表 2.7.6.26－23　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
Any Route	MT-6548	Screening period	87	347.01	879.16	86.96	(0.0, 5598.3)	(159.64, 534.39)								
		Baseline <= to < Week 2	87	313.58	911.02	37.27	(0.0, 6087.5)	(119.42, 507.75)	87	-33.43	347.01 (879.16)	133.27	0.00	(-484.5, 489.2)	(-61.84, -5.03)	0.022
		Week 2 <= to < Week 4	85	307.51	919.36	0.00	(0.0, 6087.5)	(109.21, 505.82)	85	-43.43	350.94 (889.19)	250.03	0.00	(-1521.9, 489.2)	(-97.36, 10.50)	0.113
		Week 4 <= to < Week 6	84	264.25	868.71	0.00	(0.0, 6087.5)	(75.73, 452.77)	84	-52.82	317.07 (837.55)	243.82	0.00	(-1521.9, 521.8)	(-108.73, 0.09)	0.050
		Week 6 <= to < Week 8	83	264.16	873.10	0.00	(0.0, 6087.5)	(73.51, 454.81)	83	-54.64	318.80 (842.50)	246.00	0.00	(-1521.9, 489.2)	(-108.35, -0.92)	0.046
		Week 8 <= to < Week 10	80	273.04	888.91	0.00	(0.0, 6087.5)	(75.22, 470.86)	80	-55.54	328.58 (856.63)	256.29	0.00	(-1521.9, 489.2)	(-112.57, 1.50)	0.056
		Week 10 <= to < Week 12	80	282.28	886.39	20.00	(0.0, 6087.5)	(85.02, 479.54)	80	-46.30	328.58 (856.63)	258.05	0.00	(-1521.9, 489.2)	(-103.72, 11.13)	0.118
		Week 12 <= to < Week 16	78	278.89	898.34	8.54	(0.0, 6087.5)	(76.34, 481.43)	78	-56.19	335.08 (866.63)	249.14	0.00	(-1521.9, 489.2)	(-112.37, -0.02)	0.050
		Week 16 <= to < Week 20	78	270.33	900.20	0.00	(0.0, 6087.5)	(67.36, 473.29)	78	-64.75	335.08 (866.63)	248.09	0.00	(-1521.9, 489.2)	(-120.69, -8.82)	0.024
		Week 20 <= to < Week 24	76	270.00	912.13	0.00	(0.0, 6087.5)	(61.57, 478.43)	76	-73.73	343.73 (876.42)	248.18	0.00	(-1521.9, 489.2)	(-130.45, -17.02)	0.012
		Baseline <= to < Week 24	87	294.73	906.25	66.26	(0.0, 6087.5)	(101.59, 487.88)	87	-52.29	347.01 (879.16)	220.82	0.00	(-1431.3, 489.2)	(-99.35, -5.22)	0.030

表 2.7.6.26－23　月あたりの鉄剤の平均投与量（FAS）（続き）

Iron Route	Treatment Group	Period	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Screening Period N	Change from Screening Period Mean	Mean in Screening period (SD)	Change from Screening Period SD	Change from Screening Period Median	Change from Screening Period Minimum, Maximum	Change from Screening Period 95% CI	Change from Screening Period p value
	darbepoetin	Screening period	101	202.14	655.08	40.00	(0.0, 5821.2)	(72.82, 331.46)								
		Baseline <= to < Week 2	101	163.19	701.98	0.00	(0.0, 6391.9)	(24.61, 301.77)	101	-38.95	202.14 (655.08)	140.24	0.00	(-466.9, 570.7)	(-66.64, -11.26)	0.006
		Week 2 <= to < Week 4	100	119.97	460.04	0.00	(0.0, 3424.2)	(29.69, 211.25)	100	-82.45	202.42 (658.38)	283.24	0.00	(-2397.0, 521.8)	(-138.65, -26.25)	0.004
		Week 4 <= to < Week 6	100	124.58	441.79	0.00	(0.0, 3195.9)	(36.92, 212.24)	100	-77.84	202.42 (658.38)	312.90	0.00	(-2625.2, 521.8)	(-139.91, -15.78)	0.014
		Week 6 <= to < Week 8	100	115.33	439.40	0.00	(0.0, 3195.9)	(28.14, 202.51)	100	-87.10	202.42 (658.38)	308.58	0.00	(-2625.2, 186.4)	(-148.33, -25.87)	0.006
		Week 8 <= to < Week 10	100	118.49	441.19	0.00	(0.0, 3195.9)	(30.95, 206.04)	100	-83.93	202.42 (658.38)	315.68	0.00	(-2625.2, 521.8)	(-146.57, -21.29)	0.009
		Week 10 <= to < Week 12	100	155.42	465.68	0.00	(0.0, 3195.9)	(63.02, 247.82)	100	-47.00	202.42 (658.38)	361.91	0.00	(-2625.2, 1521.9)	(-116.81, 24.81)	0.197
		Week 12 <= to < Week 16	100	164.18	528.76	8.28	(0.0, 3195.9)	(59.26, 269.10)	100	-38.24	202.42 (658.38)	446.91	0.00	(-2625.2, 3043.8)	(-126.72, 50.23)	0.393
		Week 16 <= to < Week 20	100	176.14	598.70	0.00	(0.0, 3195.9)	(57.35, 294.94)	100	-26.28	202.42 (658.38)	634.36	0.00	(-2625.2, 3043.8)	(-132.31, 79.75)	0.624
		Week 20 <= to < Week 24	99	238.19	799.57	0.00	(0.0, 5304.8)	(78.72, 397.66)	99	38.18	200.01 (661.28)	766.75	0.00	(-2625.2, 5304.8)	(-114.74, 191.11)	0.621
		Baseline <= to < Week 24	101	160.87	489.07	51.76	(0.0, 3481.3)	(64.32, 257.42)	101	-41.27	202.14 (655.08)	381.78	0.00	(-2339.9, 1665.1)	(-110.72, 28.17)	0.241

Note(s): Iron: average monthly dose (mg).
Note(s): p value is analyzed by paired t-test from screening period.
Note(s): Subjects who changed iron route in treatment period 1 or subjects who never take Iron in treatment period 1 is excluded from the analysis.
Dose of iron counts as 0 mg during the period in which subjects did not take Iron.
Note(s): Doses are expressed as elemental iron.
Data Source: Listing 16.2.4.2
Source: t_14_2_3_5_1.sas

5.3.5.1—7 表 11.4.1—3 より引用

(6)　鉄剤の投与を受けた被験者の割合

鉄剤の投与を受けた被験者の割合を表 2.7.6.26－24 に示した．

鉄剤の静脈投与を受けた被験者の割合は，MT-6548 群においてスクリーニング期間 26.5%に対し，20 週～24 週後では 20.7%であり，darbepoetin 群においてスクリーニング期間 31.7%に対し，20 週～24 週後では 28.6%であった．鉄剤の経口投与を受けた被験者の割合は，MT-6548 群においてスクリーニング期間 4.3%に対し，20 週～24 週後では 3.6%であり，darbepoetin 群においてスクリーニング期間 1.2%に対し，20 週～24 週後では 3.2%であった．

表 2.7.6.26－24　鉄剤投与を受けた被験者の割合（FAS）

		MT-6548(N=162)				darbepoetin(N=161)				Difference of proportion (MT-6548 - darbepoetin)		
Iron Route	Period	N*	n (%)	95% CI of proportion	p value from S	N*	n (%)	95% CI of proportion	p value from S	Difference	95% CI	p value
Oral	Screening period	162	7(4.3)	(1.75, 8.70)		161	2(1.2)	(0.15, 4.42)		3.1	(-7.8, 13.9)	0.174
	Baseline <= to < Week 2	162	7(4.3)	(1.75, 8.70)	-	161	2(1.2)	(0.15, 4.42)	-	3.1	(-7.8, 13.9)	0.174
	Week 2 <= to < Week 4	159	6(3.8)	(1.40, 8.03)	0.317	159	2(1.3)	(0.15, 4.47)	-	2.5	(-8.8, 13.7)	0.283
	Week 4 <= to < Week 6	156	5(3.2)	(1.05, 7.32)	0.317	159	2(1.3)	(0.15, 4.47)	-	1.9	(-9.2, 12.9)	0.280
	Week 6 <= to < Week 8	154	5(3.2)	(1.06, 7.41)	0.317	159	2(1.3)	(0.15, 4.47)	-	2.0	(-9.2, 13.0)	0.277
	Week 8 <= to < Week 10	150	5(3.3)	(1.09, 7.61)	0.317	158	2(1.3)	(0.15, 4.50)	-	2.1	(-9.1, 13.3)	0.272
	Week 10 <= to < Week 12	150	5(3.3)	(1.09, 7.61)	0.317	158	3(1.9)	(0.39, 5.45)	0.317	1.4	(-9.8, 12.6)	0.492
	Week 12 <= to < Week 16	144	5(3.5)	(1.14, 7.92)	0.317	157	3(1.9)	(0.40, 5.48)	0.317	1.6	(-9.7, 12.8)	0.486
	Week 16 <= to < Week 20	144	5(3.5)	(1.14, 7.92)	0.317	156	4(2.6)	(0.70, 6.43)	0.157	0.9	(-10.4, 12.2)	0.742
	Week 20 <= to < Week 24	140	5(3.6)	(1.17, 8.14)	0.317	154	5(3.2)	(1.06, 7.41)	0.083	0.3	(-11.1, 11.8)	1.000
	Baseline <= to < Week 24	162	7(4.3)	(1.75, 8.70)	-	161	5(3.1)	(1.02, 7.10)	0.083	1.2	(-9.6, 12.1)	0.770
Intravenous	Screening period	162	43(26.5)	(19.92, 34.04)		161	51(31.7)	(24.58, 39.46)		-5.1	(-15.8, 5.9)	0.329
	Baseline <= to < Week 2	162	38(23.5)	(17.17, 30.75)	0.132	161	44(27.3)	(20.61, 34.90)	0.090	-3.9	(-14.5, 7.2)	0.446
	Week 2 <= to < Week 4	159	34(21.4)	(15.29, 28.58)	0.162	159	35(22.0)	(15.84, 29.26)	0.005	-0.6	(-11.9, 10.6)	1.000
	Week 4 <= to < Week 6	156	30(19.2)	(13.37, 26.30)	0.034	159	41(25.8)	(19.18, 33.31)	0.139	-6.6	(-17.6, 4.7)	0.179
	Week 6 <= to < Week 8	154	35(22.7)	(16.37, 30.16)	0.384	159	42(26.4)	(19.75, 33.98)	0.228	-3.7	(-14.8, 7.4)	0.512
	Week 8 <= to < Week 10	150	29(19.3)	(13.35, 26.57)	0.096	158	41(25.9)	(19.31, 33.51)	0.180	-6.6	(-17.7, 4.6)	0.176
	Week 10 <= to < Week 12	150	35(23.3)	(16.82, 30.93)	0.527	158	45(28.5)	(21.59, 36.20)	0.456	-5.1	(-16.3, 6.1)	0.363
	Week 12 <= to < Week 16	144	35(24.3)	(17.55, 32.15)	0.732	157	47(29.9)	(22.90, 37.75)	0.674	-5.6	(-16.8, 5.7)	0.301
	Week 16 <= to < Week 20	144	29(20.1)	(13.92, 27.63)	0.170	156	42(26.9)	(20.14, 34.60)	0.248	-6.8	(-18.0, 4.6)	0.177
	Week 20 <= to < Week 24	140	29(20.7)	(14.33, 28.38)	0.237	154	44(28.6)	(21.59, 36.40)	0.475	-7.9	(-19.2, 3.6)	0.138
	Baseline <= to < Week 24	162	75(46.3)	(38.44, 54.29)	<0.001	161	87(54.0)	(46.02, 61.91)	<0.001	-7.7	(-18.7, 3.4)	0.182

表 2.7.6.26－24　鉄剤投与を受けた被験者の割合（FAS）（続き）

		MT-6548(N=162)				darbepoetin(N=161)				Difference of proportion (MT-6548 - darbepoetin)		
Iron Route	Period	N*	n (%)	95% CI of proportion	p value from S	N*	n (%)	95% CI of proportion	p value from S	Difference	95% CI	p value
Any Route	Screening period	162	50(30.9)	(23.85, 38.59)		161	53(32.9)	(25.73, 40.75)		-2.1	(-12.7, 9.0)	0.721
	Baseline <= to < Week 2	162	45(27.8)	(21.04, 35.39)	0.132	161	46(28.6)	(21.74, 36.21)	0.090	-0.8	(-11.5, 10.3)	0.902
	Week 2 <= to < Week 4	159	40(25.2)	(18.62, 32.64)	0.117	159	37(23.3)	(16.94, 30.62)	0.005	1.9	(-9.4, 13.1)	0.794
	Week 4 <= to < Week 6	156	35(22.4)	(16.15, 29.80)	0.023	159	43(27.0)	(20.31, 34.65)	0.139	-4.6	(-15.5, 6.6)	0.363
	Week 6 <= to < Week 8	154	40(26.0)	(19.25, 33.65)	0.303	159	44(27.7)	(20.88, 35.32)	0.228	-1.7	(-12.9, 9.4)	0.799
	Week 8 <= to < Week 10	150	34(22.7)	(16.24, 30.21)	0.063	158	43(27.2)	(20.45, 34.86)	0.180	-4.5	(-15.7, 6.7)	0.430
	Week 10 <= to < Week 12	150	40(26.7)	(19.78, 34.49)	0.435	158	48(30.4)	(23.32, 38.19)	0.665	-3.7	(-14.8, 7.5)	0.529
	Week 12 <= to < Week 16	144	40(27.8)	(20.64, 35.85)	0.612	157	50(31.8)	(24.65, 39.75)	0.782	-4.1	(-15.3, 7.8)	0.453
	Week 16 <= to < Week 20	144	34(23.6)	(16.94, 31.40)	0.128	156	46(29.5)	(22.47, 37.31)	0.396	-5.9	(-17.1, 5.5)	0.296
	Week 20 <= to < Week 24	140	34(24.3)	(17.44, 32.25)	0.182	154	49(31.8)	(24.55, 39.80)	0.782	-7.5	(-18.9, 3.9)	0.157
	Baseline <= to < Week 24	162	82(50.6)	(42.66, 58.55)	<0.001	161	92(57.1)	(49.12, 64.90)	<0.001	-6.5	(-17.6, 4.5)	0.265

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value from S: p value from screening period.
Note(s): p value from S is analyzed by McNemar test.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.2
Source: t_14_2_3_6_1.sas

5.3.5.1—7 表 11.4.1—4 より引用

(7)　血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合

血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合を表 2.7.6.26－25 に示した.

血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合は，MT-6548 群においてベースラインで 93.2%に対し，24 週後では 92.0%であり，darbepoetin 群においてベースラインで 90.7%に対し，24 週後では 86.2%であった.

表 2.7.6.26－25　血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合（FAS）

	MT-6548(N=162)				darbepoetin(N=161)				Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B	Difference	95% CI	p value
Baseline	162	151(93.2)	(88.18, 96.56)		161	146(90.7)	(85.10, 94.69)		2.5	(-8.4, 13.3)	0.422
Week 2	160	146(91.3)	(85.75, 95.13)	0.491	160	142(88.8)	(82.80, 93.19)	0.439	2.5	(-8.7, 13.7)	0.577
Week 4	157	147(93.6)	(88.60, 96.90)	0.808	159	143(89.9)	(84.17, 94.14)	0.827	3.7	(-7.5, 14.6)	0.306
Week 6	155	144(92.9)	(87.66, 96.40)	1.000	159	137(86.2)	(79.80, 91.12)	0.162	6.7	(-4.4, 17.7)	0.065
Week 8	151	140(92.7)	(87.34, 96.31)	1.000	158	140(88.6)	(82.59, 93.11)	0.549	4.1	(-7.1, 15.2)	0.245
Week 10	150	136(90.7)	(84.84, 94.80)	0.491	157	144(91.7)	(86.26, 95.52)	0.655	-1.1	(-12.3, 10.2)	0.841
Week 12	147	136(92.5)	(87.01, 96.21)	1.000	157	140(89.2)	(83.23, 93.56)	0.670	3.3	(-7.9, 14.6)	0.329
Week 16	144	131(91.0)	(85.06, 95.11)	0.593	156	142(91.0)	(85.40, 95.01)	0.819	-0.1	(-11.4, 11.3)	1.000
Week 20	140	130(92.9)	(87.26, 96.52)	0.782	154	136(88.3)	(82.16, 92.92)	0.549	4.5	(-6.9, 15.9)	0.233
Week 24	138	127(92.0)	(86.19, 95.95)	1.000	152	131(86.2)	(79.66, 91.24)	0.239	5.8	(-5.7, 17.2)	0.134

Note(s): N*: number of subjects at each visit.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value from B: p value from baseline value.
Note(s): p value from B is analyzed by McNemar test.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.4
Source: t_14_2_3_7_1.sas

5.3.5.1—7 表 14.2.3.7.1 より引用

(8)　血球関連評価項目

MMRM を用いた MCV，MCH，ヘマトクリット，RBC，網状赤血球数及び網状赤血球率のベースラインからの変化量を表 2.7.6.26－26，表 2.7.6.26－27，表 2.7.6.26－28，表 2.7.6.26－29，表 2.7.6.26－30 及び表 2.7.6.26－31 に示した．

MMRM を用いた MCV の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.6 fL 及び 1.3～2.0 fL，darbepoetin 群で 0.4 fL 及び 0.1～0.7 fL であった．MMRM を用いた MCV の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 1.2 fL 及び 0.8～1.7 fL であり，統計学的に有意な差が認められた（$p<0.001$）．

MMRM を用いた MCH の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.94 pg 及び 0.79～1.08 pg，darbepoetin 群で 0.32 pg 及び 0.18～0.46 pg であった．MMRM を用いた MCH の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は，0.61 pg 及び 0.41～0.81 pg であり，統計学的に有意な差が認められた（$p<0.001$）．

MMRM を用いたヘマトクリットの 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -0.87%及び -1.29%～ -0.44%，darbepoetin 群で -0.52%及び -0.94%～ -0.11%であった．

MMRM を用いた RBC の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -15.0×10^4/μL 及び -19.8×10^4/μL～ -10.3×10^4/μL，darbepoetin 群で -6.9×10^4/μL 及び -11.6×10^4/μL～ -2.2×10^4/μL であった．

MMRM を用いた網状赤血球数の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.16×10^4/μL 及び -0.12×10^4/μL～0.43×10^4/μL，darbepoetin 群で -0.25×10^4/μL 及び -0.52×10^4/μL～0.02×10^4/μL であった．

MMRM を用いた網状赤血球率の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.2‰及び 0.3‰～2.0‰，darbepoetin 群で -0.4‰及び -1.2‰～0.4‰であった．

表 2.7.6.26－26　平均赤血球容積のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	95.6 (5.3)	0.2	0.2	(-0.1, 0.5)	
	Week 4	157	95.6 (5.3)	0.1	0.2	(-0.2, 0.5)	
	Week 6	155	95.6 (5.3)	0.3	0.2	(0.0, 0.7)	
	Week 9	151	95.5 (5.3)	0.8	0.2	(0.4, 1.1)	
	Week 10	150	95.6 (5.3)	1.1	0.2	(0.8, 1.5)	
	Week 12	147	95.5 (5.2)	1.6	0.2	(1.2, 1.9)	
	Week 16	144	95.6 (5.0)	2.1	0.2	(1.8, 2.5)	
	Week 20	140	95.5 (4.9)	2.0	0.2	(1.7, 2.4)	
	Week 24	138	95.4 (4.9)	1.6	0.2	(1.3, 2.0)	
darbepoetin	Week 2	160	95.5 (4.2)	0.1	0.2	(-0.2, 0.4)	
	Week 4	159	95.5 (4.2)	0.1	0.2	(-0.2, 0.4)	
	Week 6	159	95.5 (4.2)	0.2	0.2	(-0.1, 0.6)	
	Week 9	158	95.5 (4.2)	0.1	0.2	(-0.2, 0.5)	
	Week 10	157	95.5 (4.2)	0.2	0.2	(-0.1, 0.5)	
	Week 12	157	95.5 (4.2)	0.3	0.2	(0.0, 0.6)	
	Week 16	156	95.4 (4.2)	0.1	0.2	(-0.2, 0.5)	
	Week 20	154	95.4 (4.1)	0.2	0.2	(-0.1, 0.6)	
	Week 24	152	95.4 (4.1)	0.4	0.2	(0.1, 0.7)	
Difference MT-6548 - darbepoetin	Week 2			0.1	0.2	(-0.4, 0.6)	0.658
	Week 4			0.0	0.2	(-0.4, 0.5)	0.926
	Week 6			0.1	0.2	(-0.4, 0.6)	0.641
	Week 9			0.6	0.2	(0.2, 1.1)	0.009
	Week 10			0.9	0.2	(0.5, 1.4)	<0.001
	Week 12			1.3	0.2	(0.8, 1.7)	<0.001
	Week 16			2.0	0.2	(1.5, 2.4)	<0.001
	Week 20			1.8	0.2	(1.3, 2.3)	<0.001
	Week 24			1.2	0.2	(0.8, 1.7)	<0.001

Note(s): Mean Corpuscular Volume (fL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_5.sas

5.3.5.1—7 表 11.4.1—5 より引用

表 2.7.6.26－27　平均赤血球ヘモグロビン量のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	31.64 (1.93)	0.02	0.07	(-0.12, 0.15)	
	Week 4	157	31.66 (1.94)	0.09	0.07	(-0.05, 0.23)	
	Week 6	156	31.64 (1.94)	0.13	0.07	(-0.01, 0.27)	
	Week 8	151	31.62 (1.95)	0.33	0.07	(0.19, 0.47)	
	Week 10	150	31.64 (1.94)	0.48	0.07	(0.34, 0.62)	
	Week 12	147	31.61 (1.91)	0.71	0.07	(0.57, 0.85)	
	Week 16	144	31.64 (1.84)	0.88	0.07	(0.74, 1.03)	
	Week 20	140	31.60 (1.83)	0.90	0.07	(0.76, 1.04)	
	Week 24	138	31.61 (1.82)	0.94	0.07	(0.79, 1.08)	
darbepoetin	Week 2	160	31.56 (1.65)	-0.01	0.07	(-0.14, 0.13)	
	Week 4	159	31.56 (1.65)	-0.03	0.07	(-0.17, 0.11)	
	Week 6	159	31.56 (1.65)	0.02	0.07	(-0.12, 0.16)	
	Week 8	156	31.57 (1.65)	-0.04	0.07	(-0.18, 0.10)	
	Week 10	157	31.55 (1.65)	0.04	0.07	(-0.10, 0.18)	
	Week 12	157	31.55 (1.65)	0.04	0.07	(-0.09, 0.18)	
	Week 16	156	31.54 (1.65)	0.09	0.07	(-0.05, 0.23)	
	Week 20	154	31.52 (1.63)	0.14	0.07	(0.00, 0.28)	
	Week 24	152	31.53 (1.63)	0.32	0.07	(0.18, 0.46)	
Difference MT-6548 - darbepoetin	Week 2			0.02	0.10	(-0.17, 0.22)	0.828
	Week 4			0.12	0.10	(-0.08, 0.31)	0.243
	Week 6			0.11	0.10	(-0.09, 0.31)	0.267
	Week 8			0.37	0.10	(0.17, 0.57)	<0.001
	Week 10			0.44	0.10	(0.24, 0.63)	<0.001
	Week 12			0.66	0.10	(0.46, 0.86)	<0.001
	Week 16			0.79	0.10	(0.59, 0.99)	<0.001
	Week 20			0.76	0.10	(0.56, 0.96)	<0.001
	Week 24			0.61	0.10	(0.41, 0.81)	<0.001

Note(s): Mean Corpuscular Hemoglobin (pg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_6.sas

5.3.5.1—7 表 11.4.1—6 より引用

表 2.7.6.26－28　ヘマトクリットのベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	32.46 (2.24)	-0.36	0.21	(-0.79, 0.02)
	Week 4	157	32.48 (2.25)	-1.17	0.21	(-1.58, -0.76)
	Week 6	155	32.49 (2.26)	-1.56	0.21	(-1.97, -1.15)
	Week 8	151	32.48 (2.26)	-1.69	0.21	(-2.11, -1.28)
	Week 10	150	32.49 (2.26)	-1.69	0.21	(-2.11, -1.28)
	Week 12	147	32.49 (2.24)	-1.30	0.21	(-1.72, -0.89)
	Week 16	144	32.45 (2.24)	-0.91	0.21	(-1.33, -0.49)
	Week 20	140	32.42 (2.25)	-0.56	0.22	(-1.00, -0.16)
	Week 24	138	32.44 (2.26)	-0.87	0.22	(-1.29, -0.44)
darbepoetin	Week 2	160	32.50 (2.38)	0.37	0.21	(-0.04, 0.77)
	Week 4	159	32.48 (2.37)	0.53	0.21	(0.12, 0.94)
	Week 6	159	32.48 (2.37)	0.36	0.21	(-0.04, 0.77)
	Week 8	156	32.50 (2.36)	0.41	0.21	(0.00, 0.82)
	Week 10	157	32.49 (2.36)	0.42	0.21	(0.01, 0.82)
	Week 12	157	32.49 (2.36)	0.55	0.21	(0.14, 0.96)
	Week 16	156	32.51 (2.35)	0.18	0.21	(-0.23, 0.59)
	Week 20	154	32.53 (2.35)	-0.33	0.21	(-0.74, 0.08)
	Week 24	152	32.53 (2.36)	-0.52	0.21	(-0.94, -0.11)

Note(s): Hematocrit (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_8_10_1_1.sas

5.3.5.1—7 表 11.4.1—7 より引用

表 2.7.6.26－29　RBC のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	341.0 (33.4)	-4.6	2.3	(-9.1, 0.1)
	Week 4	157	341.1 (33.6)	-12.9	2.4	(-17.6, -8.3)
	Week 6	155	341.2 (33.6)	-17.7	2.4	(-22.3, -13.1)
	Week 8	151	341.4 (33.6)	-20.4	2.4	(-25.1, -15.7)
	Week 10	150	341.3 (33.7)	-21.9	2.4	(-26.5, -17.2)
	Week 12	147	341.5 (33.2)	-19.1	2.4	(-23.9, -14.4)
	Week 16	144	340.7 (31.8)	-16.8	2.4	(-21.6, -12.1)
	Week 20	140	340.8 (31.9)	-13.0	2.4	(-17.8, -8.3)
	Week 24	138	341.0 (31.9)	-15.0	2.4	(-19.8, -10.3)
darbepoetin	Week 2	160	341.1 (29.4)	3.4	2.3	(-1.2, 8.0)
	Week 4	159	341.0 (29.4)	4.7	2.3	(0.1, 9.3)
	Week 6	159	341.0 (29.4)	2.8	2.3	(-1.8, 7.4)
	Week 8	158	341.1 (29.4)	3.5	2.4	(-1.1, 8.1)
	Week 10	157	341.0 (29.5)	3.7	2.4	(-0.9, 8.3)
	Week 12	157	341.0 (29.5)	4.6	2.4	(0.0, 9.3)
	Week 16	156	341.4 (29.3)	1.2	2.4	(-3.5, 5.8)
	Week 20	154	341.8 (29.0)	-4.4	2.4	(-9.1, 0.2)
	Week 24	152	341.7 (29.1)	-6.9	2.4	(-11.6, -2.2)

Note(s): Red Blood Cell Count (10^4/uL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_2.sas

5.3.5.1—7 表 11.4.1—8 より引用

表 2.7.6.26－30　網状赤血球数のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	4.60 (1.88)	-0.34	0.13	(-0.60, -0.07)
	Week 4	157	4.62 (1.88)	-0.37	0.14	(-0.64, -0.11)
	Week 6	155	4.61 (1.88)	0.17	0.14	(-0.10, 0.43)
	Week 8	151	4.61 (1.90)	0.08	0.14	(-0.18, 0.35)
	Week 10	150	4.59 (1.90)	0.46	0.14	(0.19, 0.73)
	Week 12	147	4.61 (1.92)	0.58	0.14	(0.31, 0.85)
	Week 16	144	4.63 (1.93)	0.47	0.14	(0.20, 0.74)
	Week 20	140	4.61 (1.94)	0.38	0.14	(0.10, 0.65)
	Week 24	138	4.63 (1.93)	0.16	0.14	(-0.12, 0.43)
darbepoetin	Week 2	160	4.73 (2.05)	0.31	0.13	(0.05, 0.58)
	Week 4	159	4.75 (2.04)	0.09	0.13	(-0.17, 0.36)
	Week 6	159	4.75 (2.04)	-0.34	0.13	(-0.61, -0.08)
	Week 8	158	4.76 (2.04)	-0.16	0.13	(-0.42, 0.10)
	Week 10	157	4.77 (2.04)	-0.15	0.14	(-0.42, 0.11)
	Week 12	157	4.77 (2.04)	-0.14	0.14	(-0.41, 0.12)
	Week 16	156	4.77 (2.05)	-0.30	0.14	(-0.56, -0.03)
	Week 20	154	4.81 (2.04)	-0.29	0.14	(-0.56, -0.03)
	Week 24	152	4.77 (2.03)	-0.25	0.14	(-0.52, 0.02)

Note(s): Reticulocyte Count (10^4/uL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_3.sas

5.3.5.1—7 表 11.4.1—9 より引用

表 2.7.6.26－31　網状赤血球率のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	13.5 (5.6)	-0.8	0.4	(-1.6, 0.0)
	Week 4	157	13.6 (5.6)	-0.6	0.4	(-1.4, 0.2)
	Week 6	155	13.6 (5.6)	1.4	0.4	(0.6, 2.3)
	Week 8	151	13.5 (5.6)	1.3	0.4	(0.5, 2.1)
	Week 10	150	13.5 (5.6)	2.6	0.4	(1.8, 3.4)
	Week 12	147	13.6 (5.7)	2.8	0.4	(2.0, 3.6)
	Week 16	144	13.6 (5.7)	2.3	0.4	(1.5, 3.2)
	Week 20	140	13.6 (5.7)	1.8	0.4	(0.9, 2.6)
	Week 24	138	13.6 (5.7)	1.2	0.4	(0.3, 2.0)
darbepoetin	Week 2	160	13.8 (5.7)	0.8	0.4	(0.0, 1.6)
	Week 4	159	13.9 (5.7)	0.1	0.4	(-0.7, 0.9)
	Week 6	159	13.9 (5.7)	-1.0	0.4	(-1.8, -0.2)
	Week 8	158	13.9 (5.7)	-0.5	0.4	(-1.3, 0.3)
	Week 10	157	13.9 (5.7)	-0.5	0.4	(-1.3, 0.3)
	Week 12	157	13.9 (5.7)	-0.5	0.4	(-1.3, 0.3)
	Week 16	156	13.9 (5.7)	-0.8	0.4	(-1.6, 0.0)
	Week 20	154	14.0 (5.7)	-0.6	0.4	(-1.4, 0.2)
	Week 24	152	13.9 (5.7)	-0.4	0.4	(-1.2, 0.4)

Note(s): Reticulocyte Ratio (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_4.sas

5.3.5.1—7 表 11.4.1—10 より引用

(9)　EPO

MMRM を用いた MT-6548 群の EPO のベースラインからの変化量を表 2.7.6.26－32，MT-6548 群の EPO の記述統計量を表 2.7.6.26－33 に示した．

MMRM を用いた EPO の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -0.11 mIU/mL 及び -2.58～2.36 mIU/mL であった．また，2 週～24 週後の EPO の最大値は 312.0 mIU/mL であった．

表 2.7.6.26－32　エリスロポエチンのベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	17.49 (28.11)	-1.60	1.19	(-3.94, 0.74)	
	Week 4	157	17.64 (28.36)	-3.03	1.20	(-5.39, -0.67)	
	Week 6	155	17.74 (28.51)	-2.10	1.21	(-4.47, 0.27)	
	Week 12	147	16.31 (22.88)	-1.14	1.23	(-3.56, 1.27)	
	Week 24	138	14.48 (19.81)	-0.11	1.26	(-2.58, 2.36)	

Note(s): Erythropoietin (mIU/mL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_7.sas

5.3.5.1—7 表 11.4.1—11 より引用

表 2.7.6.26－33　エリスロポエチンの記述統計量（FAS）

		Absolute						Change from Baseline						
Treatment Group	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Baseline	162	17.40	27.95	8.20	(2.0, 236.0)	(13.07, 21.74)							
	Week 2	160	14.85	26.14	10.25	(2.4, 312.0)	(10.77, 18.93)	160	-2.64	35.27	-0.05	(-215.4, 307.5)	(-8.15, 2.87)	0.345
	Week 4	157	13.52	16.99	9.80	(1.2, 168.0)	(10.84, 16.20)	157	-4.12	30.03	0.00	(-217.2, 119.7)	(-8.85, 0.61)	0.087
	Week 6	155	14.53	14.28	10.90	(1.6, 120.0)	(12.26, 16.79)	155	-3.21	28.48	1.10	(-205.2, 115.5)	(-7.73, 1.31)	0.162
	Week 12	147	15.45	13.70	11.70	(2.0, 99.3)	(13.21, 17.68)	147	-0.87	21.92	2.20	(-119.2, 50.6)	(-4.44, 2.70)	0.631
	Week 24	138	16.18	22.76	10.80	(2.5, 206.0)	(12.35, 20.01)	138	1.69	24.20	1.95	(-127.4, 157.3)	(-2.38, 5.77)	0.412
	Week 24 (LOCF)	161	16.88	25.59	10.20	(2.2, 206.0)	(12.90, 20.86)	161	-0.54	32.52	1.10	(-205.2, 169.0)	(-5.60, 4.52)	0.834

Note(s): Erythropoietin (mIU/mL).
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_9_1_7.sas

5.3.5.1—7 表 11.4.1—12 より引用

(10)　脂質関連評価項目

MMRM を用いた総コレステロール，LDL-C，HDL-C，LDL-C／HDL-C 比及び中性脂肪のベースラインからの変化量を表 2.7.6.26－34，表 2.7.6.26－35，表 2.7.6.26－36，表 2.7.6.26－37 及び表 2.7.6.26－38 に示した．

MMRM を用いた総コレステロールの 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 7.1 mg/dL 及び 4.3～9.9 mg/dL，darbepoetin 群で 3.6 mg/dL 及び 0.9～6.3 mg/dL であった．MMRM を用いた総コレステロールの 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 3.5 mg/dL 及び -0.4～7.4 mg/dL であり，統計学的に有意な差が認められなかった（p=0.078）．

MMRM を用いた LDL-C の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.7 mg/dL 及び -0.6～4.0 mg/dL，darbepoetin 群で -0.3 mg/dL 及び -2.5～1.9 mg/dL であった．MMRM を用いた LDL-C の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 1.9 mg/dL 及び -1.2～5.1 mg/dL であり，統計学的に有意な差が認められなかった（p=0.227）．

MMRM を用いた HDL-C の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -1.5 mg/dL 及び -2.5～ -0.5 mg/dL，darbepoetin 群で 2.1 mg/dL 及び 1.1～3.1 mg/dL であった．MMRM を用いた HDL-C の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -3.6 mg/dL 及び -5.0～ -2.2 mg/dL であり，統計学的に有意な差が認められた（p<0.001）．

MMRM を用いた LDL-C/HDL-C 比の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.11 及び 0.05～0.17，darbepoetin 群で -0.08 及び -0.14～ -0.02 であった．MMRM を用いた LDL-C/HDL-C 比の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 0.19 及び 0.10～0.27 であり，統計学的に有意な差が認められた（p<0.001）．

MMRM を用いた中性脂肪の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 26.9 mg/dL 及び 17.5～36.3 mg/dL，darbepoetin 群で-1.6 mg/dL 及び -10.7～7.5 mg/dL であった．MMRM を用いた中性脂肪の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 28.5 mg/dL 及び 15.4～41.6 mg/dL であり，統計学的に有意な差が認められた（p<0.001）．

表 2.7.6.26－34　総コレステロールのベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	158.8 (32.2)	0.2	1.4	(-2.5, 2.9)		160	0.4	0.9	(-1.3, 2.1)	
	Week 4	157	158.4 (32.3)	-1.4	1.4	(-4.1, 1.3)		157	-0.4	0.9	(-2.2, 1.3)	
	Week 6	155	158.1 (32.4)	1.0	1.4	(-1.7, 3.7)		155	1.1	0.9	(-0.7, 2.8)	
	Week 8	151	157.7 (32.3)	0.5	1.4	(-2.2, 3.2)		151	0.8	0.9	(-1.0, 2.5)	
	Week 10	150	157.7 (32.4)	1.1	1.4	(-1.6, 3.8)		150	1.2	0.9	(-0.6, 2.9)	
	Week 12	147	157.5 (32.2)	2.8	1.4	(0.1, 5.6)		147	2.3	0.9	(0.5, 4.1)	
	Week 16	144	158.0 (32.6)	2.6	1.4	(-0.1, 5.4)		144	2.3	0.9	(0.5, 4.1)	
	Week 20	140	158.2 (32.6)	7.6	1.4	(4.9, 10.4)		140	5.7	0.9	(3.9, 7.4)	
	Week 24	138	158.4 (32.7)	7.1	1.4	(4.3, 9.9)		138	5.2	0.9	(3.4, 7.0)	
darbepoetin												
	Week 2	160	158.6 (33.9)	-0.7	1.4	(-3.3, 2.0)		160	0.0	0.9	(-1.8, 1.7)	
	Week 4	159	158.6 (34.0)	-0.3	1.4	(-3.0, 2.4)		159	0.2	0.9	(-1.6, 1.9)	
	Week 6	159	158.6 (34.0)	-1.4	1.4	(-4.1, 1.3)		159	-0.6	0.9	(-2.3, 1.1)	
	Week 8	158	158.8 (34.0)	-2.8	1.4	(-5.5, -0.1)		158	-1.3	0.9	(-3.0, 0.5)	
	Week 10	157	158.7 (34.1)	-2.8	1.4	(-5.4, -0.1)		157	-1.3	0.9	(-3.1, 0.4)	
	Week 12	157	158.7 (34.1)	-1.2	1.4	(-3.9, 1.5)		157	-0.4	0.9	(-2.1, 1.3)	
	Week 16	156	158.8 (34.2)	-1.3	1.4	(-4.0, 1.4)		156	-0.4	0.9	(-2.1, 1.3)	
	Week 20	154	159.1 (34.2)	-0.3	1.4	(-3.0, 2.4)		154	0.3	0.9	(-1.5, 2.0)	
	Week 24	152	159.4 (34.3)	3.6	1.4	(0.9, 6.3)		152	2.6	0.9	(0.9, 4.4)	
Difference MT-6548 - darbepoetin												
	Week 2			0.8	1.9	(-2.9, 4.6)	0.660		0.4	1.2	(-2.0, 2.9)	0.724
	Week 4			-1.1	1.9	(-4.9, 2.7)	0.562		-0.6	1.2	(-3.1, 1.8)	0.621
	Week 6			2.4	1.9	(-1.4, 6.3)	0.207		1.7	1.3	(-0.8, 4.2)	0.174
	Week 8			3.3	1.9	(-0.5, 7.1)	0.091		2.0	1.3	(-0.4, 4.5)	0.108
	Week 10			3.9	2.0	(0.0, 7.7)	0.050		2.5	1.3	(0.0, 5.0)	0.049
	Week 12			4.0	2.0	(0.2, 7.9)	0.041		2.7	1.3	(0.2, 5.2)	0.033
	Week 16			3.9	2.0	(0.0, 7.8)	0.047		2.7	1.3	(0.2, 5.2)	0.036
	Week 20			7.9	2.0	(4.1, 11.8)	<0.001		5.4	1.3	(2.9, 7.9)	<0.001
	Week 24			3.5	2.0	(-0.4, 7.4)	0.078		2.6	1.3	(0.0, 5.1)	0.046

Note(s): Total Cholesterol (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_12.sas

5.3.5.1—7 表 11.4.1—13 より引用

表 2.7.6.26－35　LDL-C のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	88.4 (26.0)	-1.2	1.1	(-3.3, 1.0)		160	-0.5	1.4	(-3.2, 2.1)	
	Week 4	157	88.1 (26.0)	-1.3	1.1	(-3.6, 0.7)		157	-0.9	1.4	(-3.6, 1.8)	
	Week 6	155	87.9 (26.0)	-0.5	1.1	(-2.7, 1.6)		155	0.5	1.4	(-2.2, 3.2)	
	Week 8	151	87.3 (25.6)	-0.8	1.1	(-3.1, 1.4)		151	-0.1	1.4	(-2.8, 2.7)	
	Week 10	150	87.3 (25.7)	-0.8	1.1	(-3.0, 1.4)		150	0.1	1.4	(-2.6, 2.8)	
	Week 12	147	87.5 (25.4)	0.3	1.1	(-2.0, 2.5)		147	1.2	1.4	(-1.5, 3.9)	
	Week 16	144	87.5 (25.7)	0.8	1.1	(-1.5, 3.0)		144	1.9	1.4	(-0.8, 4.7)	
	Week 20	140	87.4 (25.8)	3.8	1.1	(1.8, 6.0)		140	5.7	1.4	(2.9, 8.5)	
	Week 24	138	87.4 (25.9)	1.7	1.2	(-0.6, 4.0)		138	3.1	1.4	(0.3, 5.9)	
darbepoetin												
	Week 2	160	86.2 (28.1)	-0.3	1.1	(-2.4, 1.9)		160	0.6	1.4	(-2.0, 3.3)	
	Week 4	159	86.4 (28.1)	-0.3	1.1	(-2.5, 1.8)		159	0.6	1.4	(-2.1, 3.3)	
	Week 6	159	86.4 (28.1)	-0.4	1.1	(-2.5, 1.8)		159	0.6	1.4	(-2.1, 3.3)	
	Week 8	158	86.5 (28.2)	-2.2	1.1	(-4.3, 0.0)		158	-1.3	1.4	(-4.0, 1.4)	
	Week 10	157	86.5 (28.3)	-1.8	1.1	(-4.0, 0.3)		157	-1.1	1.4	(-3.8, 1.6)	
	Week 12	157	86.5 (28.3)	-1.4	1.1	(-3.6, 0.8)		157	-0.6	1.4	(-3.3, 2.1)	
	Week 16	156	86.6 (28.3)	-1.6	1.1	(-3.8, 0.6)		156	-0.7	1.4	(-3.4, 2.0)	
	Week 20	154	86.9 (28.4)	-1.4	1.1	(-3.6, 0.8)		154	-0.5	1.4	(-3.2, 2.2)	
	Week 24	152	87.1 (28.5)	-0.3	1.1	(-2.5, 1.9)		152	0.6	1.4	(-2.1, 3.3)	
Difference MT-6548 - darbepoetin												
	Week 2			-0.9	1.6	(-4.0, 2.2)	0.567		-1.2	1.9	(-4.9, 2.6)	0.549
	Week 4			-1.1	1.6	(-4.2, 1.9)	0.469		-1.5	1.9	(-5.3, 2.3)	0.439
	Week 6			-0.2	1.6	(-3.3, 2.9)	0.907		-0.1	1.9	(-3.9, 3.7)	0.956
	Week 8			1.3	1.6	(-1.8, 4.4)	0.408		1.2	1.9	(-2.6, 5.0)	0.532
	Week 10			1.1	1.6	(-2.1, 4.2)	0.507		1.2	1.9	(-2.6, 5.0)	0.529
	Week 12			1.6	1.6	(-1.5, 4.8)	0.300		1.8	2.0	(-2.1, 5.6)	0.364
	Week 16			2.4	1.6	(-0.8, 5.5)	0.138		2.6	2.0	(-1.2, 6.5)	0.179
	Week 20			5.2	1.6	(2.0, 8.3)	0.001		6.2	2.0	(2.3, 10.1)	0.002
	Week 24			1.9	1.6	(-1.2, 5.1)	0.227		2.5	2.0	(-1.4, 6.4)	0.208

Note(s): LDL-C (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_13.sas

5.3.5.1—7 表 11.4.1—14 より引用

表 2.7.6.26－36　HDL-C のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	48.5 (15.6)	-2.9	0.5	(-3.9, -2.0)		160	-5.3	1.0	(-7.2, -3.3)	
	Week 4	157	48.3 (15.7)	-4.1	0.5	(-5.0, -3.1)		157	-7.2	1.0	(-9.2, -5.3)	
	Week 6	155	48.4 (15.7)	-4.1	0.5	(-5.1, -3.2)		155	-7.9	1.0	(-9.8, -5.9)	
	Week 8	151	48.6 (15.8)	-4.8	0.5	(-5.8, -3.8)		151	-9.7	1.0	(-10.7, -6.8)	
	Week 10	150	48.7 (15.8)	-5.0	0.5	(-6.0, -4.0)		150	-9.2	1.0	(-11.1, -7.2)	
	Week 12	147	48.6 (15.9)	-4.4	0.5	(-5.4, -3.4)		147	-7.8	1.0	(-9.8, -5.8)	
	Week 16	144	48.8 (16.0)	-3.2	0.5	(-4.2, -2.2)		144	-5.8	1.0	(-7.8, -3.8)	
	Week 20	140	48.8 (16.1)	-2.0	0.5	(-3.0, -1.0)		140	-3.2	1.0	(-5.3, -1.2)	
	Week 24	138	48.9 (16.0)	-1.5	0.5	(-2.5, -0.5)		138	-2.4	1.0	(-4.4, -0.4)	
darbepoetin												
	Week 2	160	51.0 (16.1)	-0.2	0.5	(-1.1, 0.8)		160	0.5	1.0	(-1.5, 2.4)	
	Week 4	159	50.8 (16.0)	-0.9	0.5	(-1.8, 0.1)		159	-1.1	1.0	(-3.0, 0.8)	
	Week 6	159	50.8 (16.0)	-2.0	0.5	(-3.0, -1.1)		159	-3.3	1.0	(-5.2, -1.4)	
	Week 8	158	51.0 (16.0)	-1.5	0.5	(-2.5, -0.5)		158	-2.1	1.0	(-4.0, -0.1)	
	Week 10	157	50.8 (15.9)	-2.0	0.5	(-3.0, -1.0)		157	-3.5	1.0	(-5.4, -1.5)	
	Week 12	157	50.8 (15.9)	-0.7	0.5	(-1.6, 0.3)		157	-0.8	1.0	(-2.8, 1.1)	
	Week 16	156	50.7 (15.9)	0.1	0.5	(-0.9, 1.1)		156	0.8	1.0	(-1.2, 2.7)	
	Week 20	154	50.7 (15.9)	0.2	0.5	(-0.7, 1.2)		154	1.6	1.0	(-0.3, 3.6)	
	Week 24	152	50.8 (15.9)	2.1	0.5	(1.1, 3.1)		152	5.1	1.0	(3.1, 7.1)	
Difference MT-6548 - darbepoetin												
	Week 2			-2.8	0.7	(-4.1, -1.4)	<0.001		-5.7	1.4	(-8.5, -3.0)	<0.001
	Week 4			-3.2	0.7	(-4.6, -1.8)	<0.001		-6.1	1.4	(-8.9, -3.4)	<0.001
	Week 6			-2.1	0.7	(-3.5, -0.7)	0.003		-4.6	1.4	(-7.3, -1.8)	0.001
	Week 8			-3.3	0.7	(-4.7, -1.9)	<0.001		-6.7	1.4	(-9.4, -3.9)	<0.001
	Week 10			-3.0	0.7	(-4.4, -1.6)	<0.001		-5.7	1.4	(-8.5, -3.0)	<0.001
	Week 12			-3.7	0.7	(-5.1, -2.3)	<0.001		-7.0	1.4	(-9.8, -4.2)	<0.001
	Week 16			-3.3	0.7	(-4.7, -1.9)	<0.001		-6.5	1.4	(-9.3, -3.7)	<0.001
	Week 20			-2.3	0.7	(-3.7, -0.9)	0.002		-4.9	1.4	(-7.7, -2.1)	<0.001
	Week 24			-3.6	0.7	(-5.0, -2.2)	<0.001		-7.5	1.4	(-10.3, -4.7)	<0.001

Note(s): HDL-C (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_14.sas

5.3.5.1—7 表 11.4.1—15 より引用

表 2.7.6.26－37　LDL-C／HDL-C 比のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	2.00 (0.82)	0.08	0.03	(0.02, 0.14)		160	6.07	1.62	(2.88, 9.26)	
	Week 4	157	2.00 (0.83)	0.13	0.03	(0.07, 0.19)		157	8.47	1.63	(5.26, 11.68)	
	Week 6	155	1.99 (0.83)	0.16	0.03	(0.10, 0.21)		155	10.31	1.64	(7.09, 13.53)	
	Week 8	151	1.97 (0.81)	0.17	0.03	(0.11, 0.23)		151	10.84	1.65	(7.60, 14.08)	
	Week 10	150	1.96 (0.81)	0.18	0.03	(0.12, 0.24)		150	11.96	1.65	(8.71, 15.20)	
	Week 12	147	1.97 (0.81)	0.16	0.03	(0.10, 0.22)		147	11.38	1.66	(8.12, 14.65)	
	Week 16	144	1.96 (0.81)	0.15	0.03	(0.09, 0.21)		144	9.70	1.67	(6.42, 12.98)	
	Week 20	140	1.96 (0.81)	0.17	0.03	(0.11, 0.23)		140	10.97	1.68	(7.67, 14.27)	
	Week 24	138	1.96 (0.81)	0.11	0.03	(0.05, 0.17)		138	8.04	1.69	(4.72, 11.35)	
darbepoetin												
	Week 2	160	1.86 (0.81)	-0.01	0.03	(-0.07, 0.05)		160	0.59	1.62	(-2.59, 3.76)	
	Week 4	159	1.86 (0.80)	0.02	0.03	(-0.04, 0.08)		159	2.37	1.63	(-0.82, 5.56)	
	Week 6	159	1.86 (0.80)	0.04	0.03	(-0.01, 0.10)		159	4.90	1.63	(1.71, 8.09)	
	Week 8	158	1.86 (0.80)	0.00	0.03	(-0.06, 0.05)		158	1.85	1.63	(-1.35, 5.05)	
	Week 10	157	1.86 (0.80)	0.03	0.03	(-0.03, 0.09)		157	3.48	1.63	(0.28, 6.69)	
	Week 12	157	1.86 (0.80)	-0.01	0.03	(-0.07, 0.05)		157	1.56	1.63	(-1.64, 4.76)	
	Week 16	156	1.87 (0.80)	-0.04	0.03	(-0.10, 0.02)		156	-0.03	1.63	(-3.24, 3.18)	
	Week 20	154	1.87 (0.80)	-0.06	0.03	(-0.11, 0.00)		154	-0.68	1.64	(-3.89, 2.54)	
	Week 24	152	1.87 (0.81)	-0.08	0.03	(-0.14, -0.02)		152	-2.68	1.64	(-5.90, 0.55)	
Difference MT-6548 - darbepoetin												
	Week 2			0.09	0.04	(0.01, 0.17)	0.036		5.48	2.30	(0.97, 9.99)	0.017
	Week 4			0.11	0.04	(0.02, 0.19)	0.011		6.10	2.31	(1.57, 10.63)	0.008
	Week 6			0.11	0.04	(0.03, 0.19)	0.006		5.41	2.31	(0.87, 9.95)	0.019
	Week 8			0.17	0.04	(0.09, 0.25)	<0.001		8.99	2.32	(4.43, 13.54)	<0.001
	Week 10			0.15	0.04	(0.07, 0.24)	<0.001		8.47	2.33	(3.91, 13.04)	<0.001
	Week 12			0.17	0.04	(0.09, 0.25)	<0.001		9.82	2.33	(5.24, 14.40)	<0.001
	Week 16			0.19	0.04	(0.11, 0.27)	<0.001		9.73	2.34	(5.14, 14.32)	<0.001
	Week 20			0.22	0.04	(0.14, 0.31)	<0.001		11.65	2.35	(7.03, 16.26)	<0.001
	Week 24			0.19	0.04	(0.10, 0.27)	<0.001		10.71	2.36	(6.08, 15.35)	<0.001

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visit as a fixed effect, baseline values as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_15.sas

5.3.5.1—7 表 11.4.1—16 より引用

表 2.7.6.26－38　中性脂肪のベースラインからの変化量（MMRM，FAS）

			Change from Baseline					Percent Change from Baseline				
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	116.5 (69.4)	26.3	4.6	(17.3, 35.2)		160	26.6	3.8	(19.3, 34.0)	
	Week 4	157	116.2 (69.6)	22.2	4.6	(13.2, 31.2)		157	25.2	3.8	(17.8, 32.6)	
	Week 6	155	115.6 (70.0)	29.3	4.6	(19.2, 37.3)		155	27.7	3.8	(20.2, 35.1)	
	Week 8	151	114.1 (67.3)	32.9	4.7	(23.7, 42.0)		151	33.9	3.8	(26.4, 41.5)	
	Week 10	150	113.3 (66.8)	34.7	4.7	(25.6, 43.9)		150	35.0	3.8	(27.5, 42.5)	
	Week 12	147	114.2 (66.9)	38.1	4.7	(28.9, 47.3)		147	41.7	3.9	(34.1, 49.3)	
	Week 16	144	114.0 (67.0)	26.4	4.7	(17.1, 35.7)		144	30.5	3.9	(22.9, 38.2)	
	Week 20	140	114.5 (67.4)	29.1	4.8	(19.8, 38.5)		140	34.3	3.9	(26.6, 42.1)	
	Week 24	138	114.9 (67.6)	26.9	4.8	(17.5, 36.3)		138	30.6	3.9	(22.8, 38.3)	
darbepoetin												
	Week 2	160	112.0 (67.4)	0.2	4.6	(-8.7, 9.2)		160	6.4	3.8	(-1.0, 13.7)	
	Week 4	159	112.2 (67.6)	4.3	4.6	(-4.6, 13.3)		159	11.9	3.8	(4.5, 19.3)	
	Week 6	159	112.2 (67.6)	5.5	4.6	(-3.4, 14.5)		159	15.0	3.8	(7.6, 22.4)	
	Week 8	158	112.4 (67.7)	4.7	4.6	(-4.3, 13.7)		158	13.3	3.8	(5.9, 20.7)	
	Week 10	157	112.5 (68.0)	9.4	4.6	(0.4, 18.5)		157	17.8	3.8	(10.3, 25.2)	
	Week 12	157	112.5 (68.0)	5.6	4.6	(-3.4, 14.7)		157	13.6	3.8	(6.2, 21.1)	
	Week 16	156	112.7 (68.1)	2.6	4.6	(-6.4, 11.7)		156	12.2	3.8	(4.8, 19.7)	
	Week 20	154	113.5 (68.2)	1.7	4.6	(-7.3, 10.8)		154	11.1	3.8	(3.6, 18.5)	
	Week 24	152	113.2 (68.4)	-1.6	4.6	(-10.7, 7.5)		152	8.7	3.8	(1.2, 16.2)	
Difference MT-6548 - darbepoetin												
	Week 2			26.0	6.5	(13.4, 38.7)	<0.001		20.3	5.3	(9.9, 30.7)	<0.001
	Week 4			17.9	6.5	(5.1, 30.6)	0.006		13.3	5.3	(2.9, 23.8)	0.013
	Week 6			22.7	6.5	(10.0, 35.5)	<0.001		12.7	5.3	(2.2, 23.2)	0.018
	Week 8			28.1	6.5	(15.3, 41.0)	<0.001		20.6	5.4	(10.1, 31.2)	<0.001
	Week 10			25.3	6.6	(12.4, 38.1)	<0.001		17.2	5.4	(6.7, 27.8)	0.001
	Week 12			32.4	6.6	(19.5, 45.3)	<0.001		28.1	5.4	(17.5, 38.7)	<0.001
	Week 16			23.7	6.6	(10.8, 36.7)	<0.001		18.3	5.4	(7.6, 28.9)	<0.001
	Week 20			27.4	6.6	(14.4, 40.4)	<0.001		23.3	5.5	(12.6, 34.0)	<0.001
	Week 24			28.5	6.7	(15.4, 41.6)	<0.001		21.9	5.5	(11.1, 32.7)	<0.001

Note(s): Triglyceride (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_16.sas

5.3.5.1—7 表 11.4.1—17 より引用

(11)　随時血糖

MMRM を用いた随時血糖のベースラインからの変化量を表 2.7.6.26－39 に示した．

MMRM を用いた随時血糖の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -2.7 mg/dL 及び -7.1～1.7 mg/dL，darbepoetin 群で 0.9 mg/dL 及び -3.4～5.1 mg/dL であった．MMRM を用いた随時血糖の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -3.6 mg/dL 及び -9.7～2.5 mg/dL であり，統計学的に有意な差が認められなかった（p=0.246）．

表 2.7.6.26－39　随時血糖のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	121.0 (28.9)	-2.8	2.1	(-6.6, 1.9)	
	Week 4	157	121.2 (29.1)	-2.1	2.1	(-6.4, 2.1)	
	Week 6	155	121.1 (29.2)	-4.6	2.2	(-8.9, -0.3)	
	Week 8	151	120.8 (29.2)	-3.3	2.2	(-7.5, 1.0)	
	Week 10	150	120.8 (29.3)	-3.8	2.2	(-8.0, 0.5)	
	Week 12	147	120.5 (29.1)	-1.8	2.2	(-6.1, 2.5)	
	Week 16	144	120.5 (29.4)	-2.8	2.2	(-7.1, 1.6)	
	Week 20	140	120.3 (29.7)	-1.5	2.2	(-5.8, 2.9)	
	Week 24	138	120.0 (29.3)	-2.7	2.2	(-7.1, 1.7)	
darbepoetin	Week 2	160	126.7 (39.8)	1.4	2.1	(-2.8, 5.5)	
	Week 4	159	126.6 (39.9)	-0.9	2.1	(-5.1, 3.3)	
	Week 6	159	126.6 (39.9)	0.5	2.1	(-3.7, 4.7)	
	Week 8	158	126.6 (40.0)	-3.1	2.1	(-7.3, 1.1)	
	Week 10	157	126.4 (40.1)	0.3	2.1	(-3.9, 4.5)	
	Week 12	157	126.4 (40.1)	-1.1	2.1	(-5.3, 3.1)	
	Week 16	156	126.5 (40.2)	2.7	2.1	(-1.5, 6.9)	
	Week 20	154	126.8 (40.3)	2.6	2.2	(-1.4, 7.0)	
	Week 24	152	126.4 (40.1)	0.9	2.2	(-3.4, 5.1)	
Difference MT-6548 - darbepoetin	Week 2			-3.7	3.0	(-9.6, 2.2)	0.221
	Week 4			-1.3	3.0	(-7.2, 4.7)	0.678
	Week 6			-5.1	3.0	(-11.0, 0.9)	0.095
	Week 8			-0.2	3.1	(-6.2, 5.8)	0.952
	Week 10			-4.1	3.1	(-10.1, 1.9)	0.184
	Week 12			-0.8	3.1	(-6.8, 5.3)	0.802
	Week 16			-5.5	3.1	(-11.5, 0.6)	0.076
	Week 20			-4.3	3.1	(-10.4, 1.8)	0.170
	Week 24			-3.6	3.1	(-9.7, 2.5)	0.246

Note(s): Blood Glucose (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_3.sas

5.3.5.1—7 表 11.4.1—18 より引用

(12)　血圧

MMRM を用いた収縮期血圧及び拡張期血圧のベースラインからの変化量を表 2.7.6.26－40 及び表 2.7.6.26－41 に示した.

MMRM を用いた収縮期血圧の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.2 mmHg 及び -1.6～3.9 mmHg，darbepoetin 群で 3.4 mmHg 及び 0.7～6.0 mmHg であった．MMRM を用いた収縮期血圧の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は -2.2 mmHg 及び -6.0～1.6 mmHg であり，統計学的に有意な差が認められなかった（p=0.256）.

MMRM を用いた拡張期血圧の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -0.5 mmHg 及び -2.1～1.0 mmHg，darbepoetin 群で 1.4 mmHg 及び -0.1～2.9 mmHg であった．MMRM を用いた拡張期血圧の 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -1.9 mmHg 及び -4.1～0.2 mmHg であり，統計学的に有意な差が認められなかった（p=0.081）.

表 2.7.6.26－40　収縮期血圧のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	148.6 (19.8)	-2.6	1.3	(-5.1, 0.1)	
	Week 4	157	148.5 (19.9)	-3.2	1.3	(-5.8, -0.6)	
	Week 6	156	148.5 (19.9)	-2.7	1.3	(-5.3, -0.1)	
	Week 8	151	148.4 (19.9)	-3.5	1.4	(-6.1, -0.8)	
	Week 10	150	148.4 (20.0)	-4.6	1.4	(-7.2, -1.9)	
	Week 12	147	148.3 (20.1)	-2.3	1.4	(-5.0, 0.3)	
	Week 16	144	148.0 (20.1)	-4.0	1.4	(-6.6, -1.3)	
	Week 20	140	147.8 (20.1)	-0.3	1.4	(-3.1, 2.4)	
	Week 24	138	147.9 (20.0)	1.2	1.4	(-1.6, 3.9)	
darbepoetin	Week 2	160	146.4 (18.4)	-1.0	1.3	(-3.6, 1.6)	
	Week 4	159	146.4 (18.5)	-2.0	1.3	(-4.6, 0.6)	
	Week 6	159	146.4 (18.5)	-2.9	1.3	(-5.5, -0.3)	
	Week 8	158	146.4 (18.5)	-0.6	1.3	(-3.2, 2.0)	
	Week 10	157	146.3 (18.5)	-2.7	1.3	(-5.3, -0.1)	
	Week 12	157	146.3 (18.8)	-1.5	1.3	(-4.1, 1.1)	
	Week 16	156	146.3 (18.6)	-1.0	1.3	(-3.6, 1.6)	
	Week 20	154	146.2 (18.7)	1.1	1.3	(-1.5, 3.7)	
	Week 24	152	146.4 (18.7)	3.4	1.3	(0.7, 6.0)	
Difference MT-6548 - darbepoetin	Week 2			-1.6	1.9	(-5.2, 2.1)	0.416
	Week 4			-1.2	1.9	(-4.9, 2.5)	0.534
	Week 6			0.2	1.9	(-3.5, 3.9)	0.928
	Week 8			-2.9	1.9	(-6.6, 0.8)	0.129
	Week 10			-1.9	1.9	(-5.6, 1.8)	0.316
	Week 12			-0.8	1.9	(-4.6, 2.9)	0.665
	Week 16			-3.0	1.9	(-6.7, 0.8)	0.122
	Week 20			-1.5	1.9	(-5.2, 2.3)	0.450
	Week 24			-2.2	1.9	(-6.0, 1.6)	0.256

Note(s): Systolic Blood Pressure (mmHg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_1.sas

5.3.5.1—7 表 11.4.1—19 より引用

表 2.7.6.26－41　拡張期血圧のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	81.4 (11.8)	-2.2	0.8	(-3.7, -0.7)	
	Week 4	157	81.1 (11.6)	-2.6	0.8	(-4.1, -1.1)	
	Week 6	155	81.1 (11.6)	-2.7	0.8	(-4.2, -1.2)	
	Week 8	151	80.8 (11.6)	-3.3	0.8	(-4.8, -1.8)	
	Week 10	150	80.9 (11.6)	-3.3	0.8	(-4.9, -1.8)	
	Week 12	147	80.9 (11.5)	-1.8	0.8	(-3.3, -0.3)	
	Week 16	144	80.8 (11.6)	-2.6	0.8	(-4.1, -1.1)	
	Week 20	140	80.7 (11.7)	-1.5	0.8	(-3.0, 0.1)	
	Week 24	138	80.9 (11.6)	-0.5	0.8	(-2.1, 1.0)	
darbepoetin	Week 2	160	78.9 (12.6)	-0.7	0.8	(-2.2, 0.8)	
	Week 4	159	78.9 (12.6)	-1.0	0.8	(-2.5, 0.5)	
	Week 6	159	78.8 (12.6)	-0.9	0.8	(-2.4, 0.5)	
	Week 8	156	79.0 (12.4)	0.0	0.8	(-1.5, 1.5)	
	Week 10	157	79.0 (12.5)	-1.6	0.8	(-3.1, -0.1)	
	Week 12	157	79.0 (12.5)	-0.5	0.8	(-1.9, 1.0)	
	Week 16	156	78.9 (12.5)	-0.5	0.8	(-2.0, 0.9)	
	Week 20	154	78.9 (12.5)	0.2	0.8	(-1.3, 1.7)	
	Week 24	152	78.9 (12.5)	1.4	0.8	(-0.1, 2.9)	
Difference MT-6548 - darbepoetin	Week 2			-1.5	1.1	(-3.6, 0.6)	0.162
	Week 4			-1.6	1.1	(-3.7, 0.5)	0.139
	Week 6			-1.8	1.1	(-3.9, 0.3)	0.095
	Week 8			-3.3	1.1	(-5.4, -1.1)	0.003
	Week 10			-1.7	1.1	(-3.9, 0.4)	0.109
	Week 12			-1.4	1.1	(-3.5, 0.8)	0.210
	Week 16			-2.1	1.1	(-4.2, 0.1)	0.059
	Week 20			-1.6	1.1	(-3.8, 0.5)	0.135
	Week 24			-1.9	1.1	(-4.1, 0.2)	0.081

Note(s): Diastolic Blood Pressure (mmHg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_2.sas

5.3.5.1—7 表 11.4.1—20 より引用

(13)　救済治療

ESA 製剤による救済治療を受けた被験者の割合を表 2.7.6.26－42 に，赤血球輸血による救済治療を受けた被験者の割合を表 2.7.6.26－43 に，瀉血による救済治療を受けた被験者の割合を表 2.7.6.26－44 に示した．

治療期間 I 期中に ESA 製剤による救済治療を受けた被験者の割合は，MT-6548 群で 2.5%，darbepoetin 群で 0.6%であった．治療期間 I 期中に赤血球輸血又は瀉血による救済治療を受けた被験者は両群で認められなかった．なお，中止日以降に初めて ESA 製剤による救済治療を受けた被験者は，MT-6548 群で 2 名，darbepoetin 群で 0 名であり，中止日以降に初めて赤血球輸血による救済治療を受けた被験者は MT-6548 群で 1 名，darbepoetin 群で 0 名であった．

表 2.7.6.26－42　ESA 製剤による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	159	0 (0.0)	(0.00, 2.29)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 4 <= to < Week 6	156	1 (0.6)	(0.02, 3.52)	159	0 (0.0)	(0.00, 2.29)	0.6	(-10.4, 11.7)	0.495
Week 6 <= to < Week 8	154	2 (1.3)	(0.16, 4.61)	159	0 (0.0)	(0.00, 2.29)	1.3	(-9.8, 12.4)	0.241
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	1 (0.7)	(0.02, 3.66)	158	0 (0.0)	(0.00, 2.31)	0.7	(-10.5, 11.9)	0.487
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to <= Week 24	140	0 (0.0)	(0.00, 2.60)	154	1 (0.6)	(0.02, 3.56)	-0.6	(-12.1, 10.8)	1.000
Baseline <= to <= Week 24	162	4 (2.5)	(0.68, 6.20)	161	1 (0.6)	(0.02, 3.41)	1.8	(-9.0, 12.7)	0.371

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.9
Source: t_14_2_3_2_1_1.sas

5.3.5.1—7 表 14.2.3.2.1.1 より引用

表 2.7.6.26－43　赤血球輸血による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	159	0 (0.0)	(0.00, 2.29)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 4 <= to < Week 6	156	0 (0.0)	(0.00, 2.34)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 6 <= to < Week 8	154	0 (0.0)	(0.00, 2.37)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to <= Week 24	140	0 (0.0)	(0.00, 2.60)	154	0 (0.0)	(0.00, 2.37)	-	(-, -)	-
Baseline <= to <= Week 24	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.10
Source: t_14_2_3_2_2_1.sas

5.3.5.1—7 表 14.2.3.2.2.1 より引用

表 2.7.6.26－44　瀉血による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	159	0 (0.0)	(0.00, 2.29)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 4 <= to < Week 6	156	0 (0.0)	(0.00, 2.34)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 6 <= to < Week 8	154	0 (0.0)	(0.00, 2.37)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to <= Week 24	140	0 (0.0)	(0.00, 2.60)	154	0 (0.0)	(0.00, 2.37)	-	(-, -)	-
Baseline <= to <= Week 24	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.11
Source: t_14_2_3_2_3_1.sas

5.3.5.1—7 表 14.2.3.2.3.1 より引用

(14)　QOL 指標

1)　QOL 指標（EQ-5D-5L）

MMRM を用いた EQ-5D-5L の Index Value 及び VAS スコアのベースラインからの変化量を表 2.7.6.26－45 に示した.

MMRM を用いた Index Value の 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -0.0038 及び -0.0201～0.0125，darbepoetin 群で -0.0244 及び -0.0400～ -0.0088 であった．MMRM を用いた 24 週後の Index Value の変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 0.0206 及び -0.0019～0.0431 であり，統計学的に有意な差が認められなかった（p=0.073）.

MMRM を用いた VAS スコアの 24 週後のベースラインからの変化量の LSMean 及びその 95%CI は MT-6548 群で -0.9 及び -3.3～1.4，darbepoetin 群で -3.8 及び -6.1～ -1.6 であった．MMRM を用いた VAS スコアの 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 2.9 及び -0.4～6.1 であり，統計学的に有意な差が認められなかった（p=0.082）.

表 2.7.6.26－45　EQ-5D-5L の Index Value 及び VAS スコアのベースラインからの変化量（MMRM，FAS）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Index value	MT-6548	Week 12	146	0.9127 (0.1266)	-0.0028	0.0081	(-0.0187, 0.0132)	
		Week 24	138	0.9080 (0.1318)	-0.0038	0.0083	(-0.0201, 0.0125)	
	darbepoetin	Week 12	157	0.9080 (0.1208)	-0.0139	0.0078	(-0.0293, 0.0015)	
		Week 24	152	0.9103 (0.1193)	-0.0244	0.0079	(-0.0400, -0.0088)	
	Difference MT-6548 - darbepoetin	Week 12			0.0111	0.0113	(-0.0111, 0.0333)	0.326
		Week 24			0.0206	0.0115	(-0.0019, 0.0431)	0.073
VAS score	MT-6548	Week 12	146	80.2 (15.5)	-1.6	1.2	(-3.8, 0.6)	
		Week 24	138	80.2 (15.8)	-0.9	1.2	(-3.3, 1.4)	
	darbepoetin	Week 12	156	79.5 (14.3)	-2.7	1.1	(-4.9, -0.4)	
		Week 24	151	80.1 (13.9)	-3.8	1.1	(-6.1, -1.6)	
	Difference MT-6548 - darbepoetin	Week 12			1.1	1.6	(-2.1, 4.3)	0.482
		Week 24			2.9	1.7	(-0.4, 6.1)	0.082

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.7
Source: t_14_2_3_12_2_1.sas

5.3.5.1—7 表 11.4.1—21 より引用

2)　QOL 指標（KDQOL）

MMRM を用いた KDQOL のスコアのベースラインからの変化量を表 2.7.6.26－46 に示した.

MMRM を用いた KDQOL のスコアの 24 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差について，特筆すべき差を認めたサブスケールはなかった.

表 2.7.6.26－46　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Physical Functioning	MT-6548	Week 12	144	83.70 (18.06)	-1.19	0.98	(-3.11, 0.73)	
		Week 24	136	84.10 (17.53)	-1.54	1.00	(-3.51, 0.42)	
	darbepoetin	Week 12	156	79.04 (19.18)	-2.81	0.94	(-4.66, -0.96)	
		Week 24	151	79.30 (19.17)	-2.16	0.95	(-4.03, -0.29)	
	Difference MT-6548 - darbepoetin	Week 12			1.63	1.36	(-1.05, 4.30)	0.233
		Week 24			0.62	1.39	(-2.11, 3.34)	0.656
Role Functioning Physical	MT-6548	Week 12	144	78.47 (33.27)	-1.17	2.60	(-6.27, 3.93)	
		Week 24	136	78.68 (32.99)	-0.75	2.66	(-5.98, 4.48)	
	darbepoetin	Week 12	156	73.88 (35.17)	-1.96	2.50	(-6.85, 2.96)	
		Week 24	151	74.83 (34.70)	-4.09	2.53	(-9.06, 0.88)	
	Difference MT-6548 - darbepoetin	Week 12			0.78	3.60	(-6.31, 7.86)	0.829
		Week 24			3.34	3.67	(-3.88, 10.56)	0.364
Bodily Pain	MT-6548	Week 12	144	81.48 (20.95)	0.56	1.52	(-2.42, 3.54)	
		Week 24	136	80.94 (21.07)	-0.32	1.55	(-3.37, 2.73)	
	darbepoetin	Week 12	156	78.86 (20.37)	-1.68	1.46	(-4.55, 1.18)	
		Week 24	151	79.93 (19.61)	-4.31	1.48	(-7.22, -1.41)	
	Difference MT-6548 - darbepoetin	Week 12			2.24	2.11	(-1.90, 6.37)	0.289
		Week 24			3.99	2.14	(-0.22, 8.20)	0.063
General Health Perceptions	MT-6548	Week 12	144	56.19 (16.26)	-1.66	1.04	(-3.70, 0.37)	
		Week 24	136	56.41 (16.43)	-1.90	1.06	(-3.96, 0.15)	
	darbepoetin	Week 12	156	54.36 (16.60)	-0.39	1.00	(-2.34, 1.57)	
		Week 24	151	54.64 (16.77)	-3.46	1.01	(-5.44, -1.48)	
	Difference MT-6548 - darbepoetin	Week 12			-1.28	1.44	(-4.10, 1.55)	0.375
		Week 24			1.57	1.46	(-1.31, 4.44)	0.285

表 2.7.6.26－46　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Vitality	MT-6548	Week 12	144	68.65 (18.78)	-2.72	1.27	(-5.22, -0.22)	
		Week 24	136	69.04 (19.07)	-1.77	1.30	(-4.32, 0.79)	
	darbepoetin	Week 12	156	65.83 (18.55)	-3.14	1.22	(-5.55, -0.74)	
		Week 24	151	66.32 (18.46)	-0.93	1.24	(-3.37, 1.50)	
	Difference MT-6548 - darbepoetin	Week 12			0.42	1.77	(-3.05, 3.90)	0.810
		Week 24			-0.84	1.80	(-4.37, 2.70)	0.642
Social Functioning	MT-6548	Week 12	144	90.89 (16.99)	-1.09	1.43	(-3.90, 1.72)	
		Week 24	136	89.25 (16.68)	-1.34	1.47	(-4.22, 1.54)	
	darbepoetin	Week 12	156	86.14 (19.70)	-2.57	1.38	(-5.27, 0.14)	
		Week 24	151	87.17 (18.71)	-2.53	1.39	(-5.27, 0.21)	
	Difference MT-6548 - darbepoetin	Week 12			1.48	1.99	(-2.43, 5.38)	0.458
		Week 24			1.19	2.03	(-2.78, 5.17)	0.556
Role Functioning Emotional	MT-6548	Week 12	144	84.49 (32.49)	-6.43	2.62	(-11.57, -1.28)	
		Week 24	136	85.29 (32.65)	-0.11	2.68	(-5.38, 5.16)	
	darbepoetin	Week 12	156	82.05 (33.74)	-1.13	2.52	(-6.07, 3.82)	
		Week 24	151	82.56 (33.30)	-3.88	2.55	(-8.89, 1.14)	
	Difference MT-6548 - darbepoetin	Week 12			-5.30	3.63	(-12.44, 1.84)	0.145
		Week 24			3.77	3.70	(-3.51, 11.04)	0.310
Mental Health	MT-6548	Week 12	144	78.47 (16.74)	-1.43	1.21	(-3.81, 0.96)	
		Week 24	136	78.88 (16.73)	-0.98	1.24	(-3.41, 1.46)	
	darbepoetin	Week 12	155	78.40 (16.26)	-1.38	1.17	(-3.68, 0.92)	
		Week 24	150	78.51 (16.26)	-0.43	1.19	(-2.76, 1.90)	
	Difference MT-6548 - darbepoetin	Week 12			-0.05	1.69	(-3.36, 3.27)	0.978
		Week 24			-0.55	1.72	(-3.92, 2.82)	0.749

表 2.7.6.26－46　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Symptoms/Problems	MT-6548	Week 12	144	88.20 (10.36)	-0.39	0.62	(-1.61, 0.84)	
		Week 24	136	88.31 (10.37)	-1.03	0.64	(-2.28, 0.22)	
	darbepoetin	Week 12	156	86.98 (10.02)	-0.32	0.60	(-1.49, 0.86)	
		Week 24	151	87.14 (9.99)	-0.09	0.61	(-1.29, 1.10)	
	Difference MT-6548 - darbepoetin	Week 12			-0.07	0.86	(-1.77, 1.63)	0.936
		Week 24			-0.94	0.88	(-2.67, 0.79)	0.288
Effect of kidney disease	MT-6548	Week 12	144	83.73 (13.64)	0.41	0.90	(-1.36, 2.17)	
		Week 24	136	83.82 (13.95)	0.89	0.92	(-0.91, 2.69)	
	darbepoetin	Week 12	156	82.68 (14.38)	0.88	0.86	(-0.82, 2.58)	
		Week 24	151	82.98 (14.24)	0.67	0.87	(-1.05, 2.39)	
	Difference MT-6548 - darbepoetin	Week 12			-0.47	1.25	(-2.92, 1.98)	0.706
		Week 24			0.22	1.27	(-2.27, 2.71)	0.865
Burden of kidney disease	MT-6548	Week 12	144	48.18 (23.02)	-1.95	1.46	(-4.81, 0.92)	
		Week 24	136	47.33 (22.82)	0.33	1.49	(-2.59, 3.25)	
	darbepoetin	Week 12	155	47.78 (23.66)	-3.82	1.41	(-6.58, -1.05)	
		Week 24	150	48.17 (23.77)	-3.39	1.42	(-6.19, -0.60)	
	Difference MT-6548 - darbepoetin	Week 12			1.87	2.03	(-2.11, 5.85)	0.356
		Week 24			3.73	2.06	(-0.32, 7.77)	0.071
Work status	MT-6548	Week 12	144	55.03 (34.81)	-0.47	1.89	(-4.20, 3.25)	
		Week 24	136	59.09 (35.08)	-3.22	1.94	(-7.02, 0.59)	
	darbepoetin	Week 12	156	56.73 (34.59)	-0.06	1.82	(-3.64, 3.52)	
		Week 24	151	58.61 (33.65)	-0.79	1.84	(-4.41, 2.84)	
	Difference MT-6548 - darbepoetin	Week 12			-0.41	2.63	(-5.58, 4.75)	0.876
		Week 24			-2.43	2.67	(-7.68, 2.83)	0.364

表 2.7.6.26－46　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Cognitive function	MT-6548	Week 12	143	90.26 (13.37)	-1.10	0.82	(-2.71, 0.52)	
		Week 24	135	90.67 (13.44)	0.73	0.84	(-0.93, 2.39)	
	darbepoetin	Week 12	155	91.72 (12.28)	-0.68	0.79	(-2.23, 0.87)	
		Week 24	151	91.99 (11.90)	-0.19	0.80	(-1.76, 1.38)	
	Difference MT-6548 - darbepoetin	Week 12			-0.42	1.14	(-2.66, 1.83)	0.716
		Week 24			0.91	1.16	(-1.37, 3.20)	0.433
Quality of social interaction	MT-6548	Week 12	143	91.62 (13.29)	-1.18	0.89	(-2.90, 0.54)	
		Week 24	135	91.16 (13.79)	1.45	0.90	(-0.31, 3.20)	
	darbepoetin	Week 12	156	91.67 (13.54)	-1.48	0.84	(-3.08, 0.21)	
		Week 24	151	91.57 (13.72)	-0.63	0.85	(-2.30, 1.04)	
	Difference MT-6548 - darbepoetin	Week 12			0.25	1.21	(-2.13, 2.63)	0.836
		Week 24			2.08	1.23	(-0.35, 4.50)	0.093
Sexual function	MT-6548	Week 12	5	85.00 (10.46)	3.35	5.17	(-7.63, 14.34)	
		Week 24	4	87.50 (10.21)	6.16	5.51	(-6.42, 16.74)	
	darbepoetin	Week 12	10	90.00 (23.42)	3.49	3.58	(-4.08, 11.05)	
		Week 24	9	86.11 (24.56)	1.21	3.69	(-6.54, 8.97)	
	Difference MT-6548 - darbepoetin	Week 12			-0.13	6.30	(-13.50, 13.24)	0.984
		Week 24			3.95	6.63	(-9.99, 17.89)	0.559
Sleep	MT-6548	Week 12	143	68.58 (16.49)	-1.60	1.11	(-3.78, 0.59)	
		Week 24	135	69.74 (16.54)	-1.33	1.14	(-3.57, 0.91)	
	darbepoetin	Week 12	156	70.29 (15.77)	-3.25	1.07	(-5.34, -1.16)	
		Week 24	151	70.30 (15.54)	-0.61	1.08	(-2.94, 1.31)	
	Difference MT-6548 - darbepoetin	Week 12			1.65	1.54	(-1.38, 4.67)	0.285
		Week 24			-0.52	1.57	(-3.60, 2.57)	0.743

表 2.7.6.26－46　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Social support	MT-6548	Week 12	144	79.63 (19.26)	-0.62	1.57	(-3.70, 2.46)	
		Week 24	135	79.26 (19.15)	-0.61	1.61	(-3.68, 2.66)	
	darbepoetin	Week 12	156	76.60 (21.98)	-3.05	1.50	(-6.01, -0.09)	
		Week 24	151	76.49 (22.22)	-2.66	1.53	(-5.66, 0.34)	
	Difference MT-6548 - darbepoetin	Week 12			2.43	2.17	(-1.84, 6.70)	0.264
		Week 24			2.15	2.22	(-2.22, 6.52)	0.334
Dialysis staff encouragement	MT-6548	Week 12	142	84.60 (16.69)	1.62	1.43	(-1.19, 4.43)	
		Week 24	135	84.35 (16.99)	0.39	1.46	(-2.49, 3.26)	
	darbepoetin	Week 12	156	82.37 (18.88)	-2.15	1.36	(-4.83, 0.53)	
		Week 24	150	82.00 (19.02)	-3.52	1.39	(-6.25, -0.79)	
	Difference MT-6548 - darbepoetin	Week 12			3.77	1.98	(-0.12, 7.65)	0.057
		Week 24			3.91	2.02	(-0.06, 7.87)	0.054
Patient satisfaction	MT-6548	Week 12	143	87.29 (12.66)	-0.18	1.06	(-2.26, 1.90)	
		Week 24	136	87.41 (12.63)	0.61	1.08	(-1.51, 2.74)	
	darbepoetin	Week 12	155	84.19 (14.81)	-2.06	1.02	(-4.05, -0.06)	
		Week 24	150	84.22 (14.68)	-0.29	1.03	(-2.31, 1.74)	
	Difference MT-6548 - darbepoetin	Week 12			1.87	1.47	(-1.02, 4.76)	0.204
		Week 24			0.90	1.50	(-2.04, 3.84)	0.548

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analysed by MMRM model.
Data Source: Listing 16.2.4.10
Source: t_14_2_3_12_6_1.sas

5.3.5.1—7 表 11.4.1—22 より引用

(15)　部分集団の検討

部分集団の検討で用いた評価項目及びその結果を示した図表の一覧を表 2.7.6.26－47 に示した.

表 2.7.6.26－47　部分集団解析の評価項目

評価項目	結果を示した図表
被験者背景別の 24 週後の Hb 値（MMRM，FAS）	表 2.7.6.26－48
前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）	表 2.7.6.26－49
前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）	表 2.7.6.26－50
MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）	図 2.7.6.26－12
MT-6548 群の前治療 ESA 製剤（エポエチン製剤）の用量別の Hb 値の推移（FAS）	図 2.7.6.26－13
MT-6548 群の前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）	図 2.7.6.26－14
MT-6548 群の前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）	図 2.7.6.26－15
前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）	表 2.7.6.26－51
前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）	表 2.7.6.26－52
鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の記述統計量（FAS）	表 2.7.6.26－53
鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値（MMRM，FAS）	表 2.7.6.26－54
MT-6548 群の鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の推移（FAS）	図 2.7.6.26－16
MT-6548 群のベースラインの CRP と 24 週後の Hb 値の散布図（FAS）	図 2.7.6.26－17
被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）	表 2.7.6.26－55
前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－56
前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－18
前治療 ESA 製剤（エポエチン製剤）の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－19
前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－20
前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－21
前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－57
鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－58
鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－22
ベースラインの CRP と 20 週から 24 週後の MT-6548 の 1 日平均投与量の散布図（FAS）	図 2.7.6.26－23

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Sex	Male	MT-6548	104	10.82 (0.78)	10.61	0.09	(10.44, 10.78)	
		darbepoetin	109	10.69 (0.67)	10.70	0.08	(10.54, 10.86)	
		Difference MT-6548 - darbepoetin			-0.09	0.12	(-0.33, 0.15)	0.456
	Female	MT-6548	56	10.61 (0.69)	10.63	0.12	(10.39, 10.75)	
		darbepoetin	51	10.83 (0.81)	10.50	0.12	(10.27, 10.72)	
		Difference MT-6548 - darbepoetin			0.03	0.16	(-0.29, 0.36)	0.856
Age at Informed Consent (years)	<65	MT-6548	60	10.78 (0.72)	10.44	0.11	(10.22, 10.66)	
		darbepoetin	68	10.69 (0.72)	10.63	0.10	(10.43, 10.84)	
		Difference MT-6548 - darbepoetin			-0.19	0.15	(-0.49, 0.11)	0.212
	>=65	MT-6548	100	10.72 (0.73)	10.68	0.09	(10.50, 10.85)	
		darbepoetin	92	10.77 (0.72)	10.63	0.09	(10.45, 10.80)	
		Difference MT-6548 - darbepoetin			0.05	0.13	(-0.20, 0.30)	0.684
	<75	MT-6548	122	10.76 (0.74)	10.58	0.08	(10.37, 10.69)	
		darbepoetin	129	10.76 (0.75)	10.59	0.08	(10.44, 10.73)	
		Difference MT-6548 - darbepoetin			-0.06	0.11	(-0.27, 0.16)	0.600
	>=75	MT-6548	38	10.68 (0.68)	10.77	0.14	(10.50, 11.04)	
		darbepoetin	31	10.65 (0.87)	10.84	0.15	(10.54, 11.14)	
		Difference MT-6548 - darbepoetin			-0.07	0.21	(-0.48, 0.33)	0.728

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Dry Weight (kg)	<60	MT-6548	98	10.71 (0.74)	10.58	0.09	(10.40, 10.75)	
		darbepoetin	91	10.79 (0.73)	10.54	0.09	(10.36, 10.71)	
		Difference MT-6548 - darbepoetin			0.04	0.13	(-0.21, 0.29)	0.756
	>=60	MT-6548	62	10.80 (0.70)	10.60	0.11	(10.38, 10.81)	
		darbepoetin	69	10.67 (0.71)	10.75	0.10	(10.55, 10.95)	
		Difference MT-6548 - darbepoetin			-0.15	0.15	(-0.44, 0.14)	0.318
BMI (kg/m^2)	<25	MT-6548	120	10.73 (0.71)	10.56	0.08	(10.40, 10.72)	
		darbepoetin	127	10.76 (0.73)	10.60	0.08	(10.45, 10.75)	
		Difference MT-6548 - darbepoetin			-0.04	0.11	(-0.26, 0.18)	0.721
	>=25	MT-6548	40	10.78 (0.78)	10.66	0.14	(10.39, 10.93)	
		darbepoetin	33	10.65 (0.68)	10.74	0.15	(10.44, 11.03)	
		Difference MT-6548 - darbepoetin			-0.08	0.20	(-0.47, 0.32)	0.704

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Etiology of CKD	Diabetes	MT-6548	29	10.92 (0.71)	10.85	0.16	(10.54, 10.66)	
		darbepoetin	39	10.76 (0.68)	10.86	0.13	(10.60, 11.11)	
		Difference MT-6548 - darbepoetin			-0.51	0.20	(-0.91, -0.11)	0.013
	Hypertension	MT-6548	20	10.73 (0.82)	10.77	0.18	(10.41, 11.13)	
		darbepoetin	22	10.71 (0.77)	10.66	0.17	(10.33, 11.00)	
		Difference MT-6548 - darbepoetin			0.11	0.25	(-0.39, 0.60)	0.669
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	62	10.71 (0.73)	10.55	0.11	(10.33, 10.76)	
		darbepoetin	64	10.76 (0.67)	10.55	0.10	(10.35, 10.76)	
		Difference MT-6548 - darbepoetin			-0.01	0.15	(-0.30, 0.29)	0.972
	Interstitial Nephritis/Pyelonephritis	MT-6548	4	10.45 (0.54)	10.33	0.79	(8.10, 12.57)	
		darbepoetin	1	11.90 (-)	9.97	2.13	(2.55, 17.39)	
		Difference MT-6548 - darbepoetin			0.36	2.50	(-8.06, 8.79)	0.896
	Cystic/Hereditary/Congenital Disease	MT-6548	17	10.54 (0.64)	10.52	0.27	(9.98, 11.06)	
		darbepoetin	10	10.35 (0.90)	10.87	0.35	(10.17, 11.57)	
		Difference MT-6548 - darbepoetin			-0.35	0.44	(-1.24, 0.54)	0.430
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	1	10.00 (-)				
		Difference MT-6548 - darbepoetin						

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Duration of Anemia from CKD (years)	<1	MT-6548	6	10.47 (0.79)	10.82	0.30	(10.22, 11.41)	
		darbepoetin	4	11.25 (0.44)	10.93	0.41	(10.10, 11.76)	
		Difference MT-6548 - darbepoetin			-0.11	0.52	(-1.17, 0.94)	0.832
	1<= to <5	MT-6548	64	10.85 (0.75)	10.70	0.11	(10.48, 10.91)	
		darbepoetin	67	10.63 (0.76)	10.78	0.10	(10.58, 10.98)	
		Difference MT-6548 - darbepoetin			-0.08	0.15	(-0.37, 0.22)	0.596
	>=5	MT-6548	89	10.68 (0.70)	10.48	0.10	(10.29, 10.67)	
		darbepoetin	89	10.79 (0.69)	10.51	0.09	(10.33, 10.69)	
		Difference MT-6548 - darbepoetin			-0.03	0.13	(-0.29, 0.23)	0.821
Complications	Hypertension	MT-6548	150	10.74 (0.73)	10.57	0.07	(10.43, 10.71)	
		darbepoetin	147	10.74 (0.71)	10.62	0.07	(10.48, 10.76)	
		Difference MT-6548 - darbepoetin			-0.05	0.10	(-0.25, 0.14)	0.598
	Diabetes	MT-6548	95	10.89 (0.69)	10.35	0.15	(10.09, 10.63)	
		darbepoetin	48	10.67 (0.76)	10.85	0.12	(10.61, 11.09)	
		Difference MT-6548 - darbepoetin			-0.46	0.19	(-0.84, -0.08)	0.017
	Dyslipidaemia	MT-6548	57	10.72 (0.63)	10.67	0.11	(10.47, 10.88)	
		darbepoetin	79	10.79 (0.71)	10.69	0.09	(10.52, 10.86)	
		Difference MT-6548 - darbepoetin			-0.02	0.14	(-0.29, 0.25)	0.894

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline Hb (g/dL)	<10	MT-6548	28	9.66 (0.26)	10.57	0.19	(10.19, 10.94)	
		darbepoetin	24	9.61 (0.31)	10.94	0.19	(10.58, 11.31)	
		Difference MT-6548 - darbepoetin			-0.37	0.27	(-0.90, 0.16)	0.160
	10<= to <11	MT-6548	76	10.45 (0.27)	10.41	0.09	(10.24, 10.59)	
		darbepoetin	76	10.52 (0.27)	10.48	0.09	(10.31, 10.65)	
		Difference MT-6548 - darbepoetin			-0.07	0.12	(-0.31, 0.16)	0.536
	>=11	MT-6548	61	11.51 (0.33)	10.81	0.12	(10.58, 11.04)	
		darbepoetin	60	11.46 (0.40)	10.70	0.11	(10.48, 10.92)	
		Difference MT-6548 - darbepoetin			0.11	0.16	(-0.21, 0.43)	0.512
Baseline Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	159	10.74 (0.72)	10.58	0.07	(10.44, 10.71)	
		darbepoetin	160	10.74 (0.72)	10.63	0.07	(10.50, 10.76)	
		Difference MT-6548 - darbepoetin			-0.05	0.10	(-0.24, 0.14)	0.590
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	1	11.40 (-)				
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						
	AST >80 or ALT >90	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline CRP (mg/dL)	<0.31	MT-6548	132	10.75 (0.73)	10.50	0.08	(10.35, 10.65)	
		darbepoetin	132	10.76 (0.69)	10.66	0.07	(10.51, 10.79)	
		Difference MT-6548 - darbepoetin			-0.15	0.10	(-0.35, 0.06)	0.161
	>=0.31	MT-6548	28	10.72 (0.72)	10.98	0.18	(10.63, 11.33)	
		darbepoetin	28	10.61 (0.87)	10.55	0.18	(10.20, 10.90)	
		Difference MT-6548 - darbepoetin			0.43	0.25	(-0.06, 0.93)	0.085
Baseline Serum Ferritin (ng/mL)	<82.7	MT-6548	55	10.79 (0.69)	10.59	0.12	(10.36, 10.82)	
		darbepoetin	52	10.83 (0.67)	10.66	0.11	(10.43, 10.88)	
		Difference MT-6548 - darbepoetin			-0.07	0.16	(-0.39, 0.25)	0.678
	82.7<= to <165	MT-6548	59	10.82 (0.84)	10.73	0.12	(10.48, 10.97)	
		darbepoetin	54	10.77 (0.74)	10.74	0.12	(10.51, 10.97)	
		Difference MT-6548 - darbepoetin			-0.01	0.17	(-0.35, 0.32)	0.938
	>=165	MT-6548	52	10.62 (0.61)	10.43	0.12	(10.18, 10.67)	
		darbepoetin	54	10.61 (0.74)	10.48	0.12	(10.25, 10.72)	
		Difference MT-6548 - darbepoetin			-0.05	0.17	(-0.39, 0.29)	0.762

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline TSAT (%)	<23	MT-6548	48	10.78 (0.76)	10.74	0.13	(10.48, 11.00)	
		darbepoetin	53	10.67 (0.77)	10.44	0.12	(10.20, 10.67)	
		Difference MT-6548 - darbepoetin			0.30	0.18	(-0.05, 0.66)	0.089
	23<= to <31	MT-6548	49	10.79 (0.67)	10.60	0.11	(10.38, 10.83)	
		darbepoetin	56	10.74 (0.70)	10.68	0.11	(10.46, 10.89)	
		Difference MT-6548 - darbepoetin			-0.07	0.16	(-0.38, 0.24)	0.641
	>=31	MT-6548	63	10.68 (0.74)	10.45	0.12	(10.22, 10.68)	
		darbepoetin	51	10.80 (0.70)	10.78	0.12	(10.54, 11.02)	
		Difference MT-6548 - darbepoetin			-0.33	0.17	(-0.67, 0.00)	0.053
Smoking Status	Never Smoked	MT-6548	73	10.61 (0.69)	10.53	0.10	(10.33, 10.73)	
		darbepoetin	73	10.83 (0.71)	10.57	0.10	(10.38, 10.76)	
		Difference MT-6548 - darbepoetin			-0.03	0.14	(-0.31, 0.24)	0.812
	Ex-Smoker	MT-6548	66	10.81 (0.72)	10.65	0.11	(10.43, 10.87)	
		darbepoetin	62	10.83 (0.69)	10.68	0.12	(10.46, 10.91)	
		Difference MT-6548 - darbepoetin			-0.03	0.16	(-0.35, 0.29)	0.843
	Current Smoker	MT-6548	21	11.00 (0.80)	10.58	0.18	(10.22, 10.95)	
		darbepoetin	25	10.22 (0.63)	10.69	0.16	(10.36, 11.01)	
		Difference MT-6548 - darbepoetin			-0.10	0.25	(-0.61, 0.40)	0.685

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	8	10.71 (0.44)	10.38	0.34	(9.68, 11.08)	
		darbepoetin	4	11.03 (0.53)	10.74	0.46	(9.78, 11.70)	
		Difference MT-6548 - darbepoetin			-0.36	0.58	(-1.57, 0.85)	0.544
	No	MT-6548	152	10.75 (0.74)	10.60	0.07	(10.46, 10.74)	
		darbepoetin	156	10.73 (0.73)	10.62	0.07	(10.49, 10.76)	
		Difference MT-6548 - darbepoetin			-0.03	0.10	(-0.22, 0.17)	0.788
Concomitant Medications of Oral Iron at Week 24	Yes	MT-6548	7	10.64 (0.48)	10.38	0.36	(9.66, 11.10)	
		darbepoetin	6	10.85 (0.97)	11.05	0.36	(10.31, 11.79)	
		Difference MT-6548 - darbepoetin			-0.67	0.51	(-1.70, 0.37)	0.198
	No	MT-6548	153	10.75 (0.73)	10.59	0.07	(10.45, 10.73)	
		darbepoetin	154	10.73 (0.71)	10.61	0.07	(10.48, 10.75)	
		Difference MT-6548 - darbepoetin			-0.02	0.10	(-0.21, 0.17)	0.888
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Baseline	Yes	MT-6548	59	10.85 (0.75)	10.43	0.12	(10.20, 10.67)	
		darbepoetin	61	10.75 (0.82)	10.59	0.13	(10.34, 10.84)	
		Difference MT-6548 - darbepoetin			-0.16	0.17	(-0.50, 0.18)	0.366
	No	MT-6548	101	10.68 (0.71)	10.68	0.09	(10.51, 10.84)	
		darbepoetin	109	10.73 (0.68)	10.65	0.08	(10.49, 10.80)	
		Difference MT-6548 - darbepoetin			0.03	0.12	(-0.20, 0.26)	0.802

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 24	Yes	MT-6548	56	10.88 (0.75)	10.41	0.12	(10.17, 10.65)	
		darbepoetin	49	10.76 (0.83)	10.60	0.13	(10.34, 10.85)	
		Difference MT-6548 - darbepoetin			-0.19	0.18	(-0.54, 0.17)	0.302
	No	MT-6548	104	10.67 (0.70)	10.68	0.09	(10.52, 10.85)	
		darbepoetin	111	10.73 (0.67)	10.64	0.09	(10.49, 10.80)	
		Difference MT-6548 - darbepoetin			0.04	0.12	(-0.19, 0.26)	0.744
Prior ESA Treatment: Medication	Epoetin	MT-6548	49	10.63 (0.76)	10.71	0.14	(10.44, 10.98)	
		darbepoetin	53	10.53 (0.80)	10.67	0.13	(10.41, 10.92)	
		Difference MT-6548 - darbepoetin			0.04	0.19	(-0.33, 0.41)	0.820
	Darbepoetin alfa	MT-6548	95	10.75 (0.70)	10.48	0.08	(10.31, 10.64)	
		darbepoetin	89	10.69 (0.66)	10.55	0.08	(10.39, 10.71)	
		Difference MT-6548 - darbepoetin			-0.07	0.12	(-0.30, 0.16)	0.537
	Epoetin beta pegol	MT-6548	16	11.03 (0.75)	10.79	0.24	(10.32, 11.26)	
		darbepoetin	18	10.60 (0.67)	10.95	0.21	(10.53, 11.37)	
		Difference MT-6548 - darbepoetin			-0.16	0.32	(-0.79, 0.47)	0.612
	Other	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Prior ESA Treatment: Weekly Dose (IU)	Epoetin, <3000	MT-6548	15	10.50 (0.69)	11.18	0.24	(10.70, 11.65)	
		darbepoetin	13	10.23 (0.89)	11.54	0.25	(11.04, 12.04)	
		Difference MT-6548 - darbepoetin			-0.36	0.34	(-1.05, 0.33)	0.299
	Epoetin, 3000<= to <4500	MT-6548	17	10.46 (0.75)	10.48	0.22	(10.04, 10.91)	
		darbepoetin	11	10.50 (0.68)	10.62	0.27	(10.09, 11.16)	
		Difference MT-6548 - darbepoetin			-0.14	0.35	(-0.84, 0.55)	0.682
	Epoetin, >=4500	MT-6548	17	10.93 (0.77)	10.47	0.21	(10.05, 10.89)	
		darbepoetin	29	10.69 (0.78)	10.32	0.16	(10.00, 10.64)	
		Difference MT-6548 - darbepoetin			0.15	0.27	(-0.38, 0.67)	0.586
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	20	10.83 (0.56)	10.76	0.15	(10.46, 11.05)	
		darbepoetin	14	10.71 (0.73)	11.01	0.17	(10.67, 11.35)	
		Difference MT-6548 - darbepoetin			-0.26	0.23	(-0.71, 0.19)	0.259
	Darbepoetin alfa, 10<= to <20	MT-6548	34	10.66 (0.75)	10.61	0.13	(10.26, 10.76)	
		darbepoetin	40	10.80 (0.57)	10.62	0.12	(10.39, 10.84)	
		Difference MT-6548 - darbepoetin			-0.11	0.17	(-0.45, 0.23)	0.521
	Darbepoetin alfa, >=20	MT-6548	41	10.80 (0.71)	10.30	0.13	(10.04, 10.57)	
		darbepoetin	35	11.06 (0.69)	10.30	0.13	(10.04, 10.56)	
		Difference MT-6548 - darbepoetin			0.00	0.19	(-0.37, 0.38)	0.987

表 2.7.6.26－48　被験者背景別の 24 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Prior ESA Treatment: Weekly Dose (ug)	Epoetin beta pegol, <12.5	MT-6548	3	10.80 (0.95)	11.07	0.31	(10.43, 11.72)	
		darbepoetin	4	10.83 (0.64)	11.32	0.27	(10.76, 11.88)	
		Difference MT-6548 - darbepoetin			-0.25	0.42	(-1.10, 0.61)	0.558
	Epoetin beta pegol, 12.5<= to <25	MT-6548	7	10.80 (0.55)	10.56	0.37	(9.81, 11.31)	
		darbepoetin	6	10.28 (0.70)	11.09	0.41	(10.28, 11.91)	
		Difference MT-6548 - darbepoetin			-0.53	0.56	(-1.67, 0.60)	0.345
	Epoetin beta pegol, >=25	MT-6548	6	11.40 (0.83)	11.04	0.41	(10.21, 11.87)	
		darbepoetin	8	10.73 (0.65)	10.68	0.31	(10.06, 11.30)	
		Difference MT-6548 - darbepoetin			0.36	0.53	(-0.70, 1.43)	0.498
Concomitant Medications of CYP2B6 inducer	Yes	MT-6548	12	10.98 (0.65)	10.74	0.25	(10.25, 11.23)	
		darbepoetin	23	10.90 (0.77)	10.60	0.17	(10.28, 10.93)	
		Difference MT-6548 - darbepoetin			0.14	0.30	(-0.45, 0.73)	0.640
	No	MT-6548	148	10.72 (0.73)	10.57	0.07	(10.43, 10.72)	
		darbepoetin	137	10.71 (0.71)	10.63	0.07	(10.49, 10.78)	
		Difference MT-6548 - darbepoetin			-0.06	0.10	(-0.27, 0.14)	0.548

Note(s): Hb (g/dL).
Note(s): N: number of subjects who was used in MMRM model (i.e. number of subjects with Hb at least one visit after baseline).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): Baseline Serum Ferritin, Baseline TSAT and each Prior ESA Treatment Total Weekly Dose are divided into three categories by the 3-quantiles.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.1
Source: t_14_2_5_1.sas

5.3.5.1—7 表 11.4.2—4 より引用

表 2.7.6.26－49　前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline						
Treatment Group	Prior ESA Treatment	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetin	Baseline	49	10.63	0.76	10.60	(9.4, 12.0)	(10.42, 10.85)							
		Week 2	49	10.51	0.83	10.60	(8.3, 12.5)	(10.27, 10.75)	49	-0.12	0.63	-0.10	(-1.6, 1.2)	(-0.30, 0.06)	0.183
		Week 4	48	10.37	0.98	10.25	(7.7, 12.4)	(10.08, 10.65)	48	-0.28	0.89	-0.20	(-2.2, 1.2)	(-0.54, -0.02)	0.033
		Week 6	47	10.24	1.16	10.10	(7.2, 13.2)	(9.90, 10.58)	47	-0.40	1.16	-0.20	(-2.7, 1.6)	(-0.74, -0.06)	0.022
		Week 8	47	10.25	1.14	10.30	(6.8, 13.0)	(9.91, 10.58)	47	-0.39	1.22	-0.20	(-3.1, 1.6)	(-0.75, -0.03)	0.034
		Week 10	47	10.31	1.28	10.30	(6.7, 12.8)	(9.93, 10.68)	47	-0.33	1.40	-0.20	(-3.2, 2.3)	(-0.74, 0.08)	0.112
		Week 12	46	10.54	1.26	10.45	(7.7, 13.3)	(10.17, 10.91)	46	-0.11	1.45	-0.15	(-2.8, 2.9)	(-0.54, 0.32)	0.599
		Week 16	46	10.73	1.08	10.95	(8.3, 12.9)	(10.41, 11.05)	46	0.07	1.32	0.30	(-3.1, 2.1)	(-0.32, 0.46)	0.714
		Week 20	46	10.84	1.06	10.85	(8.3, 13.1)	(10.53, 11.16)	46	0.19	1.29	0.10	(-2.8, 2.6)	(-0.20, 0.57)	0.332
		Week 24	46	10.80	1.08	10.85	(8.6, 13.3)	(10.48, 11.12)	46	0.14	1.19	0.30	(-3.1, 2.3)	(-0.21, 0.50)	0.416
		Week 24 (LOCF)	49	10.66	1.22	10.70	(6.6, 13.3)	(10.31, 11.01)	49	0.03	1.27	0.20	(-3.3, 2.3)	(-0.34, 0.39)	0.875
	Darbepoetin alfa	Baseline	97	10.74	0.70	10.70	(8.8, 12.1)	(10.60, 10.88)							
		Week 2	95	10.60	0.73	10.60	(8.8, 12.3)	(10.45, 10.75)	95	-0.16	0.52	0.00	(-1.7, 1.3)	(-0.26, -0.05)	0.005
		Week 4	93	10.32	0.81	10.30	(8.3, 11.9)	(10.15, 10.48)	93	-0.44	0.77	-0.40	(-2.3, 1.3)	(-0.60, -0.28)	<0.001
		Week 6	92	10.17	0.89	10.10	(7.8, 11.9)	(9.99, 10.35)	92	-0.59	0.87	-0.45	(-3.2, 1.3)	(-0.77, -0.41)	<0.001
		Week 8	87	10.15	0.94	10.20	(8.0, 12.5)	(9.95, 10.35)	87	-0.60	1.05	-0.60	(-3.3, 2.6)	(-0.82, -0.37)	<0.001
		Week 10	87	10.14	0.94	10.20	(7.7, 12.1)	(9.94, 10.34)	87	-0.63	1.10	-0.50	(-3.7, 2.0)	(-0.86, -0.39)	<0.001
		Week 12	85	10.33	0.95	10.40	(7.4, 12.5)	(10.12, 10.53)	85	-0.43	1.15	-0.50	(-3.9, 3.7)	(-0.68, -0.18)	<0.001
		Week 16	84	10.45	0.82	10.50	(8.5, 12.4)	(10.27, 10.63)	84	-0.30	1.09	-0.25	(-3.0, 2.6)	(-0.53, -0.06)	0.015
		Week 20	81	10.57	0.78	10.60	(8.7, 12.5)	(10.40, 10.75)	81	-0.15	1.00	0.00	(-2.9, 2.1)	(-0.38, 0.07)	0.170
		Week 24	79	10.53	0.82	10.60	(8.0, 12.2)	(10.34, 10.71)	79	-0.22	1.06	-0.20	(-3.6, 2.2)	(-0.45, 0.02)	0.071
		Week 24 (LOCF)	96	10.33	0.98	10.40	(7.4, 12.2)	(10.13, 10.53)	96	-0.41	1.17	-0.35	(-3.9, 2.2)	(-0.65, -0.18)	<0.001

表 2.7.6.26－49　前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）（続き）

Treatment Group	Prior ESA Treatment	Visit	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Baseline N	Change from Baseline Mean	Change from Baseline SD	Change from Baseline Median	Change from Baseline Minimum, Maximum	Change from Baseline 95% CI	p value
	Epoetinbeta pegol	Baseline	16	11.03	0.75	10.65	(10.2, 12.6)	(10.62, 11.43)							
		Week 2	16	10.99	0.95	11.05	(9.6, 12.9)	(10.49, 11.50)	16	-0.03	0.42	-0.05	(-0.7, 0.6)	(-0.25, 0.19)	0.770
		Week 4	16	10.80	0.78	10.90	(9.4, 12.2)	(10.38, 11.22)	16	-0.23	0.69	-0.40	(-1.2, 1.3)	(-0.59, 0.14)	0.211
		Week 6	16	10.68	0.70	10.85	(9.2, 11.7)	(10.30, 11.05)	16	-0.35	0.89	-0.40	(-1.4, 1.2)	(-0.82, 0.12)	0.137
		Week 8	16	10.68	0.88	10.95	(9.1, 11.9)	(10.21, 11.14)	16	-0.35	1.18	-0.10	(-2.2, 1.3)	(-0.98, 0.28)	0.254
		Week 10	16	10.59	1.08	10.90	(8.6, 12.2)	(10.01, 11.16)	16	-0.44	1.47	-0.40	(-2.7, 2.0)	(-1.22, 0.34)	0.252
		Week 12	16	10.66	1.15	11.10	(8.4, 11.9)	(10.04, 11.27)	16	-0.37	1.60	-0.10	(-3.2, 1.6)	(-1.22, 0.48)	0.370
		Week 16	14	10.77	1.31	11.05	(7.5, 12.5)	(10.02, 11.53)	14	-0.20	1.80	0.30	(-4.1, 2.3)	(-1.24, 0.84)	0.684
		Week 20	13	10.85	0.90	10.90	(9.4, 12.0)	(10.30, 11.39)	13	-0.18	1.22	-0.20	(-2.1, 1.5)	(-0.92, 0.56)	0.612
		Week 24	13	10.90	0.76	10.60	(10.0, 12.4)	(10.44, 11.36)	13	-0.12	0.92	-0.30	(-1.4, 1.2)	(-0.68, 0.44)	0.640
		Week 24(LOCF)	16	10.68	0.99	10.55	(8.8, 12.4)	(10.15, 11.20)	16	-0.35	1.23	-0.35	(-2.8, 1.2)	(-1.01, 0.31)	0.274

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_5_1.sas

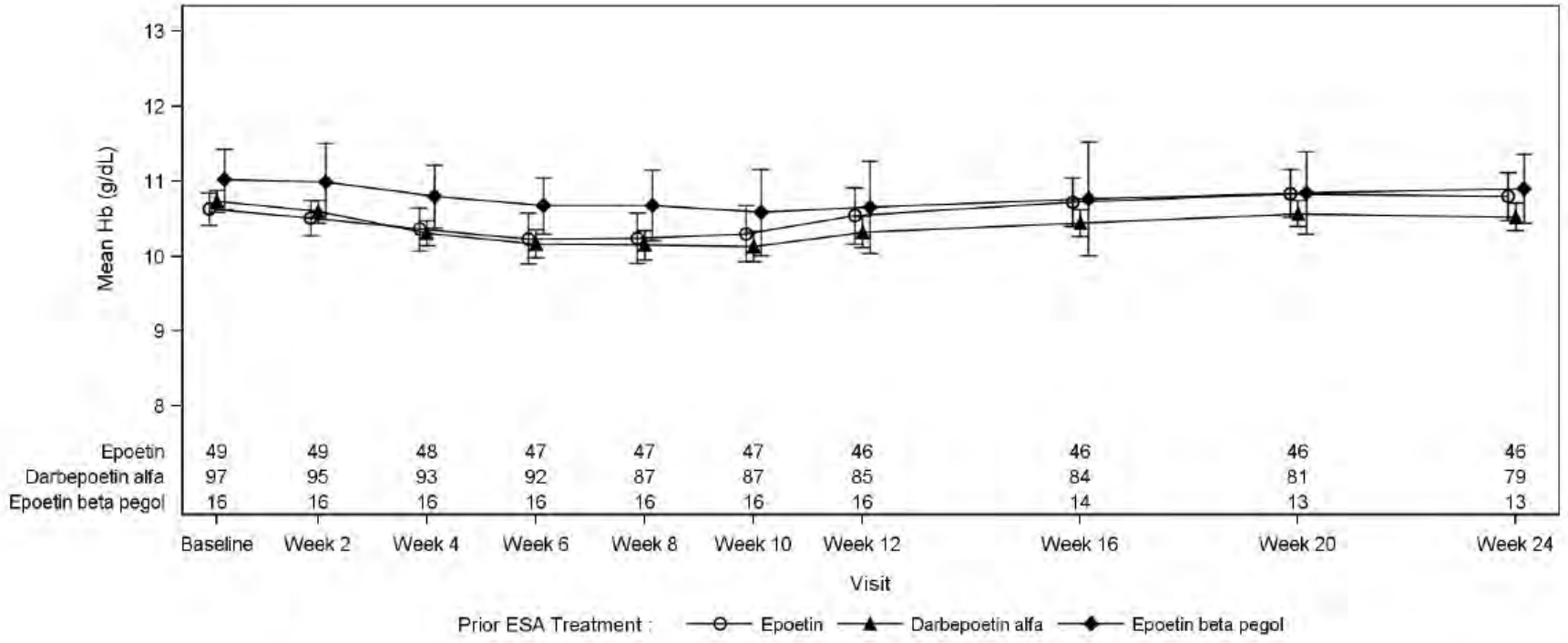
5.3.5.1—7 表 14.2.2.5.1 より引用

表 2.7.6.26－50　前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）

Treatment Group	Prior ESA Treatment	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Epoetin	Week 2	49	10.63 (0.76)	10.52	0.16	(10.20, 10.83)
		Week 4	48	10.65 (0.76)	10.35	0.16	(10.04, 10.67)
		Week 6	47	10.64 (0.76)	10.22	0.16	(9.91, 10.54)
		Week 8	47	10.64 (0.76)	10.23	0.16	(9.92, 10.55)
		Week 10	47	10.64 (0.76)	10.29	0.16	(9.97, 10.61)
		Week 12	46	10.65 (0.76)	10.46	0.16	(10.15, 10.78)
		Week 16	46	10.65 (0.76)	10.65	0.16	(10.33, 10.97)
		Week 20	46	10.65 (0.76)	10.76	0.16	(10.45, 11.08)
		Week 24	46	10.65 (0.76)	10.72	0.16	(10.40, 11.04)
	Darbepoetin alfa	Week 2	95	10.75 (0.70)	10.60	0.09	(10.42, 10.77)
		Week 4	93	10.76 (0.70)	10.31	0.09	(10.13, 10.48)
		Week 6	92	10.76 (0.70)	10.15	0.09	(9.98, 10.33)
		Week 8	87	10.75 (0.70)	10.11	0.09	(9.94, 10.29)
		Week 10	87	10.76 (0.71)	10.10	0.09	(9.92, 10.27)
		Week 12	85	10.75 (0.70)	10.27	0.09	(10.09, 10.44)
		Week 16	84	10.75 (0.70)	10.37	0.09	(10.20, 10.55)
		Week 20	81	10.73 (0.70)	10.51	0.09	(10.33, 10.69)
		Week 24	79	10.74 (0.70)	10.45	0.09	(10.27, 10.63)
	Epoetin beta pegol	Week 2	16	11.03 (0.75)	10.99	0.25	(10.50, 11.49)
		Week 4	16	11.03 (0.75)	10.80	0.25	(10.31, 11.29)
		Week 6	16	11.03 (0.75)	10.67	0.25	(10.18, 11.17)
		Week 8	16	11.03 (0.75)	10.67	0.25	(10.18, 11.17)
		Week 10	16	11.03 (0.75)	10.59	0.25	(10.09, 11.08)
		Week 12	16	11.03 (0.75)	10.66	0.25	(10.16, 11.15)
		Week 16	14	10.97 (0.78)	10.68	0.26	(10.16, 11.19)
		Week 20	13	11.02 (0.79)	10.79	0.26	(10.26, 11.31)
		Week 24	13	11.02 (0.79)	10.84	0.26	(10.31, 11.37)

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_5_2.sas

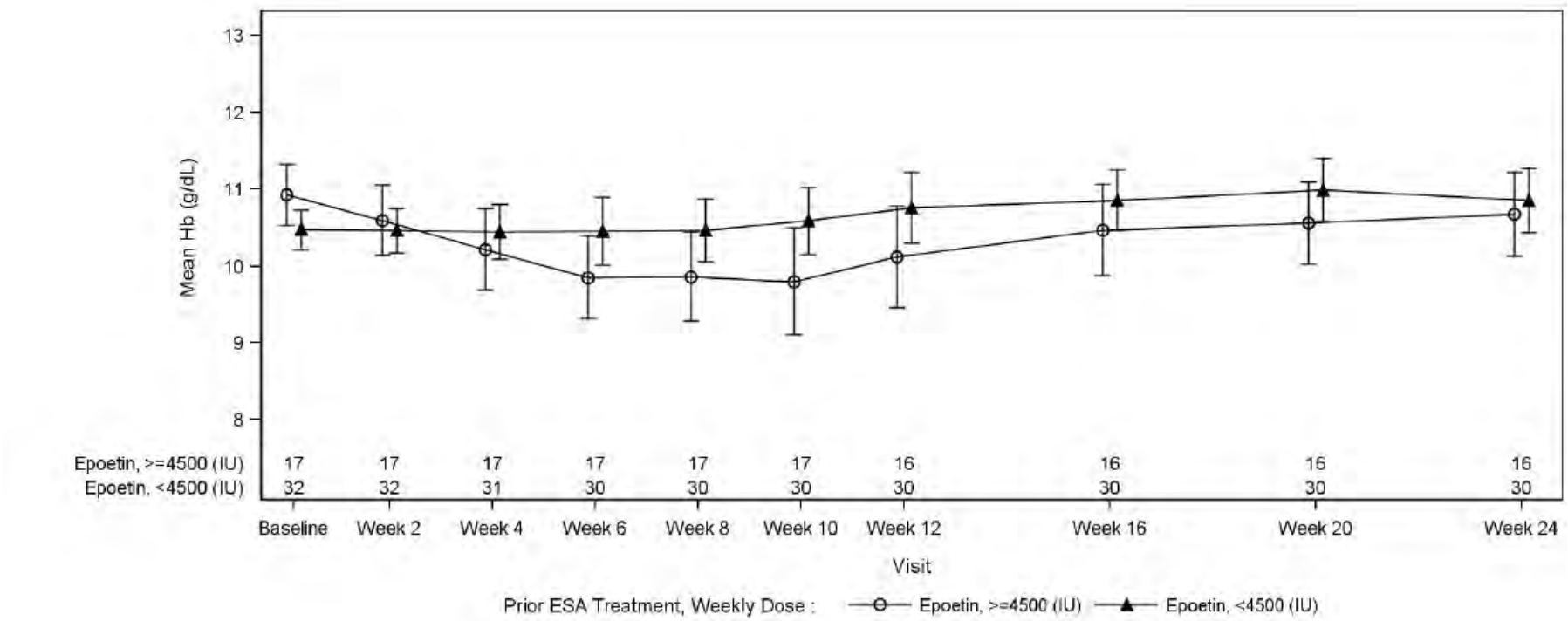
5.3.5.1—7 表 14.2.2.5.2 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.2.5.1
Source: f_14_2_1_3_1.sas

図 2.7.6.26－12　MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）

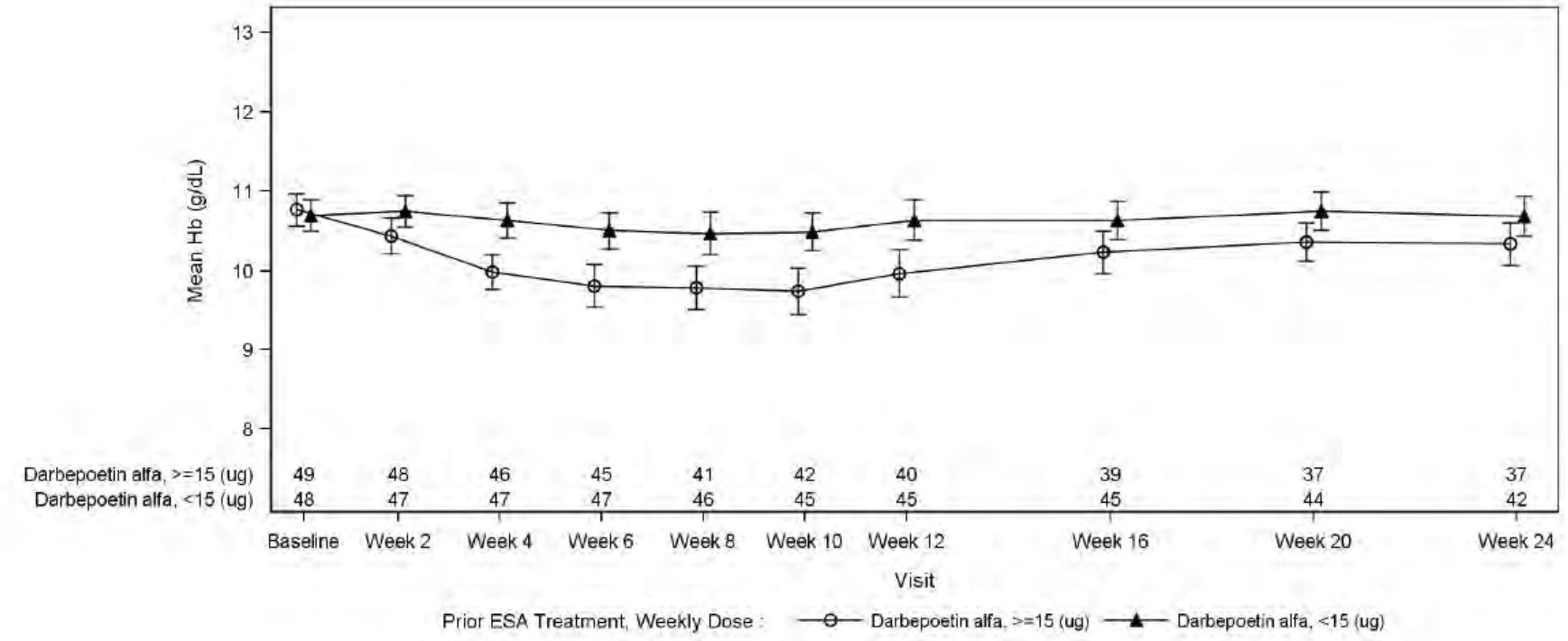
5.3.5.1—7 図 14.2.1.3.1 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_1.sas

図 2.7.6.26－13　MT-6548 群の前治療 ESA 製剤（エポエチン製剤）の用量別の Hb 値の推移（FAS）

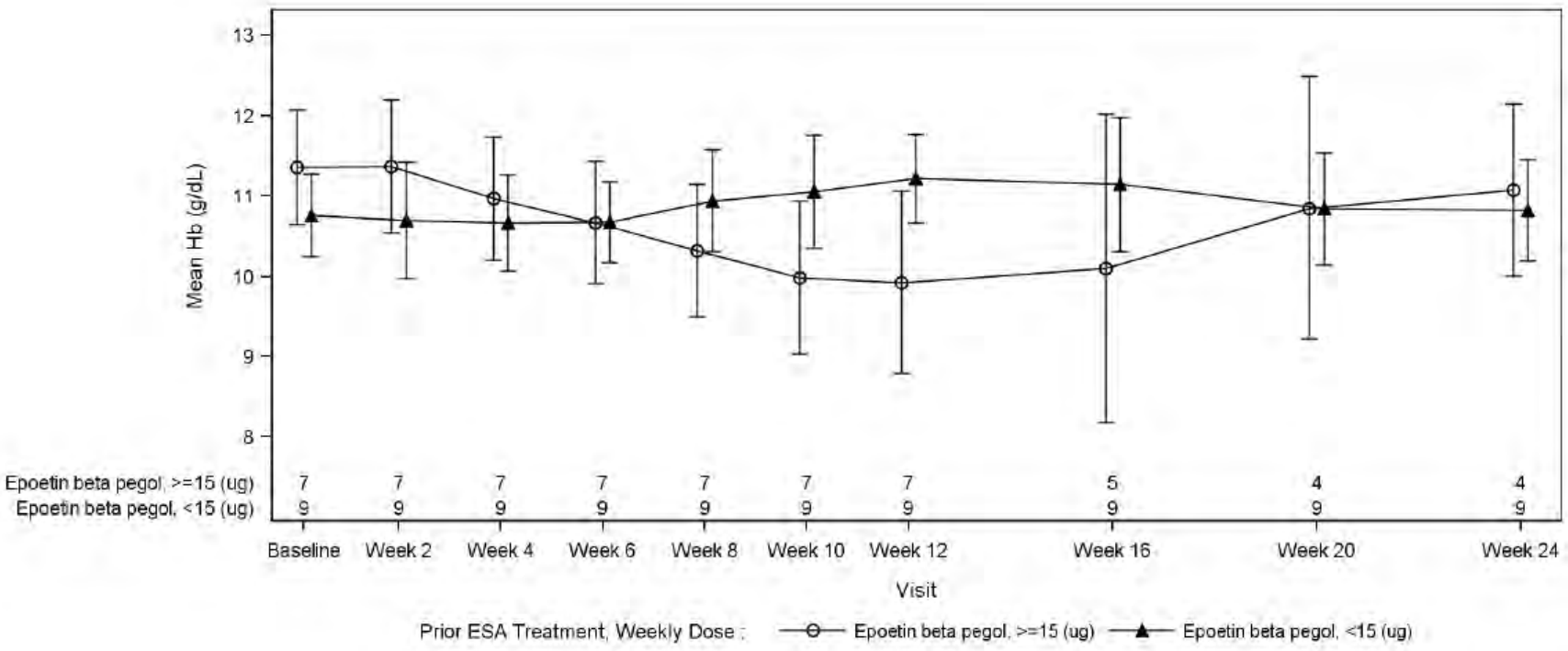
5.3.5.1—7 図 14.2.1.4.1 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_2.sas

図 2.7.6.26－14　MT-6548 群の前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）

5.3.5.1—7 図 14.2.1.4.2 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_3.sas

図 2.7.6.26－15　MT-6548 群の前治療 ESA 製剤｛エポエチンベータ ペゴル（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）

5.3.5.1—7 図 14.2.1.4.3 より引用

表 2.7.6.26－51　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline						
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetin, >=4500 (IU)	Baseline	17	10.93	0.77	10.90	(9.9, 12.0)	(10.53, 11.33)							
		Week 2	17	10.60	0.89	10.90	(8.3, 11.6)	(10.14, 11.06)	17	-0.33	0.59	-0.40	(-1.6, 0.6)	(-0.63, -0.03)	0.035
		Week 4	17	10.22	1.02	10.40	(7.7, 11.7)	(9.70, 10.75)	17	-0.71	0.79	-0.60	(-2.2, 0.5)	(-1.11, -0.30)	0.002
		Week 6	17	9.85	1.06	9.90	(7.2, 11.3)	(9.31, 10.40)	17	-1.08	1.02	-1.20	(-2.7, 0.9)	(-1.60, -0.55)	<0.001
		Week 8	17	9.86	1.15	10.00	(6.8, 11.7)	(9.28, 10.45)	17	-1.06	1.12	-1.30	(-3.1, 1.3)	(-1.64, -0.49)	0.001
		Week 10	17	9.80	1.37	9.80	(6.7, 11.9)	(9.10, 10.50)	17	-1.13	1.41	-1.50	(-3.2, 1.5)	(-1.86, -0.40)	0.005
		Week 12	16	10.13	1.24	9.90	(7.7, 12.3)	(9.47, 10.78)	16	-0.87	1.48	-1.40	(-2.6, 1.9)	(-1.66, -0.08)	0.033
		Week 16	16	10.48	1.11	10.35	(8.9, 12.4)	(9.88, 11.07)	16	-0.52	1.27	-0.65	(-2.5, 1.5)	(-1.19, 0.16)	0.122
		Week 20	16	10.56	1.00	10.50	(8.3, 11.9)	(10.03, 11.09)	16	-0.43	1.11	-0.65	(-2.3, 1.5)	(-1.02, 0.16)	0.140
		Week 24	16	10.68	1.02	10.90	(8.6, 11.9)	(10.14, 11.23)	16	-0.31	1.02	0.05	(-2.5, 1.0)	(-0.86, 0.23)	0.240
		Week 24(LOCF)	17	10.44	1.40	10.80	(6.6, 11.9)	(9.72, 11.16)	17	-0.49	1.23	0.00	(-3.3, 1.0)	(-1.12, 0.14)	0.120
	Epoetin, <4500 (IU)	Baseline	32	10.48	0.71	10.35	(9.4, 11.7)	(10.22, 10.73)							
		Week 2	32	10.47	0.81	10.55	(9.0, 12.5)	(10.17, 10.76)	32	-0.01	0.64	0.10	(-1.3, 1.2)	(-0.24, 0.22)	0.913
		Week 4	31	10.45	0.97	10.20	(8.8, 12.4)	(10.09, 10.80)	31	-0.05	0.86	0.00	(-1.8, 1.2)	(-0.37, 0.27)	0.757
		Week 6	30	10.46	1.18	10.15	(8.6, 13.2)	(10.02, 10.90)	30	-0.02	1.06	0.10	(-2.3, 1.6)	(-0.41, 0.38)	0.932
		Week 8	30	10.47	1.09	10.40	(8.2, 13.0)	(10.06, 10.87)	30	-0.01	1.12	0.30	(-2.8, 1.6)	(-0.42, 0.41)	0.974
		Week 10	30	10.59	1.16	10.45	(8.1, 12.8)	(10.16, 11.03)	30	0.12	1.20	0.10	(-2.8, 2.3)	(-0.33, 0.57)	0.587
		Week 12	30	10.76	1.23	10.70	(8.1, 13.3)	(10.30, 11.22)	30	0.29	1.26	0.40	(-2.8, 2.9)	(-0.19, 0.77)	0.224
		Week 16	30	10.86	1.05	11.00	(8.3, 12.9)	(10.47, 11.25)	30	0.39	1.25	0.55	(-3.1, 2.1)	(-0.08, 0.85)	0.102
		Week 20	30	10.99	1.09	10.90	(8.7, 13.1)	(10.58, 11.40)	30	0.52	1.28	0.35	(-2.8, 2.6)	(0.04, 0.99)	0.035
		Week 24	30	10.86	1.12	10.80	(8.6, 13.3)	(10.44, 11.28)	30	0.39	1.21	0.50	(-3.1, 2.3)	(-0.07, 0.84)	0.091
		Week 24(LOCF)	32	10.78	1.13	10.65	(8.6, 13.3)	(10.38, 11.19)	32	0.30	1.22	0.50	(-3.1, 2.3)	(-0.14, 0.74)	0.170

表 2.7.6.26－51　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

			Absolute						Change from Baseline						
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
	Darbepoetin alfa, >=15 (ug)	Baseline	49	10.77	0.72	10.70	(9.4, 12.0)	(10.56, 10.98)							
		Week 2	48	10.44	0.76	10.40	(8.8, 11.9)	(10.22, 10.66)	48	-0.35	0.50	-0.35	(-1.7, 0.6)	(-0.49, -0.21)	<0.001
		Week 4	46	9.99	0.75	10.00	(8.3, 11.7)	(9.77, 10.21)	46	-0.81	0.76	-0.85	(-2.3, 0.9)	(-1.04, -0.59)	<0.001
		Week 6	45	9.82	0.88	9.80	(7.8, 11.9)	(9.55, 10.08)	45	-1.00	0.92	-0.90	(-3.2, 0.6)	(-1.28, -0.72)	<0.001
		Week 8	41	9.79	0.86	9.70	(8.0, 11.3)	(9.51, 10.06)	41	-1.01	1.10	-1.00	(-3.3, 1.4)	(-1.36, -0.66)	<0.001
		Week 10	42	9.75	0.94	9.70	(7.7, 12.1)	(9.46, 10.05)	42	-1.07	1.17	-1.00	(-3.7, 1.4)	(-1.43, -0.70)	<0.001
		Week 12	40	9.97	0.93	10.05	(7.4, 11.4)	(9.68, 10.27)	40	-0.83	1.21	-0.80	(-3.9, 1.5)	(-1.22, -0.45)	<0.001
		Week 16	39	10.24	0.81	10.20	(8.6, 12.1)	(9.97, 10.50)	39	-0.56	1.17	-0.50	(-3.0, 1.8)	(-0.93, -0.18)	0.005
		Week 20	37	10.36	0.72	10.40	(8.7, 12.5)	(10.12, 10.60)	37	-0.41	1.01	-0.10	(-2.9, 1.4)	(-0.74, -0.07)	0.020
		Week 24	37	10.34	0.80	10.40	(8.0, 11.8)	(10.08, 10.61)	37	-0.42	1.14	-0.50	(-3.6, 2.0)	(-0.80, -0.04)	0.030
		Week 24(LOCF)	48	10.07	0.99	10.10	(7.4, 11.8)	(9.78, 10.36)	48	-0.73	1.29	-0.70	(-3.9, 2.0)	(-1.10, -0.35)	<0.001
	Darbepoetin alfa, <15 (ug)	Baseline	48	10.70	0.68	10.60	(8.8, 12.1)	(10.50, 10.90)							
		Week 2	47	10.75	0.68	10.80	(9.2, 12.3)	(10.55, 10.95)	47	0.04	0.47	0.10	(-1.0, 1.3)	(-0.10, 0.18)	0.540
		Week 4	47	10.64	0.75	10.80	(8.8, 11.9)	(10.42, 10.86)	47	-0.07	0.58	0.00	(-1.4, 1.3)	(-0.25, 0.10)	0.387
		Week 6	47	10.51	0.76	10.60	(8.7, 11.8)	(10.28, 10.73)	47	-0.20	0.60	-0.20	(-1.8, 1.3)	(-0.38, -0.03)	0.025
		Week 8	46	10.47	0.89	10.50	(8.2, 12.5)	(10.21, 10.74)	46	-0.23	0.85	-0.35	(-1.5, 2.6)	(-0.48, 0.03)	0.077
		Week 10	45	10.49	0.79	10.60	(8.3, 11.9)	(10.26, 10.73)	45	-0.22	0.86	-0.30	(-2.4, 2.0)	(-0.47, 0.04)	0.100
		Week 12	45	10.64	0.86	10.60	(8.5, 12.5)	(10.38, 10.90)	45	-0.07	0.98	0.00	(-2.0, 3.7)	(-0.36, 0.23)	0.650
		Week 16	45	10.64	0.79	10.80	(8.5, 12.4)	(10.40, 10.87)	45	-0.07	0.98	-0.10	(-1.7, 2.6)	(-0.37, 0.22)	0.619
		Week 20	44	10.75	0.80	10.90	(8.7, 12.4)	(10.51, 10.99)	44	0.06	0.96	0.20	(-1.9, 2.1)	(-0.23, 0.35)	0.695
		Week 24	42	10.69	0.82	10.80	(8.6, 12.2)	(10.43, 10.94)	42	-0.04	0.96	0.00	(-2.7, 2.2)	(-0.33, 0.26)	0.811
		Week 24(LOCF)	48	10.60	0.90	10.70	(7.7, 12.2)	(10.34, 10.86)	48	-0.10	0.96	-0.05	(-2.7, 2.2)	(-0.38, 0.18)	0.457

表 2.7.6.26－51　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Baseline N	Change from Baseline Mean	Change from Baseline SD	Change from Baseline Median	Change from Baseline Minimum, Maximum	Change from Baseline 95% CI	Change from Baseline p value
	Epoetinbeta pegol, >=15 (ug)	Baseline	7	11.36	0.77	11.60	(10.3, 12.6)	(10.65, 12.07)							
		Week 2	7	11.37	0.89	11.40	(9.9, 12.9)	(10.54, 12.20)	7	0.01	0.43	0.00	(-0.7, 0.6)	(-0.38, 0.41)	0.933
		Week 4	7	10.97	0.82	11.10	(9.7, 12.2)	(10.21, 11.73)	7	-0.39	0.80	-0.50	(-1.2, 1.3)	(-1.12, 0.35)	0.249
		Week 6	7	10.67	0.82	10.50	(9.6, 11.7)	(9.91, 11.43)	7	-0.69	0.97	-1.20	(-1.4, 1.2)	(-1.59, 0.21)	0.112
		Week 8	7	10.33	0.89	10.40	(9.3, 11.6)	(9.51, 11.15)	7	-1.03	1.26	-1.60	(-2.2, 1.3)	(-2.19, 0.13)	0.073
		Week 10	7	9.99	1.03	10.10	(8.6, 11.1)	(9.03, 10.94)	7	-1.37	1.29	-1.70	(-2.7, 0.8)	(-2.56, -0.18)	0.030
		Week 12	7	9.93	1.23	10.30	(8.4, 11.6)	(8.79, 11.07)	7	-1.43	1.66	-2.30	(-3.2, 1.3)	(-2.96, 0.10)	0.062
		Week 16	5	10.10	1.54	10.40	(7.5, 11.4)	(8.18, 12.02)	5	-1.24	2.14	-1.20	(-4.1, 1.1)	(-3.89, 1.41)	0.264
		Week 20	4	10.85	1.03	10.95	(9.5, 12.0)	(9.21, 12.49)	4	-0.75	1.55	-1.15	(-2.1, 1.4)	(-3.21, 1.71)	0.403
		Week 24	4	11.08	0.67	11.10	(10.4, 11.7)	(10.01, 12.14)	4	-0.53	1.09	-1.00	(-1.2, 1.1)	(-2.26, 1.21)	0.405
		Week 24(LOCF)	7	10.49	1.22	10.60	(8.8, 11.7)	(9.36, 11.61)	7	-0.87	1.51	-1.00	(-2.8, 1.1)	(-2.27, 0.52)	0.178
	Epoetinbeta pegol, <15 (ug)	Baseline	9	10.77	0.67	10.60	(10.2, 11.9)	(10.25, 11.28)							
		Week 2	9	10.70	0.94	10.30	(9.6, 12.1)	(9.98, 11.42)	9	-0.07	0.43	-0.10	(-0.6, 0.6)	(-0.40, 0.27)	0.656
		Week 4	9	10.67	0.77	10.80	(9.4, 11.8)	(10.07, 11.26)	9	-0.10	0.61	-0.10	(-1.2, 0.8)	(-0.57, 0.37)	0.636
		Week 6	9	10.68	0.65	10.90	(9.2, 11.4)	(10.18, 11.18)	9	-0.09	0.77	0.10	(-1.4, 0.9)	(-0.68, 0.51)	0.739
		Week 8	9	10.94	0.82	11.10	(9.1, 11.9)	(10.32, 11.57)	9	0.18	0.85	0.20	(-1.5, 1.1)	(-0.47, 0.83)	0.546
		Week 10	9	11.06	0.91	11.00	(9.1, 12.2)	(10.36, 11.75)	9	0.29	1.20	0.30	(-1.5, 2.0)	(-0.63, 1.21)	0.491
		Week 12	9	11.22	0.71	11.40	(9.5, 11.9)	(10.67, 11.77)	9	0.46	0.99	0.70	(-1.1, 1.6)	(-0.30, 1.21)	0.204
		Week 16	9	11.14	1.07	11.40	(8.8, 12.5)	(10.32, 11.97)	9	0.38	1.38	0.40	(-1.8, 2.3)	(-0.68, 1.44)	0.436
		Week 20	9	10.84	0.91	10.90	(9.4, 12.0)	(10.15, 11.54)	9	0.08	1.06	0.00	(-1.2, 1.5)	(-0.73, 0.89)	0.831
		Week 24	9	10.82	0.82	10.50	(10.0, 12.4)	(10.19, 11.45)	9	0.06	0.85	0.00	(-1.4, 1.2)	(-0.60, 0.71)	0.849
		Week 24(LOCF)	9	10.82	0.82	10.50	(10.0, 12.4)	(10.19, 11.45)	9	0.06	0.85	0.00	(-1.4, 1.2)	(-0.60, 0.71)	0.849

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_6_1.sas

5.3.5.1—7 表 14.2.2.6.1 より引用

表 2.7.6.26－52　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Epoetin, >=4500 (IU)	Week 2	17	10.93 (0.77)	10.62	0.27	(10.06, 11.17)
		Week 4	17	10.93 (0.77)	10.24	0.27	(9.68, 10.80)
		Week 6	17	10.93 (0.77)	9.87	0.27	(9.31, 10.42)
		Week 8	17	10.93 (0.77)	9.88	0.27	(9.32, 10.44)
		Week 10	17	10.93 (0.77)	9.82	0.27	(9.26, 10.37)
		Week 12	16	10.99 (0.75)	9.98	0.27	(9.42, 10.54)
		Week 16	16	10.99 (0.75)	10.33	0.27	(9.77, 10.89)
		Week 20	16	10.99 (0.75)	10.42	0.27	(9.86, 10.98)
		Week 24	16	10.99 (0.75)	10.54	0.27	(9.98, 11.10)
	Epoetin, <4500 (IU)	Week 2	32	10.48 (0.71)	10.46	0.18	(10.10, 10.83)
		Week 4	31	10.49 (0.72)	10.42	0.19	(10.05, 10.79)
		Week 6	30	10.47 (0.72)	10.43	0.19	(10.05, 10.80)
		Week 8	30	10.47 (0.72)	10.44	0.19	(10.06, 10.81)
		Week 10	30	10.47 (0.72)	10.56	0.19	(10.19, 10.94)
		Week 12	30	10.47 (0.72)	10.73	0.19	(10.36, 11.11)
		Week 16	30	10.47 (0.72)	10.83	0.19	(10.45, 11.20)
		Week 20	30	10.47 (0.72)	10.96	0.19	(10.58, 11.33)
		Week 24	30	10.47 (0.72)	10.83	0.19	(10.45, 11.20)

表 2.7.6.26－52　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
	Darbepoetin alfa, >=15 (ug)	Week 2	48	10.79 (0.71)	10.44	0.12	(10.20, 10.68)
		Week 4	46	10.80 (0.72)	9.98	0.12	(9.73, 10.22)
		Week 6	45	10.82 (0.72)	9.80	0.12	(9.55, 10.04)
		Week 8	41	10.80 (0.72)	9.72	0.13	(9.47, 9.97)
		Week 10	42	10.82 (0.72)	9.68	0.13	(9.43, 9.93)
		Week 12	40	10.81 (0.70)	9.87	0.13	(9.62, 10.13)
		Week 16	39	10.79 (0.71)	10.11	0.13	(9.85, 10.36)
		Week 20	37	10.77 (0.71)	10.26	0.13	(10.00, 10.52)
		Week 24	37	10.77 (0.71)	10.24	0.13	(9.98, 10.50)
	Darbepoetin alfa, <15 (ug)	Week 2	47	10.71 (0.69)	10.75	0.11	(10.54, 10.96)
		Week 4	47	10.71 (0.69)	10.64	0.11	(10.42, 10.85)
		Week 6	47	10.71 (0.69)	10.51	0.11	(10.30, 10.72)
		Week 8	46	10.70 (0.69)	10.49	0.11	(10.28, 10.70)
		Week 10	45	10.71 (0.70)	10.50	0.11	(10.28, 10.71)
		Week 12	45	10.71 (0.70)	10.65	0.11	(10.43, 10.86)
		Week 16	45	10.71 (0.70)	10.64	0.11	(10.43, 10.85)
		Week 20	44	10.69 (0.70)	10.76	0.11	(10.55, 10.98)
		Week 24	42	10.72 (0.70)	10.67	0.11	(10.45, 10.89)

表 2.7.6.26－52　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
	Epoetin beta pegol, >=15 (ug)	Week 2	7	11.36 (0.77)	11.37	0.40	(10.51, 12.23)
		Week 4	7	11.36 (0.77)	10.97	0.40	(10.11, 11.83)
		Week 6	7	11.36 (0.77)	10.67	0.40	(9.81, 11.53)
		Week 8	7	11.36 (0.77)	10.33	0.40	(9.47, 11.19)
		Week 10	7	11.36 (0.77)	9.98	0.40	(9.13, 10.84)
		Week 12	7	11.36 (0.77)	9.93	0.40	(9.07, 10.79)
		Week 16	5	11.34 (0.92)	9.88	0.45	(8.95, 10.82)
		Week 20	4	11.60 (0.82)	10.78	0.48	(9.79, 11.78)
		Week 24	4	11.60 (0.82)	11.01	0.48	(10.01, 12.01)
	Epoetin beta pegol, <15 (ug)	Week 2	9	10.77 (0.67)	10.70	0.29	(10.10, 11.30)
		Week 4	9	10.77 (0.67)	10.67	0.29	(10.07, 11.26)
		Week 6	9	10.77 (0.67)	10.68	0.29	(10.08, 11.27)
		Week 8	9	10.77 (0.67)	10.94	0.29	(10.35, 11.54)
		Week 10	9	10.77 (0.67)	11.06	0.29	(10.46, 11.65)
		Week 12	9	10.77 (0.67)	11.22	0.29	(10.63, 11.82)
		Week 16	9	10.77 (0.67)	11.14	0.29	(10.55, 11.74)
		Week 20	9	10.77 (0.67)	10.84	0.29	(10.25, 11.44)
		Week 24	9	10.77 (0.67)	10.82	0.29	(10.23, 11.42)

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_6_2.sas

5.3.5.1—7 表 14.2.2.6.2 より引用

表 2.7.6.26－53 鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline					
Treatment Group	Iron or Iron-containing Phosphorus	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	User	Baseline	51	10.90	0.72	10.90	(9.6, 12.0)	(10.70, 11.10)							
		Week 2	50	10.72	0.77	10.70	(9.2, 12.1)	(10.50, 10.93)	50	-0.21	0.43	-0.20	(-1.3, 0.5)	(-0.34, -0.09)	0.001
		Week 4	49	10.36	0.79	10.20	(8.8, 11.9)	(10.13, 10.58)	49	-0.59	0.68	-0.80	(-2.1, 0.6)	(-0.79, -0.40)	<0.001
		Week 6	47	10.10	0.87	10.00	(8.4, 11.7)	(9.84, 10.36)	47	-0.86	0.87	-0.70	(-3.1, 0.4)	(-1.11, -0.60)	<0.001
		Week 8	46	10.04	1.05	10.25	(8.0, 12.0)	(9.73, 10.35)	46	-0.91	1.10	-0.90	(-3.3, 1.0)	(-1.23, -0.58)	<0.001
		Week 10	46	10.05	1.14	10.10	(7.7, 12.1)	(9.72, 10.39)	46	-0.89	1.24	-0.70	(-3.6, 1.2)	(-1.26, -0.52)	<0.001
		Week 12	46	10.14	1.13	10.25	(7.4, 12.1)	(9.81, 10.48)	46	-0.80	1.29	-0.80	(-3.9, 1.5)	(-1.19, -0.42)	<0.001
		Week 16	44	10.43	1.16	10.50	(7.5, 12.4)	(10.07, 10.78)	44	-0.51	1.33	-0.35	(-4.1, 1.8)	(-0.91, -0.10)	0.015
		Week 20	43	10.64	0.95	10.70	(8.7, 12.5)	(10.35, 10.93)	43	-0.27	1.09	0.00	(-2.8, 1.5)	(-0.61, 0.06)	0.108
		Week 24	42	10.49	1.00	10.45	(8.6, 12.4)	(10.18, 10.80)	42	-0.44	1.06	-0.40	(-3.1, 1.6)	(-0.77, -0.11)	0.010
		Week 24 (LOCF)	50	10.29	1.08	10.20	(7.4, 12.4)	(9.99, 10.60)	50	-0.63	1.19	-0.60	(-3.9, 1.6)	(-0.97, -0.30)	<0.001
MT-6548	Non-user	Baseline	29	10.71	0.59	10.70	(9.8, 12.0)	(10.49, 10.94)							
		Week 2	29	10.56	0.78	10.80	(8.3, 11.5)	(10.26, 10.85)	29	-0.16	0.61	0.00	(-1.6, 1.0)	(-0.39, 0.07)	0.170
		Week 4	27	10.43	0.99	10.50	(7.7, 12.1)	(10.03, 10.82)	27	-0.30	0.89	-0.20	(-2.3, 1.1)	(-0.65, 0.05)	0.090
		Week 6	27	10.17	1.06	10.50	(7.2, 12.3)	(9.75, 10.59)	27	-0.56	1.00	-0.40	(-3.2, 1.3)	(-0.95, -0.16)	0.008
		Week 8	27	10.10	1.09	10.10	(6.8, 12.4)	(9.67, 10.54)	27	-0.62	1.06	-0.60	(-3.1, 1.4)	(-1.04, -0.20)	0.005
		Week 10	27	10.09	1.30	10.30	(6.7, 12.4)	(9.58, 10.60)	27	-0.63	1.34	-0.50	(-3.7, 2.0)	(-1.16, -0.10)	0.021
		Week 12	24	10.50	1.11	10.30	(8.3, 13.3)	(10.04, 10.97)	24	-0.23	1.11	-0.40	(-2.8, 2.3)	(-0.69, 0.24)	0.330
		Week 16	23	10.57	1.00	10.70	(8.5, 12.7)	(10.13, 11.00)	23	-0.12	1.00	-0.10	(-1.8, 2.3)	(-0.56, 0.31)	0.567
		Week 20	22	10.50	1.13	10.45	(8.3, 12.9)	(10.00, 11.00)	22	-0.18	1.10	0.00	(-1.9, 1.9)	(-0.67, 0.31)	0.459
		Week 24	21	10.60	1.00	10.70	(8.6, 12.7)	(10.14, 11.05)	21	-0.13	1.04	0.00	(-2.7, 1.7)	(-0.60, 0.34)	0.577
		Week 24 (LOCF)	29	10.09	1.34	10.40	(6.6, 12.7)	(9.58, 10.60)	29	-0.62	1.35	-0.40	(-3.6, 1.7)	(-1.14, -0.11)	0.019

Note(s): Hb (g/dL).
Note(s): p value is analyzed by paired t-test from baseline value.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_1_2.sas

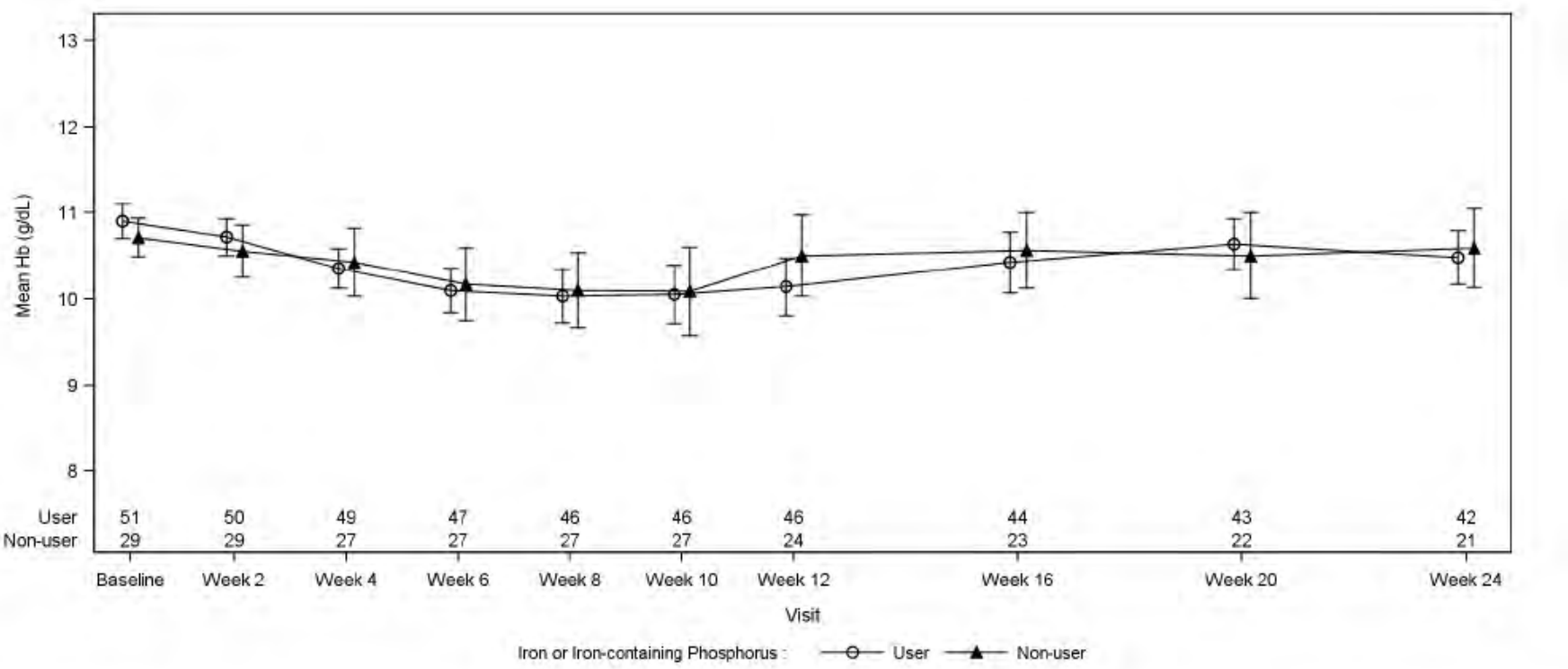
5.3.5.1—9 表 14.2.2.8.1.2 より引用

表 2.7.6.26－54　鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値（MMRM，FAS）

Treatment Group	Iron or Iron-containing Phosphorus	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	User	Week 2	50	10.93 (0.70)	10.72	0.14	(10.45, 10.99)
		Week 4	49	10.95 (0.69)	10.34	0.14	(10.07, 10.61)
		Week 6	47	10.96 (0.70)	10.07	0.14	(9.80, 10.34)
		Week 8	46	10.94 (0.70)	9.99	0.14	(9.72, 10.27)
		Week 10	46	10.94 (0.70)	10.01	0.14	(9.73, 10.28)
		Week 12	46	10.94 (0.70)	10.10	0.14	(9.82, 10.37)
		Week 16	44	10.93 (0.72)	10.34	0.14	(10.06, 10.61)
		Week 20	43	10.91 (0.71)	10.56	0.14	(10.28, 10.84)
		Week 24	42	10.98 (0.72)	10.41	0.14	(10.13, 10.69)
	Non-user	Week 2	29	10.71 (0.89)	10.56	0.20	(10.16, 10.95)
		Week 4	27	10.73 (0.61)	10.39	0.20	(9.98, 10.79)
		Week 6	27	10.73 (0.61)	10.13	0.20	(9.73, 10.53)
		Week 8	27	10.73 (0.61)	10.06	0.20	(9.66, 10.47)
		Week 10	27	10.73 (0.61)	10.05	0.20	(9.65, 10.46)
		Week 12	24	10.73 (0.56)	10.27	0.21	(9.86, 10.69)
		Week 16	23	10.69 (0.53)	10.32	0.21	(9.91, 10.74)
		Week 20	22	10.68 (0.54)	10.27	0.21	(9.85, 10.69)
		Week 24	21	10.72 (0.51)	10.30	0.21	(9.88, 10.72)

Note(s): Hb (g/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_2_2.sas

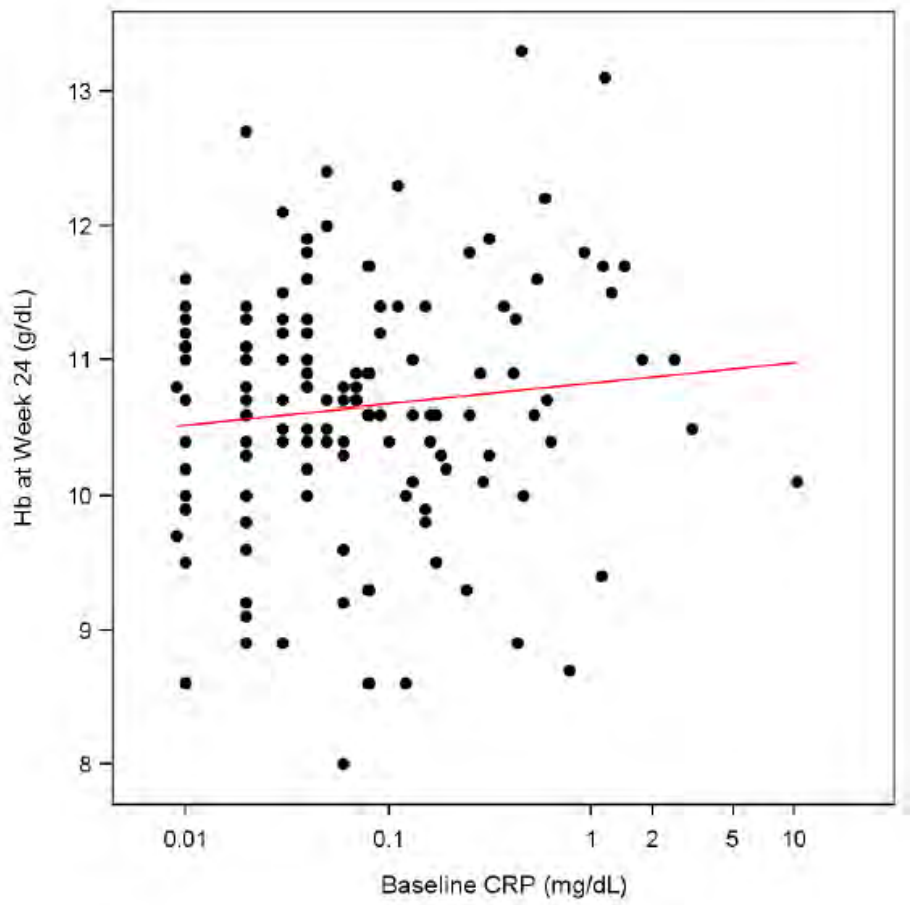
5.3.5.1—9 表 14.2.2.8.2.2 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Table 14.2.2.8.1.2
Source: f_14_2_1_6_1_2.sas

図 2.7.6.26－16　MT-6548 群の鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の推移（FAS）

5.3.5.1—9 図 14.2.1.6.1.2 より引用



Note(s): linear regression model: Y=aX + b; Y: Hb at Week 24; X: baseline CRP.
Data Source: Listing 16.2.4.1, Listing 16.2.6.4
Source: f_14_2_1_8_1.sas

図 2.7.6.26－17　MT-6548 群のベースラインの CRP と 24 週後の Hb 値の散布図（FAS）

5.3.5.1—7 図 14.2.1.8.1 より引用

表 2.7.6.26－55　被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Sex	Male	MT-6548	92	344.80	193.75	300.00	(0.0, 600.0)	(304.67, 384.92)
		darbepoetin	104	18.73	19.71	10.00	(2.5, 130.0)	(14.90, 22.56)
	Female	MT-6548	48	433.94	173.35	450.00	(150.0, 600.0)	(383.61, 484.28)
		darbepoetin	50	18.44	21.88	15.00	(0.0, 140.0)	(12.22, 24.66)
Age at Informed Consent (years)	<65	MT-6548	56	370.89	190.62	342.86	(0.0, 600.0)	(319.30, 422.47)
		darbepoetin	66	16.55	19.68	10.00	(2.5, 140.0)	(11.71, 21.39)
	>=65	MT-6548	88	376.26	192.44	375.00	(0.0, 600.0)	(336.75, 419.77)
		darbepoetin	88	20.20	20.85	15.00	(0.0, 130.0)	(15.78, 24.62)
	<75	MT-6548	108	382.17	192.33	430.67	(0.0, 600.0)	(345.48, 418.85)
		darbepoetin	126	17.71	18.36	11.25	(0.0, 140.0)	(14.47, 20.95)
	>=75	MT-6548	32	352.40	188.28	300.00	(0.0, 600.0)	(284.52, 420.28)
		darbepoetin	28	22.81	27.72	13.75	(2.5, 130.0)	(12.06, 33.56)
Dry Weight (kg)	<60	MT-6548	83	380.64	187.73	375.00	(0.0, 600.0)	(339.65, 421.64)
		darbepoetin	86	20.73	24.18	13.98	(0.0, 140.0)	(15.54, 25.91)
	>=60	MT-6548	57	367.67	197.46	332.14	(0.0, 600.0)	(315.28, 420.06)
		darbepoetin	68	15.99	13.69	10.00	(2.5, 62.5)	(12.63, 19.36)
BMI (kg/m²)	<25	MT-6548	102	367.04	185.73	316.07	(0.0, 600.0)	(330.56, 403.52)
		darbepoetin	122	17.71	16.15	11.86	(0.0, 130.0)	(14.45, 20.96)
	>=25	MT-6548	38	397.70	205.93	452.69	(0.0, 600.0)	(330.01, 465.38)
		darbepoetin	32	22.16	27.31	10.00	(3.5, 140.0)	(12.34, 32.03)

表 2.7.6.26－55　被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Etiology of CKD	Diabetes	MT-6548	25	421.29	198.95	450.00	(0.0, 600.0)	(339.16, 503.41)
		darbepoetin	39	19.67	23.24	10.00	(3.5, 130.0)	(12.14, 27.20)
	Hypertension	MT-6548	18	396.13	192.27	450.00	(75.0, 600.0)	(300.52, 491.74)
		darbepoetin	21	20.22	18.92	10.00	(5.0, 75.0)	(11.61, 28.83)
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	53	395.96	184.88	375.00	(0.0, 600.0)	(346.00, 446.92)
		darbepoetin	61	18.03	16.02	15.00	(2.5, 75.0)	(13.92, 22.13)
	Interstitial Nephritis/Pyelonephritis	MT-6548	3	400.00	228.13	450.00	(150.0, 600.0)	(-169.19, 969.19)
		darbepoetin	1	30.00	-	30.00	(30.0, 30.0)	-
	Cystic/Hereditary/Congenital Disease	MT-6548	16	313.99	176.23	300.00	(0.0, 600.0)	(220.09, 407.90)
		darbepoetin	10	13.89	10.90	11.25	(2.5, 40.0)	(6.07, 21.68)
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	1	6.25	-	6.25	(6.3, 6.3)	-
Duration of Anemia from CKD (years)	<1	MT-6548	6	450.00	199.74	525.00	(150.0, 600.0)	(260.88, 649.12)
		darbepoetin	4	5.66	2.13	5.00	(3.9, 8.8)	(2.28, 9.04)
	1<= to <5	MT-6548	55	381.75	181.26	300.00	(75.0, 600.0)	(332.75, 430.76)
		darbepoetin	63	18.44	20.86	10.00	(2.5, 140.0)	(13.18, 23.69)
	>=5	MT-6548	78	368.00	198.50	368.93	(0.0, 600.0)	(323.25, 412.76)
		darbepoetin	87	19.38	20.39	15.00	(0.0, 130.0)	(15.03, 23.72)

表 2.7.6.26－55　被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Complications	Hypertension	MT-6548	131	378.00	188.67	375.00	(0.0, 600.0)	(345.39, 410.62)
		darbepoetin	142	16.79	20.56	11.68	(2.5, 140.0)	(13.36, 22.21)
	Diabetes	MT-6548	30	416.07	196.17	450.00	(0.0, 600.0)	(342.82, 489.32)
		darbepoetin	48	18.85	22.25	10.00	(2.5, 130.0)	(12.39, 25.31)
	Dyslipidaemia	MT-6548	51	384.56	192.16	382.14	(37.5, 600.0)	(330.51, 438.61)
		darbepoetin	76	18.56	23.10	10.00	(0.0, 140.0)	(13.28, 23.84)
Baseline Hb (g/dL)	<10	MT-6548	21	376.62	166.31	417.86	(75.0, 600.0)	(300.91, 452.32)
		darbepoetin	22	23.16	29.99	15.00	(0.0, 140.0)	(9.96, 36.45)
	10<= to <11	MT-6548	69	408.73	188.91	450.00	(0.0, 600.0)	(363.00, 454.45)
		darbepoetin	74	15.80	13.71	10.63	(2.5, 65.0)	(12.62, 18.97)
	>=11	MT-6548	51	330.36	197.77	300.00	(0.0, 600.0)	(274.73, 385.98)
		darbepoetin	58	20.55	22.80	12.50	(3.9, 130.0)	(14.56, 26.54)
Baseline Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	139	375.90	191.74	375.00	(0.0, 600.0)	(343.76, 408.06)
		darbepoetin	154	18.64	20.87	11.25	(0.0, 140.0)	(15.39, 21.88)
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	1	300.00	-	300.00	(300.0, 300.0)	-
		darbepoetin	0					
	AST >80 or ALT >90	MT-6548	0					
		darbepoetin	0					
Baseline CRP (mg/dL)	<0.31	MT-6548	115	388.33	187.03	450.00	(0.0, 600.0)	(353.78, 422.88)
		darbepoetin	129	16.89	18.33	10.00	(0.0, 140.0)	(13.70, 20.09)
	>=0.31	MT-6548	25	315.71	202.39	300.00	(0.0, 600.0)	(232.17, 399.26)
		darbepoetin	25	27.63	27.45	20.00	(3.9, 130.0)	(16.30, 38.96)

表 2.7.6.26－55　被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Baseline Serum Ferritin (ng/mL)	<82.7	MT-6548	47	362.84	186.70	300.00	(75.0, 600.0)	(308.02, 417.66)
		darbepoetin	49	24.10	29.87	10.00	(2.5, 140.0)	(15.52, 32.68)
	82.7<= to <165	MT-6548	47	392.14	194.16	450.00	(0.0, 600.0)	(335.13, 449.14)
		darbepoetin	54	15.55	13.54	10.00	(2.5, 75.0)	(11.86, 19.25)
	>=165	MT-6548	46	371.02	195.50	321.43	(0.0, 600.0)	(312.96, 429.07)
		darbepoetin	51	16.65	13.24	15.00	(0.0, 60.0)	(12.93, 20.38)
Baseline TSAT (%)	<23	MT-6548	41	375.70	186.08	342.86	(0.0, 600.0)	(316.96, 434.43)
		darbepoetin	52	21.49	27.31	12.95	(0.0, 140.0)	(13.88, 29.09)
	23<= to <31	MT-6548	47	354.80	196.32	300.00	(0.0, 600.0)	(297.16, 412.44)
		darbepoetin	52	17.96	18.04	11.88	(2.5, 75.0)	(12.94, 22.99)
	>=31	MT-6548	52	393.68	192.18	450.00	(75.0, 600.0)	(340.15, 447.18)
		darbepoetin	50	16.37	12.88	10.63	(5.0, 60.0)	(12.71, 20.04)
Smoking Status	Never Smoked	MT-6548	61	404.45	179.10	450.00	(37.5, 600.0)	(358.58, 450.32)
		darbepoetin	72	15.56	19.21	10.00	(0.0, 140.0)	(11.04, 20.07)
	Ex-Smoker	MT-6548	59	354.10	204.82	300.00	(0.0, 600.0)	(300.72, 407.47)
		darbepoetin	58	22.93	22.86	15.00	(3.9, 130.0)	(16.92, 28.94)
	Current Smoker	MT-6548	20	349.38	182.01	300.00	(0.0, 600.0)	(264.19, 434.56)
		darbepoetin	24	17.51	15.75	12.00	(2.5, 60.0)	(10.86, 24.16)
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	7	361.22	192.23	300.00	(150.0, 600.0)	(183.44, 539.01)
		darbepoetin	4	21.88	18.19	18.75	(5.0, 45.0)	(-7.06, 50.81)
	No	MT-6548	133	376.11	191.60	375.00	(0.0, 600.0)	(343.21, 409.00)
		darbepoetin	150	18.55	20.47	11.25	(0.0, 140.0)	(15.25, 21.85)

表 2.7.6.26－55 被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Concomitant Medications of Oral Iron at Week 24	Yes	MT-6548	6	391.07	198.00	364.29	(150.0, 600.0)	(193.77, 588.37)
		darbepoetin	6	20.58	22.28	12.50	(3.5, 62.5)	(-2.80, 43.97)
	No	MT-6548	134	374.66	191.96	358.93	(0.0, 600.0)	(341.86, 407.46)
		darbepoetin	148	18.56	20.37	11.25	(0.0, 140.0)	(15.25, 21.87)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Baseline	Yes	MT-6548	53	386.62	202.24	375.00	(0.0, 600.0)	(330.88, 442.37)
		darbepoetin	47	17.36	15.28	12.50	(5.0, 75.0)	(12.87, 21.84)
	No	MT-6548	87	368.50	184.94	332.14	(0.0, 600.0)	(329.09, 407.92)
		darbepoetin	107	19.20	22.28	10.00	(0.0, 140.0)	(14.93, 23.47)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 24	Yes	MT-6548	50	379.82	203.34	368.93	(0.0, 600.0)	(322.03, 437.61)
		darbepoetin	45	17.46	15.47	12.50	(5.0, 75.0)	(12.82, 22.11)
	No	MT-6548	90	372.88	185.17	375.00	(0.0, 600.0)	(334.10, 411.67)
		darbepoetin	109	19.12	22.13	10.00	(0.0, 140.0)	(14.92, 23.32)
Prior ESA Treatment: Medication	Epoetin	MT-6548	46	343.18	200.55	300.00	(0.0, 600.0)	(283.63, 402.74)
		darbepoetin	51	14.17	11.98	10.00	(0.0, 60.0)	(10.80, 17.54)
	Darbepoetin alfa	MT-6548	81	408.49	185.17	450.00	(0.0, 600.0)	(367.54, 449.43)
		darbepoetin	86	19.45	19.90	15.00	(2.5, 130.0)	(15.19, 23.72)
	Epoetin beta pegol	MT-6548	13	282.83	152.25	294.64	(125.0, 600.0)	(190.82, 374.83)
		darbepoetin	17	[redacted]				
	Other	MT-6548	0					
		darbepoetin	0					

表 2.7.6.26－55 被験者背景別の 20 週～24 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Prior ESA Treatment: Weekly Dose (IU)	Epoetin, <3000	MT-6548	14	251.32	193.76	225.00	(0.0, 600.0)	(139.45, 363.19)
		darbepoetin	13	7.46	6.27	5.00	(2.5, 21.3)	(4.30, 10.66)
	Epoetin, 3000<= to <4500	MT-6548	16	363.62	194.45	375.00	(150.0, 600.0)	(260.00, 467.23)
		darbepoetin	11	9.89	6.72	10.00	(0.0, 25.0)	(5.37, 14.40)
	Epoetin, >=4500	MT-6548	16	403.13	195.34	450.00	(150.0, 600.0)	(299.04, 507.21)
		darbepoetin	27	19.13	13.79	15.00	(5.0, 60.0)	(13.67, 24.58)
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	18	306.25	186.50	300.00	(37.5, 600.0)	(213.50, 399.00)
		darbepoetin	14	9.82	7.50	8.00	(5.0, 30.0)	(5.48, 14.15)
	Darbepoetin alfa, 10<= to <20	MT-6548	32	392.30	188.53	359.93	(0.0, 600.0)	(324.33, 460.27)
		darbepoetin	39	12.67	10.87	10.00	(2.5, 60.0)	(9.10, 16.25)
	Darbepoetin alfa, >=20	MT-6548	31	484.56	149.89	600.00	(150.0, 600.0)	(429.59, 539.54)
		darbepoetin	34	31.00	25.21	25.00	(5.0, 130.0)	(22.20, 39.80)
Prior ESA Treatment: Weekly Dose (ug)	Epoetin beta pegol, <12.5	MT-6548	3	162.50	21.65	150.00	(150.0, 187.5)	(108.72, 216.28)
		darbepoetin	4	[redacted]				
	Epoetin beta pegol, 12.5<= to <25	MT-6548	6	304.46	164.89	297.32	(150.0, 600.0)	(131.42, 477.50)
		darbepoetin	5	[redacted]				
	Epoetin beta pegol, >=25	MT-6548	4	340.63	165.00	375.00	(125.0, 487.5)	(78.07, 603.18)
		darbepoetin	8	[redacted]				
Concomitant Medications of CYP2B6 Substrates	Yes	MT-6548	10	282.50	195.10	300.00	(0.0, 600.0)	(142.94, 422.06)
		darbepoetin	23	19.13	21.10	10.00	(0.0, 75.0)	(10.00, 28.25)
	No	MT-6548	130	382.50	189.73	446.74	(0.0, 600.0)	(349.58, 415.43)
		darbepoetin	131	18.55	20.32	12.50	(2.5, 140.0)	(15.04, 22.06)

Note(s): average dose: MT-6548: average daily dose (mg); darbepoetin: average weekly dose (ug).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): Baseline Serum Ferritin, Baseline TSAT and each Prior ESA Treatment Total Weekly Dose are divided into three categories by the 3-quantiles.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_5_2.sas

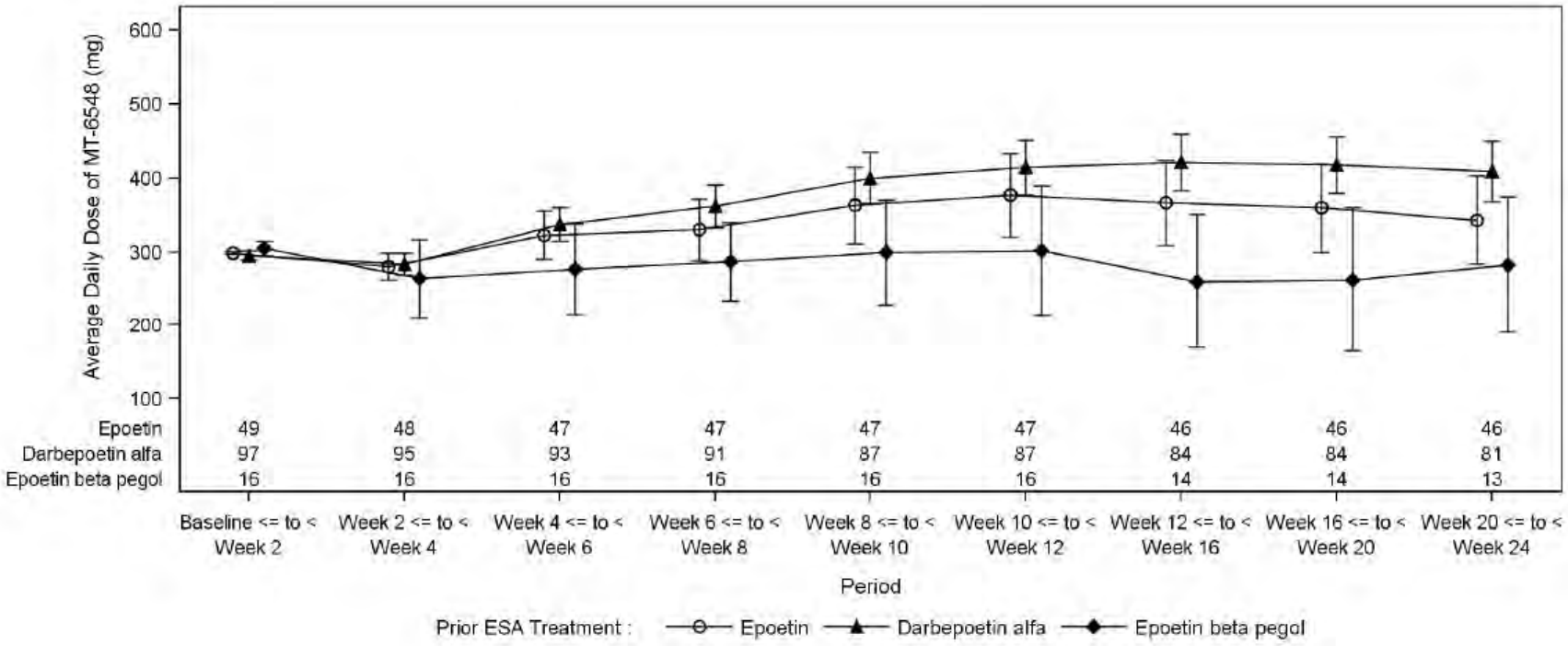
5.3.5.1—7 表 14.2.5.2 より引用

表 2.7.6.26－56　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）

Treatment Group	Prior ESA Treatment	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Epoetin	Baseline <= to < Week 2	49	298.69	6.79	300.00	(257.1, 300.0)	(296.74, 300.64)
		Week 2 <= to < Week 4	46	280.58	63.35	300.00	(42.9, 450.0)	(262.18, 298.98)
		Week 4 <= to < Week 6	47	322.60	109.58	300.00	(150.0, 600.0)	(290.62, 354.97)
		Week 6 <= to < Week 8	47	330.09	141.96	300.00	(0.0, 600.0)	(288.41, 371.77)
		Week 8 <= to < Week 10	47	362.92	175.31	300.00	(0.0, 600.0)	(311.45, 414.39)
		Week 10 <= to < Week 12	47	376.37	190.22	385.71	(0.0, 600.0)	(320.52, 432.22)
		Week 12 <= to < Week 16	46	366.27	194.46	356.25	(0.0, 600.0)	(308.52, 424.01)
		Week 16 <= to < Week 20	46	359.51	200.22	300.00	(0.0, 600.0)	(300.05, 418.97)
		Week 20 <= to < Week 24	46	343.18	200.55	300.00	(0.0, 600.0)	(283.63, 402.74)
	Darbepoetin alfa	Baseline <= to < Week 2	97	295.14	30.85	300.00	(42.9, 364.3)	(288.92, 301.36)
		Week 2 <= to < Week 4	95	283.87	73.52	300.00	(0.0, 514.3)	(268.90, 298.85)
		Week 4 <= to < Week 6	93	337.10	112.32	300.00	(0.0, 600.0)	(313.96, 360.23)
		Week 6 <= to < Week 8	91	361.70	140.39	417.86	(0.0, 600.0)	(332.46, 390.93)
		Week 8 <= to < Week 10	87	400.25	164.47	450.00	(96.4, 600.0)	(365.19, 435.30)
		Week 10 <= to < Week 12	87	414.33	173.54	450.00	(0.0, 600.0)	(377.35, 451.32)
		Week 12 <= to < Week 16	84	420.98	176.33	450.00	(0.0, 600.0)	(382.72, 459.25)
		Week 16 <= to < Week 20	84	417.49	175.64	450.00	(37.5, 600.0)	(379.37, 455.60)
		Week 20 <= to < Week 24	81	408.49	185.17	450.00	(0.0, 600.0)	(367.54, 449.43)
	Epoetin beta pegol	Baseline <= to < Week 2	16	304.69	18.75	300.00	(300.0, 375.0)	(294.70, 314.68)
		Week 2 <= to < Week 4	16	263.84	98.89	300.00	(21.4, 450.0)	(211.15, 316.53)
		Week 4 <= to < Week 6	16	276.56	115.28	300.00	(0.0, 450.0)	(215.14, 337.99)
		Week 6 <= to < Week 8	16	286.61	99.17	300.00	(150.0, 450.0)	(233.76, 339.45)
		Week 8 <= to < Week 10	16	299.33	133.39	300.00	(0.0, 450.0)	(228.25, 370.41)
		Week 10 <= to < Week 12	16	301.34	164.40	300.00	(0.0, 600.0)	(213.73, 388.94)
		Week 12 <= to < Week 16	14	260.20	157.21	249.11	(0.0, 600.0)	(169.43, 350.97)
		Week 16 <= to < Week 20	14	262.50	168.99	168.75	(112.5, 600.0)	(164.93, 360.07)
		Week 20 <= to < Week 24	13	282.83	152.25	294.64	(125.0, 600.0)	(190.82, 374.83)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_3_4_1.sas

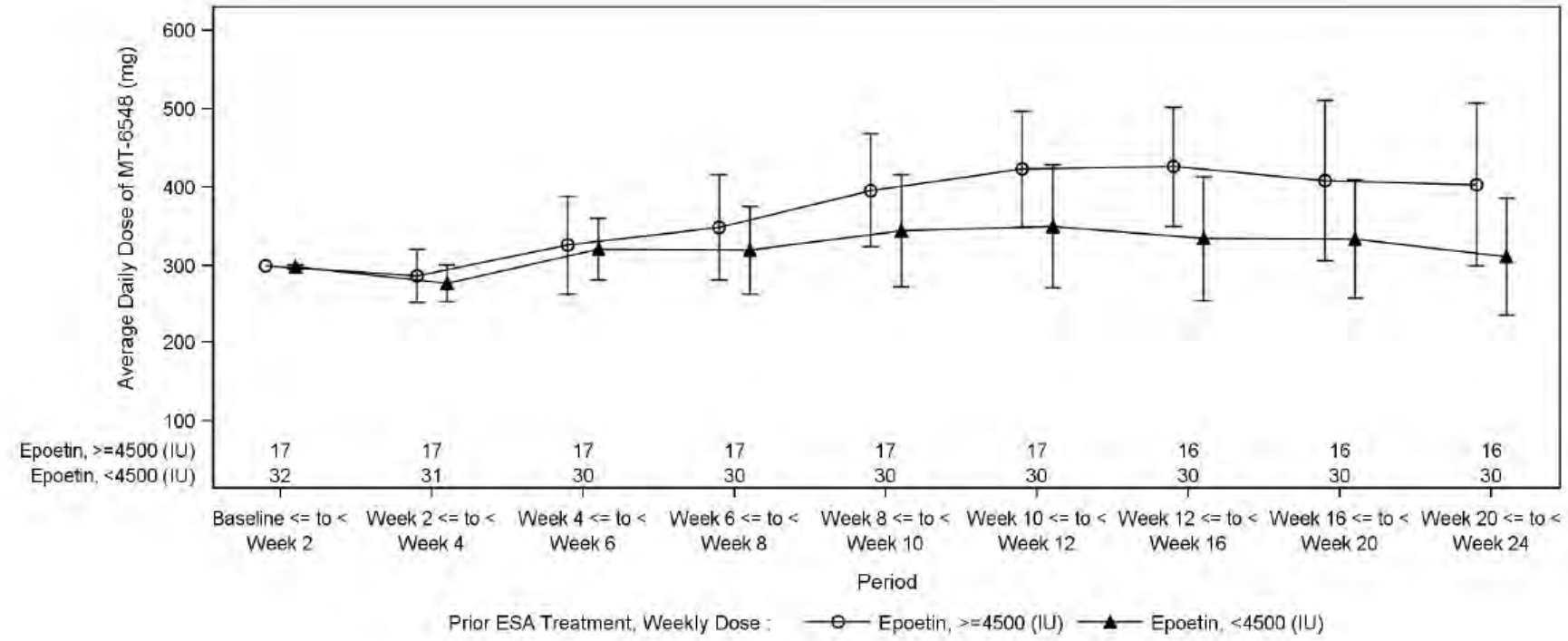
5.3.5.1—7 表 14.2.3.3.4.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.3.3.4.1
Source: f_14_2_3_4_1.sas

図 2.7.6.26－18　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量の推移（FAS）

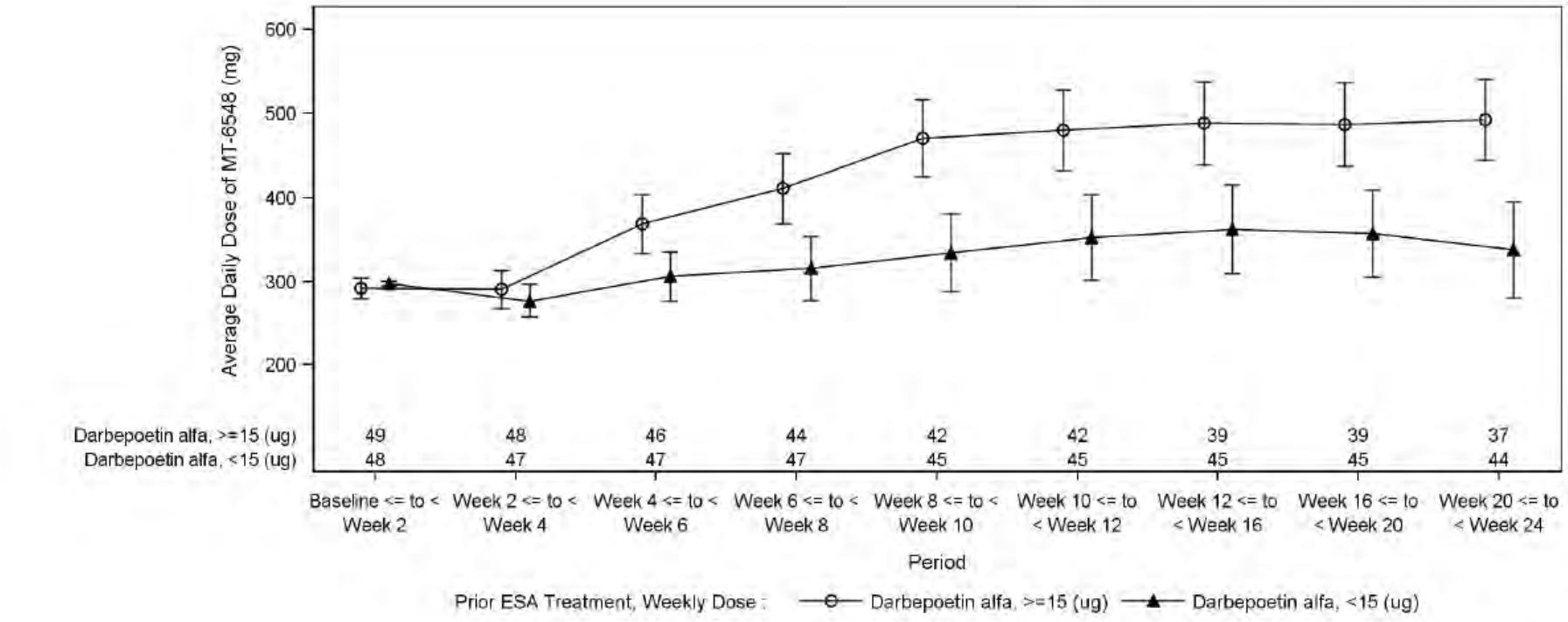
5.3.5.1—7 図 14.2.3.4.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.3.3.5.1
Source: f_14_2_3_5_1.sas

図 2.7.6.26－19　前治療 ESA 製剤（エポエチン製剤）の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

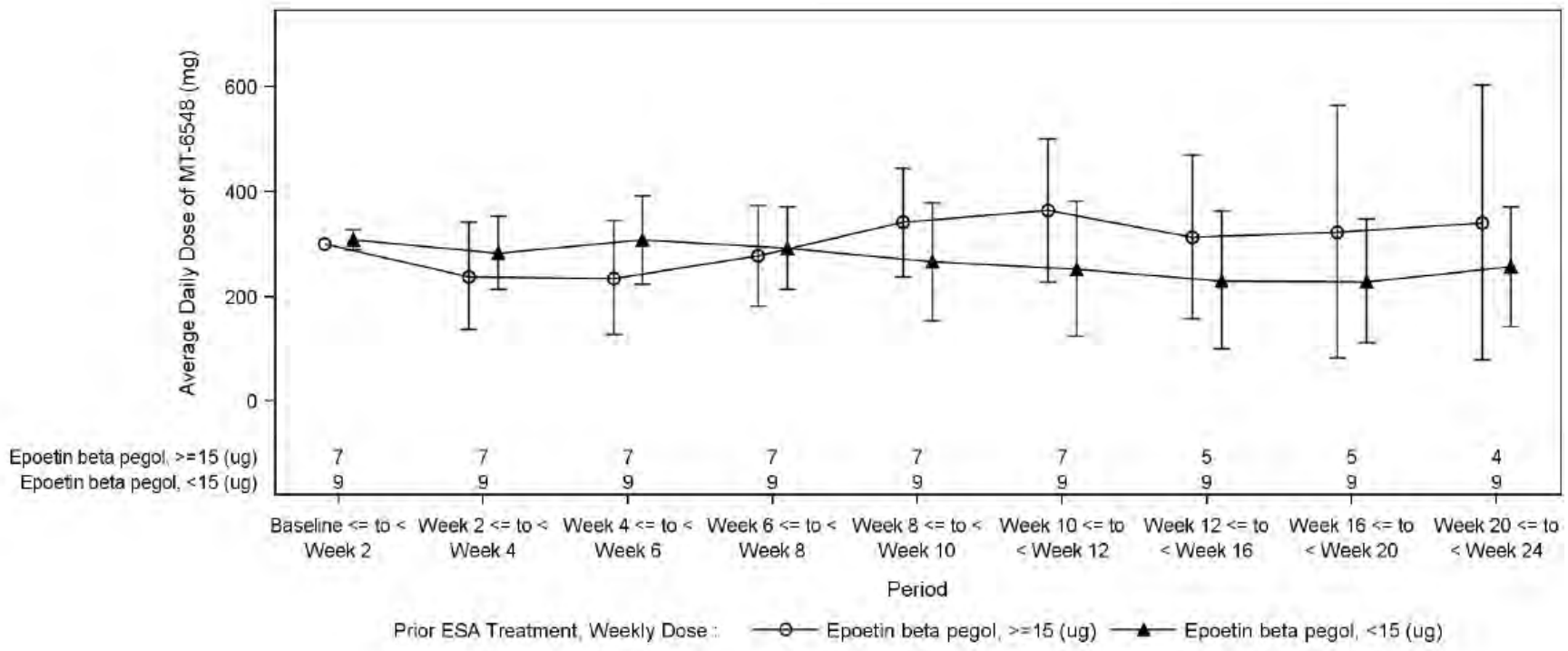
5.3.5.1—7 図 14.2.3.5.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.3.5.1
Source: f_14_2_3_5_2.sas

図 2.7.6.26－20　前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—7 図 14.2.3.5.2 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.3.5.1
Source: f_14_2_3_5_3.sas

図 2.7.6.26－21　前治療 ESA 製剤｛エポエチンベータ ペゴル（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—7 図 14.2.3.5.3 より引用

表 2.7.6.26－57　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Epoetin, >=4500 (IU)	Baseline <= to < Week 2	17	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	17	286.76	66.21	300.00	(150.0, 450.0)	(252.72, 320.81)
		Week 4 <= to < Week 6	17	325.84	120.81	300.00	(150.0, 600.0)	(263.73, 387.95)
		Week 6 <= to < Week 8	17	348.53	129.74	375.00	(150.0, 600.0)	(281.82, 415.24)
		Week 8 <= to < Week 10	17	395.80	140.34	450.00	(150.0, 600.0)	(323.64, 467.95)
		Week 10 <= to < Week 12	17	422.90	144.00	450.00	(150.0, 600.0)	(348.86, 496.94)
		Week 12 <= to < Week 16	16	426.23	143.03	450.00	(150.0, 600.0)	(350.01, 502.44)
		Week 16 <= to < Week 20	16	408.48	192.38	450.00	(85.7, 600.0)	(305.97, 510.99)
		Week 20 <= to < Week 24	16	403.13	195.34	450.00	(150.0, 600.0)	(299.04, 507.21)
	Epoetin, <4500 (IU)	Baseline <= to < Week 2	32	297.99	8.36	300.00	(257.1, 300.0)	(294.98, 301.01)
		Week 2 <= to < Week 4	31	277.19	62.58	300.00	(42.9, 300.0)	(254.23, 300.14)
		Week 4 <= to < Week 6	30	321.07	104.81	300.00	(150.0, 450.0)	(281.94, 360.21)
		Week 6 <= to < Week 8	30	319.64	149.55	300.00	(0.0, 600.0)	(263.80, 375.49)
		Week 8 <= to < Week 10	30	344.29	192.07	300.00	(0.0, 600.0)	(272.57, 416.01)
		Week 10 <= to < Week 12	30	350.00	209.68	300.00	(0.0, 600.0)	(271.70, 428.30)
		Week 12 <= to < Week 16	30	334.29	212.27	300.00	(0.0, 600.0)	(255.02, 413.55)
		Week 16 <= to < Week 20	30	333.39	202.57	300.00	(0.0, 600.0)	(257.75, 409.03)
		Week 20 <= to < Week 24	30	311.21	199.08	300.00	(0.0, 600.0)	(236.87, 385.55)

表 2.7.6.26－57　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
	Darbepoetin alfa, >=15 (ug)	Baseline <= to < Week 2	49	292.13	42.34	300.00	(42.9, 364.3)	(279.97, 304.29)
		Week 2 <= to < Week 4	48	290.85	78.39	300.00	(0.0, 514.3)	(268.09, 313.61)
		Week 4 <= to < Week 6	46	368.71	117.75	401.79	(0.0, 600.0)	(333.74, 403.68)
		Week 6 <= to < Week 8	44	410.80	136.19	450.00	(0.0, 600.0)	(369.39, 452.20)
		Week 8 <= to < Week 10	42	470.41	147.68	525.00	(150.0, 600.0)	(424.39, 516.43)
		Week 10 <= to < Week 12	42	480.46	153.60	600.00	(150.0, 600.0)	(432.59, 528.32)
		Week 12 <= to < Week 16	39	488.32	153.24	600.00	(150.0, 600.0)	(438.65, 538.00)
		Week 16 <= to < Week 20	39	486.71	153.48	600.00	(150.0, 600.0)	(436.96, 536.46)
		Week 20 <= to < Week 24	37	492.28	143.99	600.00	(150.0, 600.0)	(444.27, 540.29)
	Darbepoetin alfa, <15 (ug)	Baseline <= to < Week 2	48	298.21	9.72	300.00	(235.7, 300.0)	(295.39, 301.04)
		Week 2 <= to < Week 4	47	276.75	68.29	300.00	(21.4, 450.0)	(256.70, 296.80)
		Week 4 <= to < Week 6	47	306.16	98.45	300.00	(0.0, 450.0)	(277.25, 335.06)
		Week 6 <= to < Week 8	47	315.73	129.46	300.00	(0.0, 600.0)	(277.72, 353.74)
		Week 8 <= to < Week 10	45	334.76	153.17	300.00	(96.4, 600.0)	(288.74, 380.78)
		Week 10 <= to < Week 12	45	352.62	169.73	300.00	(0.0, 600.0)	(301.63, 403.61)
		Week 12 <= to < Week 16	45	362.62	175.70	300.00	(0.0, 600.0)	(309.83, 415.41)
		Week 16 <= to < Week 20	45	357.50	172.97	300.00	(37.5, 600.0)	(305.53, 409.47)
		Week 20 <= to < Week 24	44	338.03	187.92	300.00	(0.0, 600.0)	(280.89, 395.16)

表 2.7.6.26－57　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
	Epoetin beta pegol, >=15 (ug)	Baseline <= to < Week 2	7	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	7	238.78	110.95	300.00	(21.4, 300.0)	(136.16, 341.39)
		Week 4 <= to < Week 6	7	235.71	118.02	300.00	(0.0, 300.0)	(126.56, 344.86)
		Week 6 <= to < Week 8	7	278.57	103.51	300.00	(150.0, 450.0)	(182.84, 374.30)
		Week 8 <= to < Week 10	7	341.33	111.76	300.00	(150.0, 450.0)	(237.96, 444.69)
		Week 10 <= to < Week 12	7	364.29	146.39	300.00	(150.0, 600.0)	(228.90, 499.67)
		Week 12 <= to < Week 16	5	313.93	125.84	332.14	(150.0, 450.0)	(157.68, 470.18)
		Week 16 <= to < Week 20	5	322.50	194.13	225.00	(150.0, 600.0)	(81.45, 563.55)
		Week 20 <= to < Week 24	4	340.63	165.00	375.00	(125.0, 487.5)	(78.07, 603.18)
	Epoetin beta pegol, <15 (ug)	Baseline <= to < Week 2	9	308.33	25.00	300.00	(300.0, 375.0)	(289.12, 327.55)
		Week 2 <= to < Week 4	9	283.33	90.14	300.00	(150.0, 450.0)	(214.05, 352.62)
		Week 4 <= to < Week 6	9	308.33	108.97	300.00	(150.0, 450.0)	(224.57, 392.10)
		Week 6 <= to < Week 8	9	292.86	101.50	300.00	(150.0, 450.0)	(214.83, 370.88)
		Week 8 <= to < Week 10	9	266.67	145.77	300.00	(0.0, 450.0)	(154.62, 378.72)
		Week 10 <= to < Week 12	9	252.38	168.65	300.00	(0.0, 600.0)	(122.74, 382.02)
		Week 12 <= to < Week 16	9	230.36	171.57	225.00	(0.0, 600.0)	(98.47, 362.24)
		Week 16 <= to < Week 20	9	229.17	155.12	150.00	(112.5, 600.0)	(109.93, 348.40)
		Week 20 <= to < Week 24	9	257.14	148.82	187.50	(150.0, 600.0)	(142.75, 371.54)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_3_5_1.sas

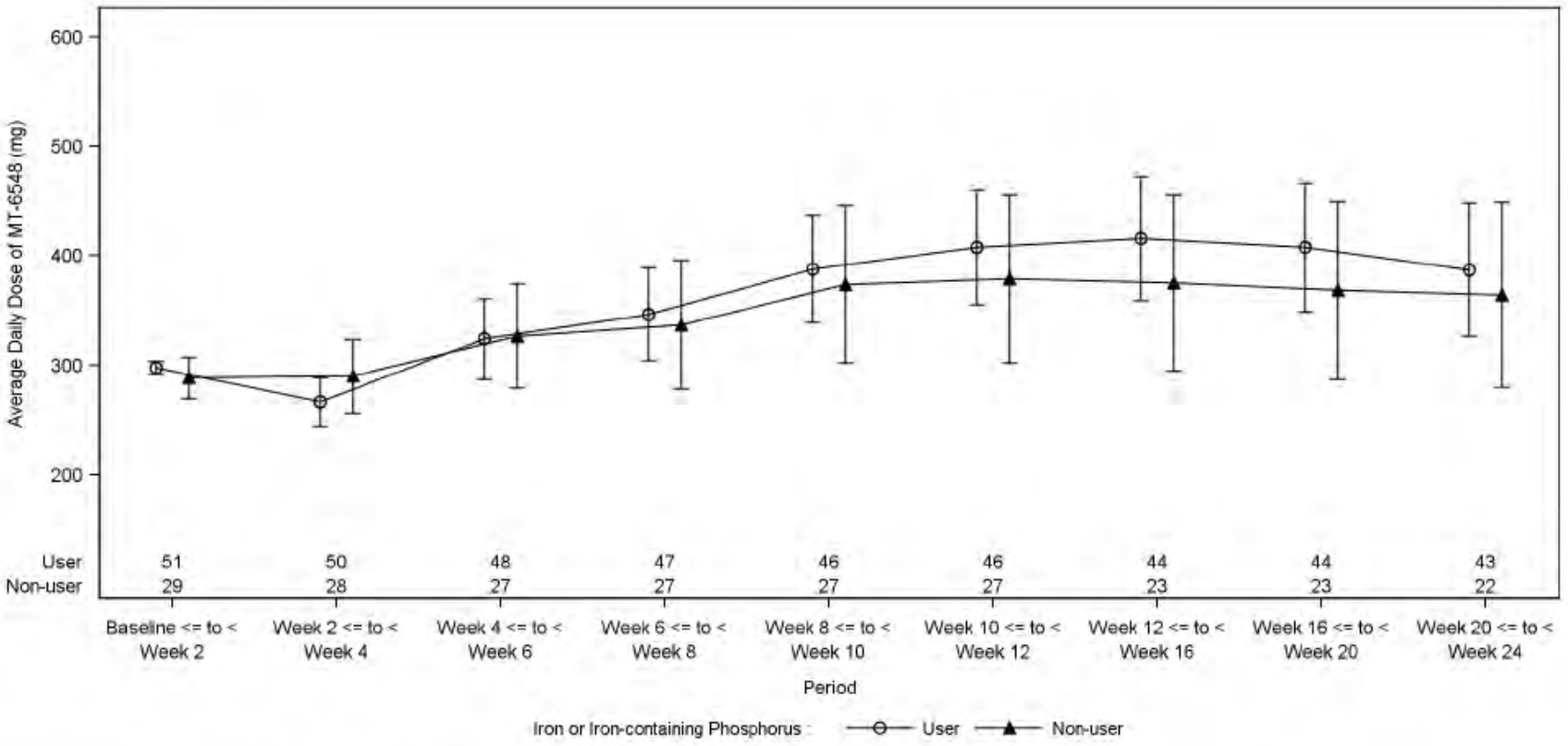
5.3.5.1—7 表 14.2.3.3.5.1 より引用

表 2.7.6.26－58　鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量（FAS）

Treatment Group	Iron or Iron-containing Phosphorus	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	User	Baseline <= to < Week 2	51	297.27	20.87	300.00	(192.9, 375.0)	(291.40, 303.14)
		Week 2 <= to < Week 4	50	266.36	79.33	300.00	(0.0, 450.0)	(243.81, 288.90)
		Week 4 <= to < Week 6	48	323.88	125.91	300.00	(0.0, 525.0)	(287.32, 360.44)
		Week 6 <= to < Week 8	47	346.50	144.86	375.00	(0.0, 600.0)	(303.97, 389.04)
		Week 8 <= to < Week 10	46	387.58	164.17	450.00	(0.0, 600.0)	(338.83, 436.33)
		Week 10 <= to < Week 12	46	407.38	177.19	450.00	(0.0, 600.0)	(354.76, 459.99)
		Week 12 <= to < Week 16	44	415.42	185.58	450.00	(0.0, 600.0)	(359.01, 471.83)
		Week 16 <= to < Week 20	44	407.41	192.91	428.57	(37.5, 600.0)	(348.76, 466.07)
		Week 20 <= to < Week 24	43	386.96	198.36	375.00	(0.0, 600.0)	(325.91, 449.01)
	Non-user	Baseline <= to < Week 2	29	288.18	49.79	300.00	(42.9, 300.0)	(269.24, 307.12)
		Week 2 <= to < Week 4	28	289.67	86.38	300.00	(0.0, 514.3)	(256.17, 323.16)
		Week 4 <= to < Week 6	27	326.59	121.16	300.00	(150.0, 600.0)	(278.66, 374.52)
		Week 6 <= to < Week 8	27	336.90	148.32	300.00	(10.7, 600.0)	(276.23, 395.58)
		Week 8 <= to < Week 10	27	373.81	181.91	375.00	(0.0, 600.0)	(301.85, 445.77)
		Week 10 <= to < Week 12	27	378.73	193.79	375.00	(0.0, 600.0)	(302.07, 455.39)
		Week 12 <= to < Week 16	28	375.00	187.05	401.79	(0.0, 600.0)	(294.11, 455.89)
		Week 16 <= to < Week 20	23	368.26	187.97	412.50	(0.0, 600.0)	(286.96, 449.53)
		Week 20 <= to < Week 24	22	364.29	191.06	300.00	(0.0, 600.0)	(279.58, 449.00)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.3.1
Source: t_14_2_3_3_7_1_2.sas

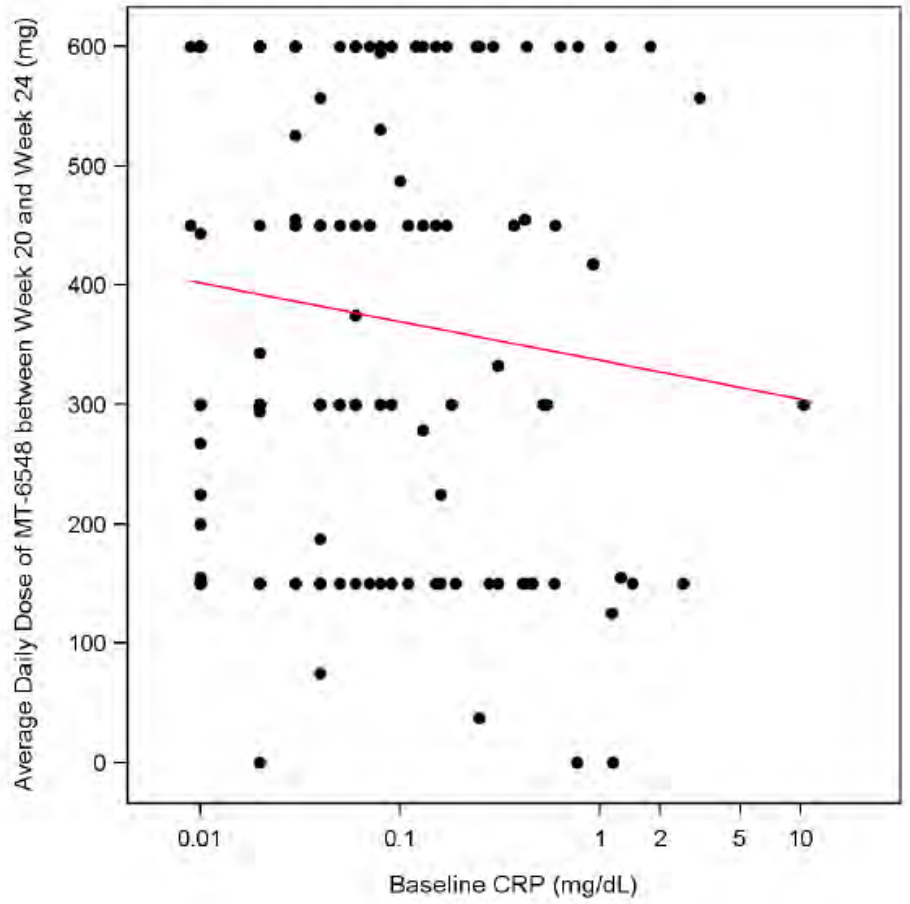
5.3.5.1—9 表 14.2.3.3.7.1.2 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Table 14.2.3.3.7.1.2
Source: f_14_2_3_7_1_2.sas

図 2.7.6.26－22　鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—9 図 14.2.3.7.1.2 より引用



Note(s): linear regression model: Y=aX + b; Y: average daily dose; X: baseline CRP.
Data Source: Listing 16.2.3.1, Listing 16.2.6.4
Source: f_14_2_3_9_1.sas

図 2.7.6.26－23　ベースラインの CRP と 20 週から 24 週後の MT-6548 の 1 日平均投与量の散布図（FAS）

5.3.5.1—7 図 14.2.3.9.1 より引用

2.7.6.26.2.1.4 安全性

(1) 治験薬投与期間及び累積投与量

安全性解析対象集団の治験薬投与期間の記述統計量を表 2.7.6.26－59 に示した. 治験薬投与期間の平均値±SD は MT-6548 群で 152.8±38.8 日，darbepoetin 群で 163.6±21.7 日であった.

治験薬の累積投与量の記述統計量を表 2.7.6.26－60 に示した. 治験薬の累積投与量の平均値±SD は MT-6548 群で 54880.6±25604.1 mg，darbepoetin 群で 411.0±302.5 μg であった.

表 2.7.6.26－59　治験薬投与期間の記述統計量（安全性解析対象集団）

Duration of Exposure (days)	MT-6548 (N=162)	darbepoetin (N=161)
Mean	152.8	163.6
SD	38.8	21.7
Median	168.0	168.0
Minimum, Maximum	(9, 170)	(4, 175)

Data Source: Listing 16.2.3.3
Source: t_14_1_4_4_1.sas

5.3.5.1—7 表 12.1—1 より引用

表 2.7.6.26－60　治験薬の累積投与量の記述統計量（安全性解析対象集団）

Cumulative Dose	MT-6548 (N=162) (mg)	darbepoetin (N=161) (ug)
Mean	54880.6	411.0
SD	25604.1	302.5
Median	51900.0	330.0
Minimum, Maximum	(600, 94800)	(20, 1700)

Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_1_4_5_2.sas

5.3.5.1—7 表 12.1—2 より引用

(2)　有害事象

1)　有害事象の簡潔な要約

有害事象の要約を表 2.7.6.26－61 に示した．有害事象の発現割合は，MT-6548 群で 89.5%（145／162 名），darbepoetin 群で 88.2%（142／161 名）であった．副作用は MT-6548 群で 10.5%（17 名），darbepoetin 群で 2.5%（4 名）であった．

重篤な有害事象の発現割合は，MT-6548 群で 13.0%（21 名），darbepoetin 群で 10.6%（17 名）であった．重篤な副作用は両群で認められなかった．

中止に至った有害事象の発現割合は，MT-6548 群で 6.2%（10 名），darbepoetin 群で 2.5%（4 名）であった．

治験薬の休薬又は減量に至った有害事象の発現割合は，MT-6548 群で 6.2%（10 名），darbepoetin 群で 2.5%（4 名）であった．

死亡に至った有害事象は，MT-6548 群で 0.6%（1 名），darbepoetin 群で 0.6%（1 名）であった．

表 2.7.6.26－61　有害事象の要約（安全性解析対象集団）

	MT-6548 (N=162) n (%)	darbepoetin (N=161) n (%)
Subjects with at least one adverse event	145 (89.5)	142 (88.2)
Subjects with at least one adverse drug reaction	17 (10.5)	4 (2.5)
Subjects with at least one serious adverse event	21 (13.0)	17 (10.6)
Subjects with at least one serious adverse drug reaction	0 (0.0)	0 (0.0)
Subjects with at least one adverse event leading to study discontinuation	10 (6.2)	4 (2.5)
Subjects who had dose reduction or interruption of study drug due to adverse event	10 (6.2)	4 (2.5)
Deaths due to adverse event	1 (0.6)	1 (0.6)

Data Source: Listing 16.2.5.1
Source: t_14_3_1_1.sas

5.3.5.1—7 表 12.2.1—1 より引用

2)　有害事象及び副作用

有害事象及び副作用を表 2.7.6.26－62 及び表 2.7.6.26－63 に示した．

有害事象のうち，MT-6548 群で発現割合が 20%以上の SOC は，「感染症および寄生虫症」｛MT-6548 群：40.1%（65 名），darbepoetin 群：47.8%（77 名）（以下，同順で記載）｝，「胃腸障害」｛28.4%（46 名），29.8%（48 名）｝，「傷害、中毒および処置合併症」｛25.9%（42 名），32.9%（53 名）｝，「筋骨格系および結合組織障害」｛24.7%（40 名），19.9%（32 名）｝及び「皮膚および皮下組織障害」｛23.5%（38 名），13.0%（21 名）｝であった．これらの SOC のうち，darbepoetin 群と比較して 10%以上高かった SOC は，「皮膚および皮下組織障害」であった．副作用のうち，MT-6548 群で発現割合が 20%以上の SOC は認められなかった．MT-6548 群で発現割合が最も高い副作用の SOC は，「胃腸障害」｛6.2%（10 名），1.2%（2 名）｝であった．

MT-6548 群で発現割合が 5%以上の有害事象は，「上咽頭炎」｛MT-6548 群：19.8%（32 名），darbepoetin 群：28.6%（46 名）（以下，同順で記載）｝，「下痢」｛10.5%（17 名），9.9%（16 名）｝，「シャント狭窄」｛8.0%（13 名），12.4%（20 名）｝，「挫傷」｛6.8%（11 名），6.2%（10 名）｝，「網膜出血」｛6.2%（10 名），3.1%（5 名）｝及び「頭痛」｛5.6%（9 名），1.9%（3 名）｝であった．これらの事象のうち，darbepoetin 群と比較して 3%以上高かった有害事象は，「網膜出血」及び「頭痛」であった．MT-6548 群で発現割合が 5%以上の副作用は認められなかった．MT-6548 群で発現割合が最も高かった副作用は，「下痢」｛2.5%（4 名），1.2%（2 名）｝続いて「悪心」｛1.9%（3 名），0%｝であった．

最も発現割合の高かった SOC「感染症および寄生虫症」，darbepoetin 群と比較して発現割合の高かった SOC「皮膚および皮下組織障害」，発現割合が 10%以上であった有害事象「上咽頭炎」，発現割合が 10%以上の有害事象かつ MT-6548 群で副作用としての発現割合が高かった「下痢」，MT-6548 群で「下痢」に次いで発現割合の高かった副作用である「悪心」，darbepoetin 群と比較して発現割合の高かった有害事象「網膜出血」及び「頭痛」に関して，下記に詳細を示した．

SOC「感染症および寄生虫症」のうち MT-6548 群で発現した主な有害事象は「上咽頭炎」であった．また，MT-6548 群で発現した SOC「皮膚および皮下組織障害」の有害事象の内訳の発現割合に，特定の傾向は認められなかった．

「上咽頭炎」は MT-6548 群で最も発現割合が高い有害事象であったが，MT-6548 群の発現割合が darbepoetin 群よりも低く，すべて軽度及び因果関係は合理的な可能性なしと判断された．「下痢」は有害事象の発現割合が 10%以上であり，副作用の発現割合が最も高い事象であったが，有害事象及び副作用の発現割合はどちらも両群で同程度であった．MT-6548 群で発現した「下痢」のうち 1 名は中等度，それ以外の 16 名は軽度と判断され，因果関係が合理的な可能性ありのものは 4 名に認められた．転帰は 4 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，それ以外の 13 名は回復であった．「下痢」に次いで MT-6548 群で副作用の発現割合が高かった「悪心」の有害事象の発現割合は MT-6548 群 3.7%（6 名），darbepoetin 群 0.6%（1 名）と MT-6548 群で darbepoetin

群よりも高かったが，副作用の発現割合は両群で同程度であった．MT-6548 群で発現した「悪心」のうち 1 名は中等度，それ以外の 5 名は軽度と判断され，因果関係は 3 名が合理的な可能性ありと判断され，転帰は 1 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，それ以外の 5 名はすべて回復であった．「網膜出血」は MT-6548 群の発現割合が darbepoetin 群よりも高かった．MT-6548 群で発現した「網膜出血」はすべて軽度，因果関係は合理的な可能性なしと判断され，転帰は 9 名が治療期間 I 期では未回復のまま治療期間 II 期に移行し，1 名は「貧血」で治療期間 I 期に中止となった．なお，MT-6548 群で「網膜出血」が発現した被験者の血管内皮増殖因子（以下，VEGF）に顕著な変動は認められなかった.「頭痛」は MT-6548 群の有害事象の発現割合が darbepoetin 群よりも高かった．MT-6548 群で発現した「頭痛」はすべて軽度，因果関係は合理的な可能性なしと判断された．転帰は 3 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，それ以外の 6 名はすべて回復であった．

表 2.7.6.26－62　有害事象（安全性解析対象集団）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Subjects with at least one adverse event		145(89.5)	142(88.2)
Infections and infestations	感染症および寄生虫症	65(40.1)	77(47.8)
Nasopharyngitis	上咽頭炎	32(19.8)	46(28.6)
Conjunctivitis	結膜炎	8(4.9)	1(0.6)
Gastroenteritis	胃腸炎	8(4.9)	0(0.0)
Upper respiratory tract infection	上気道感染	4(2.5)	5(3.1)
Pneumonia	肺炎	4(2.5)	0(0.0)
Periodontitis	歯周炎	3(1.9)	2(1.2)
Pharyngitis	咽頭炎	2(1.2)	5(3.1)
Tinea pedis	足部白癬	2(1.2)	4(2.5)
Cystitis	膀胱炎	2(1.2)	1(0.6)
Otitis media	中耳炎	2(1.2)	0(0.0)
Bronchitis	気管支炎	1(0.6)	2(1.2)
Herpes zoster	帯状疱疹	1(0.6)	1(0.6)
Skin infection	皮膚感染	1(0.6)	1(0.6)
Oral herpes	口腔ヘルペス	1(0.6)	1(0.6)
Angular cheilitis	口角口唇炎	1(0.6)	0(0.0)
Cellulitis	蜂巣炎	1(0.6)	0(0.0)
Chronic sinusitis	慢性副鼻腔炎	1(0.6)	0(0.0)
Furuncle	せつ	1(0.6)	0(0.0)
Gastroenteritis viral	ウイルス性胃腸炎	1(0.6)	0(0.0)
Otitis media chronic	慢性中耳炎	1(0.6)	0(0.0)
Paronychia	爪囲炎	1(0.6)	0(0.0)
Sinusitis	副鼻腔炎	1(0.6)	0(0.0)
Hepatic cyst infection	肝嚢胞感染	1(0.6)	0(0.0)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Upper respiratory tract infection bacterial	細菌性上気道感染	1(0.6)	0(0.0)
Enteritis infectious	感染性腸炎	1(0.6)	0(0.0)
Device related infection	医療機器関連感染	1(0.6)	0(0.0)
Infected dermal cyst	感染性皮膚嚢腫	1(0.6)	0(0.0)
Shunt infection	シャント感染	0(0.0)	5(3.1)
Folliculitis	毛包炎	0(0.0)	2(1.2)
Gingivitis	歯肉炎	0(0.0)	2(1.2)
Dermatophytosis of nail	爪の皮膚糸状菌症	0(0.0)	1(0.6)
Otitis media acute	急性中耳炎	0(0.0)	1(0.6)
Tinea cruris	股部白癬	0(0.0)	1(0.6)
Urinary tract infection	尿路感染	0(0.0)	1(0.6)
Urinary tract infection fungal	真菌性尿路感染	0(0.0)	1(0.6)
Skin bacterial infection	皮膚細菌感染	0(0.0)	1(0.6)
Abdominal infection	腹部感染	0(0.0)	1(0.6)
Staphylococcal infection	ブドウ球菌感染	0(0.0)	1(0.6)
Pneumonia bacterial	細菌性肺炎	0(0.0)	1(0.6)
Purulence	化膿	0(0.0)	1(0.6)
Mycotic endophthalmitis	真菌性眼内炎	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	4(2.5)	4(2.5)
Seborrhoeic keratosis	脂漏性角化症	1(0.6)	1(0.6)
Breast cancer	乳癌	1(0.6)	0(0.0)
Gastric cancer	胃癌	1(0.6)	0(0.0)
Laryngeal papilloma	喉頭乳頭腫	1(0.6)	0(0.0)
Pancreatic neoplasm	膵新生物	0(0.0)	1(0.6)
Urethral neoplasm	尿道新生物	0(0.0)	1(0.6)
Gastrointestinal submucosal tumour	消化管粘膜下腫瘍	0(0.0)	1(0.6)
Blood and lymphatic system disorders	血液およびリンパ系障害	6(3.7)	2(1.2)
Anaemia	貧血	1(0.6)	0(0.0)
Anaemia macrocytic	大球性貧血	1(0.6)	0(0.0)
Eosinophilia	好酸球増加症	1(0.6)	0(0.0)
Lymphadenitis	リンパ節炎	1(0.6)	0(0.0)
Lymphadenopathy	リンパ節症	1(0.6)	0(0.0)
Nephrogenic anaemia	腎性貧血	1(0.6)	0(0.0)
Aplastic anaemia	再生不良性貧血	0(0.0)	1(0.6)
Iron deficiency anaemia	鉄欠乏性貧血	0(0.0)	1(0.6)
Endocrine disorders	内分泌障害	2(1.2)	1(0.6)
Hyperparathyroidism secondary	続発性副甲状腺機能亢進症	2(1.2)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Metabolism and nutrition disorders	代謝および栄養障害	10(6.2)	7(4.3)
Decreased appetite	食欲減退	6(3.7)	2(1.2)
Hyperphosphataemia	高リン酸塩血症	1(0.6)	2(1.2)
Hypoglycaemia	低血糖	1(0.6)	2(1.2)
Hyperkalaemia	高カリウム血症	1(0.6)	0(0.0)
Dyslipidaemia	脂質異常症	1(0.6)	0(0.0)
Hypocarnitinaemia	低カルニチン血症	1(0.6)	0(0.0)
Dehydration	脱水	0(0.0)	1(0.6)
Psychiatric disorders	精神障害	5(3.1)	3(1.9)
Insomnia	不眠症	4(2.5)	3(1.9)
Abnormal behaviour	異常行動	1(0.6)	0(0.0)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Nervous system disorders	神経系障害	24(14.8)	11(6.8)
Headache	頭痛	9(5.6)	3(1.9)
Dizziness	浮動性めまい	6(3.7)	3(1.9)
Cerebral infarction	脳梗塞	1(0.6)	3(1.9)
Cerebellar infarction	小脳梗塞	1(0.6)	1(0.6)
Carotid artery stenosis	頚動脈狭窄	1(0.6)	0(0.0)
Dizziness postural	体位性めまい	1(0.6)	0(0.0)
Facial paralysis	顔面麻痺	1(0.6)	0(0.0)
Myoclonus	ミオクローヌス	1(0.6)	0(0.0)
Sciatica	坐骨神経痛	1(0.6)	0(0.0)
Somnolence	傾眠	1(0.6)	0(0.0)
Tremor	振戦	1(0.6)	0(0.0)
Intercostal neuralgia	肋間神経痛	1(0.6)	0(0.0)
Cervical radiculopathy	頚髄神経根障害	1(0.6)	0(0.0)
Loss of consciousness	意識消失	0(0.0)	1(0.6)
Seizure	痙攣発作	0(0.0)	1(0.6)
Trigeminal neuralgia	三叉神経痛	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Eye disorders	眼障害	23(14.2)	17(10.6)
Retinal haemorrhage	網膜出血	10(6.2)	5(3.1)
Conjunctival haemorrhage	結膜出血	2(1.2)	2(1.2)
Diabetic retinopathy	糖尿病網膜症	2(1.2)	1(0.6)
Cataract	白内障	1(0.6)	1(0.6)
Dry eye	眼乾燥	1(0.6)	1(0.6)
Ocular hyperaemia	眼充血	1(0.6)	1(0.6)
Optic disc haemorrhage	視神経乳頭出血	1(0.6)	0(0.0)
Punctate keratitis	点状角膜炎	1(0.6)	0(0.0)
Retinal oedema	網膜浮腫	1(0.6)	0(0.0)
Retinal vein occlusion	網膜静脈閉塞	1(0.6)	0(0.0)
Trichiasis	睫毛乱生	1(0.6)	0(0.0)
Vitreous floaters	硝子体浮遊物	1(0.6)	0(0.0)
Eye pruritus	眼そう痒症	1(0.6)	0(0.0)
Cystoid macular oedema	嚢胞様黄斑浮腫	1(0.6)	0(0.0)
Eyelid haematoma	眼瞼血腫	1(0.6)	0(0.0)
Macular oedema	黄斑浮腫	0(0.0)	2(1.2)
Chalazion	霰粒腫	0(0.0)	1(0.6)
Conjunctivitis allergic	アレルギー性結膜炎	0(0.0)	1(0.6)
Eyelid oedema	眼瞼浮腫	0(0.0)	1(0.6)
Retinal detachment	網膜剥離	0(0.0)	1(0.6)
Retinal vascular disorder	網膜血管障害	0(0.0)	1(0.6)
Vitreous detachment	硝子体剥離	0(0.0)	1(0.6)
Retinal aneurysm	網膜血管瘤	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Ear and labyrinth disorders	耳および迷路障害	5(3.1)	2(1.2)
Vertigo	回転性めまい	2(1.2)	0(0.0)
Deafness	難聴	1(0.6)	0(0.0)
Sudden hearing loss	突発性難聴	1(0.6)	0(0.0)
Eustachian tube stenosis	耳管狭窄	1(0.6)	0(0.0)
Tinnitus	耳鳴	0(0.0)	1(0.6)
Vertigo positional	頭位性回転性めまい	0(0.0)	1(0.6)
Cardiac disorders	心臓障害	6(3.7)	8(5.0)
Tachycardia paroxysmal	発作性頻脈	2(1.2)	0(0.0)
Cardiac failure	心不全	1(0.6)	0(0.0)
Cardiac failure congestive	うっ血性心不全	1(0.6)	0(0.0)
Myocardial ischaemia	心筋虚血	1(0.6)	0(0.0)
Palpitations	動悸	1(0.6)	0(0.0)
Bradycardia	徐脈	0(0.0)	2(1.2)
Atrial fibrillation	心房細動	0(0.0)	1(0.6)
Coronary artery stenosis	冠動脈狭窄	0(0.0)	1(0.6)
Ventricular extrasystoles	心室性期外収縮	0(0.0)	1(0.6)
Left ventricular dysfunction	左室機能不全	0(0.0)	1(0.6)
Coronary artery perforation	冠動脈穿孔	0(0.0)	1(0.6)
Supraventricular tachyarrhythmia	上室性頻脈性不整脈	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Vascular disorders	血管障害	14(8.6)	10(6.2)
Hypertension	高血圧	3(1.9)	3(1.9)
Internal haemorrhage	内出血	3(1.9)	3(1.9)
Hypotension	低血圧	2(1.2)	1(0.6)
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	2(1.2)	1(0.6)
Orthostatic hypotension	起立性低血圧	1(0.6)	0(0.0)
Vascular pain	血管痛	1(0.6)	0(0.0)
Vascular insufficiency	血行不全	1(0.6)	0(0.0)
Haemorrhage	出血	1(0.6)	0(0.0)
Peripheral artery occlusion	末梢動脈閉塞	0(0.0)	1(0.6)
Peripheral artery aneurysm rupture	末梢動脈瘤破裂	0(0.0)	1(0.6)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	6(3.7)	11(6.8)
Epistaxis	鼻出血	2(1.2)	2(1.2)
Upper respiratory tract inflammation	上気道の炎症	2(1.2)	2(1.2)
Haemoptysis	喀血	1(0.6)	0(0.0)
Pulmonary oedema	肺水腫	1(0.6)	0(0.0)
Rhinitis allergic	アレルギー性鼻炎	1(0.6)	0(0.0)
Cough	咳嗽	0(0.0)	3(1.9)
Dyspnoea	呼吸困難	0(0.0)	1(0.6)
Pleural effusion	胸水	0(0.0)	1(0.6)
Rhinorrhoea	鼻漏	0(0.0)	1(0.6)
Laryngeal discomfort	喉頭不快感	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Gastrointestinal disorders	胃腸障害	46(28.4)	48(29.8)
Diarrhoea	下痢	17(10.5)	16(9.9)
Vomiting	嘔吐	8(4.9)	9(5.6)
Nausea	悪心	6(3.7)	1(0.6)
Constipation	便秘	4(2.5)	5(3.1)
Gastrooesophageal reflux disease	胃食道逆流性疾患	3(1.9)	3(1.9)
Abdominal discomfort	腹部不快感	3(1.9)	1(0.6)
Dental caries	齲歯	2(1.2)	1(0.6)
Enterocolitis	腸炎	2(1.2)	1(0.6)
Stomatitis	口内炎	2(1.2)	1(0.6)
Toothache	歯痛	2(1.2)	0(0.0)
Abdominal pain	腹痛	1(0.6)	2(1.2)
Large intestine polyp	大腸ポリープ	1(0.6)	2(1.2)
Faeces soft	軟便	1(0.6)	2(1.2)
Dyspepsia	消化不良	1(0.6)	1(0.6)
Diverticulum intestinal	腸憩室	1(0.6)	0(0.0)
Dry mouth	口内乾燥	1(0.6)	0(0.0)
Duodenal ulcer	十二指腸潰瘍	1(0.6)	0(0.0)
Gastric ulcer	胃潰瘍	1(0.6)	0(0.0)
Gastritis erosive	びらん性胃炎	1(0.6)	0(0.0)
Glossitis	舌炎	1(0.6)	0(0.0)
Haemorrhoids	痔核	1(0.6)	0(0.0)
Melaena	メレナ	1(0.6)	0(0.0)
Pancreatitis	膵炎	1(0.6)	0(0.0)
Gastric disorder	胃障害	1(0.6)	0(0.0)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Gastrointestinal motility disorder	消化管運動障害	1(0.6)	0(0.0)
Loose tooth	弛緩歯	1(0.6)	0(0.0)
Anal fissure	裂肛	0(0.0)	2(1.2)
Gastritis	胃炎	0(0.0)	2(1.2)
Abdominal pain upper	上腹部痛	0(0.0)	1(0.6)
Anal fistula	痔瘻	0(0.0)	1(0.6)
Enteritis	小腸炎	0(0.0)	1(0.6)
Gastric polyps	胃ポリープ	0(0.0)	1(0.6)
Lip dry	口唇乾燥	0(0.0)	1(0.6)
Upper gastrointestinal haemorrhage	上部消化管出血	0(0.0)	1(0.6)
Haemorrhoidal haemorrhage	痔出血	0(0.0)	1(0.6)
Hepatobiliary disorders	肝胆道系障害	2(1.2)	0(0.0)
Cholelithiasis	胆石症	2(1.2)	0(0.0)
Cholangitis	胆管炎	1(0.6)	0(0.0)
Cholecystitis	胆嚢炎	1(0.6)	0(0.0)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	38(23.5)	21(13.0)
Eczema	湿疹	8(4.9)	5(3.1)
Pruritus	そう痒症	6(3.7)	4(2.5)
Haemorrhage subcutaneous	皮下出血	5(3.1)	2(1.2)
Dermatitis contact	接触皮膚炎	4(2.5)	0(0.0)
Drug eruption	薬疹	4(2.5)	0(0.0)
Skin exfoliation	皮膚剥脱	3(1.9)	2(1.2)
Ingrowing nail	嵌入爪	3(1.9)	0(0.0)
Cold sweat	冷汗	2(1.2)	0(0.0)
Rash	発疹	2(1.2)	0(0.0)
Xeroderma	乾皮症	1(0.6)	3(1.9)
Hyperkeratosis	過角化	1(0.6)	2(1.2)
Alopecia	脱毛症	1(0.6)	0(0.0)
Dermal cyst	皮膚嚢腫	1(0.6)	0(0.0)
Skin disorder	皮膚障害	1(0.6)	0(0.0)
Skin mass	皮膚腫瘤	1(0.6)	0(0.0)
Acne	ざ瘡	0(0.0)	2(1.2)
Dermatitis	皮膚炎	0(0.0)	2(1.2)
Erythema	紅斑	0(0.0)	1(0.6)
Petechiae	点状出血	0(0.0)	1(0.6)
Onychomadesis	爪甲脱落症	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	40(24.7)	32(19.9)
Back pain	背部痛	8(4.9)	3(1.9)
Pain in extremity	四肢痛	8(4.9)	2(1.2)
Musculoskeletal pain	筋骨格痛	7(4.3)	5(3.1)
Myalgia	筋肉痛	5(3.1)	3(1.9)
Arthralgia	関節痛	3(1.9)	6(3.7)
Muscle spasms	筋痙縮	3(1.9)	3(1.9)
Neck pain	頸部痛	3(1.9)	3(1.9)
Osteoarthritis	変形性関節症	3(1.9)	0(0.0)
Periarthritis	関節周囲炎	2(1.2)	3(1.9)
Lumbar spinal stenosis	腰部脊柱管狭窄症	2(1.2)	1(0.6)
Spinal osteoarthritis	変形性脊椎症	1(0.6)	2(1.2)
Trigger finger	弾発指	1(0.6)	1(0.6)
Bursitis	滑液包炎	1(0.6)	0(0.0)
Haemarthrosis	出血性関節症	1(0.6)	0(0.0)
Osteoporosis	骨粗鬆症	1(0.6)	0(0.0)
Tenosynovitis	腱鞘炎	1(0.6)	0(0.0)
Musculoskeletal discomfort	筋骨格不快感	1(0.6)	0(0.0)
Bone pain	骨痛	0(0.0)	1(0.6)
Tendonitis	腱炎	0(0.0)	1(0.6)
Musculoskeletal chest pain	筋骨格系胸痛	0(0.0)	1(0.6)
Musculoskeletal stiffness	筋骨格硬直	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Renal and urinary disorders	腎および尿路障害	2(1.2)	4(2.5)
Ureterolithiasis	尿管結石症	1(0.6)	1(0.6)
Pollakiuria	頻尿	1(0.6)	0(0.0)
Haematuria	血尿	0(0.0)	1(0.6)
Urethral haemorrhage	尿道出血	0(0.0)	1(0.6)
Renal mass	腎腫瘤	0(0.0)	1(0.6)
Reproductive system and breast disorders	生殖系および乳房障害	3(1.9)	2(1.2)
Benign prostatic hyperplasia	良性前立腺肥大症	2(1.2)	0(0.0)
Acquired hydrocele	後天性陰嚢水瘤	1(0.6)	0(0.0)
Menorrhagia	月経過多	0(0.0)	1(0.6)
Scrotal pain	陰嚢痛	0(0.0)	1(0.6)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	12(7.4)	8(5.0)
Oedema peripheral	末梢性浮腫	6(3.1)	0(0.0)
Pyrexia	発熱	3(1.9)	2(1.2)
Chest discomfort	胸部不快感	1(0.6)	1(0.6)
Puncture site haemorrhage	穿刺部位出血	1(0.6)	1(0.6)
Feeling abnormal	異常感	1(0.6)	0(0.0)
Injection site reaction	注射部位反応	1(0.6)	0(0.0)
Peripheral swelling	末梢腫脹	1(0.6)	0(0.0)
Injection site bruising	注射部位内出血	0(0.0)	1(0.6)
Catheter site pain	カテーテル留置部位疼痛	0(0.0)	1(0.6)
Catheter site bruise	カテーテル留置部位内出血	0(0.0)	1(0.6)
Mucosal hyperaemia	粘膜充血	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Investigations	臨床検査	9(5.6)	14(8.7)
Blood pressure decreased	血圧低下	3(1.9)	3(1.9)
Blood pressure increased	血圧上昇	1(0.6)	3(1.9)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1(0.6)	0(0.0)
C-reactive protein increased	C－反応性蛋白増加	1(0.6)	0(0.0)
Haemoglobin decreased	ヘモグロビン減少	1(0.6)	0(0.0)
Prostatic specific antigen increased	前立腺特異性抗原増加	1(0.6)	0(0.0)
Serum ferritin decreased	血清フェリチン減少	1(0.6)	0(0.0)
Transferrin saturation decreased	トランスフェリン飽和度低下	1(0.6)	0(0.0)
Salmonella test positive	サルモネラ検査陽性	1(0.6)	0(0.0)
Blood parathyroid hormone increased	血中副甲状腺ホルモン増加	0(0.0)	2(1.2)
Electrocardiogram QT prolonged	心電図ＱＴ延長	0(0.0)	2(1.2)
Blood calcium decreased	血中カルシウム減少	0(0.0)	1(0.6)
Carnitine decreased	カルニチン減少	0(0.0)	1(0.6)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0(0.0)	1(0.6)
Haemoglobin increased	ヘモグロビン増加	0(0.0)	1(0.6)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	42(25.9)	53(32.9)
Shunt stenosis	シャント狭窄	13(8.0)	20(12.4)
Contusion	挫傷	11(6.8)	10(6.2)
Skin abrasion	皮膚擦過傷	4(2.5)	6(3.7)
Wound	創傷	4(2.5)	3(1.9)
Shunt occlusion	シャント閉塞	3(1.9)	1(0.6)
Thermal burn	熱傷	2(1.2)	2(1.2)
Limb injury	四肢損傷	2(1.2)	2(1.2)
Joint injury	関節損傷	2(1.2)	0(0.0)
Dental restoration failure	歯科修復不成功	2(1.2)	0(0.0)
Procedural hypotension	処置による低血圧	1(0.6)	3(1.9)
Foot fracture	足骨折	1(0.6)	2(1.2)
Rib fracture	肋骨骨折	1(0.6)	2(1.2)
Subcutaneous haematoma	皮下血腫	1(0.6)	1(0.6)
Heat illness	熱中症	1(0.6)	1(0.6)
Skin wound	皮膚創傷	1(0.6)	1(0.6)
Animal bite	動物咬傷	1(0.6)	0(0.0)
Ligament sprain	靭帯捻挫	1(0.6)	0(0.0)
Tooth injury	歯牙損傷	1(0.6)	0(0.0)
Vascular access complication	血管確保合併症	1(0.6)	0(0.0)
Procedural hypertension	処置による高血圧	1(0.6)	0(0.0)
Shunt blood flow excessive	シャント血流過剰	1(0.6)	0(0.0)
Vascular access site inflammation	血管確保部位炎症	1(0.6)	0(0.0)
Arthropod sting	節足動物刺傷	0(0.0)	1(0.6)
Femoral neck fracture	大腿骨頸部骨折	0(0.0)	1(0.6)

表 2.7.6.26－62　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Fractured ischium	坐骨骨折	0 (0.0)	1 (0.6)
Joint dislocation	関節脱臼	0 (0.0)	1 (0.6)
Laceration	裂傷	0 (0.0)	1 (0.6)
Radius fracture	橈骨骨折	0 (0.0)	1 (0.6)
Scratch	引っかき傷	0 (0.0)	1 (0.6)
Subarachnoid haemorrhage	くも膜下出血	0 (0.0)	1 (0.6)
Postoperative ileus	術後イレウス	0 (0.0)	1 (0.6)
Arteriovenous fistula site complication	動静脈瘻部位合併症	0 (0.0)	1 (0.6)
Coronary artery restenosis	冠動脈再狭窄	0 (0.0)	1 (0.6)
Upper limb fracture	上肢骨折	0 (0.0)	1 (0.6)
Ear abrasion	耳擦過傷	0 (0.0)	1 (0.6)
Shunt malfunction	シャント機能不全	0 (0.0)	1 (0.6)
Post-traumatic pain	外傷後疼痛	0 (0.0)	1 (0.6)
Procedural headache	処置による頭痛	0 (0.0)	1 (0.6)
Dialysis related complication	透析関連合併症	0 (0.0)	1 (0.6)

Note(s): MedDRA Version 20.1 and MedDRA/J Version 20.1.
Data Source: Listing 16.2.9.1
Source: t_14_3_1_2.sas

5.3.5.1—7 表 12.2.3—1 より引用

表 2.7.6.26－63　副作用（安全性解析対象集団）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Subjects with at least one adverse drug reaction		17(10.5)	4(2.5)
Infections and infestations	感染症および寄生虫症	1(0.6)	0(0.0)
Gastroenteritis	胃腸炎	1(0.6)	0(0.0)
Eye disorders	眼障害	1(0.6)	0(0.0)
Retinal oedema	網膜浮腫	1(0.6)	0(0.0)
Vascular disorders	血管障害	1(0.6)	0(0.0)
Hypertension	高血圧	1(0.6)	0(0.0)
Gastrointestinal disorders	胃腸障害	10(6.2)	2(1.2)
Diarrhoea	下痢	4(2.5)	2(1.2)
Nausea	悪心	3(1.9)	0(0.0)
Abdominal discomfort	腹部不快感	2(1.2)	0(0.0)
Vomiting	嘔吐	2(1.2)	0(0.0)
Stomatitis	口内炎	1(0.6)	0(0.0)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	4(2.5)	0(0.0)
Alopecia	脱毛症	1(0.6)	0(0.0)
Cold sweat	冷汗	1(0.6)	0(0.0)
Drug eruption	薬疹	1(0.6)	0(0.0)
Pruritus	そう痒症	1(0.6)	0(0.0)
Renal and urinary disorders	腎および尿路障害	1(0.6)	0(0.0)
Pollakiuria	頻尿	1(0.6)	0(0.0)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	1(0.6)	0(0.0)
Chest discomfort	胸部不快感	1(0.6)	0(0.0)

表 2.7.6.26－63　副作用（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Investigations	臨床検査	2(1.2)	2(1.2)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1(0.6)	0(0.0)
Serum ferritin decreased	血清フェリチン減少	1(0.6)	0(0.0)
Transferrin saturation decreased	トランスフェリン飽和度低下	1(0.6)	0(0.0)
Blood pressure increased	血圧上昇	0(0.0)	1(0.6)
Haemoglobin increased	ヘモグロビン増加	0(0.0)	1(0.6)

Note(s): MedDRA Version 20.1 and MedDRA/J Version 20.1.
Data Source: Listing 16.2.5.1
Source: t_14_3_1_3.sas

5.3.5.1—7 表 12.2.3—2 より引用

3)　程度別の有害事象

高度と判断された有害事象の発現割合は，MT-6548 群で 3.7%（6 名）であり，内訳は「肺炎」が 2 名，「肝嚢胞感染」，「乳癌」，「脳梗塞」，「心不全」，「胆管炎」及び「シャント閉塞」が各 1 名であった．そのうち「肺炎」及び「心不全」並びに「肝嚢胞感染」及び「胆管炎」は同一被験者で認められた．darbepoetin 群では 3.7%（6 名）であり，内訳は「細菌性肺炎」，「真菌性眼内炎」，「再生不良性貧血」，「脳梗塞」，「網膜剥離」，「末梢動脈瘤破裂」，「大腿骨頚部骨折」及び「術後イレウス」が各 1 名であった．そのうち「真菌性眼内炎」及び「網膜剥離」並びに「末梢動脈瘤破裂」及び「術後イレウス」は同一被験者で認められた．

中等度と判断された有害事象の発現割合は，MT-6548 群で 16.0%（26 名），darbepoetin 群で 13.0%（21 名）であった．

4)　発現時期別の有害事象

発現時期別の有害事象の発現割合は，MT-6548 群では 84 日後までが 71.6%（116／162 名），85 日後以降が 77.8%（112／144 名）であり，darbepoetin 群では 84 日後までが 64.0%（103／161 名），85 日後以降が 72.6%（114／157 名）であった．MT-6548 群で 84 日後までと比較し，85 日後以降の発現割合が 10%以上高かった SOC は「眼障害」であり，その発現割合は 84 日後までが 2.5%（4 名），85 日後以降が 13.9%（20 名）であった．

5)　発現直前の投与量別の有害事象

発現直前の投与量別の総曝露日数あたりの有害事象の発現率は，MT-6548 群では 0 mg，150 mg，300 mg，450 mg 及び 600 mg でそれぞれ 2.2%（16 件），1.6%（72 件），2.1%（203 件），2.1%（93 件）及び 1.9%（104 件）であり，darbepoetin 群では週あたりの投与量として 0 μg，0 μg 超 30 μg 以下，30 μg 超 60 μg 以下，60 μg 超 90 μg 以下，90 μg 超 120 μg 以下及び 120 μg 超でそれぞれ 4.0%（14 件），1.6%（381 件），1.7%（38 件），0.7%（1 件），0%（0 件）及び 0%（0 件）であった．

なお，MT-6548 群で過量投与のあった被験者（被験者識別コード J313416）が 1200 mg を 1 日服用した際に「悪心」が認められた．当該事象は軽度，治験薬との因果関係は合理的な可能性ありと判断され，転帰は発現日当日のうちに回復となった．治験責任医師は本事象が 1 日で回復していること，問診やその他臨床的な所見より，治験継続には問題ないと判断しており，被験者自身も治験継続の意思があることを確認したため，治験は継続した．

6)　累積投与量別の有害事象

累積投与量別の有害事象の発現割合は，最大累積投与量に 0 から 1/4 を乗じた範囲，1/4 から 2/4 を乗じた範囲，2/4 から 3/4 を乗じた範囲及び 3/4 から 1 を乗じた範囲を累積投与量の分類として，MT-6548 群ではそれぞれ 67.3%（109／162 名），56.2%（82／

146 名），48.1%（50／104 名）及び 45.5%（30／66 名）であり，darbepoetin 群ではそれぞれ 80.7%（130／161 名），57.5%（50／87 名），44.4%（12／27 名）及び 21.4%（3／14 名）であった．

7)　休薬前後別の有害事象

休薬前後別の有害事象の発現割合は，MT-6548 群では休薬前 4 週間で 8.0%（2／25 名），休薬後 4 週間で 8.0%（2／25 名）であり，darbepoetin 群ではそれぞれ 6.3%（1／16 名）及び 18.8%（3／16 名）であった．

(3)　死亡，その他の重篤な有害事象及び他の重要な有害事象

1)　死亡

MT-6548 群で，1 名に「肺炎」による死亡を認めた．本事象の程度は高度，重篤性は重篤，治験薬との因果関係は合理的な可能性なしと判断され，治験薬投与 134 日目に本事象により中止され，中止から 13 日後に死亡した．治験薬との因果関係について，「偶発的に発生したものであり MT-6548 錠，ダルベポエチンアルファ注の作用機序を考え因果関係はなしと判断した．」と治験責任医師は報告した．

なお，MT-6548 群で，安全性評価期間外に 1 名の死亡（報告事象名：突然死）が報告された．当該被験者は重篤な有害事象「乳癌」により治験薬投与 117 日目に中止となっており，中止から 31 日後に死亡した．治験責任医師は，「剖検を実施しておらず死因は不明であることを確認したため突然死として報告する．乳癌による死亡ではないと考える．」と報告した．

darbepoetin 群で，1 名に「末梢動脈瘤破裂」による死亡を認めた．本事象の程度は高度，重篤性は重篤，治験薬との因果関係は合理的な可能性なしと判断され，治験薬投与 56 日目に本事象により中止され，中止から 26 日後に死亡した．治験薬との因果関係について，「治験開始前より動脈瘤は形成されていた可能性が高く，腎不全及び高血圧等の合併症により悪化したと考えるため，因果関係はなしと判断した．」と治験責任医師は報告した．なお，本事象に対する処置として，腹部大動脈人工血管置換術が施行された．手術後の入院期間中に意識レベルの低下が見られ，脳梗塞と診断され，その後死亡した．

2)　重篤な有害事象及び副作用

重篤な有害事象を表 2.7.6.26－64 に示した．

MT-6548 群で 2 名以上に認められた重篤な有害事象は，「肺炎」｛MT-6548 群：1.9%（3 名），darbepoetin 群：0%，以下同順で記載｝，「シャント閉塞」｛1.9%（3 名），0%｝，「胃腸炎」｛1.2%（2 名），0%｝及び「シャント狭窄」｛1.2%（2 名），1.9%（3 名）｝であった．

重篤な副作用は，MT-6548 群及び darbepoetin 群で認められなかった．

表 2.7.6.26－64　重篤な有害事象（安全性解析対象集団）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Subjects with at least one serious adverse event		21(13.0)	17(10.6)
Infections and infestations	感染症および寄生虫症	6(3.7)	4(2.5)
Pneumonia	肺炎	3(1.9)	0(0.0)
Gastroenteritis	胃腸炎	2(1.2)	0(0.0)
Hepatic cyst infection	肝嚢胞感染	1(0.6)	0(0.0)
Device related infection	医療機器関連感染	1(0.6)	0(0.0)
Herpes zoster	帯状疱疹	0(0.0)	1(0.6)
Staphylococcal infection	ブドウ球菌感染	0(0.0)	1(0.6)
Pneumonia bacterial	細菌性肺炎	0(0.0)	1(0.6)
Mycotic endophthalmitis	真菌性眼内炎	0(0.0)	1(0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2(1.2)	0(0.0)
Breast cancer	乳癌	1(0.6)	0(0.0)
Gastric cancer	胃癌	1(0.6)	0(0.0)
Blood and lymphatic system disorders	血液およびリンパ系障害	1(0.6)	1(0.6)
Lymphadenitis	リンパ節炎	1(0.6)	0(0.0)
Aplastic anaemia	再生不良性貧血	0(0.0)	1(0.6)
Metabolism and nutrition disorders	代謝および栄養障害	2(1.2)	0(0.0)
Hyperkalaemia	高カリウム血症	1(0.6)	0(0.0)
Decreased appetite	食欲減退	1(0.6)	0(0.0)
Nervous system disorders	神経系障害	1(0.6)	3(1.9)
Cerebral infarction	脳梗塞	1(0.6)	2(1.2)
Cerebellar infarction	小脳梗塞	0(0.0)	1(0.6)
Eye disorders	眼障害	0(0.0)	1(0.6)
Retinal detachment	網膜剥離	0(0.0)	1(0.6)

表 2.7.6.26－64　重篤な有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Ear and labyrinth disorders	耳および迷路障害	1(0.6)	0(0.0)
Sudden hearing loss	突発性難聴	1(0.6)	0(0.0)
Cardiac disorders	心臓障害	2(1.2)	2(1.2)
Cardiac failure	心不全	1(0.6)	0(0.0)
Myocardial ischaemia	心筋虚血	1(0.6)	0(0.0)
Coronary artery stenosis	冠動脈狭窄	0(0.0)	1(0.6)
Coronary artery perforation	冠動脈穿孔	0(0.0)	1(0.6)
Vascular disorders	血管障害	1(0.6)	2(1.2)
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1(0.6)	0(0.0)
Peripheral artery occlusion	末梢動脈閉塞	0(0.0)	1(0.6)
Peripheral artery aneurysm rupture	末梢動脈瘤破裂	0(0.0)	1(0.6)
Gastrointestinal disorders	胃腸障害	1(0.6)	2(1.2)
Gastrocesophageal reflux disease	胃食道逆流性疾患	1(0.6)	0(0.0)
Abdominal pain	腹痛	0(0.0)	1(0.6)
Gastritis	胃炎	0(0.0)	1(0.6)
Hepatobiliary disorders	肝胆道系障害	1(0.6)	0(0.0)
Cholangitis	胆管炎	1(0.6)	0(0.0)

表 2.7.6.26－64　重篤な有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	6(3.7)	8(5.0)
Shunt occlusion	シャント閉塞	3(1.9)	0(0.0)
Shunt stenosis	シャント狭窄	2(1.2)	3(1.9)
Shunt blood flow excessive	シャント血流過剰	1(0.6)	0(0.0)
Femoral neck fracture	大腿骨頸部骨折	0(0.0)	1(0.6)
Radius fracture	橈骨骨折	0(0.0)	1(0.6)
Rib fracture	肋骨骨折	0(0.0)	1(0.6)
Subarachnoid haemorrhage	くも膜下出血	0(0.0)	1(0.6)
Coronary artery restenosis	冠動脈再狭窄	0(0.0)	1(0.6)
Upper limb fracture	上肢骨折	0(0.0)	1(0.6)

Note(s): MedDRA Version 20.1 and MedDRA/J Version 20.1.
Data Source: Listing 16.2.8.2
Source: t_14_3_1_4.sas

5.3.5.1—7 表 12.3.1—1 より引用

3)　中止に至った有害事象

MT-6548 群で中止に至った有害事象は，「薬疹」が 2 名，「肺炎」，「乳癌」，「胃癌」，「貧血」，「腎性貧血」，「脳梗塞」，「冷汗」，「胸部不快感」及び「ヘモグロビン減少」が各 1 名であった．そのうち「冷汗」及び「胸部不快感」は同一被験者で認められた．darbepoetin 群で中止に至った有害事象は，「脳梗塞」が 2 名，「末梢動脈瘤破裂」及び「大腿骨頚部骨折」が各 1 名であった．

MT-6548 群で中止に至った有害事象の詳細を下記に示した．「薬疹」のうち被験者識別コード J305501 で認められた事象は軽度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は未回復であった．被験者識別コード J311102 で認められた「薬疹」は，軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった．「肺炎」は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は死亡であった．「乳癌」は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は不明であったが，治験中止から 31 日後に死亡（報告事象名：突然死）が報告された．「胃癌」は，軽度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は軽快であった．「貧血」は，軽度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった．「腎性貧血」は中等度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった．「脳梗塞」は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復したが後遺症ありであった．「冷汗」及び「胸部不快感」は同一の被験者で発現し，どちらも軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった．「ヘモグロビン減少」は中等度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった．

darbepoetin 群で中止に至った有害事象の詳細を下記に示した．「脳梗塞」のうち被験者識別コード J303211 に認められた事象は，中等度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復したが後遺症ありであった．「脳梗塞」のうち被験者識別コード J314803 に認められた事象は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は未回復であった．「末梢動脈瘤破裂」は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は死亡であった．「大腿骨頚部骨折」は，高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は軽快であった．

4)　休薬又は減量に至った有害事象

MT-6548 群で休薬又は減量に至った有害事象は，「下痢」が 3 名（休薬 2 名，減量 1 名），「肝嚢胞感染」，「高カリウム血症」，「ミオクローヌス」，「傾眠」，「口内炎」及び「胆管炎」が各 1 名（休薬），「胃腸炎」及び「腹部不快感」が各 1 名（減量）であった．そのうち「肝嚢胞感染」及び「胆管炎」は同一被験者で認められた．darbepoetin 群で休薬又は減量に至った有害事象は，「細菌性肺炎」，「真菌性眼内炎」，「小脳梗塞」及び「へ

モグロビン増加」が各 1 名（休薬）であった.

MT-6548 群で休薬に至った有害事象の詳細を下記に示した.「下痢」のうち被験者識別コード J303212 に認められた事象は，軽度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「下痢」のうち被験者識別コード J311308 に認められた事象は，中等度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は治療期間 I 期で未回復であり治療期間 II 期に移行した.「肝嚢胞感染」及び「胆管炎」は同一の被験者で発現し，どちらも高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「高カリウム血症」は,中等度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「ミオクローヌス」は，軽度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「傾眠」は，軽度，非重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「口内炎」は軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった.

darbepoetin 群で休薬に至った有害事象の詳細を下記に示した.「細菌性肺炎」は高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「真菌性眼内炎」は高度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は軽快であった.「小脳梗塞」は中等度，重篤，治験薬との因果関係は合理的な可能性なしと判断され，転帰は回復であった.「ヘモグロビン増加」は軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった.

MT-6548 群で減量に至った有害事象の詳細を下記に示した.「下痢」は，軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は治療期間 I 期で未回復であり治療期間 II 期に移行した.「胃腸炎」は，軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった.「腹部不快感」は軽度，非重篤，治験薬との因果関係は合理的な可能性ありと判断され，転帰は回復であった.

darbepoetin 群で減量に至った有害事象は認められなかった.

(4) 臨床検査値の評価

1) 治験期間を通しての臨床検査値

中性脂肪は MT-6548 群でベースライン以降上昇し，12 週後に最大値を示し，その平均値±SD 及びベースラインからの変化量の平均値±SD は 153.115±93.692 mg/dL 及び 38.831±57.719 mg/dL であり，その後も同程度で推移した．darbepoetin 群では，大きな変動を示さなかった.

上記以外に顕著な変動を示した臨床検査値はなかった.

2) 個々の臨床的に重要な異常

SOC「臨床検査」のうち，臨床検査値の異常に関連する有害事象は，MT-6548 群では「アスパラギン酸アミノトランスフェラーゼ増加」,「C-反応性蛋白増加」,「ヘモグロビ

ン減少」,「前立腺特異性抗原増加」,「血清フェリチン減少」及び「トランスフェリン飽和度低下」が各 1 名であり，darbepoetin 群では「血中副甲状腺ホルモン増加」が 2 名，「血中カルシウム減少」,「カルニチン減少」,「γ−グルタミルトランスフェラーゼ増加」,「ヘモグロビン増加」及び「血中アルカリホスファターゼ増加」が各 1 名であった．SOC「代謝および栄養障害」のうち MT-6548 群で「高カリウム血症」が 1 名に認められた．

また，VEGF がベースラインより後に 200 pg/mL 以上かつベースライン値の 2 倍以上となった被験者は MT-6548 群で 5 名，darbepoetin 群で 1 名であったが，これらの被験者において SOC「眼障害」及び SOC「良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む)」に該当する有害事象の発現は認められなかった．

3)　Hb 値が 12.0 g/dL 以上又は 13.0 g/dL 以上になった被験者の割合

治療期間 I 期中に Hb 値が 12.0 g/dL 以上又は 13.0 g/dL 以上になった被験者の割合の記述統計量を表 2.7.6.26－65 に示した．

治療期間 I 期中に Hb 値が 12.0 g/dL 以上になった被験者の割合は MT-6548 群で 17.9%（29 名），darbepoetin 群で 22.4%（36 名）であった．また，治療期間 I 期中に Hb 値が 13.0 g/dL 以上になった被験者の割合は MT-6548 群で 1.9%（3 名），darbepoetin 群で 2.5%（4 名）であった．

表 2.7.6.26－65　Hb 値が 12.0 g/dL 以上又は 13.0 g/dL 以上になった被験者の割合（安全性解析対象集団）

Criteria	Period	MT-6548(N=162)			darbepoetin(N=161)		
		N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb >=12.0 g/dL	Baseline	162	6 (3.7)	(1.37, 7.89)	161	9 (5.6)	(2.59, 10.35)
	Baseline < to <= Week 2	159	6 (3.8)	(1.40, 8.03)	160	10 (6.3)	(3.04, 11.19)
	Week 2 < to <= Week 4	153	5 (3.3)	(1.07, 7.46)	156	14 (9.0)	(4.99, 14.60)
	Week 4 < to <= Week 6	148	4 (2.7)	(0.74, 6.78)	152	12 (7.9)	(4.15, 13.38)
	Week 6 < to <= Week 8	152	8 (5.3)	(2.30, 10.11)	158	10 (6.3)	(3.06, 11.33)
	Week 8 < to <= Week 10	148	5 (3.4)	(1.11, 7.71)	155	13 (8.4)	(4.54, 13.92)
	Week 10 < to <= Week 12	143	10 (7.0)	(3.40, 12.48)	155	8 (5.2)	(2.25, 9.92)
	Week 12 < to <= Week 16	135	8 (5.9)	(2.59, 11.34)	147	7 (4.8)	(1.94, 9.57)
	Week 16 < to <= Week 20	135	9 (6.7)	(3.09, 12.28)	152	7 (4.6)	(1.87, 9.26)
	Week 20 < to <= Week 24	141	10 (7.1)	(3.45, 12.66)	153	9 (5.9)	(2.72, 10.87)
	Baseline < to <= Week 24	162	29 (17.9)	(12.33, 24.69)	161	36 (22.4)	(16.18, 29.59)
Hb >=13.0 g/dL	Baseline	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)
	Baseline < to <= Week 2	159	0 (0.0)	(0.00, 2.29)	160	0 (0.0)	(0.00, 2.28)
	Week 2 < to <= Week 4	153	0 (0.0)	(0.00, 2.38)	156	0 (0.0)	(0.00, 2.34)
	Week 4 < to <= Week 6	148	1 (0.7)	(0.02, 3.71)	152	0 (0.0)	(0.00, 2.40)
	Week 6 < to <= Week 8	152	1 (0.7)	(0.02, 3.61)	158	1 (0.6)	(0.02, 3.48)
	Week 8 < to <= Week 10	148	0 (0.0)	(0.00, 2.46)	155	2 (1.3)	(0.16, 4.58)
	Week 10 < to <= Week 12	143	1 (0.7)	(0.02, 3.83)	155	0 (0.0)	(0.00, 2.35)
	Week 12 < to <= Week 16	135	0 (0.0)	(0.00, 2.70)	147	1 (0.7)	(0.02, 3.73)
	Week 16 < to <= Week 20	135	1 (0.7)	(0.02, 4.06)	152	0 (0.0)	(0.00, 2.40)
	Week 20 < to <= Week 24	141	2 (1.4)	(0.17, 5.03)	153	1 (0.7)	(0.02, 3.59)
	Baseline < to <= Week 24	162	3 (1.9)	(0.38, 5.32)	161	4 (2.5)	(0.68, 6.24)

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.4.1
Source: t_14_3_6_1.sas

5.3.5.1—7 表 12.4.3—1 より引用

4)　Hb 値が 9.0 g/dL 未満又は 8.0 g/dL 未満になった被験者の割合

治療期間 I 期中に Hb 値が 9.0 g/dL 未満又は 8.0 g/dL 未満になった被験者の割合の記述統計量を表 2.7.6.26－66 に示した.

治療期間 I 期中に Hb 値が 9.0 g/dL 未満になった被験者の割合は, MT-6548 群で 21.0%（34 名）, darbepoetin 群で 4.3%（7 名）であった. また, 治療期間 I 期中に Hb 値が 8.0 g/dL 未満になった被験者の割合は, MT-6548 群で 4.3%（7 名）, darbepoetin 群で 0.6%（1 名）であった.

表 2.7.6.26－66　Hb 値が 9.0 g/dL 未満又は 8.0 g/dL 未満になった被験者の割合（安全性解析対象集団）

Criteria	Period	MT-6548(N=162)			darbepoetin(N=161)		
		N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb <9.0 g/dL	Baseline	162	1 (0.6)	(0.02, 3.39)	161	1 (0.6)	(0.02, 3.41)
	Baseline < to <= Week 2	159	3 (1.9)	(0.39, 5.41)	160	1 (0.6)	(0.02, 3.43)
	Week 2 < to <= Week 4	153	5 (3.3)	(1.07, 7.46)	156	1 (0.6)	(0.02, 3.52)
	Week 4 < to <= Week 6	148	13 (8.8)	(4.76, 14.55)	152	0 (0.0)	(0.00, 2.40)
	Week 6 < to <= Week 8	152	14 (9.2)	(5.13, 14.97)	158	0 (0.0)	(0.00, 2.31)
	Week 8 < to <= Week 10	148	14 (9.5)	(5.27, 15.36)	155	0 (0.0)	(0.00, 2.35)
	Week 10 < to <= Week 12	143	17 (11.9)	(7.08, 18.35)	155	1 (0.6)	(0.02, 3.54)
	Week 12 < to <= Week 16	135	8 (5.9)	(2.59, 11.34)	147	1 (0.7)	(0.02, 3.73)
	Week 16 < to <= Week 20	135	6 (4.4)	(1.65, 9.42)	152	2 (1.3)	(0.16, 4.67)
	Week 20 < to <= Week 24	141	9 (6.4)	(2.96, 11.77)	153	2 (1.3)	(0.16, 4.64)
	Baseline < to <= Week 24	162	34 (21.0)	(14.99, 28.07)	161	7 (4.3)	(1.77, 8.75)
Hb <8.0 g/dL	Baseline	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)
	Baseline < to <= Week 2	159	0 (0.0)	(0.00, 2.29)	160	1 (0.6)	(0.02, 3.43)
	Week 2 < to <= Week 4	153	1 (0.7)	(0.02, 3.59)	156	0 (0.0)	(0.00, 2.34)
	Week 4 < to <= Week 6	148	3 (2.0)	(0.42, 5.81)	152	0 (0.0)	(0.00, 2.40)
	Week 6 < to <= Week 8	152	1 (0.7)	(0.02, 3.61)	158	0 (0.0)	(0.00, 2.31)
	Week 8 < to <= Week 10	148	3 (2.0)	(0.42, 5.81)	155	0 (0.0)	(0.00, 2.35)
	Week 10 < to <= Week 12	143	3 (2.1)	(0.43, 6.01)	155	0 (0.0)	(0.00, 2.35)
	Week 12 < to <= Week 16	135	1 (0.7)	(0.02, 4.06)	147	0 (0.0)	(0.00, 2.48)
	Week 16 < to <= Week 20	135	0 (0.0)	(0.00, 2.70)	152	0 (0.0)	(0.00, 2.40)
	Week 20 < to <= Week 24	141	1 (0.7)	(0.02, 3.89)	153	0 (0.0)	(0.00, 2.38)
	Baseline < to <= Week 24	162	7 (4.3)	(1.75, 8.70)	161	1 (0.6)	(0.02, 3.41)

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.4.1
Source: t_14_3_8_2.sas

5.3.5.1—7 表 12.4.4—1 より引用

5)　Hb 値の上昇速度が 0.5 g/dL/week 超になった被験者の割合

治療期間 I 期中に Hb 値の上昇速度が 0.5 g/dL/week 超になった被験者の割合の記述統計量を表 2.7.6.26－67 に示した.

MT-6548 群，darbepoetin 群ともに治療期間 I 期中に Hb 値の上昇速度が 0.5 g/dL/week 超になった被験者は認められなかった.

表 2.7.6.26－67　Hb 値の上昇速度が 0.5 g/dL/week 超になった被験者の割合（安全性解析対象集団）

Criteria	Visit	MT-6548(N=162)			darbepoetin(N=161)		
		N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Increase of >0.5 g/dL/week in Hb	Week 4	157	0 (0.0)	(0.00, 2.32)	159	0 (0.0)	(0.00, 2.29)
	Week 8	151	0 (0.0)	(0.00, 2.41)	156	0 (0.0)	(0.00, 2.31)
	Week 12	148	0 (0.0)	(0.00, 2.46)	157	0 (0.0)	(0.00, 2.32)
	Week 16	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)
	Week 20	140	0 (0.0)	(0.00, 2.60)	154	0 (0.0)	(0.00, 2.37)
	Week 24	138	0 (0.0)	(0.00, 2.64)	153	0 (0.0)	(0.00, 2.38)
	Baseline < to <= Week 24	157	0 (0.0)	(0.00, 2.32)	159	0 (0.0)	(0.00, 2.29)

Note(s): N*: number of subjects at each visit.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.4.1
Source: t_14_3_9_1.sas

5.3.5.1—7 表 12.4.5—1 より引用

6)　減量・休薬前後の Hb 値

治験薬の減量・休薬時及びその 4 週後に最も近い Hb 値と，その前後間の Hb 値の変化量の記述統計量を表 2.7.6.26－68 に示した．

治験薬の減量・休薬時及びその 4 週後に最も近い時点の Hb 値の平均値±SD は，MT-6548 群でそれぞれ 11.85±0.55 g/dL 及び 11.31±0.84 g/dL，その間の Hb 値の変化量の平均値±SD は -0.55±0.65 g/dL であった．darbepoetin 群ではそれぞれ 11.83±0.52 g/dL 及び 11.26±0.69 g/dL，その間の Hb 値の変化量の平均値±SD は -0.59±0.63 g/dL であった．

表 2.7.6.26－68　減量，休薬前後の Hb 値の記述統計量（安全性解析対象集団）

Parameter(unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Hb (g/dL)	At interruption or dose reduction	MT-6548	70	11.86	0.55	11.80	(10.0, 13.3)	(11.72, 11.96)
		darbepoetin	126	11.83	0.52	11.80	(9.5, 13.2)	(11.74, 11.93)
	4 weeks after interruption or dose reduction	MT-6548	62	11.31	0.84	11.30	(8.7, 13.2)	(11.10, 11.53)
		darbepoetin	119	11.26	0.69	11.30	(9.3, 12.9)	(11.14, 11.39)
	Difference of Hb	MT-6548	62	-0.55	0.65	-0.55	(-1.9, 1.0)	(-0.72, -0.39)
		darbepoetin	119	-0.59	0.63	-0.60	(-2.5, 1.0)	(-0.70, -0.47)
Interval (days)		MT-6548	62	30.37	4.37	29.00	(22.0, 43.0)	(29.26, 31.48)
		darbepoetin	119	29.34	3.47	29.00	(16.0, 43.0)	(28.72, 29.97)

Note(s): N: Number interruption or dose reduction.
Note(s): Difference of Hb: difference of Hb between 2 time points (At interruption or dose reduction - 4 weeks after interruption or dose reduction).
Note(s): Interval (days): interval between 'At interruption or dose reduction' and '4 weeks after interruption or dose reduction'.
Data Source: Listing 16.2.4.1
Source: t_14_3_10_1.sas

5.3.5.1—7 表 12.4.6—1 より引用

(5) バイタルサイン，身体的所見及び安全性に関連する他の観察項目

1) 安静時標準 12 誘導心電図

判定結果がベースラインでは正常又は臨床的に問題とならない異常であったが，24 週後に臨床的に問題となる異常になった被験者は，MT-6548 群でそれぞれ 0.7%（1／138 名）及び 0%，darbepoetin 群で 0%及び 1.3%（2／153 名）であった．

2) 透析後体重及びドライウェイト

透析後体重の 24 週後のベースラインからの変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で 0.01±1.60 kg 及び 0.25±1.44 kg であった．ドライウェイトのベースラインから 24 週後の変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で 0.00±1.60 kg 及び 0.20±1.27 kg であった．

3) バイタルサイン

収縮期血圧の 24 週後のベースラインからの変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で 0.6±22.8 mmHg 及び 3.8±21.0 mmHg であった．拡張期血圧のベースラインから 24 週後の変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で -1.0±12.1 mmHg 及び 1.8±10.7 mmHg であった．脈拍のベースラインから 24 週後の変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で 2.2±9.0 beats/min 及び 0.4±8.2 beats/min であった．

4) 眼底検査

判定結果がスクリーニングでは正常又は臨床的に問題とならない異常であったが，20 週～24 週後に臨床的に問題となる異常になった被験者の割合は，MT-6548 群でそれぞれ 4.3%（6／140 名）及び 2.1%（3／140 名），darbepoetin 群で 2.6%（4／154 名）及び 2.6%（4／154 名）であった．

当該被験者で報告された SOC「眼障害」の有害事象は，MT-6548 群で「網膜出血」が 6 名，「糖尿病網膜症」が 2 名，「網膜浮腫」及び「硝子体浮遊物」が各 1 名，darbepoetin 群で「網膜出血」が 5 名，「黄斑浮腫」が 2 名，「網膜血管瘤」，「網膜血管障害」，「糖尿病網膜症」及び「霰粒腫」が各 1 名であった．

なお，SOC が「眼障害」の有害事象は，MT-6548 群で「網膜出血」が 10 名，「結膜出血」及び「糖尿病網膜症」が各 2 名，「白内障」，「眼乾燥」「眼充血」，「視神経乳頭出血」，「点状角膜炎」，「網膜浮腫」，「網膜静脈閉塞」，「睫毛乱生」，「硝子体浮遊物」，「眼そう痒症」，「嚢胞様黄斑浮腫」及び「眼瞼血腫」が各 1 名，darbepoetin 群で「網膜出血」が 5 名，「結膜出血」及び「黄斑浮腫」が各 2 名，「糖尿病網膜症」，「白内障」，「眼乾燥」，「眼充血」，「霰粒腫」，「アレルギー性結膜炎」，「眼瞼浮腫」，「網膜剥離」，「網膜血管障害」，「硝子体剥離」及び「網膜血管瘤」が各 1 名で認められた．MT-6548 群で 1 名に認められた「網膜浮腫」は合理的な可能性ありと判断され，程度は軽度，転帰は治療期間

I 期で未回復であり治療期間 II 期に移行した．なお，本被験者の VEGF はベースラインで 42.7 pg/mL，12 週後で 52.9 pg/mL，24 週後で 59.3 pg/mL と大きな変動は認められなかった．

5) 胸部 X 線検査

判定結果がスクリーニングでは正常又は臨床的に問題とならない異常であったが, 20 週～24 週後に臨床的に問題となる異常になった被験者は，MT-6548 群でそれぞれ 0.7%（1／139 名）及び 0%，darbepoetin 群で 0.6%（1／154 名）及び 0%であった．

6) 標準化透析量（以下，Kt/V）

Kt/V の 24 週後のベースラインからの変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で 0.0281±0.1673 及び 0.0085±0.2824 であった．

7) 安全性に関する部分集団解析

有害事象及び副作用の発現割合に関して, 特筆すべき差のある部分集団は認められなかった．

2.7.6.26.2.2 結論

(1) 有効性

主要評価項目である MMRM を用いた 20 週後及び 24 週後の平均 Hb 値の LSMean 及びその 95%CI は，MT-6548 群で 10.61 g/dL 及び 10.45～10.76 g/dL，darbepoetin 群で 10.65 g/dL 及び 10.50～10.80 g/dL であり，いずれの群においても治療期間 20 週及び 24 週後の平均 Hb 値の 95%CI は，目標範囲内（10.0 g/dL 以上 12.0 g/dL 未満）であった．

また, MMRM を用いた 20 週及び 24 週後の平均 Hb 値の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は -0.05 g/dL 及び -0.26～0.17 g/dL であった. 群間差（MT-6548 群 －darbepoetin 群）の 95%CI の下限が -0.75 g/dL 以上であったため，MT-6548 群の darbepoetin 群に対する非劣性が検証された．

MT-6548 群に関して，Hb 値の平均値は，ESA 製剤からの切り替え直後に急な変動なく推移し，24 週間にわたり目標範囲内で維持した．

24 週後に Hb 値が目標範囲内の被験者の割合は，MT-6548 群で 75.4%であった．

以上より，MT-6548 の ESA 製剤からの切替え維持効果が確認された．

MMRM を用いた 24 週後のベースラインからの変化量に関して [redacted] は MT-6548 群で darbepoetin 群と比較して統計学的に有意に[redacted]し，[redacted]，MCV 及び MCH は MT-6548 群で darbepoetin 群と比較して統計学的に有意に[redacted]した．MT-6548 群で darbepoetin 群と比較して[redacted]の[redacted]及び[redacted]の[redacted]が認められたことから，MT-6548 により[redacted]が[redacted]する可能性が考えられ，MCV 及び MCH の上昇は当該[redacted]の[redacted]を

反映している可能性が考えられた.

MT-6548 群の EPO の 2～24 週後の最大値は 312.0 mIU/mL であり，生理学的な変動の範囲内であった.

(2) 安全性

有害事象の発現割合は MT-6548 群と darbepoetin 群で同程度であり，副作用の発現割合は，darbepoetin 群と比較して MT-6548 群で高かった.

有害事象のうち，MT-6548 群で発現割合が 20%以上の有害事象の SOC は,「感染症および寄生虫症」,「胃腸障害」,「傷害、中毒および処置合併症」,「筋骨格系および結合組織障害」及び「皮膚および皮下組織障害」であった．これらの SOC のうち，darbepoetin 群と比較して 10%以上高かった SOC は,「皮膚および皮下組織障害」であった．副作用のうち，MT-6548 群で発現割合が 20%以上の SOC は認められなかった．MT-6548 群で発現割合が最も高い副作用の SOC は「胃腸障害」であった.

MT-6548 群で最も発現割合の高い SOC「感染症および寄生虫症」のうち，MT-6548 群で発現した主な有害事象は「上咽頭炎」であった．darbepoetin 群と比較して発現割合の高かった SOC「皮膚および皮下組織障害」の有害事象の内訳の発現割合に特定の傾向は認められなかった.

MT-6548 群で発現割合が 5%以上の有害事象は,「上咽頭炎」,「下痢」,「シャント狭窄」,「挫傷」,「網膜出血」及び「頭痛」であった．これらの事象のうち，darbepoetin 群と比較して 3%以上高かった有害事象は,「網膜出血」及び「頭痛」であった．MT-6548 群で発現割合が 5%以上の副作用は認められなかった．MT-6548 群で発現割合が最も高かった副作用は,「下痢」続いて「悪心」であった．本治験では，副作用が darbepoetin 群と比較して MT-6548 群に多く認められたが, 個々の副作用の発現割合に両群で大きな差は認められなかった.

発現割合が 10%以上の有害事象かつ MT-6548 群で副作用としての発現割合が高かった「下痢」，MT-6548 群で「下痢」に次いで発現割合の高かった副作用である「悪心」，darbepoetin 群と比較して発現割合の高かった有害事象「網膜出血」及び「頭痛」に関して，下記に詳細を示した.

「下痢」は，MT-6548 群で有害事象の発現割合が 10%以上であり，副作用の発現割合が最も高い事象であったが，有害事象及び副作用の発現割合は両群で同程度であった．MT-6548 群で発現した「下痢」のうち 1 名は中等度，それ以外の 16 名は軽度と判断され，因果関係が合理的な可能性ありのものは 4 名に認められた．転帰は 4 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，それ以外の 13 名は回復であった．「下痢」に次いで MT-6548 群で副作用の発現割合が高かった「悪心」の有害事象の発現割合は MT-6548 群で darbepoetin 群よりも高かったが，副作用の発現割合は両群で同程度であった．MT-6548 群で発現した「悪心」のうち 1 名は中等度，それ以外の 5 名は軽度と判断され，因果関係は 3 名が合理的な可能性ありと判断され, 転帰は 1 名が治療期間 I 期で未回復であり治療

期間 II 期に移行し，それ以外の 5 名はすべて回復であった．「網膜出血」は MT-6548 群の有害事象の発現割合が darbepoetin 群よりも高かった．MT-6548 群で発現した「網膜出血」はすべて軽度，治験薬との因果関係は合理的な可能性なしと判断され，転帰は 9 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，1 名は「貧血」で中止となり，「網膜出血」の転帰は未回復であった．なお，MT-6548 群で「網膜出血」が発現した被験者の VEGF に顕著な変動は認められなかった．「頭痛」は MT-6548 群の有害事象の発現割合が darbepoetin 群よりも高かった．MT-6548 群で発現した「頭痛」はすべて軽度，因果関係は合理的な可能性なしと判断された．転帰は 3 名が治療期間 I 期で未回復であり治療期間 II 期に移行し，それ以外の 6 名はすべて回復であった．

MT-6548 群で，1 名に「肺炎」による死亡が，darbepoetin 群で 1 名に「末梢動脈瘤破裂」による死亡が認められた．いずれの事象も治験薬との因果関係は合理的な可能性なしと判断された．なお，MT-6548 群で，治験中止から 31 日後に死亡（報告事象名：突然死）が 1 名で報告された．

重篤な有害事象の発現割合は，両群で大きな差は認められなかった．MT-6548 群で 2 名以上に認められた重篤な有害事象は，「肺炎」，「シャント閉塞」，「胃腸炎」及び「シャント狭窄」であった．重篤な有害事象は，特定の事象が多く発現する傾向は認められなかった．なお，重篤な副作用は，両群で認められなかった．

MT-6548 群で中止に至った有害事象は，「薬疹」が 2 名，「肺炎」，「乳癌」，「胃癌」，「貧血」，「腎性貧血」，「脳梗塞」，「冷汗」，「胸部不快感」及び「ヘモグロビン減少」が各 1 名であった．そのうち「冷汗」及び「胸部不快感」は同一被験者で認められた．darbepoetin 群で中止に至った有害事象は，「脳梗塞」が 2 名，「末梢動脈瘤破裂」及び「大腿骨頚部骨折」が各 1 名であった．中止に至った有害事象は MT-6548 群で多く認められたが，特定の事象に偏っていなかった．

MT-6548 群で休薬に至った有害事象は，「下痢」が 2 名，「肝嚢胞感染」，「高カリウム血症」，「ミオクローヌス」，「傾眠」，「口内炎」及び「胆管炎」が各 1 名であった．そのうち「肝嚢胞感染」及び「胆管炎」は同一被験者で認められた．darbepoetin 群で休薬に至った有害事象は，「細菌性肺炎」，「真菌性眼内炎」，「小脳梗塞」及び「ヘモグロビン増加」が各 1 名であった．MT-6548 群で減量に至った有害事象は「下痢」，「腹部不快感」及び「胃腸炎」が各 1 名であった．darbepoetin 群で減量に至った有害事象は認められなかった．休薬又は減量に至った有害事象は MT-6548 群で多く認められたが，特定の事象に偏っていなかった．

治療期間 I 期で，MT-6548 群で治療期間が長くなるに従って有害事象の発現割合が高くなる傾向は認められなかった．

MT-6548 群の投与量又は累積投与量が高くなるに従って有害事象の発現割合が高くなる傾向は認められなかった．

MT-6548 群は休薬前後で有害事象の発現割合に大きな差は認められなかった．

治療期間 I 期中に変動があった臨床検査値は，中性脂肪であったが，臨床的に問題とな

る顕著な変動は認められなかった．また，VEGF がベースライン以降に 200 pg/mL 以上かつベースライン値の 2 倍以上となった被験者は MT-6548 群で 5 名，darbepoetin 群で 1 名であったが，これらの被験者において SOC「眼障害」及び SOC「良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む)」に該当する有害事象の発現は認められなかった．

治療期間 I 期中に透析後体重，ドライウェイト及びバイタルサインは特に臨床的に問題となる異常は認められなかった．安静時標準 12 誘導心電図，胸部 X 線検査に関して，判定結果がベースラインでは正常又は臨床的に問題とならない異常であったが，20 週～24 週後に臨床的に問題となる異常になった被験者の割合は両群で同程度であった．

眼底検査に関して，判定結果がスクリーニングでは正常又は臨床的に問題とならない異常であったが，20 週～24 週後に臨床的に問題となる異常になった被験者の割合は，両群で同程度であった．当該被験者で報告された SOC「眼障害」の有害事象は，MT-6548 群で「網膜出血」が 6 名，「糖尿病網膜症」が 2 名，「網膜浮腫」及び「硝子体浮遊物」が各 1 名，darbepoetin 群で「網膜出血」が 5 名，「黄斑浮腫」が 2 名，「網膜血管瘤」，「網膜血管障害」，「糖尿病網膜症」及び「霰粒腫」が各 1 名であった．MT-6548 群の「網膜浮腫」1 名は治験薬との因果関係が合理的な可能性ありと判断され，程度は軽度，転帰は治療期間 I 期で未回復であり治療期間 II 期に移行した．なお，本被験者の VEGF に大きな変動は認められなかった．

本治験で設定した MT-6548 の初回用量及び維持用量で Hb 値の過剰な上昇，過度な低下及び急速な上昇は起こしにくいと考えられた．また，Hb 値が必要以上に上昇した際に，MT-6548 を休薬又は減量することにより，Hb 値を目標範囲内にコントロールしやすいと考えられた．

以上の結果から，本治験では治験薬投与による安全性への大きな懸念は認められなかった．

(3)　全般的な結論

血液透析を実施中の慢性腎臓病に伴う貧血患者を対象に，MT-6548 を初回用量 300 mg/日，維持用量 150～600 mg/日で投与した．その結果，20 週及び 24 週後の平均 Hb 値に対して，MT-6548 群の darbepoetin 群に対する非劣性が検証された．MT-6548 は良好な Hb 値のコントロールが可能であり，MT-6548 の血液透析を実施中の慢性腎臓病に伴う貧血患者に対する貧血治療効果が確認された．更に，鉄関連指標等の推移より，MT-6548 が[redacted]を[redacted]することが示唆された．

安全性に関して，MT-6548 の投与による安全性に関する大きな懸念は認められなかった．

以上の結果から，MT-6548 は血液透析を実施中の慢性腎臓病に伴う貧血患者に対して，有効かつ安全に使用できると考えられた．

2.7.6.26.3　最終固定データ

2.7.6.26.3.1　結果の要約

2.7.6.26.3.1.1　被験者の内訳

被験者の内訳を図 2.7.6.26－24 に示した.

同意登録被験者数は 475 名であり，そのうち 152 名が治療期間移行前に脱落し，323 名が MT-6548 群又は darbepoetin 群に割付けられた. 各群の被験者数は MT-6548 群 162 名, darbepoetin 群 161 名であった．治療期間 I 期を完了した被験者は MT-6548 群で 136 名，darbepoetin 群で 152 名であり，治療期間を完了した被験者は MT-6548 群で 120 名，darbepoetin 群で 135 名であった．治療期間に中止した被験者は MT-6548 群で 42 名（治療期間 I 期 26 名，治療期間 II 期 16 名），darbepoetin 群で 26 名（治療期間 I 期 9 名，治療期間 II 期 17 名）であった.

治療期間に中止した被験者の割合及び理由を表 2.7.6.26－69，休薬に至った理由を表 2.7.6.26－70 に示した.

治療期間に中止した被験者の割合は，MT-6548 群 25.9%（42／162 名），darbepoetin 群 16.1%（26／161 名）であった. 中止理由は,「被験者からの申し入れ」が MT-6548 群 14 名, darbepoetin 群 4 名,「有害事象」が MT-6548 群 16 名，darbepoetin 群 12 名,「24 週後の規定検査終了前の救済治療の実施」が MT-6548 群 2 名，darbepoetin 群 1 名,「過粘稠度症候群又は Hb 値コントロール困難」が MT-6548 群 10 名，darbepoetin 群 2 名,「腎移植の実施」が MT-6548 群 0 名，darbepoetin 群 2 名及び「その他，治験責任（分担）医師判断」が MT-6548 群 0 名，darbepoetin 群 5 名であった．中止理由が「過粘稠度症候群又は Hb 値コントロール困難」の MT-6548 群 10 名の中止時の Hb 値は 6.6 g/dL，7.4 g/dL，8.4 g/dL，8.5 g/dL，9.4 g/dL，9.9 g/dL，10.3 g/dL，11.2 g/dL，12.7 g/dL 及び 13.0 g/dL であった．なお，有害事象として過粘稠度症候群は認められなかった.

治療期間中の休薬は MT-6548 群 53 回，darbepoetin 群 39 回であり，休薬理由は,「Hb 値の推移」が MT-6548 群で 21 回，darbepoetin 群で 6 回,「用量調節アルゴリズムに準じた休薬」が MT-6548 群 16 回，darbepoetin 群 18 回,「有害事象」が MT-6548 群で 15 回，darbepoetin 群で 11 回,「肝機能値異常」が MT-6548 群で 0 回，darbepoetin 群で 1 回，及び「その他」が MT-6548 群で 4 回，darbepoetin 群 3 回であった.

有効性の解析対象集団は FAS とした．安全性の解析は，安全性解析対象集団を対象に行った.

各解析対象集団に含まれる被験者の内訳を表 2.7.6.26－71 に示した.

治療期間に移行した 323 名（MT-6548 群 162 名，darbepoetin 群 161 名）すべてを FAS 及び安全性解析対象集団とした.

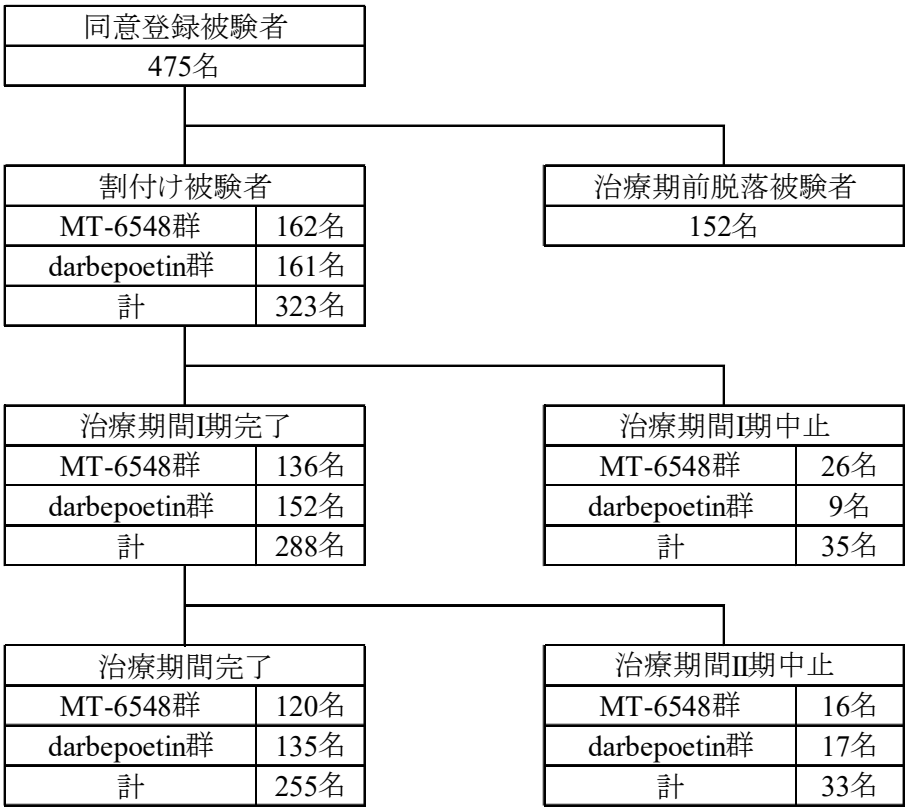


図 2.7.6.26－24　被験者の内訳

5.3.5.1—9 図 10.1—1 より引用

表 2.7.6.26－69　治療期間に中止した被験者の割合及び理由（治療期間移行例）

	Statistic	MT-6548 (N=162)	darbepoetin (N=161)
Subject discontinued during treatment period	n (%)	42 (25.9)	26 (16.1)
Primary reason for discontinuation			
Subject withdrawal of consent	n (%)	14 (8.6)	4 (2.5)
Inappropriate for participating in the study	n (%)	0 (0.0)	0 (0.0)
Adverse Events	n (%)	16 (9.9)	12 (7.5)
Hepatic function abnormalities	n (%)	0 (0.0)	0 (0.0)
Conducting rescue therapy before completing the scheduled examinations at Week 24	n (%)	2 (1.2)	1 (0.6)
Hyperviscosity syndrome, difficult to control of Hb within target range	n (%)	10 (6.2)	2 (1.2)
No longer require hemodialysis or hemodiafiltration treatment	n (%)	0 (0.0)	0 (0.0)
Initiation of a renal transplant	n (%)	0 (0.0)	2 (1.2)
Proven to be pregnant	n (%)	0 (0.0)	0 (0.0)
Other, Investigator discretion	n (%)	0 (0.0)	5 (3.1)

Data Source: Listing 16.2.1.4
Source: t_14_1_2_1.sas

5.3.5.1—9 表 10.1—1 より引用

表 2.7.6.26－70　休薬に至った理由（治療期間移行例）

	Statistic	MT-6548 (N=162)	darbepoetin (N=161)
Number of study drug interruption during treatment period	N*	53	39
Based on dose adjustment algorithm	n (%)	16 (30.2)	18 (46.2)
Not based on dose adjustment algorithm	n (%)	37 (69.8)	21 (53.8)
Adverse events	n (%)	15 (28.3)	11 (28.2)
Hepatic function abnormalities	n (%)	0 (0.0)	1 (2.6)
Decreased body fluid volume	n (%)	0 (0.0)	0 (0.0)
Increased body fluid volume	n (%)	0 (0.0)	0 (0.0)
Change of Hb	n (%)	21 (39.6)	6 (15.4)
Treated with maximum or minimum dose	n (%)	0 (0.0)	0 (0.0)
Other	n (%)	4 (7.5)	3 (7.7)

Note(s): N*: total number of interruption of study drug in each treatment group.
Note(s): Percentages are based on the total number of interruption of study drug in each treatment group.
Note(s): When there were plural reasons for one interruption, all reasons were counted.
Data Source: Listing 16.2.3.4
Source: t_14_1_2_3.sas

5.3.5.1—9 表 10.1—2 より引用

表 2.7.6.26－71　各解析対象集団に含まれる被験者の内訳（治療期間移行例）

	Statistic	MT-6549	darbepoetin
Subjects enrolled in Treatment Period	N	162	161
Subjects completed	n (%)	120 (74.1)	135 (83.9)
Subjects withdrawn	n (%)	42 (25.9)	26 (16.1)
Subjects received rescue therapy	n (%)	14 (8.6)	7 (4.3)
Subjects in FAS	n (%)	162 (100.0)	161 (100.0)
Subjects excluded from FAS	n (%)	0 (0.0)	0 (0.0)
Subjects in Safety Analysis Set	n (%)	162 (100.0)	161 (100.0)
Subjects excluded from Safety Analysis Set	n (%)	0 (0.0)	0 (0.0)

Data Source: Listing 16.2.1.1, Listing 16.2.2.1, Listing 16.2.2.9, Listing 16.2.2.10, Listing 16.2.2.11
Source: t_14_1_1_1.sas

5.3.5.1—9 表 11.1—1 より引用

2.7.6.26.3.1.2 被験者背景

FAS の人口統計学的及び他の基準値の特性については，治療期間 24 週固定データ解析時の「2.7.6.26.2.1.2　被験者背景」と同一であった.

2.7.6.26.3.1.3　有効性

(1)　服用遵守割合

FAS の治療期間における MT-6548 錠 150 mg 及びダルベポエチンアルファ注実薬の服用／投与遵守割合を表 2.7.6.26－72 に示した.

MT-6548 群の服用遵守割合の平均値±SD は 98.76±2.92%，darbepoetin 群の投与遵守割合の平均値±SD は 99.84±0.85%であった.

表 2.7.6.26－72　治験薬の服用／投与遵守割合（FAS）

	Statistic	MT-6548 (N=162)	darbepoetin (N=161)
Compliance (%)	Mean	98.76	99.84
	SD	2.92	0.85
	Median	99.86	100.00
	Minimum, Maximum	(72.7, 100.0)	(90.4, 100.0)
Category			
<80%	n (%)	1 (0.6)	0 (0.0)
>=80%	n (%)	161 (99.4)	161 (100.0)

Data Source: Listing 16.2.3.3
Source: t_14_1_4_1_1.sas

5.3.5.1—9 表 11.3—1 より引用

(2)　貧血治療効果（切替え維持効果）

1)　48 週及び 52 週後の平均 Hb 値

MMRM を用いた 48 週及び 52 週後の平均 Hb 値を表 2.7.6.26－73 に示した．

MMRM を用いた 48 週及び 52 週後の平均 Hb 値の LSMean 及びその 95%CI は，MT-6548 群で 10.42 g/dL 及び 10.27～10.56 g/dL，darbepoetin 群で 10.62 g/dL 及び 10.49～10.76 g/dL であった．いずれの群も 48 週及び 52 週後の平均 Hb 値の 95%CI は目標範囲内（10.0 g/dL 以上 12.0 g/dL 未満）であった．

表 2.7.6.26－73　48 週及び 52 週後の平均 Hb 値（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 48 and Week 52	160	10.74 (0.72)	10.42	0.07	(10.27, 10.56)
darbepoetin	Week 48 and Week 52	160	10.74 (0.72)	10.62	0.07	(10.49, 10.76)
Difference MT-6548 - darbepoetin	Week 48 and Week 52			-0.20	0.10	(-0.40, -0.01)

Note(s): Hb (g/dL).
Note(s): N: number of subjects who was used in MMRM model (i.e. number of subjects with Hb at least one visit after baseline).
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect. (covariance matrix: unstructured)
Data Source: Listing 16.2.4.1
Source: t_14_2_1_2_1.sas

5.3.5.1—9 表 11.4.1—1 より引用

2)　Hb 値の推移

Hb 値の平均値の推移を図 2.7.6.26－25，Hb 値の記述統計量を表 2.7.6.26－74 に示した．また，MMRM を用いた Hb 値を表 2.7.6.26－75 に示した．

MT-6548 群，darbepoetin 群ともに Hb 値の平均値は ESA 製剤からの切り替え後に急な変動なく推移し，52 週間にわたり目標範囲内を維持した．

MMRM を用いた 52 週後の Hb 値の LSMean 及びその 95%CI は，MT-6548 群で 10.39 g/dL 及び 10.24～10.54 g/dL，darbepoetin 群で 10.62 g/dL 及び 10.48～10.76 g/dL であった．

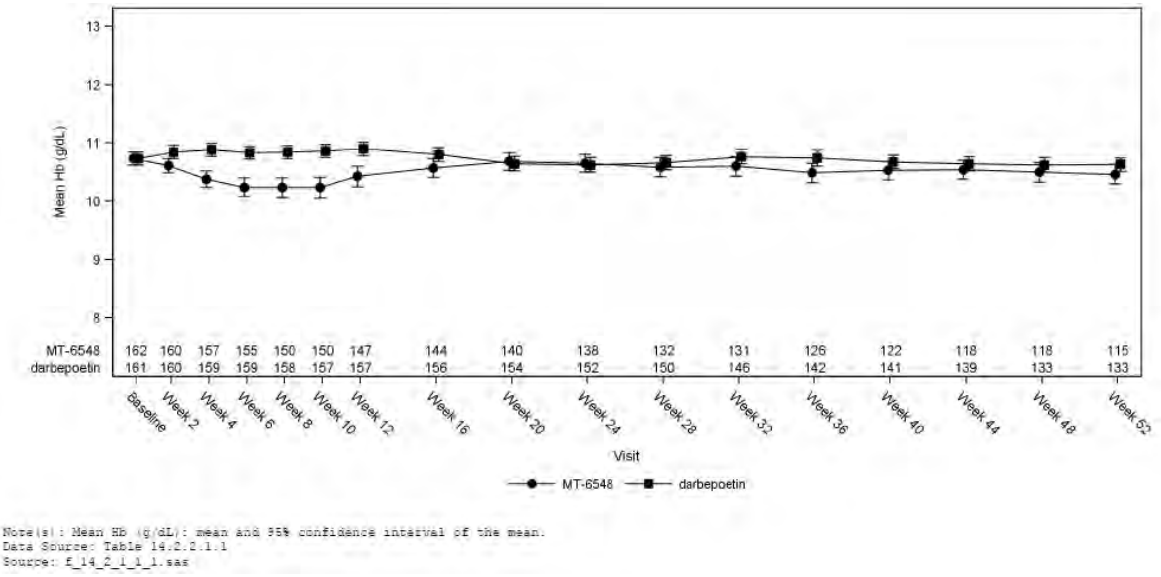


図 2.7.6.26－25　Hb 値の推移（FAS）

5.3.5.1—9 図 11.4.1—1 より引用

表 2.7.6.26－74　各評価時点の Hb 値の記述統計量（FAS）

		Absolute						Change from Baseline						
Treatment Group	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Baseline	162	10.73	0.73	10.65	(8.8, 12.6)	(10.62, 10.86)							
	Week 2	160	10.61	0.79	10.70	(8.3, 12.9)	(10.49, 10.73)	160	-0.13	0.55	-0.05	(-1.7, 1.3)	(-0.22, -0.05)	0.003
	Week 4	157	10.38	0.87	10.30	(7.7, 12.4)	(10.24, 10.52)	157	-0.37	0.80	-0.40	(-2.3, 1.3)	(-0.50, -0.24)	<0.001
	Week 6	155	10.24	0.97	10.10	(7.2, 13.2)	(10.09, 10.40)	155	-0.51	0.97	-0.40	(-3.2, 1.6)	(-0.66, -0.36)	<0.001
	Week 8	150	10.24	1.01	10.30	(6.8, 13.0)	(10.08, 10.40)	150	-0.51	1.12	-0.50	(-3.3, 2.6)	(-0.69, -0.33)	<0.001
	Week 10	150	10.24	1.07	10.30	(6.7, 12.8)	(10.06, 10.41)	150	-0.51	1.24	-0.45	(-3.7, 2.3)	(-0.71, -0.31)	<0.001
	Week 12	147	10.43	1.08	10.50	(7.4, 13.3)	(10.25, 10.61)	147	-0.32	1.30	-0.30	(-3.9, 3.7)	(-0.53, -0.11)	0.003
	Week 16	144	10.57	0.97	10.60	(7.5, 12.9)	(10.41, 10.73)	144	-0.17	1.25	-0.10	(-4.1, 2.6)	(-0.38, 0.04)	0.105
	Week 20	140	10.69	0.90	10.70	(8.3, 13.1)	(10.54, 10.84)	140	-0.04	1.13	0.00	(-2.9, 2.6)	(-0.23, 0.14)	0.644
	Week 24	138	10.65	0.92	10.70	(8.0, 13.3)	(10.50, 10.81)	138	-0.09	1.10	0.00	(-3.6, 2.3)	(-0.27, 0.10)	0.345
	Week 28	132	10.58	0.96	10.60	(7.8, 12.8)	(10.42, 10.75)	132	-0.15	1.13	-0.10	(-3.2, 2.8)	(-0.35, 0.04)	0.123
	Week 32	131	10.60	0.95	10.70	(7.6, 13.5)	(10.43, 10.76)	131	-0.13	1.09	0.00	(-3.4, 2.6)	(-0.32, 0.05)	0.161
	Week 36	126	10.49	0.95	10.60	(7.8, 13.4)	(10.32, 10.66)	126	-0.25	1.11	-0.20	(-3.8, 2.0)	(-0.44, -0.05)	0.013
	Week 40	122	10.53	0.87	10.50	(7.8, 12.7)	(10.37, 10.68)	122	-0.21	1.10	-0.20	(-3.6, 3.1)	(-0.40, -0.01)	0.040
	Week 44	118	10.54	0.90	10.70	(8.2, 12.6)	(10.38, 10.71)	118	-0.20	1.09	-0.10	(-3.4, 2.5)	(-0.40, 0.00)	0.049
	Week 48	118	10.50	0.92	10.50	(7.7, 12.5)	(10.33, 10.66)	118	-0.25	1.08	-0.10	(-3.9, 1.7)	(-0.44, -0.05)	0.015
	Week 52	115	10.47	0.87	10.50	(8.1, 13.4)	(10.30, 10.63)	115	-0.29	1.09	-0.30	(-3.6, 1.7)	(-0.49, -0.09)	0.005
	Week 52(LOCF)	161	10.24	1.06	10.30	(6.6, 13.4)	(10.08, 10.41)	161	-0.50	1.23	-0.40	(-3.9, 1.7)	(-0.69, -0.31)	<0.001

表 2.7.6.26－74　各評価時点の Hb 値の記述統計量（FAS）（続き）

		Absolute						Change from Baseline						
Treatment Group	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
darbepoetin	Baseline	161	10.73	0.72	10.70	(8.6, 12.3)	(10.62, 10.84)							
	Week 2	160	10.85	0.74	10.80	(9.1, 12.6)	(10.73, 10.96)	160	0.11	0.48	0.10	(-1.4, 1.4)	(0.03, 0.19)	-
	Week 4	159	10.88	0.71	10.80	(8.8, 12.9)	(10.77, 10.99)	159	0.15	0.57	0.10	(-1.5, 2.0)	(0.06, 0.24)	-
	Week 6	159	10.83	0.69	10.70	(9.4, 12.8)	(10.72, 10.94)	159	0.10	0.74	0.10	(-2.1, 2.0)	(-0.01, 0.22)	-
	Week 8	158	10.84	0.68	10.80	(9.4, 13.1)	(10.74, 10.95)	158	0.10	0.80	0.00	(-2.0, 2.3)	(-0.02, 0.23)	-
	Week 10	157	10.86	0.72	10.90	(9.5, 13.1)	(10.75, 10.98)	157	0.13	0.94	0.00	(-2.4, 3.2)	(-0.02, 0.28)	-
	Week 12	157	10.90	0.72	10.90	(8.5, 12.9)	(10.79, 11.01)	157	0.17	1.00	0.10	(-3.1, 3.0)	(0.01, 0.32)	-
	Week 16	156	10.80	0.76	10.80	(8.6, 13.2)	(10.68, 10.92)	156	0.06	1.17	0.00	(-2.9, 3.9)	(-0.12, 0.25)	-
	Week 20	154	10.65	0.81	10.60	(8.9, 12.5)	(10.52, 10.78)	154	-0.10	1.21	-0.10	(-3.0, 3.9)	(-0.29, 0.09)	-
	Week 24	152	10.63	0.77	10.70	(8.6, 13.3)	(10.50, 10.75)	152	-0.12	1.10	-0.10	(-2.5, 3.3)	(-0.29, 0.06)	-
	Week 28	150	10.66	0.75	10.70	(8.4, 12.6)	(10.54, 10.78)	150	-0.09	1.06	0.00	(-2.8, 2.7)	(-0.27, 0.08)	-
	Week 32	146	10.77	0.78	10.80	(8.3, 12.9)	(10.64, 10.89)	146	0.00	1.00	0.10	(-3.2, 2.3)	(-0.17, 0.16)	-
	Week 36	142	10.75	0.84	10.80	(8.2, 12.9)	(10.61, 10.88)	142	-0.03	1.08	0.00	(-3.7, 2.2)	(-0.21, 0.15)	-
	Week 40	141	10.67	0.70	10.70	(8.2, 13.0)	(10.56, 10.79)	141	-0.09	0.91	-0.10	(-2.5, 2.3)	(-0.24, 0.06)	-
	Week 44	139	10.64	0.71	10.70	(8.2, 12.3)	(10.52, 10.76)	139	-0.12	0.94	-0.10	(-2.5, 2.0)	(-0.28, 0.04)	-
	Week 48	133	10.63	0.71	10.60	(9.0, 12.4)	(10.50, 10.75)	133	-0.14	0.96	-0.20	(-2.7, 2.1)	(-0.30, 0.03)	-
	Week 52	133	10.63	0.66	10.60	(9.1, 12.7)	(10.52, 10.74)	133	-0.13	0.85	-0.10	(-2.4, 2.6)	(-0.29, 0.02)	-
	Week 52(LOCF)	161	10.61	0.76	10.60	(8.2, 12.7)	(10.49, 10.73)	161	-0.12	1.01	-0.10	(-3.7, 3.0)	(-0.28, 0.04)	-

Note(s): Hb (g/dL).
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_1_1.sas

5.3.5.1—9 表 14.2.2.1.1 より引用

表 2.7.6.26－75　各評価時点の Hb 値（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	10.74 (0.72)	10.61	0.07	(10.48, 10.74)
	Week 4	157	10.75 (0.73)	10.37	0.07	(10.24, 10.51)
	Week 6	155	10.75 (0.73)	10.23	0.07	(10.10, 10.37)
	Week 8	150	10.74 (0.73)	10.21	0.07	(10.08, 10.35)
	Week 10	150	10.75 (0.73)	10.21	0.07	(10.08, 10.35)
	Week 12	147	10.75 (0.73)	10.38	0.07	(10.24, 10.51)
	Week 16	144	10.74 (0.73)	10.50	0.07	(10.37, 10.64)
	Week 20	140	10.73 (0.73)	10.63	0.07	(10.49, 10.77)
	Week 24	138	10.74 (0.73)	10.59	0.07	(10.45, 10.73)
	Week 28	132	10.74 (0.74)	10.51	0.07	(10.37, 10.66)
	Week 32	131	10.73 (0.74)	10.53	0.07	(10.39, 10.67)
	Week 36	126	10.74 (0.74)	10.44	0.07	(10.30, 10.58)
	Week 40	122	10.74 (0.74)	10.47	0.07	(10.32, 10.61)
	Week 44	118	10.74 (0.74)	10.47	0.07	(10.33, 10.62)
	Week 48	118	10.74 (0.74)	10.43	0.07	(10.28, 10.57)
	Week 52	115	10.76 (0.76)	10.39	0.08	(10.24, 10.54)
darbepoetin	Week 2	160	10.74 (0.72)	10.86	0.07	(10.72, 10.98)
	Week 4	159	10.73 (0.72)	10.88	0.07	(10.75, 11.02)
	Week 6	159	10.73 (0.72)	10.84	0.07	(10.70, 10.97)
	Week 8	158	10.74 (0.72)	10.84	0.07	(10.71, 10.98)
	Week 10	157	10.73 (0.71)	10.87	0.07	(10.74, 11.00)
	Week 12	157	10.73 (0.71)	10.91	0.07	(10.77, 11.04)
	Week 16	156	10.74 (0.71)	10.81	0.07	(10.69, 10.94)
	Week 20	154	10.75 (0.71)	10.65	0.07	(10.52, 10.78)
	Week 24	152	10.75 (0.71)	10.63	0.07	(10.50, 10.76)
	Week 28	150	10.76 (0.71)	10.67	0.07	(10.53, 10.80)
	Week 32	146	10.77 (0.71)	10.77	0.07	(10.63, 10.90)
	Week 36	142	10.77 (0.70)	10.74	0.07	(10.60, 10.88)
	Week 40	141	10.77 (0.70)	10.66	0.07	(10.52, 10.80)
	Week 44	139	10.76 (0.69)	10.63	0.07	(10.49, 10.77)
	Week 48	133	10.76 (0.69)	10.62	0.07	(10.48, 10.76)
	Week 52	133	10.76 (0.69)	10.62	0.07	(10.48, 10.76)

Note(s): Hb (g/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_2_1.sas

5.3.5.1—9 表 14.2.2.2.1 より引用

3)　Hb 値が目標範囲内の被験者の割合

Hb 値が目標範囲内の被験者の割合について，MT-6548 群を図 2.7.6.26－26，darbepoetin 群を図 2.7.6.26－27 に示した．また，Hb 値が目標範囲内の被験者割合を表 2.7.6.26－76 に示した．

MT-6548 群の Hb 値が目標範囲内の被験者の割合は，ベースラインで 81.5%であり，24 週後は 75.4%，52 週後は 75.7%であった．また，darbepoetin 群の Hb 値が目標範囲内の被験者の割合は，ベースラインで 78.9%であり，24 週後は 75.7%，52 週後は 86.5%であった．

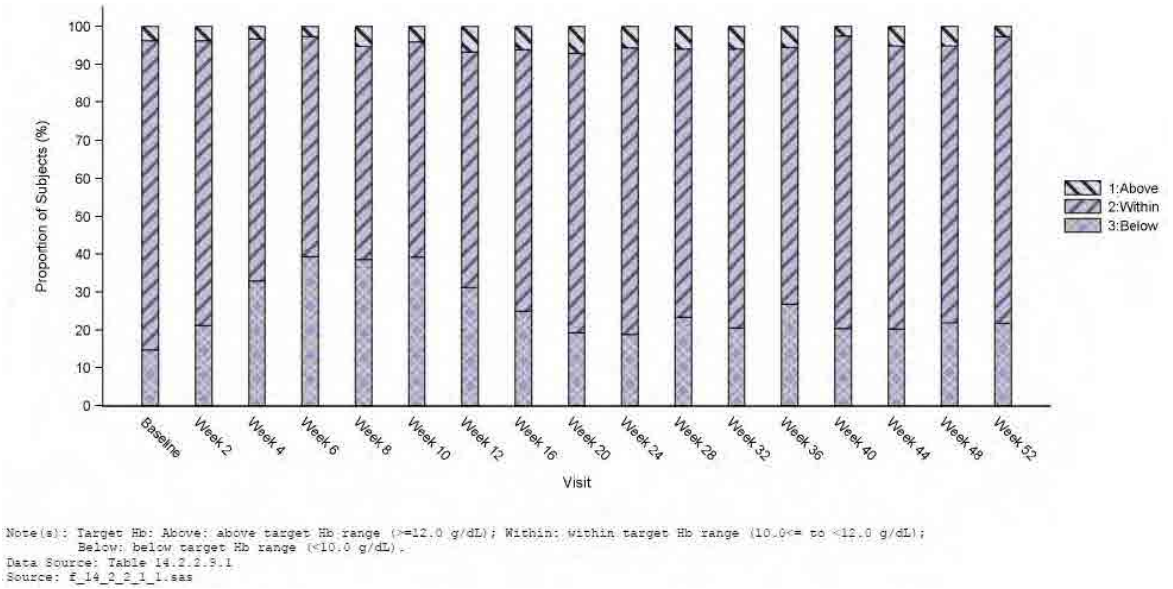
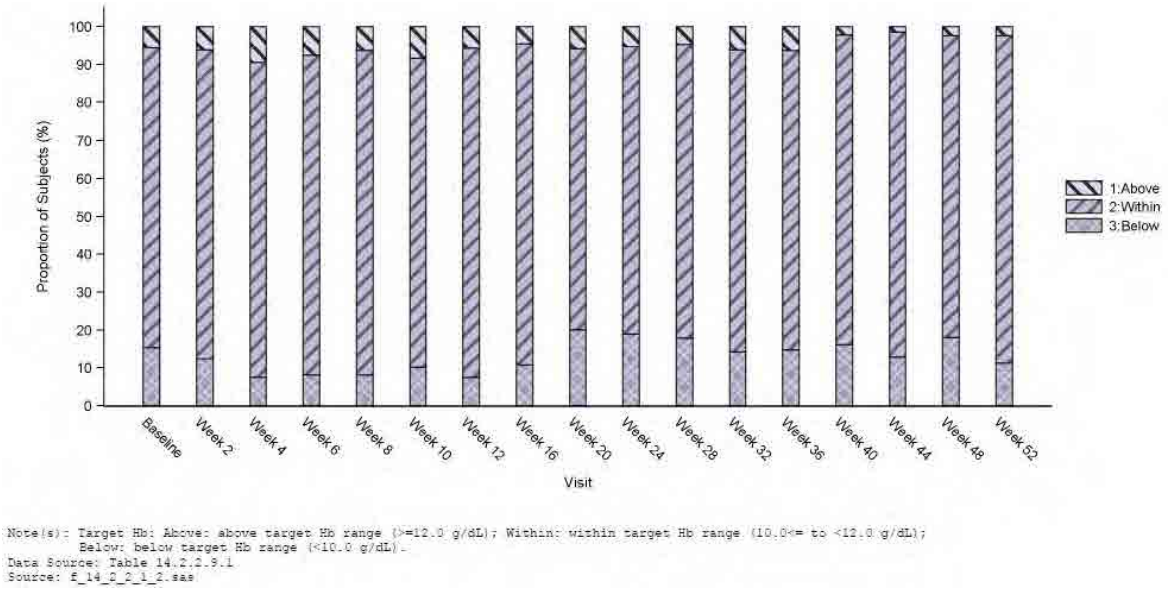


図 2.7.6.26－26　MT-6548 群の Hb 値が目標範囲内の被験者割合（FAS）

5.3.5.1—9 図 11.4.1—2 より引用



Note(s): Target Hb: Above: above target Hb range (>=12.0 g/dL); Within: within target Hb range (10.0<= to <12.0 g/dL);
Below: below target Hb range (<10.0 g/dL).
Data Source: Table 14.2.2.9.1
Source: f_14_2_2_1_2.sas

図 2.7.6.26－27　darbepoetin 群の Hb 値が目標範囲内の被験者割合（FAS）

5.3.5.1—9 図 11.4.1—3 より引用

表 2.7.6.26－76　Hb 値が目標範囲内の被験者割合（FAS）

		MT-6548(N=162)				darbepoetin(N=161)			
Visit	Target Hb Range	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B
Baseline		162				161			
	Above		6 (3.7)	(1.37, 7.89)			9 (5.6)	(2.69, 10.35)	
	Within		132 (81.5)	(74.63, 87.14)			127 (78.9)	(71.76, 84.91)	
	Below		24 (14.8)	(9.73, 21.24)			25 (15.5)	(10.31, 22.06)	
Week 2		160				160			
	Above		6 (3.8)	(1.39, 7.98)			10 (6.3)	(3.04, 11.19)	
	Within		120 (75.0)	(67.58, 81.50)	0.101		130 (81.3)	(74.33, 86.98)	-
	Below		34 (21.3)	(15.19, 28.41)			20 (12.5)	(7.81, 18.64)	
Week 4		157				159			
	Above		5 (3.2)	(1.04, 7.28)			15 (9.4)	(5.38, 15.06)	
	Within		100 (63.7)	(55.65, 71.21)	<0.001		132 (83.0)	(76.26, 88.50)	-
	Below		52 (33.1)	(25.82, 41.07)			12 (7.5)	(3.96, 12.81)	
Week 6		155				159			
	Above		4 (2.6)	(0.71, 6.49)			12 (7.5)	(3.96, 12.81)	
	Within		90 (58.1)	(49.88, 65.93)	<0.001		134 (84.3)	(77.67, 89.56)	-
	Below		61 (39.4)	(31.61, 47.51)			13 (8.2)	(4.48, 13.58)	
Week 8		150				158			
	Above		8 (5.3)	(2.33, 10.24)			10 (6.3)	(3.08, 11.33)	
	Within		84 (56.0)	(47.67, 64.09)	<0.001		135 (85.4)	(78.96, 90.84)	-
	Below		58 (38.7)	(30.84, 46.95)			13 (8.2)	(4.45, 13.66)	
Week 10		150				157			
	Above		6 (4.0)	(1.48, 8.50)			13 (8.3)	(4.48, 13.74)	
	Within		86 (56.7)	(48.34, 64.73)	<0.001		128 (81.5)	(74.56, 87.27)	-
	Below		59 (39.3)	(31.47, 47.63)			16 (10.2)	(5.94, 16.02)	

表 2.7.6.26－76　Hb 値が目標範囲内の被験者割合（FAS）（続き）

		MT-6548(N=162)				darbepoetin(N=161)			
Visit	Target Hb Range	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B
Week 12		147				157			
	Above		10 (6.8)	(3.31, 12.15)			9 (5.7)	(2.65, 10.60)	
	Within		91 (61.9)	(53.54, 69.78)	<0.001		136 (86.6)	(80.28, 91.53)	-
	Below		46 (31.3)	(23.91, 39.45)			12 (7.6)	(4.01, 12.97)	
Week 16		144				156			
	Above		9 (6.3)	(2.90, 11.53)			7 (4.5)	(1.82, 9.03)	
	Within		99 (68.8)	(60.50, 76.21)	0.018		132 (84.6)	(77.98, 89.89)	-
	Below		36 (25.0)	(18.16, 32.89)			17 (10.9)	(6.48, 16.87)	
Week 20		140				154			
	Above		10 (7.1)	(3.48, 12.74)			9 (5.8)	(2.71, 10.80)	
	Within		103 (73.6)	(65.46, 80.66)	0.131		114 (74.0)	(66.35, 80.75)	-
	Below		27 (19.3)	(13.11, 26.81)			31 (20.1)	(14.11, 27.84)	
Week 24		138				152			
	Above		8 (5.8)	(2.54, 11.10)			8 (5.3)	(2.30, 10.11)	
	Within		104 (75.4)	(67.31, 82.29)	0.208		115 (75.7)	(68.04, 82.25)	-
	Below		26 (18.8)	(12.69, 26.37)			29 (19.1)	(13.17, 26.24)	
Week 28		132				150			
	Above		8 (6.1)	(2.65, 11.59)			7 (4.7)	(1.90, 9.38)	
	Within		93 (70.5)	(61.89, 78.07)	0.048		116 (77.3)	(69.79, 83.76)	-
	Below		31 (23.5)	(16.55, 31.65)			27 (18.0)	(12.21, 25.10)	
Week 32		131				146			
	Above		8 (6.1)	(2.67, 11.68)			9 (6.2)	(2.86, 11.38)	
	Within		96 (73.3)	(64.85, 80.63)	0.166		116 (79.5)	(71.98, 85.69)	-
	Below		27 (20.6)	(14.04, 28.55)			21 (14.4)	(9.13, 21.14)	

表 2.7.6.26－76　Hb 値が目標範囲内の被験者割合（FAS）（続き）

		MT-6548(N=162)				darbepoetin(N=161)			
Visit	Target Hb Range	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B
Week 36		126				142			
	Above		7 (5.6)	(2.26, 11.11)			9 (6.3)	(2.94, 11.69)	
	Within		86 (67.5)	(58.54, 75.54)	0.013		112 (78.9)	(71.23, 85.27)	-
	Below		34 (27.0)	(19.47, 35.62)			21 (14.8)	(9.39, 21.71)	
Week 40		122				141			
	Above		3 (2.5)	(0.51, 7.02)			3 (2.1)	(0.44, 6.09)	
	Within		94 (77.0)	(69.57, 84.18)	0.435		115 (81.6)	(74.16, 87.59)	-
	Below		25 (20.5)	(13.72, 28.75)			23 (16.3)	(10.63, 23.46)	
Week 44		118				139			
	Above		6 (5.1)	(1.89, 10.74)			2 (1.4)	(0.17, 5.10)	
	Within		88 (74.6)	(65.74, 82.14)	0.286		119 (85.6)	(78.66, 90.98)	-
	Below		24 (20.3)	(13.49, 28.73)			18 (12.9)	(7.86, 19.69)	
Week 48		118				133			
	Above		6 (5.1)	(1.89, 10.74)			3 (2.3)	(0.47, 6.45)	
	Within		86 (72.9)	(63.92, 80.65)	0.199		106 (79.7)	(71.86, 86.17)	-
	Below		26 (22.0)	(14.93, 30.59)			24 (18.0)	(11.92, 26.65)	
Week 52		115				133			
	Above		3 (2.6)	(0.54, 7.43)			3 (2.3)	(0.47, 6.46)	
	Within		87 (75.7)	(66.77, 83.17)	0.456		115 (86.5)	(79.46, 91.78)	-
	Below		25 (21.7)	(14.59, 30.40)			15 (11.3)	(6.45, 17.92)	

Note(s): Target Hb: Above: above target Hb range (>=12.0 g/dL); Within: within target Hb range (10.0<= to <12.0 g/dL);
Below: below target Hb range (<10.0 g/dL).
Note(s): N*: number of subjects at each visit.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): p value from B: p value from baseline value.
Note(s): p value from B is analyzed by McNemar test to comparer proportion of subjects in target range (Within) and proportion of subjects out of target range (Above + Below).
Data Source: Listing 16.2.4.1
Source: t_14_2_2_9_1.sas

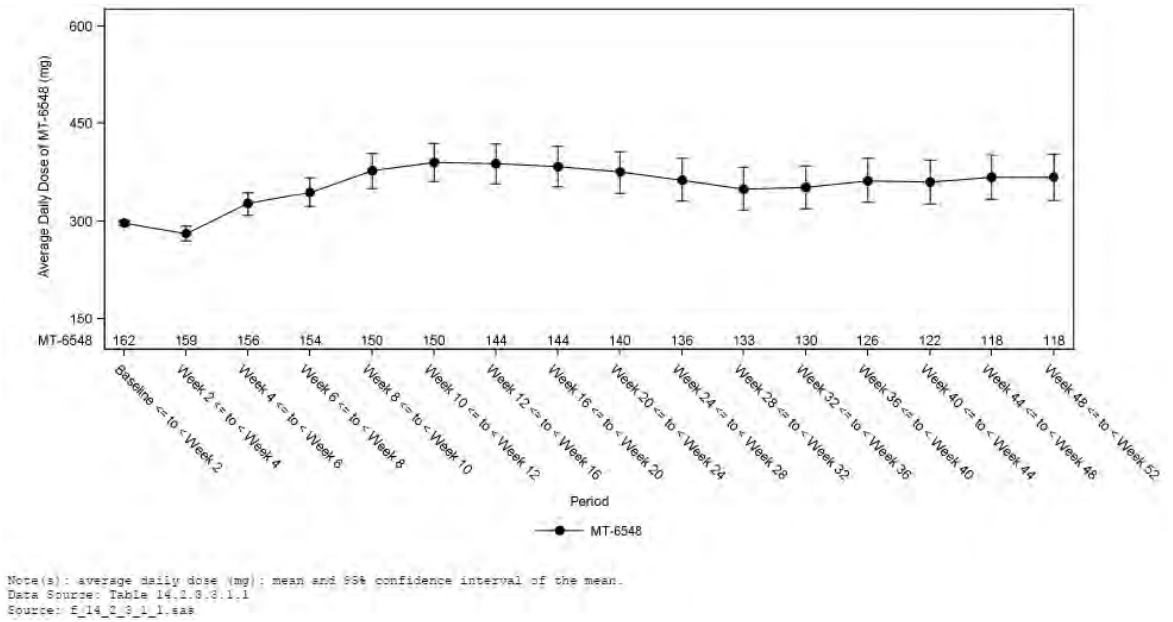
5.3.5.1—9 表 14.2.2.9.1 より引用

4)　治験薬の投与量

規定来院間の治験薬の平均投与量の推移について，MT-6548 群を図 2.7.6.26－28，その記述統計量を表 2.7.6.26－77 に示した．また，規定来院日における MT-6548 錠の 1 日投与量の分布を図 2.7.6.26－29，治験薬の投与量の分布を表 2.7.6.26－78 に示した．

MT-6548 は 300 mg/日で投与を開始し，，MT-6548 の 1 日平均投与量の平均値及びその 95%CI は，20 週～24 週後で 375.34 mg/日及び 343.45～407.23 mg/日，48 週～52 週後で 367.65 mg/日及び 331.91～403.39 mg/日であった．ダルベポエチンアルファ（遺伝子組換え）の週あたりの平均投与量の平均値及びその 95%CI は，ベースライン～2 週後までで 19.31 μg/週及び 17.43～21.19 μg/週，20 週～24 週後で 18.67 μg/週及び 15.43～21.91 μg/週，48 週～52 週後で 24.15 μg/週及び 19.12～29.18 μg/週であった．

MT-6548 錠の 20 週後の 1 日投与量の分布は，0 mg，150 mg，300 mg，450 mg 及び 600 mg でそれぞれ 2.1%，27.9%，20.0%，14.3%及び 35.7%であった．また，MT-6548 錠の 48 週後の 1 日投与量の分布は，0 mg，150 mg，300 mg，450 mg 及び 600 mg でそれぞれ 0.8%，33.9%，17.8%，11.9%及び 35.6%であった．ダルベポエチンアルファ注の 20 週後の週あたりの投与量の分布は，0 μg，0 μg 超 30 μg 以下，30 μg 超 60 μg 以下，60 μg 超 90 μg 以下，90 μg 超 120 μg 以下及び 120 μg 超でそれぞれ 0.6%，86.5%，11.6%，0%，0.6%及び 0.6%であった．また，ダルベポエチンアルファ注の 48 週後の週あたりの投与量の分布は，0 μg，0 μg 超 30 μg 以下，30 μg 超 60 μg 以下，60 μg 超 90 μg 以下，90 μg 超 120 μg 以下及び 120 μg 超でそれぞれ 0.8%，78.9%，12.0%，4.5%，2.3%及び 1.5%であった．



Note(s): average daily dose (mg); mean and 95% confidence interval of the mean.
Data Source: Table 14.2.9.3.1.1
Source: f_14_2_9_1_1.sas

図 2.7.6.26－28　MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—9 図 11.4.1—4 より引用

表 2.7.6.26－77　治験薬の平均投与量の記述統計量（FAS）

Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Baseline <= to < Week 2	162	297.16	24.96	300.00	(42.9, 375.0)	(293.28, 301.03)
	Week 2 <= to < Week 4	159	280.66	73.30	300.00	(0.0, 514.3)	(269.38, 292.34)
	Week 4 <= to < Week 6	156	326.58	112.55	300.00	(0.0, 600.0)	(308.78, 344.38)
	Week 6 <= to < Week 8	154	344.25	138.59	300.00	(0.0, 600.0)	(322.19, 366.31)
	Week 8 <= to < Week 10	150	377.79	167.08	407.14	(0.0, 600.0)	(350.83, 404.74)
	Week 10 <= to < Week 12	150	390.39	180.34	439.29	(0.0, 600.0)	(361.29, 419.48)
	Week 12 <= to < Week 16	144	387.87	185.97	412.50	(0.0, 600.0)	(367.24, 408.51)
	Week 16 <= to < Week 20	144	383.90	188.18	393.75	(0.0, 600.0)	(352.90, 414.90)
	Week 20 <= to < Week 24	140	375.34	190.85	358.93	(0.0, 600.0)	(343.45, 407.23)
	Week 24 <= to < Week 28	136	363.19	193.21	300.00	(0.0, 600.0)	(330.42, 395.96)
	Week 28 <= to < Week 32	133	349.66	190.99	300.00	(0.0, 600.0)	(316.91, 382.42)
	Week 32 <= to < Week 36	130	351.92	188.94	300.00	(0.0, 600.0)	(319.14, 384.71)
	Week 36 <= to < Week 40	126	362.45	192.63	300.00	(0.0, 600.0)	(329.49, 396.42)
	Week 40 <= to < Week 44	122	359.94	189.17	300.00	(0.0, 600.0)	(326.03, 393.86)
	Week 44 <= to < Week 48	118	367.51	186.26	300.00	(150.0, 600.0)	(333.55, 401.47)
	Week 48 <= to < Week 52	118	367.65	196.03	300.00	(0.0, 600.0)	(331.91, 403.39)
darbepoetin	Baseline <= to < Week 2	160	19.31	12.03	15.00	(5.0, 60.0)	(17.43, 21.19)
	Week 2 <= to < Week 4	158	18.13	10.69	15.00	(2.5, 60.0)	(16.45, 19.81)
	Week 4 <= to < Week 6	159	17.17	10.48	15.00	(0.0, 60.0)	(15.53, 18.81)
	Week 6 <= to < Week 8	159	16.86	10.96	15.00	(0.0, 60.0)	(15.14, 18.58)
	Week 8 <= to < Week 10	158	16.80	11.62	15.00	(0.0, 60.0)	(14.98, 18.63)
	Week 10 <= to < Week 12	158	16.95	12.74	15.00	(0.0, 60.0)	(14.95, 18.95)
	Week 12 <= to < Week 16	157	17.03	14.23	12.50	(0.9, 90.0)	(14.79, 19.28)
	Week 16 <= to < Week 20	156	17.23	16.78	10.00	(0.0, 110.0)	(14.58, 19.89)
	Week 20 <= to < Week 24	154	18.67	20.38	11.25	(0.0, 140.0)	(15.43, 21.91)
	Week 24 <= to < Week 28	152	21.29	23.94	15.00	(2.5, 160.0)	(17.45, 25.13)
	Week 28 <= to < Week 32	150	22.60	25.81	15.00	(2.5, 140.0)	(18.44, 26.77)
	Week 32 <= to < Week 36	146	22.91	28.03	15.00	(0.0, 180.0)	(18.33, 27.50)
	Week 36 <= to < Week 40	143	23.21	27.89	15.00	(2.5, 180.0)	(18.60, 27.83)
	Week 40 <= to < Week 44	141	23.30	29.83	13.75	(1.3, 180.0)	(18.33, 28.27)
	Week 44 <= to < Week 48	137	23.40	29.52	11.25	(0.0, 180.0)	(18.41, 28.38)
	Week 48 <= to < Week 52	133	24.15	29.31	15.00	(2.5, 180.0)	(19.12, 29.18)

Note(s): average dose: MT-6548: average daily dose (mg); darbepoetin: average weekly dose (ug).
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_3_1_1.sas

5.3.5.1—9 表 14.2.3.3.1.1 より引用

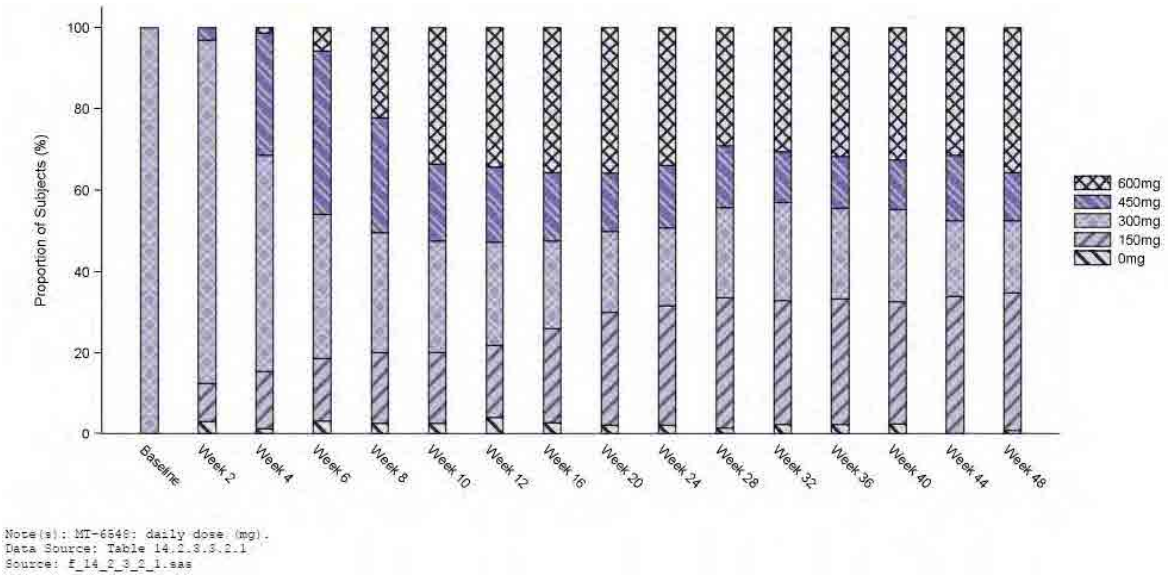


図 2.7.6.26－29　MT-6548 錠の 1 日投与量の分布（FAS）

5.3.5.1—9 図 11.4.1—5 より引用

表 2.7.6.26－78　治験薬の投与量の分布（FAS）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
MT-6548	Baseline		162		
		0mg		0 (0.0)	(0.00, 2.25)
		150mg		0 (0.0)	(0.00, 2.25)
		300mg		162 (100.0)	(97.75, 100.00)
		450mg		0 (0.0)	(0.00, 2.25)
		600mg		0 (0.0)	(0.00, 2.25)
	Week 2		161		
		0mg		5 (3.1)	(1.02, 7.10)
		150mg		15 (9.3)	(5.31, 14.90)
		300mg		136 (84.5)	(77.94, 89.69)
		450mg		5 (3.1)	(1.02, 7.10)
		600mg		0 (0.0)	(0.00, 2.27)
	Week 4		156		
		0mg		2 (1.3)	(0.16, 4.55)
		150mg		22 (14.1)	(9.05, 20.57)
		300mg		83 (53.2)	(45.06, 61.23)
		450mg		47 (30.1)	(23.05, 37.98)
		600mg		2 (1.3)	(0.16, 4.55)
	Week 6		155		
		0mg		5 (3.2)	(1.06, 7.37)
		150mg		24 (15.5)	(10.18, 22.16)
		300mg		55 (35.5)	(27.97, 43.56)
		450mg		62 (40.0)	(32.22, 48.17)
		600mg		9 (5.8)	(2.69, 10.74)
	Week 8		149		
		0mg		4 (2.7)	(0.74, 6.73)
		150mg		26 (17.4)	(11.73, 24.51)
		300mg		44 (29.5)	(22.35, 37.55)
		450mg		42 (28.2)	(21.13, 36.13)
		600mg		33 (22.1)	(15.76, 29.67)
	Week 10		149		
		0mg		4 (2.7)	(0.74, 6.73)
		150mg		26 (17.4)	(11.73, 24.51)
		300mg		41 (27.5)	(20.53, 35.43)
		450mg		28 (18.8)	(12.87, 26.00)
		600mg		50 (33.6)	(26.04, 41.74)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 12		146		
		0mg		6 (4.1)	(1.52, 8.73)
		150mg		26 (17.8)	(11.98, 24.95)
		300mg		37 (25.3)	(18.51, 33.20)
		450mg		27 (18.5)	(12.56, 25.75)
		600mg		50 (34.2)	(26.60, 42.55)
	Week 16		143		
		0mg		4 (2.8)	(0.77, 7.01)
		150mg		33 (23.1)	(16.48, 30.85)
		300mg		31 (21.7)	(15.23, 29.34)
		450mg		24 (16.8)	(11.06, 23.94)
		600mg		51 (35.7)	(27.84, 44.10)
	Week 20		140		
		0mg		3 (2.1)	(0.44, 6.13)
		150mg		39 (27.9)	(20.62, 36.06)
		300mg		28 (20.0)	(13.72, 27.69)
		450mg		20 (14.3)	(8.95, 21.20)
		600mg		50 (35.7)	(27.80, 44.25)
	Week 24		136		
		0mg		3 (2.2)	(0.46, 6.31)
		150mg		40 (29.4)	(21.91, 37.83)
		300mg		26 (19.1)	(12.88, 26.74)
		450mg		21 (15.4)	(9.82, 22.63)
		600mg		46 (33.8)	(25.94, 42.43)
	Week 28		131		
		0mg		2 (1.5)	(0.19, 5.41)
		150mg		42 (32.1)	(24.18, 40.77)
		300mg		29 (22.1)	(15.35, 30.22)
		450mg		20 (15.3)	(9.58, 22.59)
		600mg		38 (29.0)	(21.41, 37.58)
	Week 32		128		
		0mg		3 (2.3)	(0.49, 6.70)
		150mg		39 (30.5)	(22.65, 39.22)
		300mg		31 (24.2)	(17.09, 32.58)
		450mg		16 (12.5)	(7.32, 19.50)
		600mg		39 (30.5)	(22.65, 39.22)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 36		126		
		0mg		3 (2.4)	(0.49, 6.80)
		150mg		39 (31.0)	(23.02, 39.80)
		300mg		28 (22.2)	(15.30, 30.49)
		450mg		16 (12.7)	(7.44, 19.80)
		600mg		40 (31.7)	(23.74, 40.63)
	Week 40		123		
		0mg		3 (2.4)	(0.51, 6.96)
		150mg		37 (30.1)	(22.14, 39.00)
		300mg		28 (22.8)	(15.69, 31.19)
		450mg		15 (12.2)	(6.99, 19.32)
		600mg		40 (32.5)	(24.35, 41.58)
	Week 44		118		
		0mg		0 (0.0)	(0.00, 3.08)
		150mg		40 (33.9)	(25.44, 43.19)
		300mg		22 (18.6)	(12.07, 26.86)
		450mg		19 (16.1)	(9.98, 24.00)
		600mg		37 (31.4)	(23.13, 40.54)
	Week 48		118		
		0mg		1 (0.8)	(0.02, 4.63)
		150mg		40 (33.9)	(25.44, 43.19)
		300mg		21 (17.8)	(11.37, 25.91)
		450mg		14 (11.9)	(6.64, 19.10)
		600mg		42 (35.6)	(27.00, 44.93)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
darbepoetin	Baseline		160		
		0ug		0 (0.0)	(0.00, 2.28)
		0ug < to <= 30ug		143 (89.4)	(83.53, 93.69)
		30ug < to <= 60ug		17 (10.6)	(6.31, 16.47)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.28)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.28)
		> 120ug		0 (0.0)	(0.00, 2.28)
	Week 2		158		
		0ug		1 (0.6)	(0.02, 3.48)
		0ug < to <= 30ug		146 (92.4)	(87.11, 96.01)
		30ug < to <= 60ug		11 (7.0)	(3.53, 12.12)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.31)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.31)
		> 120ug		0 (0.0)	(0.00, 2.31)
	Week 4		158		
		0ug		1 (0.6)	(0.02, 3.48)
		0ug < to <= 30ug		148 (93.7)	(89.67, 96.92)
		30ug < to <= 60ug		9 (5.7)	(2.64, 10.54)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.31)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.31)
		> 120ug		0 (0.0)	(0.00, 2.31)
	Week 6		159		
		0ug		3 (1.9)	(0.39, 5.41)
		0ug < to <= 30ug		144 (90.6)	(84.92, 94.62)
		30ug < to <= 60ug		12 (7.5)	(3.96, 12.81)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.29)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.29)
		> 120ug		0 (0.0)	(0.00, 2.29)
	Week 8		158		
		0ug		1 (0.6)	(0.02, 3.48)
		0ug < to <= 30ug		144 (91.1)	(85.58, 95.07)
		30ug < to <= 60ug		13 (8.2)	(4.45, 13.66)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.31)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.31)
		> 120ug		0 (0.0)	(0.00, 2.31)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 10		156		
		0ug		5 (3.2)	(1.04, 7.23)
		0ug < to <= 30ug		140 (89.6)	(82.59, 93.11)
		30ug < to <= 60ug		13 (8.2)	(4.45, 13.66)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.31)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.31)
		> 120ug		0 (0.0)	(0.00, 2.31)
	Week 12		157		
		0ug		4 (2.5)	(0.70, 6.39)
		0ug < to <= 30ug		137 (87.3)	(81.01, 92.04)
		30ug < to <= 60ug		15 (9.6)	(5.45, 15.27)
		60ug < to <= 90ug		1 (0.6)	(0.02, 3.50)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.32)
		> 120ug		0 (0.0)	(0.00, 2.32)
	Week 16		156		
		0ug		2 (1.3)	(0.16, 4.55)
		0ug < to <= 30ug		138 (88.5)	(82.88, 93.02)
		30ug < to <= 60ug		13 (8.3)	(4.51, 13.83)
		60ug < to <= 90ug		2 (1.3)	(0.16, 4.55)
		90ug < to <= 120ug		1 (0.6)	(0.02, 3.52)
		> 120ug		0 (0.0)	(0.00, 2.34)
	Week 20		155		
		0ug		1 (0.6)	(0.02, 3.54)
		0ug < to <= 30ug		134 (86.5)	(80.04, 91.41)
		30ug < to <= 60ug		18 (11.6)	(7.03, 17.73)
		60ug < to <= 90ug		0 (0.0)	(0.00, 2.35)
		90ug < to <= 120ug		1 (0.6)	(0.02, 3.54)
		> 120ug		1 (0.6)	(0.02, 3.54)
	Week 24		152		
		0ug		1 (0.7)	(0.02, 3.61)
		0ug < to <= 30ug		128 (84.2)	(77.42, 89.61)
		30ug < to <= 60ug		15 (9.9)	(5.63, 15.75)
		60ug < to <= 90ug		6 (3.9)	(1.46, 8.39)
		90ug < to <= 120ug		0 (0.0)	(0.00, 2.40)
		> 120ug		2 (1.3)	(0.16, 4.67)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 28		149		
		0ug		3 (2.0)	(0.42, 5.77)
		0ug < to <= 30ug		120 (80.5)	(73.26, 86.56)
		30ug < to <= 60ug		18 (12.1)	(7.32, 18.42)
		60ug < to <= 90ug		5 (3.4)	(1.10, 7.66)
		90ug < to <= 120ug		2 (1.3)	(0.16, 4.76)
		> 120ug		1 (0.7)	(0.02, 3.68)
	Week 32		146		
		0ug		1 (0.7)	(0.02, 3.76)
		0ug < to <= 30ug		124 (84.9)	(78.08, 90.31)
		30ug < to <= 60ug		11 (7.5)	(3.82, 13.08)
		60ug < to <= 90ug		5 (3.4)	(1.12, 7.81)
		90ug < to <= 120ug		2 (1.4)	(0.17, 4.86)
		> 120ug		3 (2.1)	(0.43, 5.89)
	Week 36		144		
		0ug		3 (2.1)	(0.43, 5.97)
		0ug < to <= 30ug		119 (82.6)	(75.45, 88.44)
		30ug < to <= 60ug		10 (6.9)	(3.36, 12.40)
		60ug < to <= 90ug		5 (3.5)	(1.14, 7.92)
		90ug < to <= 120ug		5 (3.5)	(1.14, 7.92)
		> 120ug		2 (1.4)	(0.17, 4.93)
	Week 40		141		
		0ug		1 (0.7)	(0.02, 3.89)
		0ug < to <= 30ug		118 (83.7)	(76.64, 89.37)
		30ug < to <= 60ug		12 (8.5)	(4.48, 14.39)
		60ug < to <= 90ug		4 (2.8)	(0.78, 7.10)
		90ug < to <= 120ug		3 (2.1)	(0.44, 6.09)
		> 120ug		3 (2.1)	(0.44, 6.09)
	Week 44		137		
		0ug		1 (0.7)	(0.02, 4.00)
		0ug < to <= 30ug		112 (81.8)	(74.25, 87.83)
		30ug < to <= 60ug		14 (10.2)	(5.70, 16.55)
		60ug < to <= 90ug		5 (3.6)	(1.20, 8.31)
		90ug < to <= 120ug		2 (1.5)	(0.18, 5.17)
		> 120ug		3 (2.2)	(0.46, 6.27)

表 2.7.6.26－78　治験薬の投与量の分布（FAS）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 48		133		
		0ug		1 (0.8)	(0.02, 4.12)
		0ug < to <= 30ug		105 (78.9)	(71.03, 85.53)
		30ug < to <= 60ug		16 (12.0)	(7.04, 18.60)
		60ug < to <= 90ug		6 (4.5)	(1.67, 9.56)
		90ug < to <= 120ug		3 (2.3)	(0.47, 6.45)
		> 120ug		2 (1.5)	(0.18, 5.33)

Note(s): Dose: MT-6548: daily dose (mg); darbepoetin: weekly dose (ug).
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analysed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.8.1, Listing 16.2.8.2
Source: t_14_2_8_3_2_1.sas

5.3.5.1—9 表 14.2.3.3.2.1 より引用

5)　用量調節の累計回数

52 週後までの MT-6548 錠の用量調節の累計回数及び規定来院間に用量調節を行った被験者の割合を表 2.7.6.26－79 に示した.

MT-6548 錠の用量調節を行った被験者の割合は 4 週～6 週後が最も多く 45.8%であり，20 週～24 週後では 19.6%，48 週～52 週後では 18.7%であった.

表 2.7.6.26－79　MT-6548 錠の用量調節の累計回数及び用量調節を行った被験者の割合（FAS）

Parameter	Period	Category	N*	MT-6548(N=162) n (%)	95% CI of proportion
Cumulative number of dose adjustment		0		6 (3.7)	(1.37, 7.89)
		1		26 (16.0)	(10.76, 22.63)
		2		43 (26.5)	(19.92, 34.04)
		3		30 (18.5)	(12.86, 25.37)
		4		20 (12.3)	(7.71, 18.42)
		5		12 (7.4)	(3.89, 12.58)
		6		17 (10.5)	(6.23, 16.27)
		7		6 (3.7)	(1.37, 7.89)
		8		1 (0.6)	(0.02, 3.39)
		9		1 (0.6)	(0.02, 3.39)
Proportion of subjects by category of dose adjustment	Baseline <= to < Week 2		162		
		No change		155 (95.7)	(91.30, 99.25)
		Dose adjustment		7 (4.3)	(1.75, 8.70)
		Increase		2 (1.2)	(0.15, 4.39)
		Decrease		1 (0.6)	(0.02, 3.39)
		Interrupt		4 (2.5)	(0.69, 6.20)
	Week 2 <= to < Week 4		157		
		No change		133 (84.7)	(78.11, 89.95)
		Dose adjustment		24 (15.3)	(10.05, 21.89)
		Increase		5 (3.2)	(1.04, 7.28)
		Decrease		15 (9.6)	(5.45, 15.27)
		Interrupt		5 (3.2)	(1.04, 7.28)
	Week 4 <= to < Week 6		155		
		No change		84 (54.2)	(46.01, 62.21)
		Dose adjustment		71 (45.8)	(37.79, 53.99)
		Increase		62 (40.0)	(32.22, 48.17)
		Decrease		8 (5.2)	(2.25, 9.92)
		Interrupt		2 (1.3)	(0.16, 4.58)

表 2.7.6.26－79　MT-6548 錠の用量調節の累計回数及び用量調節を行った被験者の割合（FAS）（続き）

Parameter	Period	Category	N[a]	MT-6548(N=162) n (%)	95% CI of proportion
	Week 6 <= to < Week 8		153		
		No change		118 (77.1)	(69.65, 83.52)
		Dose adjustment		35 (22.9)	(16.48, 30.35)
		Increase		22 (14.4)	(9.24, 20.96)
		Decrease		12 (7.8)	(4.12, 13.30)
		Interrupt		2 (1.3)	(0.16, 4.64)
	Week 8 <= to < Week 10		149		
		No change		100 (67.1)	(59.05, 74.58)
		Dose adjustment		49 (32.9)	(25.42, 41.05)
		Increase		42 (28.2)	(21.13, 36.13)
		Decrease		4 (2.7)	(0.74, 6.73)
		Interrupt		3 (2.0)	(0.42, 5.77)
	Week 10 <= to < Week 12		149		
		No change		129 (86.6)	(80.03, 91.60)
		Dose adjustment		20 (13.4)	(8.40, 19.97)
		Increase		15 (10.1)	(5.74, 16.06)
		Decrease		4 (2.7)	(0.74, 6.73)
		Interrupt		1 (0.7)	(0.02, 3.68)
	Week 12 <= to < Week 16		143		
		No change		107 (74.8)	(66.89, 81.70)
		Dose adjustment		36 (25.2)	(18.30, 33.11)
		Increase		19 (13.3)	(8.19, 19.97)
		Decrease		14 (9.8)	(5.46, 15.88)
		Interrupt		3 (2.1)	(0.43, 6.01)
	Week 16 <= to < Week 20		143		
		No change		117 (81.8)	(74.51, 87.77)
		Dose adjustment		26 (18.2)	(12.23, 25.49)
		Increase		10 (7.0)	(3.40, 12.48)
		Decrease		16 (11.2)	(6.53, 17.53)
		Interrupt		3 (2.1)	(0.43, 6.01)

表 2.7.6.26－79　MT-6548 錠の用量調節の累計回数及び用量調節を行った被験者の割合（FAS）（続き）

Parameter	Period	Category	N*	MT-6548(N=162) n (%)	95% CI of proportion
	Week 20 <= to < Week 24		138		
		No change		111 (80.4)	(72.83, 86.69)
		Dose adjustment		27 (19.6)	(13.31, 27.17)
		Increase		8 (5.8)	(2.54, 11.10)
		Decrease		13 (9.4)	(5.11, 15.57)
		Interrupt		6 (4.3)	(1.61, 9.22)
	Week 24 <= to < Week 28		135		
		No change		108 (80.0)	(72.25, 86.39)
		Dose adjustment		27 (20.0)	(13.61, 27.75)
		Increase		7 (5.2)	(2.11, 10.39)
		Decrease		16 (11.9)	(6.93, 18.53)
		Interrupt		6 (4.4)	(1.65, 9.42)
	Week 28 <= to < Week 32		130		
		No change		105 (80.8)	(72.93, 87.15)
		Dose adjustment		25 (19.2)	(12.85, 27.07)
		Increase		11 (8.5)	(4.30, 14.64)
		Decrease		13 (10.0)	(5.43, 16.48)
		Interrupt		1 (0.8)	(0.02, 4.21)
	Week 32 <= to < Week 36		127		
		No change		96 (75.6)	(67.18, 82.77)
		Dose adjustment		31 (24.4)	(17.23, 32.82)
		Increase		18 (14.2)	(8.62, 21.47)
		Decrease		10 (7.9)	(3.84, 14.00)
		Interrupt		4 (3.1)	(0.86, 7.87)
	Week 36 <= to < Week 40		127		
		No change		96 (75.6)	(67.18, 82.77)
		Dose adjustment		31 (24.4)	(17.23, 32.82)
		Increase		18 (14.2)	(8.62, 21.47)
		Decrease		9 (7.1)	(3.29, 13.03)
		Interrupt		5 (3.9)	(1.29, 8.95)

表 2.7.6.26－79　MT-6548 錠の用量調節の累計回数及び用量調節を行った被験者の割合（FAS）（続き）

Parameter	Period	Category	N*	MT-6548(N=162) n (%)	95% CI of proportion
	Week 40 <= to < Week 44		126		
		No change		98 (77.8)	(69.51, 84.70)
		Dose adjustment		28 (22.2)	(15.30, 30.49)
		Increase		12 (9.5)	(5.02, 16.05)
		Decrease		13 (10.3)	(5.61, 17.00)
		Interrupt		3 (2.4)	(0.49, 6.80)
	Week 44 <= to < Week 48		123		
		No change		104 (84.6)	(76.93, 90.44)
		Dose adjustment		19 (15.4)	(9.66, 23.07)
		Increase		10 (8.1)	(3.97, 14.44)
		Decrease		9 (7.3)	(3.40, 13.44)
		Interrupt		0 (0.0)	(0.00, 2.95)
	Week 48 <= to < Week 52		123		
		No change		100 (81.3)	(73.28, 87.76)
		Dose adjustment		23 (18.7)	(12.24, 26.72)
		Increase		10 (8.1)	(3.97, 14.44)
		Decrease		10 (8.1)	(3.97, 14.44)
		Interrupt		3 (2.4)	(0.51, 6.96)
	Baseline <= to < Week 52		162		
		No change		6 (3.7)	(1.37, 7.89)
		Dose adjustment		156 (96.3)	(92.11, 98.63)
		Increase		126 (77.8)	(70.59, 83.92)
		Decrease		103 (63.6)	(55.67, 70.99)
		Interrupt		37 (22.8)	(16.62, 30.08)

Note(s): N*: number of subjects in MT-6548 group in each period.
Note(s): Percentages in 'Cumulative number of dose adjustment' are based on the number of subjects in MT-6548 group.
Note(s): Percentages in 'Proportion of subjects by category of dose adjustment' are based on the number of subjects in MT-6548 group by period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analysed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.3.1
Source: t_14_2_3_4_1.sas

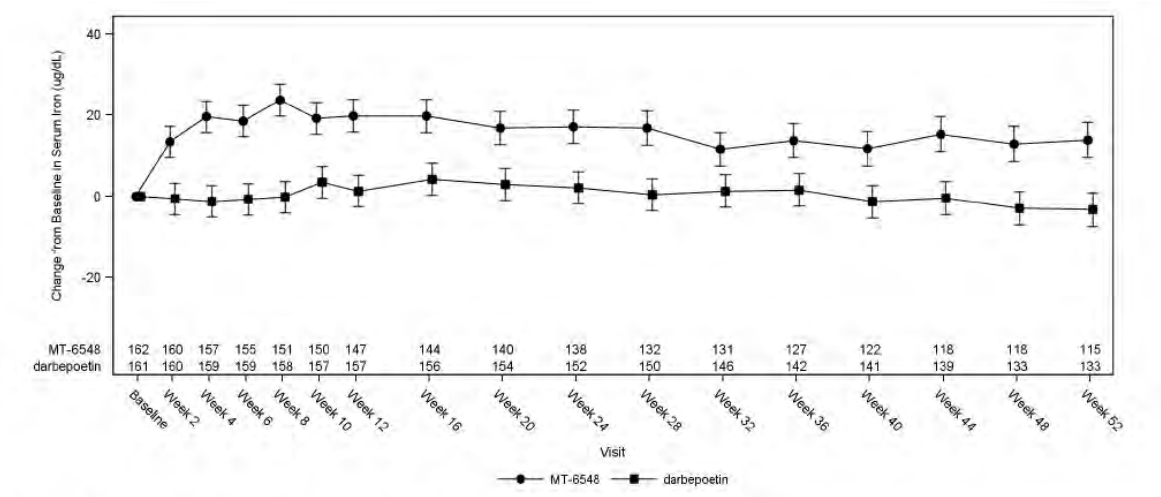
5.3.5.1—9 表 11.4.1—2 より引用

(3)　鉄関連指標（血清鉄，TIBC，TSAT 及び血清フェリチン値）及びヘプシジン

1)　血清鉄

MMRM を用いた血清鉄のベースラインからの変化量の推移を図 2.7.6.26－30 に示した．MMRM を用いた血清鉄のベースラインからの変化量を表 2.7.6.26－80 に示した．

MMRM を用いた血清鉄の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 13.9 µg/dL 及び 9.5～18.3 µg/dL，darbepoetin 群で -3.3 µg/dL 及び -7.4～0.8 µg/dL であった．MMRM を用いた血清鉄の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 17.2 µg/dL 及び 11.2～23.2 µg/dL であり，統計学的に有意な差が認められた（p<0.001）．



Note(s): Change from baseline in serum iron (ug/dL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.8.2.1
Source: f_14_2_4_1_1.sas

図 2.7.6.26－30　血清鉄のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—9 図 11.4.1—6 より引用

表 2.7.6.26－80　血清鉄のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	68.4 (29.0)	13.4	2.0	(9.6, 17.3)		160	30.0	3.6	(23.1, 36.9)	
	Week 4	157	68.4 (28.5)	19.6	2.0	(15.7, 23.5)		157	40.7	3.5	(33.7, 47.6)	
	Week 6	155	68.7 (28.5)	18.6	2.0	(14.6, 22.5)		155	38.0	3.5	(31.1, 45.0)	
	Week 8	151	68.1 (28.2)	23.7	2.0	(19.8, 27.7)		151	48.0	3.6	(40.9, 55.0)	
	Week 10	150	68.2 (28.2)	19.2	2.0	(15.2, 23.2)		150	40.3	3.6	(33.2, 47.3)	
	Week 12	147	68.4 (28.4)	19.8	2.0	(15.8, 23.8)		147	41.2	3.6	(34.1, 48.3)	
	Week 16	144	68.3 (28.1)	19.8	2.0	(15.8, 23.8)		144	40.9	3.6	(33.8, 48.1)	
	Week 20	140	68.2 (28.4)	16.8	2.1	(12.7, 20.9)		140	37.0	3.7	(29.7, 44.2)	
	Week 24	138	68.3 (28.6)	17.1	2.1	(13.0, 21.1)		138	38.0	3.7	(30.8, 45.3)	
	Week 28	132	68.7 (28.9)	16.8	2.1	(12.7, 21.0)		132	36.9	3.8	(29.5, 44.2)	
	Week 32	131	69.2 (29.1)	11.6	2.1	(7.4, 15.8)		131	30.0	3.8	(22.6, 37.3)	
	Week 36	127	69.4 (29.3)	13.7	2.1	(9.5, 17.9)		127	31.8	3.8	(24.4, 39.3)	
	Week 40	122	68.6 (28.9)	11.7	2.2	(7.5, 16.0)		122	28.6	3.9	(21.1, 36.2)	
	Week 44	118	68.4 (28.5)	15.3	2.2	(11.0, 19.7)		118	33.8	3.9	(26.2, 41.4)	
	Week 48	118	68.4 (28.5)	12.9	2.2	(8.5, 17.2)		118	32.6	3.5	(24.9, 40.1)	
	Week 52	115	68.8 (28.6)	13.9	2.2	(9.5, 18.3)		115	31.3	3.9	(23.6, 39.0)	

表 2.7.6.26－80　血清鉄のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	64.6 (22.2)	-0.6	2.0	(-4.5, 3.2)		160	4.7	3.5	(-2.2, 11.6)	
	Week 4	159	64.6 (22.3)	-1.3	2.0	(-5.1, 2.6)		159	3.9	3.5	(-3.0, 10.8)	
	Week 6	159	64.6 (22.3)	-0.8	2.0	(-4.6, 3.1)		159	5.6	3.5	(-1.4, 12.4)	
	Week 8	158	64.6 (22.4)	-0.2	2.0	(-4.1, 3.6)		158	7.2	3.5	(0.3, 14.1)	
	Week 10	157	64.5 (22.4)	3.4	2.0	(-0.5, 7.3)		157	12.9	3.5	(6.0, 19.8)	
	Week 12	157	64.5 (22.4)	1.3	2.0	(-2.6, 5.1)		157	11.1	3.5	(4.2, 18.0)	
	Week 16	156	64.6 (22.5)	4.2	2.0	(0.3, 8.1)		156	15.3	3.5	(8.3, 22.2)	
	Week 20	154	64.5 (22.4)	2.9	2.0	(-1.0, 6.9)		154	12.4	3.6	(5.4, 19.3)	
	Week 24	152	65.0 (22.5)	2.1	2.0	(-1.9, 6.0)		152	11.1	3.6	(4.1, 18.1)	
	Week 28	150	64.9 (22.6)	0.4	2.0	(-3.6, 4.3)		150	9.1	3.6	(2.1, 16.1)	
	Week 32	146	65.2 (22.7)	1.3	2.0	(-2.7, 5.3)		146	11.6	3.6	(4.5, 18.7)	
	Week 36	142	65.0 (22.9)	1.6	2.1	(-2.5, 5.6)		142	10.6	3.6	(3.5, 17.8)	
	Week 40	141	64.8 (22.8)	-1.4	2.1	(-5.4, 2.7)		141	5.5	3.7	(-1.7, 12.7)	
	Week 44	139	65.0 (22.8)	-0.4	2.1	(-4.5, 3.7)		139	8.6	3.7	(1.4, 15.8)	
	Week 48	133	65.3 (23.0)	-3.0	2.1	(-7.1, 1.1)		133	3.7	3.7	(-3.6, 11.0)	
	Week 52	133	65.3 (23.0)	-3.3	2.1	(-7.4, 0.8)		133	2.3	3.7	(-5.0, 9.6)	

表 2.7.6.26－80　血清鉄のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			14.0	2.8	(8.6, 19.5)	<0.001		25.3	5.0	(15.6, 35.0)	<0.001
	Week 4			20.8	2.8	(15.3, 26.3)	<0.001		36.7	5.0	(27.0, 46.5)	<0.001
	Week 6			19.3	2.8	(13.8, 24.8)	<0.001		32.5	5.0	(22.7, 42.3)	<0.001
	Week 8			24.0	2.8	(18.4, 29.6)	<0.001		40.3	5.0	(30.9, 50.7)	<0.001
	Week 10			15.8	2.8	(10.2, 21.3)	<0.001		27.4	5.0	(17.5, 37.2)	<0.001
	Week 12			18.6	2.8	(13.0, 24.1)	<0.001		30.1	5.1	(20.2, 40.0)	<0.001
	Week 16			15.6	2.9	(10.0, 21.2)	<0.001		25.7	5.1	(15.7, 35.6)	<0.001
	Week 20			13.9	2.9	(8.2, 19.5)	<0.001		24.6	5.1	(14.6, 34.6)	<0.001
	Week 24			15.0	2.9	(9.3, 20.6)	<0.001		26.9	5.1	(16.8, 37.0)	<0.001
	Week 28			16.4	2.9	(10.7, 22.2)	<0.001		27.8	5.2	(17.6, 37.9)	<0.001
	Week 32			10.3	2.9	(4.6, 16.1)	<0.001		18.4	5.2	(8.2, 28.6)	<0.001
	Week 36			12.2	3.0	(6.3, 18.0)	<0.001		21.2	5.3	(10.9, 31.5)	<0.001
	Week 40			13.1	3.0	(7.2, 19.0)	<0.001		23.1	5.3	(12.7, 33.6)	<0.001
	Week 44			15.7	3.0	(9.8, 21.7)	<0.001		25.2	5.4	(14.7, 35.8)	<0.001
	Week 48			15.8	3.1	(9.9, 21.8)	<0.001		28.8	5.4	(18.2, 39.3)	<0.001
	Week 52			17.2	3.1	(11.2, 23.2)	<0.001		29.0	5.4	(18.3, 39.6)	<0.001

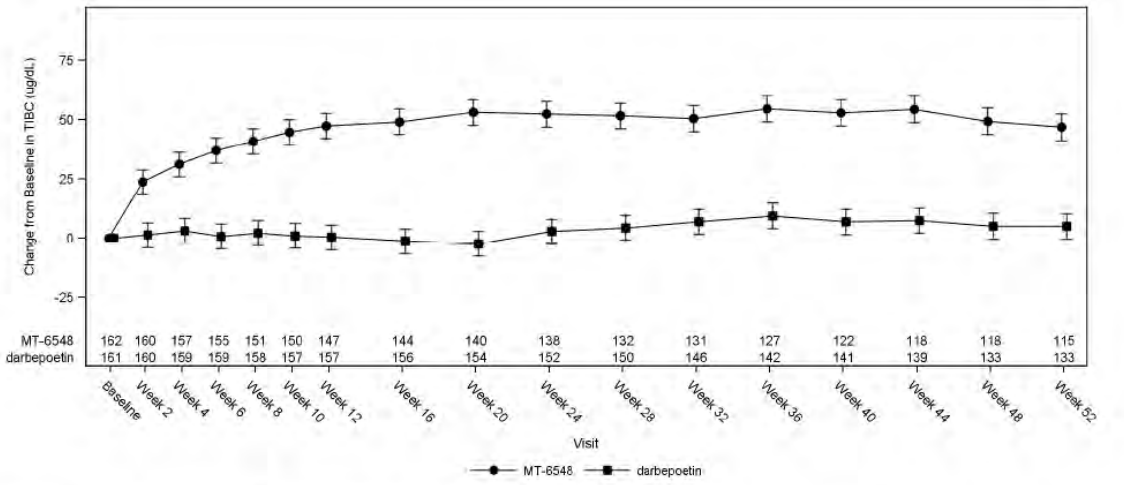
Note(s): Serum Iron (ug/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.3
Source: t_14_2_3_8_2_1.sas

5.3.5.1—9 表 14.2.3.8.2.1 より引用

2)　TIBC

MMRM を用いた TIBC のベースラインからの変化量の推移を図 2.7.6.26－31 に示した．MMRM を用いた TIBC のベースラインからの変化量を表 2.7.6.26－81 に示した．

MMRM を用いた TIBC の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 46.8 μg/dL 及び 41.2～52.5 μg/dL，darbepoetin 群で 4.9 μg/dL 及び -0.5～10.4 μg/dL であった．MMRM を用いた TIBC の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 41.9 μg/dL 及び 34.0～49.8 μg/dL であり，統計学的に有意な差が認められた（p<0.001）．



Note(s): Change from baseline in TIBC (ug/dL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.8.2.2
Source: f_14_2_4_2_1.sas

図 2.7.6.26－31　TIBC のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—9 図 11.4.1—7 より引用

表 2.7.6.26－81　TIBC のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	239.4 (36.3)	23.7	2.6	(18.5, 28.9)		160	10.0	1.1	(7.9, 12.1)	
	Week 4	157	239.7 (36.4)	31.2	2.7	(25.9, 36.4)		157	13.2	1.1	(11.0, 15.3)	
	Week 6	155	240.0 (36.6)	37.0	2.7	(31.7, 42.2)		155	15.8	1.1	(13.7, 17.9)	
	Week 8	151	240.2 (36.6)	40.8	2.7	(35.5, 46.1)		151	17.4	1.1	(15.2, 19.5)	
	Week 10	150	240.3 (36.7)	44.7	2.7	(39.4, 50.0)		150	19.1	1.1	(17.0, 21.3)	
	Week 12	147	240.5 (36.8)	47.4	2.7	(42.0, 52.7)		147	20.1	1.1	(18.0, 22.3)	
	Week 16	144	241.7 (36.7)	49.1	2.7	(43.8, 54.5)		144	20.6	1.1	(18.4, 22.8)	
	Week 20	140	241.5 (37.1)	53.1	2.7	(47.7, 58.4)		140	22.4	1.1	(20.2, 24.5)	
	Week 24	138	242.2 (37.2)	52.4	2.8	(47.0, 57.8)		138	22.1	1.1	(19.9, 24.3)	
	Week 28	132	243.0 (37.5)	51.6	2.8	(46.1, 57.1)		132	22.0	1.1	(19.8, 24.2)	
	Week 32	131	242.4 (37.7)	50.5	2.8	(45.0, 56.0)		131	21.6	1.1	(19.4, 23.8)	
	Week 36	127	242.6 (38.2)	54.6	2.8	(49.1, 60.1)		127	23.2	1.1	(20.9, 25.4)	
	Week 40	122	241.5 (38.4)	52.9	2.9	(47.3, 58.5)		122	22.5	1.2	(20.2, 24.8)	
	Week 44	118	240.8 (37.9)	54.4	2.9	(48.7, 60.0)		118	23.1	1.2	(20.9, 25.4)	
	Week 48	118	240.8 (37.9)	45.4	2.9	(43.7, 55.0)		118	21.1	1.2	(18.8, 23.4)	
	Week 52	115	241.4 (38.0)	46.8	2.9	(41.2, 52.5)		115	20.3	1.2	(18.0, 22.6)	

表 2.7.6.26－81　TIBC のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	242.4 (35.6)	1.3	2.6	(-3.8, 6.5)		160	0.8	1.1	(-1.3, 2.9)	
	Week 4	159	242.3 (35.7)	3.1	2.6	(-2.1, 8.3)		159	1.6	1.1	(-0.5, 3.7)	
	Week 6	159	242.3 (35.7)	0.7	2.6	(-4.5, 5.9)		159	0.6	1.1	(-1.5, 2.7)	
	Week 8	158	242.2 (35.8)	2.2	2.7	(-3.0, 7.4)		158	1.3	1.1	(-0.8, 3.4)	
	Week 10	157	242.2 (35.9)	1.0	2.7	(-4.2, 6.2)		157	0.7	1.1	(-1.4, 2.8)	
	Week 12	157	242.2 (35.9)	0.4	2.7	(-4.8, 5.6)		157	0.6	1.1	(-1.5, 2.7)	
	Week 16	156	242.4 (36.9)	-1.3	2.7	(-6.5, 3.9)		156	0.0	1.1	(-2.1, 2.2)	
	Week 20	154	242.6 (35.7)	-2.3	2.7	(-7.6, 2.9)		154	-0.4	1.1	(-2.6, 1.7)	
	Week 24	152	242.8 (35.9)	2.7	2.7	(-2.5, 8.0)		152	1.5	1.1	(-0.6, 3.7)	
	Week 28	150	243.0 (36.1)	4.4	2.7	(-0.9, 9.7)		150	2.1	1.1	(0.0, 4.3)	
	Week 32	146	242.8 (35.3)	6.9	2.7	(1.6, 12.2)		146	3.3	1.1	(1.1, 5.5)	
	Week 36	142	241.9 (35.2)	9.4	2.7	(4.1, 14.8)		142	4.3	1.1	(2.1, 6.5)	
	Week 40	141	242.1 (35.5)	6.9	2.7	(1.5, 12.2)		141	3.2	1.1	(1.0, 5.4)	
	Week 44	139	242.4 (35.7)	7.4	2.7	(2.0, 12.8)		139	3.5	1.1	(1.3, 5.6)	
	Week 48	133	242.7 (36.0)	5.3	2.8	(-0.5, 10.4)		133	2.5	1.1	(0.3, 4.7)	
	Week 52	133	242.7 (36.0)	4.9	2.8	(-0.5, 10.4)		133	2.6	1.1	(0.4, 4.8)	

表 2.7.6.26－81　TIBC のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			22.4	3.7	(15.0, 29.7)	<0.001		9.2	1.5	(6.2, 12.2)	<0.001
	Week 4			28.0	3.8	(20.7, 35.4)	<0.001		11.6	1.5	(8.6, 14.6)	<0.001
	Week 6			36.2	3.8	(28.9, 43.6)	<0.001		15.2	1.5	(12.2, 18.2)	<0.001
	Week 8			38.6	3.8	(31.2, 46.1)	<0.001		16.1	1.5	(13.1, 19.1)	<0.001
	Week 10			43.8	3.8	(36.3, 51.2)	<0.001		18.4	1.5	(15.4, 21.5)	<0.001
	Week 12			47.0	3.8	(39.5, 54.4)	<0.001		19.5	1.5	(16.5, 22.6)	<0.001
	Week 16			50.5	3.8	(43.0, 57.9)	<0.001		20.5	1.5	(17.5, 23.6)	<0.001
	Week 20			55.4	3.8	(47.9, 62.9)	<0.001		22.8	1.6	(19.7, 25.9)	<0.001
	Week 24			49.7	3.8	(42.2, 57.2)	<0.001		20.6	1.6	(17.5, 23.7)	<0.001
	Week 28			47.2	3.9	(39.6, 54.8)	<0.001		19.9	1.6	(16.8, 23.0)	<0.001
	Week 32			43.6	3.9	(36.0, 51.2)	<0.001		18.3	1.6	(15.2, 21.4)	<0.001
	Week 36			45.2	3.8	(37.6, 52.9)	<0.001		18.9	1.6	(15.8, 22.0)	<0.001
	Week 40			46.1	4.0	(38.3, 53.8)	<0.001		19.3	1.6	(16.1, 22.4)	<0.001
	Week 44			47.0	4.0	(39.2, 54.8)	<0.001		19.6	1.6	(16.5, 22.8)	<0.001
	Week 48			44.4	4.0	(36.5, 52.2)	<0.001		18.6	1.6	(15.4, 21.8)	<0.001
	Week 52			41.9	4.0	(34.0, 49.8)	<0.001		17.7	1.6	(14.5, 20.9)	<0.001

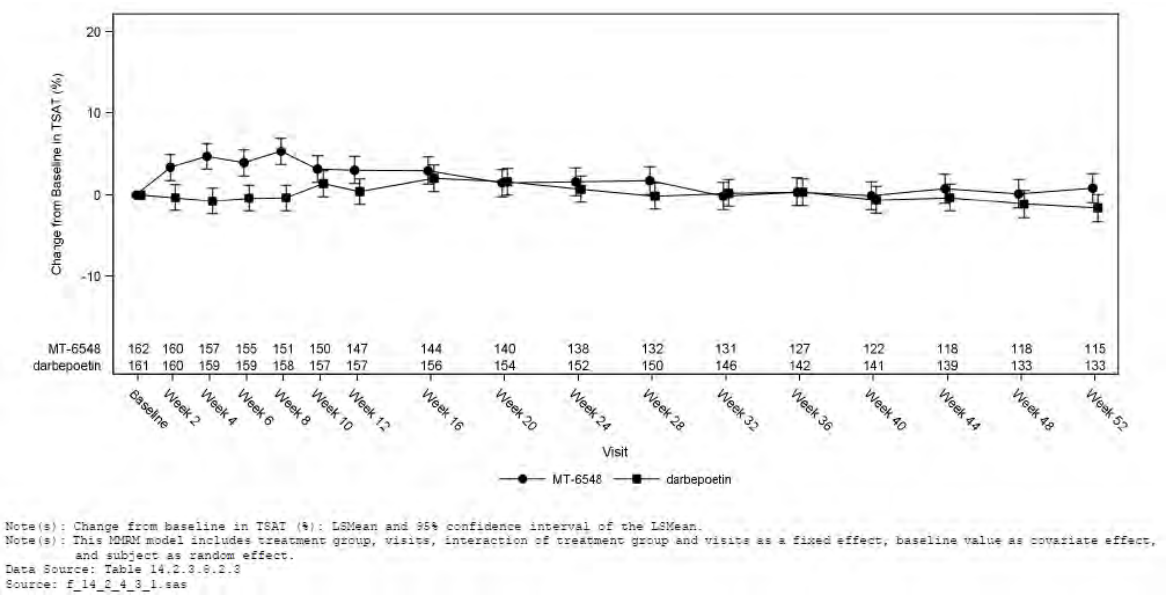
Note(s): TIBC (ug/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.3
Source: t_14_2_3_8_2_2.sas

5.3.5.1—9 表 14.2.3.8.2.2 より引用

3)　TSAT

MMRM を用いた TSAT のベースラインからの変化量の推移を図 2.7.6.26－32 に示した．MMRM を用いた TSAT のベースラインからの変化量を表 2.7.6.26－82 に示した．

MMRM を用いた TSAT の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.8%及び -1.0%～2.6%，darbepoetin 群で -1.6%及び -3.3%～0.1%であった．MMRM を用いた TSAT の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 2.4%及び -0.1%～4.9%であり，統計学的に有意な差は認められなかった．



Note(s): Change from baseline in TSAT (%): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.6.2.3
Source: f_14_2_4_3_1.sas

図 2.7.6.26－32　TSAT のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—9 図 11.4.1—8 より引用

表 2.7.6.26－82　TSAT のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	28.6 (10.6)	3.3	0.8	(1.7, 4.9)		160	18.5	3.4	(11.9, 25.2)	
	Week 4	157	28.6 (10.5)	4.7	0.8	(3.1, 6.3)		157	25.6	3.4	(18.9, 32.2)	
	Week 6	155	28.7 (10.5)	3.9	0.8	(2.3, 5.5)		155	20.8	3.4	(14.1, 27.5)	
	Week 8	151	28.6 (10.4)	5.3	0.8	(3.7, 7.0)		151	27.3	3.5	(20.5, 34.0)	
	Week 10	150	28.6 (10.4)	3.1	0.8	(1.5, 4.8)		150	19.0	3.5	(12.2, 25.7)	
	Week 12	147	28.5 (10.5)	3.0	0.8	(1.4, 4.7)		147	19.4	3.5	(12.6, 26.2)	
	Week 16	144	28.3 (10.0)	3.0	0.8	(1.3, 4.6)		144	18.0	3.5	(11.2, 24.9)	
	Week 20	140	28.3 (10.1)	1.4	0.8	(-0.2, 3.1)		140	13.5	3.6	(6.6, 20.4)	
	Week 24	138	28.3 (10.2)	1.6	0.9	(-0.1, 3.3)		138	14.8	3.6	(7.8, 21.7)	
	Week 28	132	28.3 (10.2)	1.8	0.9	(0.1, 3.4)		132	14.1	3.6	(7.1, 21.2)	
	Week 32	131	28.6 (10.3)	-0.1	0.9	(-1.8, 1.6)		131	8.8	3.6	(1.7, 15.9)	
	Week 36	127	28.7 (10.4)	0.4	0.9	(-1.4, 2.1)		127	9.8	3.7	(2.6, 17.0)	
	Week 40	122	28.5 (10.4)	-0.1	0.9	(-1.9, 1.6)		122	7.7	3.7	(0.4, 14.9)	
	Week 44	118	28.6 (10.3)	0.7	0.9	(-1.0, 2.5)		118	10.9	3.7	(3.6, 18.3)	
	Week 48	118	28.6 (10.3)	0.1	0.9	(-1.6, 1.9)		118	11.4	3.7	(4.1, 18.8)	
	Week 52	115	28.7 (10.3)	0.9	0.9	(-1.0, 2.6)		115	11.1	3.8	(3.7, 18.5)	

表 2.7.6.26－82　TSAT のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline				Percent Change from Baseline				
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	26.9 (9.3)	-0.3	0.8	(-1.9, 1.2)		160	3.3	3.4	(-2.9, 10.4)	
	Week 4	159	26.9 (9.4)	-0.8	0.8	(-2.3, 0.8)		159	2.8	3.4	(-3.8, 9.5)	
	Week 6	159	26.9 (9.4)	-0.4	0.8	(-2.0, 1.2)		159	5.4	3.4	(-1.2, 12.1)	
	Week 8	158	26.9 (9.4)	-0.4	0.8	(-2.0, 1.2)		158	6.3	3.4	(-0.3, 13.0)	
	Week 10	157	26.9 (9.4)	1.4	0.8	(-0.2, 3.0)		157	13.1	3.4	(6.4, 19.7)	
	Week 12	157	26.9 (9.4)	0.4	0.8	(-1.2, 2.0)		157	10.4	3.4	(3.7, 17.1)	
	Week 16	156	26.9 (9.4)	2.0	0.8	(0.4, 3.6)		156	16.3	3.4	(9.6, 23.0)	
	Week 20	154	27.0 (9.5)	1.6	0.8	(0.0, 3.2)		154	14.3	3.4	(7.5, 21.0)	
	Week 24	152	27.0 (9.5)	0.7	0.8	(-0.9, 2.3)		152	10.6	3.4	(3.8, 17.3)	
	Week 28	150	27.0 (9.5)	-0.1	0.8	(-1.8, 1.6)		150	7.9	3.4	(1.2, 14.7)	
	Week 32	146	27.1 (9.6)	0.2	0.8	(-1.4, 1.9)		146	9.6	3.5	(2.8, 16.5)	
	Week 36	142	27.1 (9.7)	0.3	0.8	(-1.3, 2.0)		142	8.7	3.5	(1.8, 15.6)	
	Week 40	141	27.0 (9.6)	-0.6	0.8	(-2.3, 1.0)		141	4.6	3.5	(-2.3, 11.5)	
	Week 44	139	27.1 (9.7)	-0.4	0.8	(-2.0, 1.3)		139	7.6	3.5	(0.7, 14.6)	
	Week 48	138	27.2 (9.8)	-1.1	0.9	(-2.8, 0.6)		138	3.1	3.6	(-3.9, 10.1)	
	Week 52	133	27.2 (9.8)	-1.6	0.9	(-3.3, 0.1)		133	1.0	3.6	(-6.0, 8.0)	

表 2.7.6.26－82　TSAT のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			3.7	1.1	(1.4, 5.9)	0.001		14.9	4.9	(5.4, 24.2)	0.002
	Week 4			5.5	1.1	(3.2, 7.7)	<0.001		22.7	4.8	(13.3, 32.2)	<0.001
	Week 6			4.4	1.2	(2.1, 6.6)	<0.001		15.3	4.8	(5.9, 24.8)	0.001
	Week 8			5.7	1.2	(3.5, 8.0)	<0.001		21.0	4.8	(11.5, 30.5)	<0.001
	Week 10			1.8	1.2	(-0.5, 4.0)	0.128		9.9	4.9	(-3.7, 15.4)	0.227
	Week 12			2.6	1.2	(0.3, 4.9)	0.024		9.0	4.9	(-0.5, 18.6)	0.064
	Week 16			0.9	1.2	(-1.4, 3.2)	0.425		1.7	4.9	(-7.9, 11.3)	0.725
	Week 20			-0.2	1.2	(-2.5, 2.1)	0.860		-0.6	4.9	(-10.4, 8.9)	0.878
	Week 24			0.9	1.2	(-1.5, 3.2)	0.462		4.2	4.9	(-5.5, 13.9)	0.396
	Week 28			1.9	1.2	(-0.4, 4.2)	0.113		6.2	5.0	(-3.6, 16.0)	0.215
	Week 32			-0.4	1.2	(-2.7, 2.0)	0.763		-0.8	5.0	(-10.7, 9.0)	0.869
	Week 36			0.0	1.2	(-2.4, 2.4)	0.986		1.1	5.1	(-8.9, 11.0)	0.829
	Week 40			0.5	1.2	(-1.9, 2.9)	0.678		3.1	5.1	(-7.0, 13.1)	0.550
	Week 44			1.1	1.2	(-1.3, 3.5)	0.382		3.3	5.2	(-6.8, 13.4)	0.522
	Week 48			1.2	1.2	(-1.2, 3.7)	0.318		8.4	5.2	(-1.8, 18.5)	0.108
	Week 52			2.4	1.3	(-0.1, 4.9)	0.055		10.1	5.2	(-0.1, 20.3)	0.053

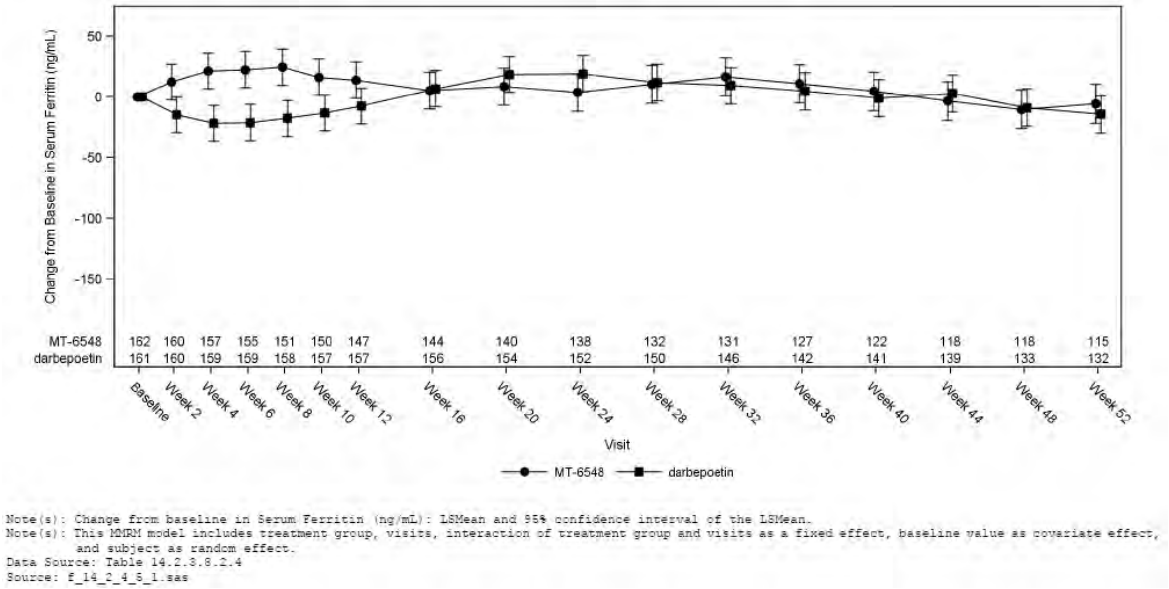
Note(s): TSAT (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.3
Source: t_14_2_3_8_2_3.sas

5.3.5.1—9 表 14.2.3.8.2.3 より引用

4)　血清フェリチン値

MMRM を用いた血清フェリチン値のベースラインからの変化量の推移を図 2.7.6.26－33 に示した．MMRM を用いた血清フェリチン値のベースラインからの変化量を表 2.7.6.26－83 に示した．

MMRM を用いた血清フェリチン値の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -5.64 ng/mL 及び -21.69～10.41 ng/mL，darbepoetin 群で -14.20 ng/mL 及び -29.61～1.20 ng/mL であった．MMRM を用いた血清フェリチン値の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 8.56 ng/mL 及び -13.69～30.81 ng/mL であり，統計学的に有意な差は認められなかった．



Note(s): Change from baseline in Serum Ferritin (ng/mL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.8.2.4
Source: f_14_2_4_5_1.sas

図 2.7.6.26－33　血清フェリチン値のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—9 図 11.4.1—9 より引用

表 2.7.6.26－83　血清フェリチン値のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	144.01 (140.40)	12.49	7.46	(-2.16, 27.13)		160	18.92	10.07	(-0.85, 38.69)	
	Week 4	157	143.88 (141.67)	21.28	7.51	(6.53, 36.02)		157	39.70	10.14	(19.79, 59.60)	
	Week 6	155	144.13 (142.49)	22.35	7.54	(7.54, 37.15)		155	43.53	10.19	(23.54, 63.52)	
	Week 8	151	146.22 (143.66)	24.42	7.60	(9.51, 39.33)		151	50.11	10.27	(29.95, 70.26)	
	Week 10	150	146.69 (144.03)	16.30	7.61	(1.35, 31.24)		150	42.74	10.29	(22.54, 62.94)	
	Week 12	147	146.53 (145.34)	14.00	7.66	(-1.02, 29.02)		147	43.87	10.36	(23.55, 64.19)	
	Week 16	144	145.98 (146.28)	5.15	7.70	(-9.96, 20.25)		144	32.86	10.42	(12.42, 53.31)	
	Week 20	140	147.97 (147.84)	8.67	7.76	(-6.55, 23.89)		140	28.59	10.51	(7.98, 49.20)	
	Week 24	138	147.99 (148.37)	3.81	7.79	(-11.47, 19.09)		138	29.25	10.55	(8.55, 49.95)	
	Week 28	132	148.08 (151.15)	10.52	7.88	(-4.94, 25.98)		132	40.43	10.69	(19.46, 61.40)	
	Week 32	131	149.07 (151.51)	16.76	7.90	(1.27, 32.25)		131	53.69	10.71	(32.66, 74.70)	
	Week 36	127	149.09 (153.70)	10.89	7.96	(-4.73, 26.51)		127	47.53	10.81	(26.32, 68.74)	
	Week 40	122	150.15 (154.75)	4.69	8.05	(-11.10, 20.48)		122	58.99	10.94	(37.52, 80.45)	
	Week 44	118	152.34 (156.61)	-3.40	8.12	(-19.34, 12.54)		118	37.31	11.05	(15.63, 58.99)	
	Week 48	118	152.34 (156.61)	-10.12	8.12	(-26.05, 5.82)		118	35.72	11.05	(14.04, 57.40)	
	Week 52	115	152.12 (158.49)	-5.64	8.18	(-21.69, 10.41)		115	69.60	11.14	(47.76, 91.45)	

表 2.7.6.26－83　血清フェリチン値のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	139.85 (95.57)	-14.69	7.46	(-29.34, -0.04)		160	-9.69	10.07	(-29.46, 10.08)	
	Week 4	159	140.37 (95.65)	-21.69	7.48	(-36.37, -7.00)		159	-10.43	10.10	(-30.24, 9.39)	
	Week 6	159	140.37 (95.65)	-20.93	7.48	(-35.61, -6.26)		159	-3.86	10.10	(-23.66, 16.97)	
	Week 8	158	140.84 (95.76)	-17.55	7.49	(-32.25, -2.84)		158	0.67	10.12	(-19.19, 20.52)	
	Week 10	157	140.59 (96.01)	-13.19	7.51	(-27.92, 1.54)		157	1.62	10.14	(-18.27, 21.51)	
	Week 12	157	140.59 (96.01)	-7.43	7.51	(-22.17, 7.30)		157	8.40	10.14	(-11.49, 28.29)	
	Week 16	156	139.78 (95.78)	6.87	7.52	(-7.89, 21.63)		156	27.16	10.16	(7.23, 47.09)	
	Week 20	154	139.61 (95.56)	18.48	7.54	(3.67, 33.28)		154	38.10	10.19	(18.09, 58.10)	
	Week 24	152	139.19 (95.92)	19.07	7.57	(4.22, 33.93)		152	36.18	10.23	(16.10, 56.25)	
	Week 28	150	139.13 (96.41)	11.93	7.60	(-2.97, 26.84)		150	32.01	10.27	(11.86, 52.16)	
	Week 32	146	140.63 (97.22)	9.34	7.65	(-5.67, 24.35)		146	35.43	10.35	(15.12, 55.73)	
	Week 36	142	141.13 (97.87)	4.58	7.70	(-10.53, 19.70)		142	31.56	10.43	(11.10, 52.02)	
	Week 40	141	141.42 (98.16)	-0.75	7.72	(-15.99, 14.40)		141	24.64	10.45	(4.14, 45.15)	
	Week 44	139	141.82 (98.81)	2.86	7.75	(-12.35, 18.06)		139	31.19	10.49	(10.60, 51.77)	
	Week 48	133	141.63 (99.18)	-8.78	7.83	(-24.16, 6.59)		133	22.18	10.63	(1.34, 43.03)	
	Week 52	132	141.43 (99.53)	-14.20	7.85	(-29.61, 1.20)		132	16.48	10.65	(-4.41, 37.38)	

表 2.7.6.26－83　血清フェリチン値のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			27.17	10.56	(6.46, 47.89)	0.010		28.61	14.26	(0.66, 56.57)	0.045
	Week 4			42.96	10.60	(22.16, 63.77)	<0.001		50.12	14.31	(22.04, 78.21)	<0.001
	Week 6			43.27	10.62	(22.43, 64.12)	<0.001		47.38	14.34	(19.23, 75.52)	<0.001
	Week 8			41.97	10.67	(21.02, 62.91)	<0.001		49.44	14.42	(21.15, 77.73)	<0.001
	Week 10			29.49	10.69	(8.50, 50.47)	0.006		41.12	14.45	(12.77, 69.47)	0.005
	Week 12			21.43	10.72	(0.39, 42.48)	0.046		35.47	14.49	(7.03, 63.90)	0.015
	Week 16			-1.72	10.76	(-22.84, 19.40)	0.873		5.70	14.55	(-22.85, 34.25)	0.695
	Week 20			-9.81	10.82	(-31.04, 11.43)	0.365		-9.51	14.64	(-38.23, 19.22)	0.516
	Week 24			-15.27	10.96	(-36.58, 6.04)	0.160		-6.93	14.70	(-35.77, 21.91)	0.637
	Week 28			-1.42	10.94	(-22.89, 20.06)	0.897		8.42	14.82	(-20.66, 37.50)	0.570
	Week 32			7.42	10.99	(-14.15, 28.99)	0.500		18.26	14.89	(-10.97, 47.48)	0.221
	Week 36			6.31	11.08	(-15.43, 28.05)	0.569		15.97	15.02	(-13.51, 45.44)	0.288
	Week 40			5.44	11.15	(-16.44, 27.32)	0.626		34.34	15.13	(4.66, 64.03)	0.023
	Week 44			-6.25	11.22	(-28.27, 15.77)	0.578		6.12	15.24	(-23.78, 36.02)	0.688
	Week 48			-1.33	11.29	(-23.48, 20.81)	0.906		13.54	15.33	(-16.54, 43.61)	0.377
	Week 52			8.56	11.34	(-13.69, 30.81)	0.450		53.12	15.41	(22.89, 83.35)	<0.001

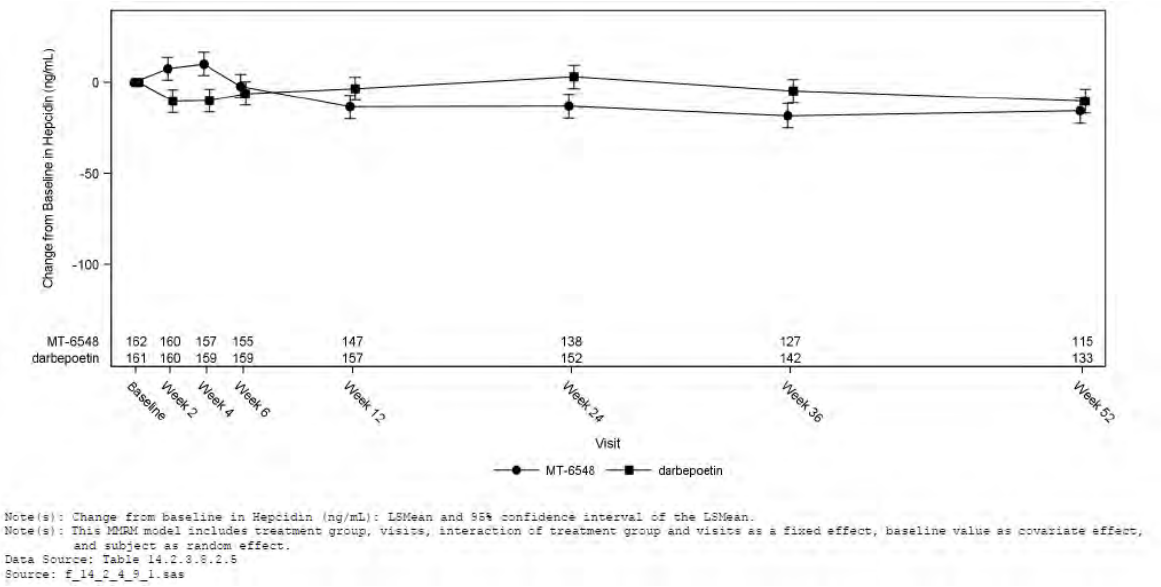
Note(s): Serum Ferritin (ng/mL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.3
Source: t_14_2_3_8_2_4.sas

5.3.5.1—9 表 14.2.3.8.2.4 より引用

5)　ヘプシジン

MMRM を用いたヘプシジンのベースラインからの変化量の推移を図 2.7.6.26－34 に示した．MMRM を用いたヘプシジンのベースラインからの変化量を表 2.7.6.26－84 に示した．

MMRM を用いたヘプシジンの 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -15.270 ng/mL 及び -22.258～ -8.282 ng/mL，darbepoetin 群で -10.127 ng/mL 及び -16.764～ -3.490 ng/mL であった．MMRM を用いたヘプシジンの 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は -5.143 ng/mL 及び -14.789～ 4.504 ng/mL であり，統計学的に有意な差は認められなかった．



Note(s): Change from baseline in Hepcidin (ng/mL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.8.2.5
Source: f_14_2_4_9_1.sas

図 2.7.6.26－34　ヘプシジンのベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—9 図 11.4.1—10 より引用

表 2.7.6.26－84　ヘプシジンのベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	66.214 (49.631)	7.905	3.185	(1.253, 13.756)		160	40.176	77.103	(-111.034, 191.385)	
	Week 4	167	65.435 (49.872)	10.183	3.208	(3.886, 16.480)		167	58.483	77.829	(-94.148, 211.115)	
	Week 6	155	65.526 (49.883)	-1.898	3.223	(-8.224, 4.428)		155	32.204	78.330	(-121.411, 185.818)	
	Week 12	147	66.016 (50.858)	-13.327	3.282	(-19.767, -6.887)		147	14.766	80.436	(-142.980, 172.512)	
	Week 24	138	66.537 (50.612)	-12.857	3.351	(-19.433, -6.281)		138	18.194	83.022	(-144.622, 181.010)	
	Week 36	127	67.998 (52.025)	-18.127	3.445	(-24.887, -11.367)		127	12.395	86.556	(-157.353, 182.142)	
	Week 52	115	69.641 (51.983)	-15.270	3.562	(-22.258, -8.282)		115	393.721	90.977	(215.303, 572.139)	
darbepoetin												
	Week 2	160	67.976 (47.913)	-10.169	3.186	(-16.421, -3.917)		160	-0.715	77.105	(-151.928, 150.498)	
	Week 4	159	68.095 (48.041)	-9.916	3.193	(-16.183, -3.649)		159	27.051	77.346	(-124.634, 178.736)	
	Week 6	159	68.095 (48.041)	-5.962	3.193	(-12.229, 0.305)		159	18.928	77.346	(-132.757, 170.613)	
	Week 12	157	68.140 (48.319)	-3.220	3.207	(-9.513, 3.073)		157	42.726	77.836	(-109.922, 195.371)	
	Week 24	152	67.355 (48.091)	3.184	3.241	(-3.176, 9.544)		152	80.703	79.114	(-74.449, 235.855)	
	Week 36	142	67.950 (49.158)	-4.662	3.312	(-11.161, 1.837)		142	97.702	81.844	(-62.804, 258.207)	
	Week 52	133	68.446 (49.949)	-10.127	3.383	(-16.764, -3.490)		133	37.628	84.561	(-128.207, 203.463)	

表 2.7.6.26－84　ヘプシジンのベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			17.674	4.509	(8.824, 26.523)	<0.001		40.891	109.075	(-173.018, 254.800)	0.708
	Week 4			20.099	4.631	(11.207, 28.990)	<0.001		31.433	109.751	(-183.803, 246.668)	0.775
	Week 6			4.064	4.541	(-4.848, 12.976)	0.371		13.276	110.108	(-202.659, 229.211)	0.904
	Week 12			-10.107	4.592	(-19.120, -1.095)	0.029		-27.959	111.960	(-247.526, 191.609)	0.803
	Week 24			-16.041	4.666	(-25.193, -6.884)	<0.001		-62.509	114.718	(-287.486, 162.468)	0.586
	Week 36			-13.465	4.783	(-22.851, -4.079)	0.005		-85.307	119.165	(-319.005, 148.391)	0.474
	Week 52			-5.143	4.916	(-14.789, 4.504)	0.296		356.093	124.253	(112.418, 599.769)	0.004

Note(s): Hepcidin (ng/mL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.3
Source: t_14_2_3_8_2_5.sas

5.3.5.1—9 表 14.2.3.8.2.5 より引用

(4)　鉄剤の投与量

鉄剤の月あたりの平均投与量の記述統計量を表 2.7.6.26－85 に示した．

静脈投与した鉄剤における，月あたりの平均投与量の 48 週～52 週後の投与前値（スクリーニング期間の鉄剤の平均投与量）からの変化量の平均値及びその 95%CI は，MT-6548 群で -20.88 mg/月及び -58.82～ 17.06 mg/月，darbepoetin 群で -33.36 mg/月及び -66.66～ -0.06 mg/月であった．静脈投与した鉄剤における，月あたりの平均投与量の平均値の 48 週～52 週後の投与前値（スクリーニング期間の鉄剤の平均投与量）からの変化量の MT-6548 群と darbepoetin 群の差の平均値及びその 95%CI は，12.48 mg/月及び -37.73～ 62.69 mg/月であり，統計学的に有意な差は認められなかった．

表 2.7.6.26－85 月あたりの鉄剤の平均投与量（FAS）

			Absolute					Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
Oral	MT-6548	Screening period	7	2995.61	1364.12	3043.75	(1521.9, 5598.3)	(1734.00, 4257.21)								
		Baseline <= to < Week 2	7	3003.37	1603.17	3043.75	(1087.1, 6087.5)	(1520.69, 4486.06)	7	7.76	2995.61 (1364.12)	267.06	0.00	(-434.8, 489.2)	(-239.23, 254.76)	0.941
		Week 2 <= to < Week 4	7	2848.08	1852.93	3043.75	(0.0, 6087.5)	(1134.41, 4561.75)	7	-147.53	2995.61 (1364.12)	632.86	0.00	(-1521.9, 489.2)	(-732.82, 437.77)	0.560
		Week 4 <= to < Week 6	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 6 <= to < Week 8	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 8 <= to < Week 10	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 10 <= to < Week 12	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 12 <= to < Week 16	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 16 <= to < Week 20	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 20 <= to < Week 24	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 24 <= to < Week 28	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 28 <= to < Week 32	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 32 <= to < Week 36	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 36 <= to < Week 40	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period					
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Week 40 <= to < Week 44	6	2790.10	2022.82	3043.75	(0.0, 6087.5)	(667.29, 4912.92)	6	-172.12	2962.22 (1491.19)	689.59	0.00	(-1521.9, 489.2)	(-895.79, 551.56)	0.568
		Week 44 <= to < Week 48	5	2739.38	2257.31	3043.75	(0.0, 6087.5)	(-63.44, 5542.19)	5	-206.54	2945.92 (1666.60)	765.20	0.00	(-1521.9, 489.2)	(-1156.66, 743.58)	0.579
		Week 48 <= to < Week 52	5	2739.38	2257.31	3043.75	(0.0, 6087.5)	(-63.44, 5542.19)	5	-206.54	2945.92 (1666.60)	765.20	0.00	(-1521.9, 489.2)	(-1156.66, 743.58)	0.579
		Baseline <= to < Week 52	7	2654.05	1842.26	3043.75	(41.8, 6087.5)	(1150.25, 4557.86)	7	-141.56	2995.61 (1364.12)	617.74	0.00	(-1480.1, 489.2)	(-712.87, 429.76)	0.567

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

Iron Route	Treatment Group	Period	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Screening Period N	Change from Screening Period Mean	Mean in Screening period (SD)	Change from Screening Period SD	Change from Screening Period Median	Change from Screening Period Minimum, Maximum	Change from Screening Period 95% CI	p value
	darbepoetin	Screening period	6	1477.49	2451.64	0.00	(0.0, 5821.2)	(-1095.35, 4050.32)								
		Baseline <= to < Week 2	6	1572.60	2656.39	0.00	(0.0, 6391.9)	(-1215.10, 4360.31)	6	95.12	1477.49 (2451.64)	232.99	0.00	(0.0, 570.7)	(-149.39, 339.62)	0.363
		Week 2 <= to < Week 4	6	1077.99	1674.35	0.00	(0.0, 3424.2)	(-679.13, 2835.12)	6	-399.49	1477.49 (2451.64)	978.56	0.00	(-2397.0, 0.0)	(-1426.42, 627.44)	0.363
		Week 4 <= to < Week 6	6	1039.95	1611.80	0.00	(0.0, 3195.9)	(-651.53, 2731.43)	6	-437.54	1477.49 (2451.64)	1071.75	0.00	(-2625.2, 0.0)	(-1562.27, 687.19)	0.363
		Week 6 <= to < Week 8	6	1039.95	1611.80	0.00	(0.0, 3195.9)	(-651.53, 2731.43)	6	-437.54	1477.49 (2451.64)	1071.75	0.00	(-2625.2, 0.0)	(-1562.27, 687.19)	0.363
		Week 8 <= to < Week 10	6	1039.95	1611.80	0.00	(0.0, 3195.9)	(-651.53, 2731.43)	6	-437.54	1477.49 (2451.64)	1071.75	0.00	(-2625.2, 0.0)	(-1562.27, 687.19)	0.363
		Week 10 <= to < Week 12	6	1293.69	1533.25	760.94	(0.0, 3195.9)	(-315.45, 2902.64)	6	-183.89	1477.49 (2451.64)	1342.02	0.00	(-2625.2, 1521.9)	(-1592.25, 1224.47)	0.751
		Week 12 <= to < Week 16	6	1547.24	1695.83	1521.88	(0.0, 3195.9)	(-232.42, 3326.90)	6	69.75	1477.49 (2451.64)	1795.94	0.00	(-2625.2, 3043.8)	(-1814.98, 1954.48)	0.928
		Week 16 <= to < Week 20	6	2041.85	1583.35	3005.70	(0.0, 3195.9)	(380.23, 3703.47)	6	564.36	1477.49 (2451.64)	2147.19	0.00	(-2625.2, 3043.8)	(-1688.98, 2817.70)	0.549
		Week 20 <= to < Week 24	6	2424.13	1262.09	3043.75	(0.0, 3195.9)	(1099.65, 3748.61)	6	946.64	1477.49 (2451.64)	2247.64	1032.70	(-2625.2, 3195.9)	(-1412.11, 3305.39)	0.350
		Week 24 <= to < Week 28	6	2949.54	387.13	3043.75	(2174.1, 3195.9)	(2543.27, 3355.81)	6	1472.05	1477.49 (2451.64)	2339.22	2608.93	(-2625.2, 3195.9)	(-982.81, 3926.92)	0.184
		Week 28 <= to < Week 32	6	3094.48	78.59	3043.75	(3043.8, 3195.9)	(3012.00, 3176.95)	6	1616.99	1477.49 (2451.64)	2417.07	3043.75	(-2625.2, 3195.9)	(-919.57, 4153.55)	0.162
		Week 32 <= to < Week 36	6	3094.48	78.59	3043.75	(3043.8, 3195.9)	(3012.00, 3176.95)	6	1616.99	1477.49 (2451.64)	2417.07	3043.75	(-2625.2, 3195.9)	(-919.57, 4153.55)	0.162
		Week 36 <= to < Week 40	6	2967.66	343.69	3043.75	(2282.8, 3195.9)	(2606.98, 3328.33)	6	1490.17	1477.49 (2451.64)	2346.16	2663.28	(-2625.2, 3195.9)	(-971.97, 3952.31)	0.190

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period					
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Week 40 <= to < Week 44	6	2092.58	1535.32	3043.75	(0.0, 3195.9)	(481.36, 3703.80)	6	615.09	1477.49 (2451.64)	2154.19	114.14	(-2625.2, 3043.8)	(-1645.60, 2875.78)	0.515
		Week 44 <= to < Week 48	6	2054.53	1592.52	3043.75	(0.0, 3195.9)	(383.28, 3725.78)	6	577.04	1477.49 (2451.64)	2164.39	0.00	(-2625.2, 3043.8)	(-1694.34, 2848.43)	0.543
		Week 48 <= to < Week 52	5	1826.25	1667.13	3043.75	(0.0, 3043.8)	(-243.77, 3896.27)	5	1217.50	608.75 (1361.21)	1667.13	0.00	(0.0, 3043.8)	(-852.52, 3287.52)	0.178
		Baseline <= to < Week 52	6	2146.20	966.68	2098.85	(811.1, 3349.6)	(1131.73, 3160.67)	6	668.71	1477.49 (2451.64)	1746.48	1143.08	(-2471.6, 2399.9)	(-1164.10, 2501.53)	0.391

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
Intravenous	MT-6548	Screening period	93	99.15	149.39	0.00	(0.0, 521.8)	(69.38, 129.92)								
		Baseline <= to < Week 2	93	67.29	101.52	0.00	(0.0, 521.8)	(46.38, 88.20)	93	-31.86	99.15 (149.39)	109.44	0.00	(-484.5, 149.1)	(-54.40, -9.32)	0.006
		Week 2 <= to < Week 4	91	68.15	117.07	0.00	(0.0, 521.8)	(43.77, 92.54)	91	-29.22	97.37 (150.54)	175.70	0.00	(-521.8, 447.2)	(-65.81, 7.38)	0.116
		Week 4 <= to < Week 6	91	57.51	97.25	0.00	(0.0, 521.8)	(37.25, 77.76)	91	-39.86	97.37 (150.54)	167.28	0.00	(-521.8, 521.8)	(-74.70, -5.03)	0.025
		Week 6 <= to < Week 8	90	51.81	83.48	0.00	(0.0, 447.2)	(34.32, 69.29)	90	-44.71	96.62 (151.17)	175.69	0.00	(-521.8, 447.2)	(-81.51, -7.91)	0.018
		Week 8 <= to < Week 10	87	52.65	90.60	0.00	(0.0, 447.2)	(33.34, 71.96)	87	-45.20	97.85 (152.84)	185.99	0.00	(-521.8, 447.2)	(-84.84, -5.56)	0.026
		Week 10 <= to < Week 12	87	61.15	88.91	0.00	(0.0, 372.7)	(42.20, 80.10)	87	-36.70	97.85 (152.84)	187.75	0.00	(-521.8, 372.7)	(-76.71, 3.32)	0.072
		Week 12 <= to < Week 16	85	52.83	79.47	0.00	(0.0, 323.0)	(35.69, 69.97)	85	-45.56	98.89 (154.27)	174.79	0.00	(-521.8, 323.0)	(-83.26, -7.85)	0.018
		Week 16 <= to < Week 20	85	44.98	76.12	0.00	(0.0, 354.1)	(28.56, 61.39)	85	-53.41	98.89 (154.27)	173.92	0.00	(-521.8, 354.1)	(-90.92, -15.90)	0.006
		Week 20 <= to < Week 24	83	39.25	67.39	0.00	(0.0, 242.3)	(24.53, 53.96)	83	-61.36	100.61 (155.45)	172.40	0.00	(-521.8, 242.3)	(-99.00, -23.71)	0.002
		Week 24 <= to < Week 28	82	43.89	73.05	0.00	(0.0, 316.8)	(27.83, 59.94)	82	-52.86	96.74 (152.35)	154.23	0.00	(-521.8, 173.9)	(-86.75, -18.97)	0.003
		Week 28 <= to < Week 32	80	51.44	85.55	0.00	(0.0, 354.1)	(32.40, 70.48)	80	-41.67	93.11 (147.52)	175.40	0.00	(-521.8, 354.1)	(-80.70, -2.64)	0.037
		Week 32 <= to < Week 36	78	47.72	71.18	0.00	(0.0, 316.8)	(31.67, 63.77)	78	-45.38	93.10 (148.85)	173.76	0.00	(-521.8, 316.8)	(-84.56, -6.20)	0.024
		Week 36 <= to < Week 40	76	67.79	86.07	0.00	(0.0, 354.1)	(48.35, 87.23)	76	-25.47	93.27 (150.15)	187.16	0.00	(-521.8, 354.1)	(-68.24, 17.29)	0.239

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Week 40 <= to < Week 44	74	56.53	74.11	0.00	(0.0, 223.6)	(39.36, 73.70)	74	-38.09	94.61 (151.79)	171.14	0.00	(-521.8, 223.6)	(-77.73, 1.57)	0.060
		Week 44 <= to < Week 48	72	53.10	71.08	0.00	(0.0, 180.1)	(36.39, 69.80)	72	-44.14	97.24 (153.07)	167.79	0.00	(-521.8, 180.1)	(-83.57, -4.72)	0.029
		Week 48 <= to < Week 52	72	76.36	92.31	35.53	(0.0, 472.1)	(54.67, 98.05)	72	-20.88	97.24 (153.07)	161.47	0.00	(-521.8, 250.5)	(-58.82, 17.06)	0.276
		Baseline <= to < Week 52	93	57.62	46.86	43.00	(0.0, 178.9)	(47.97, 67.27)	93	-41.53	99.15 (149.39)	183.44	19.11	(-493.6, 167.0)	(-73.13, -9.93)	0.011

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
	darbepoetin	Screening period	112	96.93	151.12	0.00	(0.0, 521.8)	(68.63, 125.22)								
		Baseline <= to < Week 2	112	56.70	103.26	0.00	(0.0, 521.8)	(37.37, 76.04)	112	-40.22	96.93 (151.12)	120.55	0.00	(-466.9, 372.7)	(-62.79, -17.65)	<0.001
		Week 2 <= to < Week 4	111	43.54	89.90	0.00	(0.0, 521.8)	(26.63, 60.45)	111	-52.69	96.23 (151.63)	152.81	0.00	(-521.8, 521.8)	(-81.43, -23.94)	<0.001
		Week 4 <= to < Week 6	111	54.12	97.21	0.00	(0.0, 521.8)	(35.83, 72.41)	111	-42.11	96.23 (151.63)	164.29	0.00	(-521.8, 521.8)	(-73.01, -11.21)	0.008
		Week 6 <= to < Week 8	111	46.12	79.72	0.00	(0.0, 521.8)	(31.12, 61.11)	111	-50.11	96.23 (151.63)	157.91	0.00	(-521.8, 186.4)	(-79.82, -20.41)	0.001
		Week 8 <= to < Week 10	111	47.63	90.04	0.00	(0.0, 521.8)	(30.69, 64.57)	111	-48.60	96.23 (151.63)	169.86	0.00	(-521.8, 521.8)	(-80.55, -16.65)	0.003
		Week 10 <= to < Week 12	111	66.96	118.02	0.00	(0.0, 521.8)	(44.76, 89.16)	111	-29.27	96.23 (151.63)	181.98	0.00	(-521.8, 521.8)	(-63.50, 4.96)	0.093
		Week 12 <= to < Week 16	111	61.14	102.53	0.00	(0.0, 559.1)	(41.86, 80.43)	111	-35.09	96.23 (151.63)	173.10	0.00	(-521.8, 559.1)	(-67.65, -2.53)	0.035
		Week 16 <= to < Week 20	111	45.18	82.62	0.00	(0.0, 521.8)	(29.64, 60.72)	111	-51.05	96.23 (151.63)	160.78	0.00	(-521.8, 173.9)	(-81.29, -20.81)	0.001
		Week 20 <= to < Week 24	110	49.54	87.86	0.00	(0.0, 521.8)	(32.93, 66.14)	110	-43.56	93.09 (148.66)	160.18	0.00	(-521.8, 260.9)	(-73.83, -13.29)	0.005
		Week 24 <= to < Week 28	108	53.80	89.67	0.00	(0.0, 521.8)	(36.70, 70.91)	108	-40.48	94.28 (149.73)	145.02	0.00	(-521.8, 316.8)	(-68.14, -12.81)	0.005
		Week 28 <= to < Week 32	107	53.19	94.61	0.00	(0.0, 521.8)	(35.06, 71.32)	107	-41.97	95.16 (150.15)	165.81	0.00	(-521.8, 447.2)	(-73.75, -10.19)	0.010
		Week 32 <= to < Week 36	103	51.56	79.81	0.00	(0.0, 347.9)	(35.96, 67.16)	103	-40.54	92.10 (146.26)	158.81	0.00	(-521.8, 298.2)	(-71.58, -9.50)	0.011
		Week 36 <= to < Week 40	101	51.38	84.26	0.00	(0.0, 484.5)	(34.75, 68.02)	101	-41.68	93.06 (147.44)	159.86	0.00	(-521.8, 298.2)	(-73.24, -10.13)	0.010

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Week 40 <= to < Week 44	100	53.17	73.63	0.00	(0.0, 223.6)	(38.56, 67.78)	100	-39.09	92.26 (147.96)	156.41	0.00	(-521.8, 173.9)	(-70.12, -8.06)	0.014
		Week 44 <= to < Week 48	98	51.50	70.31	0.00	(0.0, 223.6)	(37.40, 65.59)	98	-40.87	92.36 (148.95)	161.68	0.00	(-521.8, 173.9)	(-73.28, -8.45)	0.014
		Week 48 <= to < Week 52	96	60.93	82.72	0.00	(0.0, 347.9)	(44.17, 77.69)	96	-33.36	94.29 (149.90)	164.36	0.00	(-521.8, 316.8)	(-66.66, -0.06)	0.050
		Baseline <= to < Week 52	112	55.51	57.89	43.48	(0.0, 521.8)	(44.67, 66.35)	112	-41.42	96.93 (151.12)	143.11	14.57	(-489.5, 145.3)	(-68.21, -14.62)	0.003

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
Any Route	MT-6548	Screening period	100	301.90	827.76	4.14	(0.0, 5898.3)	(137.66, 466.15)								
		Baseline <= to < Week 2	100	272.82	855.69	0.00	(0.0, 6087.5)	(103.03, 442.60)	100	-29.09	301.90 (827.76)	124.73	0.00	(-484.5, 489.2)	(-53.83, -4.34)	0.022
		Week 2 <= to < Week 4	98	266.72	861.94	0.00	(0.0, 6087.5)	(93.91, 439.53)	98	-37.67	304.39 (836.06)	233.14	0.00	(-1521.9, 489.2)	(-84.41, 9.08)	0.113
		Week 4 <= to < Week 6	97	226.53	812.28	0.00	(0.0, 6087.5)	(62.82, 390.24)	97	-48.04	274.58 (786.32)	228.10	0.00	(-1521.9, 521.8)	(-94.02, -2.07)	0.041
		Week 6 <= to < Week 8	96	222.95	816.00	0.00	(0.0, 6087.5)	(57.61, 388.29)	96	-52.67	276.63 (790.38)	234.32	0.00	(-1521.9, 489.2)	(-100.15, -5.20)	0.030
		Week 8 <= to < Week 10	93	229.26	829.00	0.00	(0.0, 6087.5)	(58.53, 399.99)	93	-53.38	282.65 (802.03)	243.24	0.00	(-1521.9, 489.2)	(-103.48, -3.29)	0.037
		Week 10 <= to < Week 12	93	237.21	827.12	0.00	(0.0, 6087.5)	(66.87, 407.55)	93	-45.44	282.65 (802.03)	244.78	0.00	(-1521.9, 489.2)	(-95.85, 4.96)	0.077
		Week 12 <= to < Week 16	91	233.31	836.54	0.00	(0.0, 6087.5)	(59.09, 407.53)	91	-53.90	287.21 (810.23)	236.49	0.00	(-1521.9, 489.2)	(-103.15, -4.65)	0.032
		Week 16 <= to < Week 20	91	225.97	837.85	0.00	(0.0, 6087.5)	(51.48, 400.46)	91	-61.24	287.21 (810.23)	235.64	0.00	(-1521.9, 489.2)	(-110.31, -12.16)	0.015
		Week 20 <= to < Week 24	89	224.70	847.28	0.00	(0.0, 6087.5)	(46.22, 403.18)	89	-69.83	293.53 (818.26)	235.57	0.00	(-1521.9, 489.2)	(-118.45, -19.20)	0.007
		Week 24 <= to < Week 28	88	231.13	851.34	0.00	(0.0, 6087.5)	(50.75, 411.51)	88	-60.99	292.12 (822.84)	224.48	0.00	(-1521.9, 489.2)	(-108.55, -13.43)	0.013
		Week 28 <= to < Week 32	86	242.51	860.23	0.00	(0.0, 6087.5)	(59.07, 426.94)	86	-50.77	293.28 (831.60)	240.16	0.00	(-1521.9, 489.2)	(-102.27, 0.72)	0.053
		Week 32 <= to < Week 36	84	243.61	869.50	0.00	(0.0, 6087.5)	(54.92, 432.30)	84	-54.43	298.04 (840.88)	240.26	0.00	(-1521.9, 489.2)	(-106.58, -2.29)	0.041
		Week 36 <= to < Week 40	82	266.99	876.40	15.53	(0.0, 6087.5)	(74.42, 459.55)	82	-36.20	303.19 (850.42)	251.52	0.00	(-1521.9, 489.2)	(-91.47, 19.06)	0.196

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Week 40 <= to < Week 44	80	261.55	888.26	0.00	(0.0, 6087.5)	(63.88, 459.22)	80	-48.13	309.68 (860.08)	241.71	0.00	(-1521.9, 489.2)	(-101.92, 5.66)	0.079
		Week 44 <= to < Week 48	77	227.53	846.65	0.00	(0.0, 6087.5)	(35.36, 419.70)	77	-54.69	282.22 (816.88)	242.36	0.00	(-1521.9, 489.2)	(-109.70, 0.32)	0.051
		Week 48 <= to < Week 52	77	249.28	844.04	43.48	(0.0, 6087.5)	(57.71, 440.85)	77	-32.94	282.22 (816.88)	239.36	0.00	(-1521.9, 489.2)	(-87.27, 21.39)	0.231
		Baseline <= to < Week 52	100	253.37	849.68	44.20	(0.0, 6087.5)	(84.77, 421.96)	100	-48.53	301.90 (827.76)	213.69	12.54	(-1460.1, 489.2)	(-90.93, -6.13)	0.025

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

			Absolute						Change from Screening Period						
Iron Route	Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
	darbepoetin	Screening period	118	167.12	609.34	0.00	(0.0, 6821.2)	(56.03, 278.22)								
		Baseline <= to < Week 2	118	133.78	650.79	0.00	(0.0, 6391.9)	(15.14, 252.43)	118	-33.34	167.12 (609.34)	130.38	0.00	(-466.9, 570.7)	(-57.11, -9.57)	0.006
		Week 2 <= to < Week 4	117	96.59	425.46	0.00	(0.0, 3424.2)	(18.69, 174.50)	117	-70.47	167.07 (611.96)	263.29	0.00	(-2397.0, 521.8)	(-118.68, -22.26)	0.005
		Week 4 <= to < Week 6	117	104.68	410.65	0.00	(0.0, 3195.9)	(29.48, 179.87)	117	-62.39	167.07 (611.96)	287.71	0.00	(-2625.2, 521.8)	(-116.07, -9.71)	0.021
		Week 6 <= to < Week 8	117	97.08	408.01	0.00	(0.0, 3195.9)	(22.37, 171.79)	117	-69.98	167.07 (611.96)	283.76	0.00	(-2625.2, 186.4)	(-121.94, -18.02)	0.009
		Week 8 <= to < Week 10	117	98.52	409.86	0.00	(0.0, 3195.9)	(23.47, 173.57)	117	-68.55	167.07 (611.96)	290.33	0.00	(-2625.2, 521.8)	(-121.71, -15.39)	0.012
		Week 10 <= to < Week 12	117	129.87	434.02	0.00	(0.0, 3195.9)	(50.39, 209.34)	117	-37.20	167.07 (611.96)	331.97	0.00	(-2625.2, 1521.9)	(-97.99, 23.59)	0.228
		Week 12 <= to < Week 16	117	137.35	492.24	0.00	(0.0, 3195.9)	(47.22, 227.48)	117	-29.71	167.07 (611.96)	409.85	0.00	(-2625.2, 3043.8)	(-104.76, 45.33)	0.435
		Week 16 <= to < Week 20	117	147.53	556.92	0.00	(0.0, 3195.9)	(45.60, 249.46)	117	-19.49	167.07 (611.96)	491.76	0.00	(-2625.2, 3043.8)	(-109.53, 70.56)	0.669
		Week 20 <= to < Week 24	116	172.36	596.28	0.00	(0.0, 3195.9)	(62.70, 282.02)	116	7.66	164.70 (614.08)	540.91	0.00	(-2625.2, 3195.9)	(-91.80, 107.12)	0.879
		Week 24 <= to < Week 28	114	206.21	660.34	0.00	(0.0, 3195.9)	(83.68, 328.74)	114	39.13	167.08 (619.21)	614.10	0.00	(-2625.2, 3195.9)	(-74.82, 153.08)	0.498
		Week 28 <= to < Week 32	113	214.68	691.33	0.00	(0.0, 3195.9)	(85.82, 343.53)	113	46.12	168.56 (621.77)	653.03	0.00	(-2625.2, 3195.9)	(-75.60, 167.84)	0.454
		Week 32 <= to < Week 36	109	219.06	701.71	0.00	(0.0, 3195.9)	(85.84, 352.28)	109	50.70	168.36 (631.85)	662.21	0.00	(-2625.2, 3195.9)	(-75.03, 176.42)	0.426
		Week 36 <= to < Week 40	107	214.91	693.13	0.00	(0.0, 3195.9)	(83.98, 345.84)	107	44.21	170.70 (637.52)	639.63	0.00	(-2625.2, 3195.9)	(-78.38, 166.81)	0.476

表 2.7.6.26－85　月あたりの鉄剤の平均投与量（FAS）（続き）

Iron Route	Treatment Group	Period	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Screening Period N	Change from Screening Period Mean	Mean in Screening period (SD)	Change from Screening Period SD	Change from Screening Period Median	Change from Screening Period Minimum, Maximum	Change from Screening Period 95% CI	Change from Screening Period p value
		Week 40 <= to < Week 44	106	168.61	584.44	0.00	(0.0, 3196.9)	(56.05, 281.16)	106	-2.06	170.67 (640.55)	516.83	0.00	(-2625.2, 3043.8)	(-101.59, 97.48)	0.967
		Week 44 <= to < Week 48	104	167.06	589.92	0.00	(0.0, 3196.9)	(52.33, 281.78)	104	-5.22	172.28 (646.51)	522.48	0.00	(-2625.2, 3043.8)	(-106.83, 96.39)	0.919
		Week 48 <= to < Week 52	101	148.32	515.54	0.00	(0.0, 3043.8)	(46.55, 250.09)	101	28.56	119.76 (328.69)	459.56	0.00	(-521.8, 3043.8)	(-62.16, 119.29)	0.534
		Baseline <= to < Week 52	118	161.81	505.84	45.15	(0.0, 3349.6)	(69.59, 254.04)	118	-5.31	167.12 (609.34)	417.52	16.01	(-2471.6, 2389.9)	(-81.43, 70.81)	0.890

Note(s): Iron: average monthly dose (mg).
Note(s): p value is analyzed by paired t-test from screening period.
Note(s): Subjects who changed iron route in treatment period or subjects who never take Iron in treatment period is excluded from the analysis.
Dose of iron counts as 0 mg during the period in which subjects did not take Iron.
Note(s): Doses are expressed as elemental iron.
Data Source: Listing 16.2.4.2
Source: t_14_2_3_5_1.sas

5.3.5.1—9 表 11.4.1—3 より引用

(5)　鉄剤の投与を受けた被験者の割合

鉄剤の投与を受けた被験者の割合を表 2.7.6.26－86 に示した．

鉄剤の静脈投与を受けた被験者の割合は，MT-6548 群においてスクリーニング期間 26.5%に対し，48 週～52 週後では 30.9%であり，darbepoetin 群においてスクリーニング期間 30.4%に対し，48 週～52 週後では 33.3%であった．鉄剤の経口投与を受けた被験者の割合は，MT-6548 群においてスクリーニング期間 4.3%に対し，48 週～52 週後では 3.3%であり，darbepoetin 群においてスクリーニング期間 1.2%に対し，48 週～52 週後では 2.2%であった．

表 2.7.6.26－86 鉄剤投与を受けた被験者の割合（FAS）

Iron Route	Period	MT-6548(N=162) N*	n (%)	95% CI of proportion	p value from S	darbepoetin(N=161) N*	n (%)	95% CI of proportion	p value from S	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Oral	Screening period	162	7(4.3)	(1.75, 8.70)		161	2(1.2)	(0.15, 4.42)		3.1	(-7.8, 13.9)	0.174
	Baseline <= to < Week 2	162	7(4.3)	(1.75, 8.70)	-	161	2(1.2)	(0.15, 4.42)	-	3.1	(-7.8, 13.9)	0.174
	Week 2 <= to < Week 4	159	6(3.8)	(1.40, 8.03)	0.317	159	2(1.3)	(0.15, 4.47)	-	2.5	(-8.6, 13.7)	0.283
	Week 4 <= to < Week 6	156	5(3.2)	(1.05, 7.32)	0.317	159	2(1.3)	(0.15, 4.47)	-	1.9	(-9.2, 12.9)	0.280
	Week 6 <= to < Week 8	154	5(3.2)	(1.06, 7.41)	0.317	159	2(1.3)	(0.15, 4.47)	-	2.0	(-9.2, 13.0)	0.277
	Week 8 <= to < Week 10	150	5(3.3)	(1.09, 7.61)	0.317	158	2(1.3)	(0.15, 4.50)	-	2.1	(-9.1, 13.3)	0.272
	Week 10 <= to < Week 12	150	5(3.3)	(1.09, 7.61)	0.317	158	3(1.9)	(0.39, 5.45)	0.317	1.4	(-9.8, 12.6)	0.492
	Week 12 <= to < Week 16	144	5(3.5)	(1.14, 7.92)	0.317	157	3(1.9)	(0.40, 5.48)	0.317	1.6	(-9.7, 12.8)	0.486
	Week 16 <= to < Week 20	144	5(3.5)	(1.14, 7.92)	0.317	156	4(2.6)	(0.70, 6.43)	0.157	0.9	(-10.4, 12.2)	0.742
	Week 20 <= to < Week 24	140	5(3.6)	(1.17, 8.14)	0.317	154	5(3.2)	(1.06, 7.41)	0.083	0.3	(-11.1, 11.8)	1.000
	Week 24 <= to < Week 28	136	5(3.7)	(1.20, 8.37)	0.317	152	6(3.9)	(1.46, 8.39)	0.046	-0.3	(-11.8, 11.3)	1.000
	Week 28 <= to < Week 32	133	5(3.8)	(1.23, 8.56)	0.317	150	6(4.0)	(1.48, 8.50)	0.046	-0.2	(-11.9, 11.4)	1.000
	Week 32 <= to < Week 36	131	5(3.8)	(1.25, 8.68)	0.317	147	6(4.1)	(1.51, 8.67)	0.046	-0.3	(-12.0, 11.5)	1.000
	Week 36 <= to < Week 40	129	5(3.9)	(1.27, 8.81)	0.317	145	6(4.1)	(1.53, 8.79)	0.046	-0.3	(-12.1, 11.6)	1.000
	Week 40 <= to < Week 44	127	5(3.9)	(1.29, 8.95)	0.317	143	5(3.5)	(1.14, 7.97)	0.083	0.4	(-11.5, 12.3)	1.000
	Week 44 <= to < Week 48	124	4(3.2)	(0.89, 8.05)	0.317	138	4(2.9)	(0.80, 7.26)	0.157	0.3	(-11.8, 12.4)	1.000
	Week 48 <= to < Week 52	123	4(3.3)	(0.89, 8.12)	0.317	138	3(2.2)	(0.46, 6.36)	0.157	1.0	(-11.1, 13.2)	0.712
	Baseline <= to < Week 52	162	7(4.3)	(1.75, 8.70)	-	161	6(3.7)	(1.38, 7.93)	0.046	0.6	(-10.3, 11.5)	1.000

表 2.7.6.26－86　鉄剤投与を受けた被験者の割合（FAS）（続き）

Iron Route	Period	MT-6548(N=162) N*	MT-6548(N=162) n (%)	MT-6548(N=162) 95% CI of proportion	MT-6548(N=162) p value from S	darbepoetin(N=161) N*	darbepoetin(N=161) n (%)	darbepoetin(N=161) 95% CI of proportion	darbepoetin(N=161) p value from S	Difference of proportion (MT-6548 − darbepoetin) Difference	95% CI	p value
Intravenous	Screening period	162	43(26.5)	(19.92, 34.04)		161	49(30.4)	(23.44, 38.17)		-3.9	(-14.5, 7.2)	0.461
	Baseline <= to < Week 2	162	38(23.5)	(17.17, 30.75)	0.132	161	42(26.1)	(19.49, 33.58)	0.090	-2.6	(-13.3, 8.4)	0.608
	Week 2 <= to < Week 4	159	34(21.4)	(15.29, 28.58)	0.162	159	33(20.8)	(14.74, 27.89)	0.005	0.6	(-10.6, 11.9)	1.000
	Week 4 <= to < Week 6	156	30(19.2)	(13.37, 26.30)	0.034	159	39(24.5)	(18.06, 31.97)	0.139	-5.3	(-16.3, 5.9)	0.278
	Week 6 <= to < Week 8	154	34(22.1)	(15.80, 29.46)	0.303	159	41(25.8)	(19.18, 33.31)	0.286	-3.7	(-14.8, 7.3)	0.508
	Week 8 <= to < Week 10	150	28(18.7)	(12.78, 25.84)	0.063	158	39(24.7)	(18.18, 32.16)	0.180	-6.0	(-17.1, 5.2)	0.216
	Week 10 <= to < Week 12	150	34(22.7)	(16.24, 30.21)	0.435	158	43(27.2)	(20.45, 34.86)	0.456	-4.5	(-15.7, 6.7)	0.430
	Week 12 <= to < Week 16	144	34(23.6)	(16.94, 31.40)	0.612	157	45(28.7)	(21.74, 36.41)	0.674	-5.1	(-16.3, 6.3)	0.359
	Week 16 <= to < Week 20	144	28(19.4)	(13.33, 26.86)	0.128	156	40(25.6)	(18.99, 33.24)	0.248	-6.2	(-17.4, 5.1)	0.216
	Week 20 <= to < Week 24	140	28(20.0)	(13.72, 27.69)	0.182	154	42(27.3)	(20.42, 35.03)	0.475	-7.3	(-18.6, 4.2)	0.171
	Week 24 <= to < Week 28	136	28(20.6)	(14.14, 28.36)	0.237	152	41(27.0)	(20.10, 34.76)	0.411	-6.4	(-17.9, 5.2)	0.216
	Week 28 <= to < Week 32	133	27(20.3)	(13.83, 28.14)	0.250	150	38(25.3)	(18.59, 33.07)	0.238	-5.0	(-16.6, 6.7)	0.326
	Week 32 <= to < Week 36	131	30(22.9)	(16.02, 31.05)	0.739	147	39(26.5)	(19.60, 34.44)	0.466	-3.6	(-15.3, 9.1)	0.491
	Week 36 <= to < Week 40	129	36(27.9)	(20.37, 36.48)	0.435	145	42(29.0)	(21.74, 37.07)	0.886	-1.1	(-12.8, 10.8)	0.894
	Week 40 <= to < Week 44	127	33(26.0)	(18.61, 34.51)	0.622	143	41(28.7)	(21.42, 36.82)	0.881	-2.7	(-14.6, 9.2)	0.682
	Week 44 <= to < Week 48	124	30(24.2)	(16.96, 32.70)	1.000	138	40(29.0)	(21.58, 37.31)	0.881	-4.8	(-16.8, 7.3)	0.404
	Week 48 <= to < Week 52	123	38(30.9)	(22.88, 39.86)	0.170	135	45(33.3)	(25.46, 41.96)	0.546	-2.4	(-14.6, 9.8)	0.691
	Baseline <= to < Week 52	162	89(54.9)	(46.94, 62.75)	<0.001	161	107(66.5)	(58.60, 73.70)	<0.001	-11.5	(-22.5, -0.8)	0.040

表 2.7.6.26－86　鉄剤投与を受けた被験者の割合（FAS）（続き）

Iron Route	Period	MT-6548(N=162) N*	MT-6548(N=162) n (%)	MT-6548(N=162) 95% CI of proportion	MT-6548(N=162) p value from S	darbepoetin(N=161) N*	darbepoetin(N=161) n (%)	darbepoetin(N=161) 95% CI of proportion	darbepoetin(N=161) p value from S	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Any Route	Screening period	162	50(30.9)	(23.85, 38.59)		161	51(31.7)	(24.58, 39.46)		-0.8	(-11.5, 10.3)	0.905
	Baseline <= to < Week 2	162	45(27.8)	(21.04, 35.35)	0.132	161	44(27.3)	(20.61, 34.90)	0.090	0.4	(-10.3, 11.5)	1.000
	Week 2 <= to < Week 4	159	40(25.2)	(18.62, 32.64)	0.117	159	35(22.0)	(15.84, 29.26)	0.005	3.1	(-8.1, 14.4)	0.597
	Week 4 <= to < Week 6	156	35(22.4)	(16.15, 29.80)	0.023	159	41(25.8)	(19.18, 33.31)	0.139	-3.4	(-14.3, 7.9)	0.512
	Week 6 <= to < Week 8	154	39(25.3)	(18.67, 32.95)	0.237	159	43(27.0)	(20.31, 34.65)	0.286	-1.7	(-12.9, 9.4)	0.797
	Week 8 <= to < Week 10	150	33(22.0)	(15.65, 29.49)	0.046	158	41(25.9)	(19.31, 33.51)	0.180	-3.9	(-15.1, 7.3)	0.427
	Week 10 <= to < Week 12	150	39(26.0)	(19.19, 33.79)	0.355	158	46(29.1)	(22.17, 36.86)	0.555	-3.1	(-14.2, 8.1)	0.610
	Week 12 <= to < Week 16	144	39(27.1)	(20.02, 35.11)	0.505	157	48(30.6)	(23.46, 38.42)	0.782	-3.5	(-14.7, 7.8)	0.527
	Week 16 <= to < Week 20	144	33(22.9)	(16.33, 30.65)	0.096	156	44(28.2)	(21.30, 35.96)	0.396	-5.3	(-16.5, 6.1)	0.355
	Week 20 <= to < Week 24	140	33(23.6)	(16.81, 31.48)	0.139	154	47(30.5)	(23.36, 38.44)	0.782	-6.9	(-18.3, 4.5)	0.192
	Week 24 <= to < Week 28	136	33(24.3)	(17.33, 32.36)	0.182	152	47(30.9)	(23.68, 38.92)	0.876	-6.7	(-18.1, 4.9)	0.236
	Week 28 <= to < Week 32	133	32(24.1)	(17.08, 32.23)	0.194	150	44(29.3)	(22.19, 37.31)	0.572	-5.3	(-16.8, 6.4)	0.348
	Week 32 <= to < Week 36	131	35(26.7)	(19.37, 35.15)	0.622	147	45(30.6)	(23.28, 38.74)	0.889	-3.9	(-15.6, 7.9)	0.509
	Week 36 <= to < Week 40	129	41(31.8)	(23.87, 40.56)	0.537	145	48(33.1)	(25.52, 41.40)	0.680	-1.3	(-13.1, 10.5)	0.897
	Week 40 <= to < Week 44	127	38(29.9)	(22.12, 38.68)	0.746	143	46(32.2)	(24.61, 40.49)	0.773	-2.2	(-14.2, 9.7)	0.695
	Week 44 <= to < Week 48	124	34(27.4)	(19.79, 36.15)	0.866	138	44(31.9)	(24.21, 40.35)	0.884	-4.5	(-16.5, 7.6)	0.499
	Week 48 <= to < Week 52	123	42(34.1)	(25.84, 43.24)	0.237	135	48(35.6)	(27.51, 44.25)	0.376	-1.4	(-13.6, 10.8)	0.896
	Baseline <= to < Week 52	162	96(59.3)	(51.27, 66.90)	<0.001	161	113(70.2)	(62.48, 77.13)	<0.001	-10.9	(-21.8, -0.2)	0.048

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value from S: p value from screening period.
Note(s): p value from S is analyzed by McNemar test.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.2
Source: t_14_2_3_6_1.sas

5.3.5.1—9 表 11.4.1—4 より引用

(6)　血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合

血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合を表 2.7.6.26－87 に示した.

血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合は，MT-6548 群においてベースラインで 93.2%に対し，52 週後では 88.7%であり，darbepoetin 群においてベースラインで 90.7%に対し，52 週後では 85.0%であった.

表 2.7.6.26－87　血清フェリチン値 100 ng/mL 以上又は TSAT 20%以上の被験者の割合（FAS）

	MT-6548(N=162)				darbepoetin(N=161)				Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B	Difference	95% CI	p value
Baseline	162	151(93.2)	(88.18, 96.56)		161	146(90.7)	(85.10, 94.69)		2.5	(-3.4, 13.3)	0.422
Week 2	160	146(91.3)	(85.75, 95.13)	0.491	160	142(88.8)	(82.80, 93.19)	0.439	2.5	(-3.7, 13.7)	0.577
Week 4	157	147(93.6)	(88.60, 96.90)	0.808	159	143(89.9)	(84.17, 94.14)	0.827	3.7	(-2.5, 14.6)	0.306
Week 6	155	144(92.9)	(87.66, 96.40)	1.000	159	137(86.2)	(79.80, 91.12)	0.162	6.7	(-1.4, 17.7)	0.065
Week 8	151	140(92.7)	(87.34, 96.31)	1.000	158	140(88.6)	(82.59, 93.11)	0.549	4.1	(-3.1, 15.2)	0.245
Week 10	150	136(90.7)	(84.84, 94.80)	0.491	157	144(91.7)	(86.26, 95.52)	0.655	-1.1	(-12.3, 10.2)	0.841
Week 12	147	136(92.5)	(87.01, 96.21)	1.000	157	140(89.2)	(83.23, 93.56)	0.670	3.3	(-3.9, 14.6)	0.329
Week 16	144	131(91.0)	(85.06, 95.11)	0.593	156	142(91.0)	(85.40, 95.01)	0.819	-0.1	(-11.4, 11.3)	1.000
Week 20	140	130(92.9)	(87.26, 96.52)	0.792	154	136(88.3)	(82.16, 92.92)	0.549	4.5	(-6.9, 15.9)	0.233
Week 24	138	127(92.0)	(86.19, 95.95)	1.000	152	131(86.2)	(79.66, 91.24)	0.239	5.8	(-5.7, 17.2)	0.184
Week 28	132	119(90.2)	(83.75, 94.65)	0.439	150	128(85.3)	(78.64, 90.57)	0.178	4.8	(-6.9, 16.4)	0.278
Week 32	131	116(88.5)	(81.82, 93.45)	0.157	146	120(82.2)	(75.01, 88.02)	0.020	6.4	(-5.4, 18.0)	0.175
Week 36	127	117(92.1)	(86.00, 96.16)	0.808	142	115(81.0)	(73.55, 87.08)	0.011	11.1	(-0.8, 22.9)	0.012
Week 40	122	109(89.3)	(82.47, 94.20)	0.285	141	116(82.3)	(74.95, 88.18)	0.019	7.1	(-5.0, 19.1)	0.116
Week 44	118	110(93.2)	(87.08, 97.03)	0.796	139	116(83.5)	(76.21, 89.21)	0.068	9.8	(-2.5, 21.8)	0.020
Week 48	118	103(87.3)	(79.90, 92.71)	0.201	133	108(81.2)	(73.52, 87.45)	0.023	6.1	(-6.3, 18.3)	0.227
Week 52	115	102(88.7)	(81.45, 93.84)	0.371	133	113(85.0)	(77.74, 90.57)	0.144	3.7	(-8.7, 16.1)	0.455

Note(s): N*: number of subjects at each visit.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value from B: p value from baseline value.
Note(s): p value from B is analyzed by McNemar test.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.4
Source: t_14_2_3_7_1.sas

5.3.5.1—9 表 14.2.3.7.1 より引用

(7)　血球関連評価項目

MMRM を用いた MCV，MCH，ヘマトクリット，RBC，網状赤血球数及び網状赤血球率のベースラインからの変化量を表 2.7.6.26－88，表 2.7.6.26－89，表 2.7.6.26－90，表 2.7.6.26－91，表 2.7.6.26－92 及び表 2.7.6.26－93 に示した．

MMRM を用いた MCV の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.2 fL 及び 0.8～1.6 fL，darbepoetin 群で -0.2 fL 及び -0.6～0.2 fL であった．MMRM を用いた MCV の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は 1.4 fL 及び 0.9～2.0 fL であり，統計学的に有意な差が認められた（p<0.001）．

MMRM を用いた MCH の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.87 pg 及び 0.69～1.05 pg，darbepoetin 群で 0.15 pg 及び -0.02～0.32 pg であった．MMRM を用いた MCH の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は，0.72 pg 及び 0.47～0.97 pg であり，統計学的に有意な差が認められた（p<0.001）．

MMRM を用いたヘマトクリットの 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -1.54%及び -1.99%～ -1.08%，darbepoetin 群で -0.56%及び -0.99%～ -0.13%であった．

MMRM を用いた RBC の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -20.5×10^4/μL 及び -25.7～ -15.2×10^4/μL，darbepoetin 群で -4.6×10^4/μL 及び -9.6～0.4×10^4/μL であった．

MMRM を用いた網状赤血球数の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.11×10^4/μL 及び -0.18～0.41×10^4/μL，darbepoetin 群で -0.01×10^4/μL 及び -0.30～0.27×10^4/μL であった．

MMRM を用いた網状赤血球率の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 1.3‰及び 0.4‰～2.2‰，darbepoetin 群で 0.2‰及び -0.7‰～1.0‰であった．

表 2.7.6.26－88　平均赤血球容積のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	95.6 (5.3)	0.2	0.2	(-0.2, 0.6)	
	Week 4	157	95.6 (5.3)	0.1	0.2	(-0.2, 0.5)	
	Week 6	155	95.6 (5.3)	0.3	0.2	(0.0, 0.7)	
	Week 8	151	95.5 (5.3)	0.8	0.2	(0.4, 1.2)	
	Week 10	150	95.6 (5.3)	1.1	0.2	(0.7, 1.5)	
	Week 12	147	95.5 (5.2)	1.6	0.2	(1.2, 2.0)	
	Week 16	144	95.6 (5.0)	2.1	0.2	(1.7, 2.5)	
	Week 20	140	95.5 (4.9)	2.0	0.2	(1.7, 2.4)	
	Week 24	138	95.4 (4.9)	1.6	0.2	(1.2, 2.0)	
	Week 28	132	95.6 (4.7)	1.5	0.2	(1.1, 1.9)	
	Week 32	131	95.6 (4.8)	1.2	0.2	(0.8, 1.6)	
	Week 36	127	95.6 (4.6)	1.1	0.2	(0.7, 1.5)	
	Week 40	122	95.5 (4.8)	1.0	0.2	(0.6, 1.4)	
	Week 44	118	95.4 (4.7)	1.0	0.2	(0.6, 1.4)	
	Week 48	118	95.4 (4.7)	1.2	0.2	(0.7, 1.6)	
	Week 52	115	95.5 (4.6)	1.2	0.2	(0.8, 1.6)	
darbepoetin	Week 2	160	95.5 (4.2)	0.1	0.2	(-0.3, 0.5)	
	Week 4	159	95.5 (4.2)	0.1	0.2	(-0.3, 0.5)	
	Week 6	159	95.5 (4.2)	0.2	0.2	(-0.2, 0.6)	
	Week 8	158	95.5 (4.2)	0.2	0.2	(-0.2, 0.5)	
	Week 10	157	95.5 (4.2)	0.2	0.2	(-0.2, 0.6)	
	Week 12	157	95.5 (4.2)	0.3	0.2	(-0.1, 0.7)	
	Week 16	156	95.4 (4.2)	0.2	0.2	(-0.2, 0.5)	
	Week 20	154	95.4 (4.1)	0.3	0.2	(-0.1, 0.6)	
	Week 24	152	95.4 (4.1)	0.4	0.2	(0.0, 0.8)	
	Week 28	150	95.3 (4.1)	0.2	0.2	(-0.2, 0.6)	
	Week 32	146	95.3 (3.9)	0.1	0.2	(-0.3, 0.5)	
	Week 36	142	95.3 (4.0)	-0.3	0.2	(-0.7, 0.1)	
	Week 40	141	95.3 (3.9)	-0.4	0.2	(-0.8, 0.0)	
	Week 44	139	95.3 (3.9)	-0.5	0.2	(-0.9, -0.2)	
	Week 48	133	95.3 (4.0)	-0.4	0.2	(-0.8, 0.0)	
	Week 52	133	95.3 (4.0)	-0.2	0.2	(-0.6, 0.2)	

表 2.7.6.26－88　平均赤血球容積のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference	Week 2			0.1	0.3	(-0.4, 0.6)	0.704
MT-6548 - darbepoetin							
	Week 4			0.0	0.3	(-0.6, 0.6)	0.935
	Week 6			0.1	0.3	(-0.4, 0.7)	0.689
	Week 8			0.6	0.3	(0.1, 1.2)	0.025
	Week 10			0.9	0.3	(0.4, 1.5)	<0.001
	Week 12			1.3	0.3	(0.7, 1.8)	<0.001
	Week 16			2.0	0.3	(1.4, 2.5)	<0.001
	Week 20			1.6	0.3	(1.2, 2.3)	<0.001
	Week 24			1.2	0.3	(0.7, 1.8)	<0.001
	Week 28			1.2	0.3	(0.7, 1.8)	<0.001
	Week 32			1.1	0.3	(0.5, 1.6)	<0.001
	Week 36			1.3	0.3	(0.8, 1.9)	<0.001
	Week 40			1.4	0.3	(0.8, 2.0)	<0.001
	Week 44			1.5	0.3	(1.0, 2.1)	<0.001
	Week 48			1.6	0.3	(1.0, 2.2)	<0.001
	Week 52			1.4	0.3	(0.9, 2.0)	<0.001

Note(s): Mean Corpuscular Volume (fL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_5.sas

5.3.5.1—9 表 11.4.1—5 より引用

表 2.7.6.26－89　平均赤血球ヘモグロビン量のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	31.64 (1.93)	0.02	0.08	(-0.15, 0.18)	
	Week 4	157	31.66 (1.94)	0.09	0.08	(-0.08, 0.25)	
	Week 6	155	31.64 (1.94)	0.13	0.08	(-0.04, 0.30)	
	Week 8	151	31.62 (1.95)	0.33	0.08	(0.17, 0.50)	
	Week 10	150	31.64 (1.94)	0.48	0.08	(0.31, 0.64)	
	Week 12	147	31.61 (1.91)	0.71	0.09	(0.54, 0.88)	
	Week 16	144	31.64 (1.84)	0.88	0.09	(0.72, 1.05)	
	Week 20	140	31.60 (1.83)	0.90	0.09	(0.73, 1.07)	
	Week 24	136	31.61 (1.82)	0.94	0.09	(0.77, 1.11)	
	Week 28	132	31.65 (1.74)	0.91	0.09	(0.74, 1.08)	
	Week 32	131	31.70 (1.79)	0.81	0.09	(0.64, 0.98)	
	Week 36	127	31.67 (1.78)	0.74	0.09	(0.56, 0.91)	
	Week 40	122	31.64 (1.79)	0.67	0.09	(0.50, 0.85)	
	Week 44	116	31.63 (1.74)	0.74	0.09	(0.56, 0.91)	
	Week 48	118	31.63 (1.74)	0.84	0.09	(0.66, 1.02)	
	Week 52	115	31.64 (1.72)	0.87	0.09	(0.69, 1.05)	
darbepoetin	Week 2	160	31.56 (1.55)	-0.01	0.08	(-0.17, 0.16)	
	Week 4	159	31.56 (1.55)	-0.03	0.08	(-0.19, 0.13)	
	Week 6	159	31.56 (1.55)	0.02	0.08	(-0.16, 0.18)	
	Week 8	158	31.57 (1.55)	-0.04	0.08	(-0.20, 0.13)	
	Week 10	157	31.55 (1.55)	0.04	0.08	(-0.12, 0.21)	
	Week 12	157	31.55 (1.55)	0.05	0.08	(-0.12, 0.21)	
	Week 16	156	31.54 (1.55)	0.09	0.08	(-0.07, 0.26)	
	Week 20	154	31.52 (1.53)	0.14	0.08	(-0.02, 0.31)	
	Week 24	152	31.53 (1.53)	0.33	0.08	(0.16, 0.49)	
	Week 28	150	31.50 (1.52)	0.34	0.08	(0.17, 0.51)	
	Week 32	146	31.52 (1.48)	0.25	0.09	(0.09, 0.42)	
	Week 36	142	31.51 (1.48)	0.16	0.09	(-0.01, 0.33)	
	Week 40	141	31.50 (1.46)	-0.03	0.09	(-0.20, 0.14)	
	Week 44	139	31.51 (1.47)	0.08	0.09	(-0.08, 0.25)	
	Week 48	133	31.51 (1.48)	0.18	0.09	(0.01, 0.35)	
	Week 52	133	31.51 (1.48)	0.15	0.09	(-0.02, 0.32)	

表 2.7.6.26－89　平均赤血球ヘモグロビン量のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin	Week 2			0.02	0.12	(-0.21, 0.25)	0.854
	Week 4			0.12	0.12	(-0.12, 0.35)	0.323
	Week 6			0.11	0.12	(-0.12, 0.34)	0.347
	Week 8			0.37	0.12	(0.14, 0.60)	0.002
	Week 10			0.44	0.12	(0.20, 0.67)	<0.001
	Week 12			0.66	0.12	(0.43, 0.90)	<0.001
	Week 16			0.79	0.12	(0.56, 1.03)	<0.001
	Week 20			0.76	0.12	(0.52, 0.99)	<0.001
	Week 24			0.61	0.12	(0.38, 0.85)	<0.001
	Week 28			0.57	0.12	(0.33, 0.81)	<0.001
	Week 32			0.56	0.12	(0.32, 0.80)	<0.001
	Week 36			0.58	0.12	(0.33, 0.82)	<0.001
	Week 40			0.70	0.12	(0.46, 0.94)	<0.001
	Week 44			0.65	0.13	(0.41, 0.90)	<0.001
	Week 48			0.66	0.13	(0.41, 0.90)	<0.001
	Week 52			0.72	0.13	(0.47, 0.97)	<0.001

Note(s): Mean Corpuscular Hemoglobin (pg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_8_10_1_6.sas

5.3.5.1—9 表 11.4.1—6 より引用

表 2.7.6.26－90　ヘマトクリットのベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	32.46 (2.24)	-0.39	0.21	(-0.80, 0.02)
	Week 4	157	32.46 (2.25)	-1.17	0.21	(-1.59, -0.76)
	Week 6	155	32.49 (2.26)	-1.56	0.21	(-1.97, -1.15)
	Week 8	151	32.48 (2.26)	-1.69	0.21	(-2.11, -1.28)
	Week 10	150	32.49 (2.26)	-1.70	0.21	(-2.11, -1.28)
	Week 12	147	32.49 (2.24)	-1.80	0.21	(-1.72, -0.88)
	Week 16	144	32.45 (2.24)	-0.90	0.22	(-1.33, -0.48)
	Week 20	140	32.42 (2.25)	-0.58	0.22	(-1.01, -0.15)
	Week 24	138	32.44 (2.26)	-0.86	0.22	(-1.29, -0.43)
	Week 28	132	32.42 (2.28)	-1.16	0.22	(-1.59, -0.72)
	Week 32	131	32.39 (2.27)	-1.09	0.22	(-1.53, -0.65)
	Week 36	126	32.41 (2.28)	-1.32	0.23	(-1.77, -0.88)
	Week 40	122	32.41 (2.24)	-1.17	0.23	(-1.62, -0.72)
	Week 44	118	32.43 (2.27)	-1.23	0.23	(-1.68, -0.78)
	Week 48	118	32.43 (2.27)	-1.40	0.23	(-1.85, -0.95)
	Week 52	115	32.46 (2.27)	-1.54	0.23	(-1.99, -1.09)
darbepoetin	Week 2	160	32.50 (2.38)	0.36	0.21	(-0.05, 0.77)
	Week 4	159	32.46 (2.37)	0.52	0.21	(0.11, 0.93)
	Week 6	159	32.49 (2.37)	0.36	0.21	(-0.05, 0.77)
	Week 8	156	32.50 (2.36)	0.40	0.21	(-0.01, 0.81)
	Week 10	157	32.49 (2.36)	0.41	0.21	(0.00, 0.82)
	Week 12	157	32.49 (2.36)	0.54	0.21	(0.13, 0.95)
	Week 16	156	32.51 (2.35)	0.17	0.21	(-0.24, 0.58)
	Week 20	154	32.53 (2.35)	-0.34	0.21	(-0.75, 0.07)
	Week 24	152	32.53 (2.36)	-0.53	0.21	(-0.95, -0.12)
	Week 28	150	32.57 (2.35)	-0.49	0.21	(-0.91, -0.07)
	Week 32	146	32.59 (2.36)	-0.15	0.21	(-0.57, 0.27)
	Week 36	142	32.62 (2.34)	-0.25	0.22	(-0.67, 0.18)
	Week 40	141	32.59 (2.33)	-0.31	0.22	(-0.74, 0.11)
	Week 44	139	32.56 (2.31)	-0.59	0.22	(-1.01, -0.16)
	Week 48	133	32.58 (2.29)	-0.67	0.22	(-1.10, -0.24)
	Week 52	133	32.58 (2.29)	-0.56	0.22	(-0.99, -0.13)

Note(s): Hematocrit (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_1.sas

5.3.5.1—9 表 11.4.1—7 より引用

表 2.7.6.26－91　RBC のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	341.0 (33.4)	-4.6	2.4	(-9.3, 0.1)
	Week 4	157	341.1 (33.6)	-13.0	2.4	(-17.7, -8.2)
	Week 6	155	341.2 (33.6)	-17.7	2.4	(-22.5, -13.0)
	Week 8	151	341.4 (33.6)	-20.4	2.5	(-25.2, -15.6)
	Week 10	150	341.3 (33.7)	-21.9	2.5	(-26.7, -17.0)
	Week 12	147	341.5 (33.2)	-19.1	2.5	(-24.0, -14.2)
	Week 16	144	340.7 (31.8)	-16.8	2.5	(-21.7, -11.9)
	Week 20	140	340.8 (31.9)	-13.0	2.5	(-17.9, -8.1)
	Week 24	138	341.0 (31.9)	-15.0	2.5	(-20.0, -10.0)
	Week 28	132	340.3 (31.5)	-17.2	2.6	(-22.2, -12.2)
	Week 32	131	339.7 (31.7)	-15.5	2.6	(-20.6, -10.5)
	Week 36	126	340.2 (31.4)	-17.6	2.6	(-22.7, -12.5)
	Week 40	122	340.4 (31.3)	-16.0	2.6	(-21.1, -10.9)
	Week 44	118	340.7 (30.8)	-16.4	2.6	(-21.6, -11.2)
	Week 48	118	340.7 (30.8)	-18.7	2.6	(-23.9, -13.5)
	Week 52	115	341.0 (30.7)	-20.5	2.7	(-25.7, -15.2)
darbepoetin	Week 2	160	341.1 (29.4)	3.4	2.4	(-1.4, 8.1)
	Week 4	159	341.0 (29.4)	4.6	2.4	(-0.1, 9.3)
	Week 6	159	341.0 (29.4)	2.7	2.4	(-2.0, 7.5)
	Week 8	156	341.1 (29.4)	3.5	2.4	(-1.3, 8.2)
	Week 10	157	341.0 (29.5)	3.6	2.4	(-1.2, 8.3)
	Week 12	157	341.0 (29.5)	4.6	2.4	(-0.2, 9.3)
	Week 16	156	341.4 (29.3)	1.1	2.4	(-3.7, 5.8)
	Week 20	154	341.8 (29.0)	-4.5	2.4	(-9.3, 0.3)
	Week 24	152	341.7 (29.1)	-7.0	2.4	(-11.8, -2.2)
	Week 28	150	342.3 (28.8)	-6.0	2.5	(-10.8, -1.2)
	Week 32	146	342.5 (28.6)	-1.8	2.5	(-6.6, 3.1)
	Week 36	142	342.7 (28.5)	-1.5	2.5	(-6.4, 3.4)
	Week 40	141	342.6 (28.4)	-1.8	2.5	(-6.7, 3.1)
	Week 44	139	342.2 (28.4)	-3.8	2.5	(-8.7, 1.1)
	Week 48	133	342.4 (28.6)	-5.0	2.5	(-10.0, 0.0)
	Week 52	133	342.4 (28.6)	-4.6	2.6	(-9.6, 0.4)

Note(s): Red Blood Cell Count (10^4/uL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_2.sas

5.3.5.1—9 表 11.4.1—8 より引用

表 2.7.6.26－92　網状赤血球数のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	4.60 (1.88)	-0.35	0.14	(-0.61, -0.08)
	Week 4	157	4.62 (1.88)	-0.38	0.14	(-0.65, -0.12)
	Week 6	155	4.61 (1.88)	0.16	0.14	(-0.11, 0.42)
	Week 8	151	4.61 (1.90)	0.07	0.14	(-0.20, 0.35)
	Week 10	150	4.59 (1.90)	0.45	0.14	(0.17, 0.72)
	Week 12	147	4.61 (1.92)	0.57	0.14	(0.30, 0.84)
	Week 16	144	4.63 (1.93)	0.46	0.14	(0.19, 0.74)
	Week 20	140	4.61 (1.94)	0.37	0.14	(0.09, 0.65)
	Week 24	136	4.63 (1.93)	0.15	0.14	(-0.13, 0.43)
	Week 28	132	4.67 (1.95)	0.04	0.14	(-0.24, 0.33)
	Week 32	131	4.71 (1.94)	0.19	0.14	(-0.10, 0.47)
	Week 36	127	4.73 (1.95)	0.28	0.15	(-0.01, 0.57)
	Week 40	122	4.75 (1.95)	0.44	0.15	(0.15, 0.73)
	Week 44	118	4.77 (1.94)	0.32	0.15	(0.02, 0.61)
	Week 48	118	4.77 (1.94)	0.31	0.15	(0.02, 0.61)
	Week 52	115	4.74 (1.95)	0.11	0.15	(-0.18, 0.41)
darbepoetin	Week 2	160	4.73 (2.05)	0.30	0.14	(0.04, 0.57)
	Week 4	159	4.75 (2.04)	0.09	0.14	(-0.18, 0.35)
	Week 6	159	4.75 (2.04)	-0.35	0.14	(-0.62, -0.09)
	Week 8	158	4.76 (2.04)	-0.17	0.14	(-0.44, 0.10)
	Week 10	157	4.77 (2.04)	-0.16	0.14	(-0.43, 0.10)
	Week 12	157	4.77 (2.04)	-0.15	0.14	(-0.42, 0.11)
	Week 16	156	4.77 (2.05)	-0.31	0.14	(-0.57, -0.04)
	Week 20	154	4.81 (2.04)	-0.30	0.14	(-0.57, -0.04)
	Week 24	152	4.77 (2.03)	-0.26	0.14	(-0.53, 0.01)
	Week 28	150	4.77 (2.03)	-0.27	0.14	(-0.54, 0.00)
	Week 32	146	4.77 (1.97)	-0.26	0.14	(-0.53, 0.02)
	Week 36	142	4.80 (1.98)	-0.43	0.14	(-0.71, -0.16)
	Week 40	141	4.78 (1.96)	-0.05	0.14	(-0.33, 0.22)
	Week 44	139	4.78 (1.98)	-0.23	0.14	(-0.51, 0.05)
	Week 48	133	4.73 (1.99)	-0.08	0.14	(-0.36, 0.20)
	Week 52	133	4.73 (1.99)	-0.01	0.14	(-0.30, 0.27)

Note(s): Reticulocyte Count (10^4/uL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_8_10_1_3.sas

5.3.5.1—9 表 11.4.1—9 より引用

表 2.7.6.26－93　網状赤血球率のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	160	13.5 (5.6)	-0.8	0.4	(-1.7, 0.0)
	Week 4	157	13.6 (5.6)	-0.6	0.4	(-1.4, 0.2)
	Week 6	155	13.6 (5.6)	1.4	0.4	(0.6, 2.2)
	Week 8	151	13.5 (5.6)	1.3	0.4	(0.4, 2.1)
	Week 10	150	13.5 (5.6)	2.5	0.4	(1.7, 3.4)
	Week 12	147	13.6 (5.7)	2.8	0.4	(1.9, 3.6)
	Week 16	144	13.6 (5.7)	2.3	0.4	(1.5, 3.1)
	Week 20	140	13.6 (5.7)	1.8	0.4	(0.9, 2.6)
	Week 24	136	13.6 (5.7)	1.1	0.4	(0.3, 2.0)
	Week 28	132	13.7 (5.7)	1.0	0.4	(0.1, 1.9)
	Week 32	131	13.9 (5.7)	1.3	0.4	(0.4, 2.1)
	Week 36	126	13.9 (5.7)	1.7	0.4	(0.8, 2.6)
	Week 40	122	14.0 (5.7)	2.1	0.5	(1.2, 3.0)
	Week 44	118	14.0 (5.7)	1.7	0.5	(0.8, 2.6)
	Week 48	118	14.0 (5.7)	1.8	0.5	(0.9, 2.7)
	Week 52	115	13.9 (5.7)	1.3	0.5	(0.4, 2.2)
darbepoetin	Week 2	160	13.9 (5.7)	0.8	0.4	(0.0, 1.6)
	Week 4	159	13.9 (5.7)	0.1	0.4	(-0.7, 0.9)
	Week 6	159	13.9 (5.7)	-1.0	0.4	(-1.8, -0.2)
	Week 8	156	13.9 (5.7)	-0.6	0.4	(-1.3, 0.3)
	Week 10	157	13.9 (5.7)	-0.5	0.4	(-1.3, 0.3)
	Week 12	157	13.9 (5.7)	-0.6	0.4	(-1.3, 0.3)
	Week 16	156	13.9 (5.7)	-0.9	0.4	(-1.7, 0.0)
	Week 20	154	14.0 (5.7)	-0.6	0.4	(-1.5, 0.2)
	Week 24	152	13.9 (5.7)	-0.5	0.4	(-1.3, 0.4)
	Week 28	150	13.9 (5.7)	-0.5	0.4	(-1.4, 0.3)
	Week 32	146	13.9 (5.6)	-0.7	0.4	(-1.5, 0.2)
	Week 36	142	14.0 (5.6)	-1.2	0.4	(-2.0, -0.4)
	Week 40	141	14.0 (5.6)	-0.1	0.4	(-0.9, 0.8)
	Week 44	139	14.0 (5.6)	-0.6	0.4	(-1.4, 0.3)
	Week 48	133	13.9 (5.6)	0.0	0.4	(-0.8, 0.9)
	Week 52	133	13.9 (5.6)	0.2	0.4	(-0.7, 1.0)

Note(s): Reticulocyte Ratio (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_4.sas

5.3.5.1—9 表 11.4.1—10 より引用

(8)　EPO

MMRM を用いた MT-6548 群の EPO のベースラインからの変化量を表 2.7.6.26－94，MT-6548 群の EPO の記述統計量を表 2.7.6.26－95 に示した．

MMRM を用いた EPO の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -3.45 mIU/mL 及び -6.25～ -0.65 mIU/mL であった．MT-6548 群の 52 週後の EPO の平均値±SD は，11.47±12.20 mIU/mL であった．また，2 週～52 週後の EPO の最大値は 312.0 mIU/mL であった．

表 2.7.6.26－94　エリスロポエチンのベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	17.49 (28.11)	-1.35	1.26	(-3.86, 1.15)	
	Week 4	157	17.64 (28.36)	-2.79	1.28	(-5.31, -0.27)	
	Week 6	155	17.74 (28.51)	-1.86	1.29	(-4.39, 0.67)	
	Week 12	147	16.31 (22.88)	-0.90	1.31	(-3.48, 1.68)	
	Week 24	138	14.46 (19.81)	0.13	1.34	(-2.50, 2.77)	
	Week 36	127	14.32 (19.45)	-0.05	1.38	(-2.76, 2.65)	
	Week 52	115	13.95 (20.02)	-3.45	1.43	(-6.25, -0.65)	

Note(s): Erythropoietin (mIU/mL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_10_1_7.sas

5.3.5.1—9 表 11.4.1—11 より引用

表 2.7.6.26－95　エリスロポエチンの記述統計量（FAS）

		Absolute						Change from Baseline						
Treatment Group	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Baseline	162	17.40	27.95	8.20	(2.0, 236.0)	(13.07, 21.74)							
	Week 2	160	14.85	26.14	10.25	(2.4, 312.0)	(10.77, 18.93)	160	-2.64	35.27	-0.05	(-215.4, 307.5)	(-8.15, 2.87)	0.345
	Week 4	157	13.52	16.99	9.90	(1.2, 168.0)	(10.84, 16.20)	157	-4.12	30.03	0.00	(-217.2, 119.7)	(-8.85, 0.61)	0.087
	Week 6	155	14.53	14.28	10.90	(1.6, 120.0)	(12.26, 16.79)	155	-3.21	28.48	1.10	(-205.2, 115.5)	(-7.73, 1.31)	0.162
	Week 12	147	15.45	13.70	11.70	(2.0, 99.3)	(13.21, 17.68)	147	-0.87	21.92	2.20	(-119.2, 60.6)	(-4.44, 2.70)	0.631
	Week 24	138	16.18	22.76	10.80	(2.5, 206.0)	(12.35, 20.01)	138	1.69	24.20	1.95	(-127.4, 157.3)	(-2.38, 5.77)	0.412
	Week 36	127	14.99	16.81	10.40	(2.1, 124.0)	(12.04, 17.94)	127	0.67	22.34	2.10	(-131.8, 78.0)	(-3.25, 4.59)	0.736
	Week 52	115	11.47	12.20	7.70	(1.5, 101.0)	(9.22, 13.73)	115	-2.48	20.78	0.00	(-130.1, 62.7)	(-6.32, 1.36)	0.204
	Week 52(LOCF)	161	15.05	24.83	7.70	(1.5, 206.0)	(11.19, 18.92)	161	-2.37	32.36	-0.20	(-205.2, 169.0)	(-7.40, 2.67)	0.355

Note(s): Erythropoietin (mIU/mL).
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.5
Source: t_14_2_3_9_1_7.sas

5.3.5.1—9 表 11.4.1—12 より引用

(9)　脂質関連評価項目

MMRM を用いた総コレステロール，LDL-C，HDL-C，LDL-C／HDL-C 比及び中性脂肪のベースラインからの変化量を表 2.7.6.26－96，表 2.7.6.26－97，表 2.7.6.26－98，表 2.7.6.26－99 及び表 2.7.6.26－100 に示した．

MMRM を用いた総コレステロールの 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 5.1 mg/dL 及び 1.8～8.3 mg/dL，darbepoetin 群で 1.7 mg/dL 及び -1.4～4.8 mg/dL であった．MMRM を用いた総コレステロールの 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 3.3 mg/dL 及び -1.1～7.8 mg/dL であり，統計学的に有意な差は認められなかった．

MMRM を用いた LDL-C の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 2.0 mg/dL 及び -0.7～4.6 mg/dL，darbepoetin 群で 0.1 mg/dL 及び -2.4～2.6 mg/dL であった．MMRM を用いた LDL-C の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 1.8 mg/dL 及び -1.8～5.5 mg/dL であり，統計学的に有意な差は認められなかった．

MMRM を用いた HDL-C の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -1.5 mg/dL 及び -2.7～ -0.3 mg/dL，darbepoetin 群で 0.4 mg/dL 及び -0.7～1.5 mg/dL であった．MMRM を用いた HDL-C の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -1.9 mg/dL 及び -3.6～ -0.3 mg/dL であり，統計学的に有意な差が認められた（p=0.024）．

MMRM を用いた LDL-C/HDL-C 比の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 0.17 及び 0.10～0.24，darbepoetin 群で -0.02 及び -0.09～0.05 であった．MMRM を用いた LDL-C/HDL-C 比の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 0.19 及び 0.09～0.29 であり，統計学的に有意な差が認められた（p<0.001）．

MMRM を用いた中性脂肪の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で 17.6 mg/dL 及び 7.7～27.5 mg/dL，darbepoetin 群で-0.4 mg/dL 及び -9.8～9.0 mg/dL であった．MMRM を用いた中性脂肪の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 18.0 mg/dL 及び 4.4～31.6 mg/dL であり，統計学的に有意な差が認められた（p=0.010）．

表 2.7.6.26－96　総コレステロールのベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	158.8 (32.2)	0.2	1.5	(-2.7, 3.1)		160	0.4	1.0	(-1.5, 2.3)	
	Week 4	157	158.4 (32.3)	-1.4	1.5	(-4.3, 1.6)		157	-0.4	1.0	(-2.3, 1.5)	
	Week 6	155	158.1 (32.4)	1.0	1.5	(-1.9, 4.0)		155	1.1	1.0	(-0.9, 3.0)	
	Week 8	151	157.7 (32.3)	0.5	1.5	(-2.5, 3.5)		151	0.8	1.0	(-1.2, 2.7)	
	Week 10	150	157.7 (32.4)	1.1	1.5	(-1.9, 4.1)		150	1.1	1.0	(-0.8, 3.1)	
	Week 12	147	157.9 (32.2)	2.8	1.5	(-0.2, 5.8)		147	2.3	1.0	(0.3, 4.2)	
	Week 16	144	158.0 (32.6)	2.6	1.5	(-0.4, 5.6)		144	2.3	1.0	(0.3, 4.2)	
	Week 20	140	158.2 (32.6)	7.6	1.6	(4.6, 10.7)		140	5.6	1.0	(3.7, 7.6)	
	Week 24	139	158.4 (32.7)	7.1	1.6	(4.0, 10.2)		139	5.2	1.0	(3.2, 7.2)	
	Week 28	132	158.3 (31.8)	11.4	1.6	(8.3, 14.5)		132	7.9	1.0	(5.9, 9.9)	
	Week 32	131	158.5 (31.9)	13.2	1.6	(10.1, 16.3)		131	9.3	1.0	(7.3, 11.3)	
	Week 36	127	159.0 (32.2)	12.7	1.6	(9.6, 15.8)		127	9.3	1.0	(7.3, 11.4)	
	Week 40	122	158.3 (32.2)	12.3	1.6	(9.2, 15.5)		122	8.9	1.1	(6.8, 11.0)	
	Week 44	118	158.8 (31.4)	11.4	1.6	(8.2, 14.6)		118	8.4	1.1	(6.3, 10.5)	
	Week 48	118	158.8 (31.4)	7.8	1.6	(4.6, 11.0)		118	6.0	1.1	(3.9, 8.0)	
	Week 52	115	159.0 (31.7)	5.1	1.6	(1.8, 8.3)		115	4.0	1.1	(1.9, 6.1)	

表 2.7.6.26－96　総コレステロールのベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	158.6 (33.9)	-0.7	1.5	(-3.6, 2.3)		160	0.0	1.0	(-2.0, 1.9)	
	Week 4	159	158.6 (34.0)	-0.3	1.5	(-3.3, 2.6)		159	0.2	1.0	(-1.7, 2.1)	
	Week 6	159	158.6 (34.0)	-1.4	1.5	(-4.4, 1.5)		159	-0.6	1.0	(-2.6, 1.3)	
	Week 8	158	158.8 (34.0)	-2.8	1.5	(-5.7, 0.1)		158	-1.3	1.0	(-3.2, 0.6)	
	Week 10	157	158.7 (34.1)	-2.8	1.5	(-5.7, 0.2)		157	-1.3	1.0	(-3.3, 0.6)	
	Week 12	157	158.7 (34.1)	-1.2	1.5	(-4.1, 1.7)		157	-0.4	1.0	(-2.3, 1.5)	
	Week 16	156	158.8 (34.2)	-1.3	1.5	(-4.3, 1.7)		156	-0.4	1.0	(-2.3, 1.6)	
	Week 20	154	159.1 (34.2)	-0.3	1.5	(-3.3, 2.6)		154	0.3	1.0	(-1.7, 2.2)	
	Week 24	152	159.4 (34.3)	3.6	1.5	(0.6, 6.6)		152	2.6	1.0	(0.7, 4.5)	
	Week 28	150	159.3 (34.4)	5.3	1.5	(2.8, 8.8)		150	4.0	1.0	(2.1, 6.0)	
	Week 32	146	159.0 (34.4)	9.6	1.5	(6.6, 11.6)		146	8.9	1.0	(4.9, 7.9)	
	Week 36	142	158.9 (34.5)	6.4	1.5	(3.4, 9.4)		142	4.6	1.0	(2.7, 6.6)	
	Week 40	141	159.0 (34.7)	7.3	1.5	(4.3, 10.3)		141	5.1	1.0	(3.1, 7.0)	
	Week 44	139	159.0 (34.9)	6.6	1.6	(3.5, 9.6)		139	4.5	1.0	(2.5, 6.5)	
	Week 48	133	159.1 (34.7)	4.1	1.6	(1.0, 7.2)		133	2.9	1.0	(0.9, 4.9)	
	Week 52	133	159.1 (34.7)	1.7	1.6	(-1.4, 4.8)		133	1.6	1.0	(-0.4, 3.6)	

表 2.7.6.26－96　総コレステロールのベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			0.8	2.1	(-3.3, 5.0)	0.689		0.4	1.4	(-2.3, 3.1)	0.748
	Week 4			-1.1	2.1	(-5.2, 3.1)	0.615		-0.6	1.4	(-3.3, 2.1)	0.655
	Week 6			2.4	2.1	(-1.7, 6.6)	0.250		1.7	1.4	(-1.0, 4.4)	0.219
	Week 8			3.3	2.1	(-0.9, 7.5)	0.123		2.0	1.4	(-0.7, 4.8)	0.147
	Week 10			3.8	2.1	(-0.4, 8.0)	0.073		2.6	1.4	(-0.3, 5.2)	0.075
	Week 12			4.0	2.1	(-0.2, 8.2)	0.062		2.7	1.4	(0.0, 5.4)	0.054
	Week 16			3.9	2.2	(-0.3, 8.1)	0.070		2.7	1.4	(-0.1, 5.4)	0.058
	Week 20			7.9	2.2	(3.7, 12.2)	<0.001		5.4	1.4	(2.6, 8.1)	<0.001
	Week 24			3.5	2.2	(-0.8, 7.8)	0.108		2.6	1.4	(-0.2, 5.3)	0.072
	Week 28			5.6	2.2	(1.3, 9.9)	0.011		3.9	1.4	(1.1, 6.7)	0.007
	Week 32			4.6	2.2	(0.3, 9.0)	0.036		3.3	1.4	(0.5, 6.1)	0.020
	Week 36			6.3	2.2	(1.9, 10.7)	0.005		4.7	1.4	(1.9, 7.5)	0.001
	Week 40			5.0	2.2	(0.6, 9.4)	0.025		3.8	1.5	(1.0, 6.7)	0.008
	Week 44			4.8	2.3	(0.4, 9.2)	0.034		3.8	1.5	(1.0, 6.7)	0.009
	Week 48			3.8	2.3	(-0.7, 8.2)	0.097		3.0	1.5	(0.1, 5.9)	0.041
	Week 52			3.3	2.3	(-1.1, 7.8)	0.143		2.4	1.5	(-0.5, 5.3)	0.109

Note(s): Total Cholesterol (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_12.sas

5.3.5.1—9 表 11.4.1—13 より引用

表 2.7.6.26－97　LDL-C のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	88.4 (26.0)	-1.2	1.2	(-3.6, 1.2)		160	-0.5	1.5	(-3.5, 2.5)	
	Week 4	157	88.1 (26.0)	-1.5	1.2	(-3.9, 0.9)		157	-0.9	1.5	(-3.9, 2.2)	
	Week 6	155	87.8 (26.0)	-0.5	1.2	(-3.0, 1.9)		155	0.5	1.5	(-2.6, 3.5)	
	Week 8	151	87.3 (25.6)	-0.9	1.2	(-3.3, 1.6)		151	0.0	1.6	(-3.1, 3.0)	
	Week 10	150	87.3 (25.7)	-0.8	1.2	(-3.2, 1.6)		150	0.1	1.6	(-2.9, 3.2)	
	Week 12	147	87.5 (25.4)	0.3	1.3	(-2.2, 2.7)		147	1.2	1.6	(-1.9, 4.3)	
	Week 16	144	87.5 (25.7)	0.8	1.3	(-1.7, 3.3)		144	2.0	1.6	(-1.1, 5.1)	
	Week 20	140	87.4 (25.8)	3.8	1.3	(1.3, 6.3)		140	5.7	1.6	(2.6, 8.8)	
	Week 24	138	87.4 (25.9)	1.7	1.3	(-0.8, 4.2)		138	3.1	1.6	(0.0, 6.2)	
	Week 28	132	87.6 (25.9)	4.3	1.3	(1.7, 6.8)		132	6.1	1.6	(2.9, 9.3)	
	Week 32	131	87.5 (26.0)	6.2	1.3	(3.7, 8.8)		131	9.1	1.6	(5.9, 12.2)	
	Week 36	127	88.1 (26.1)	5.6	1.3	(3.2, 8.3)		127	9.3	1.6	(6.1, 12.5)	
	Week 40	122	87.4 (26.0)	4.9	1.3	(2.3, 7.5)		122	7.5	1.7	(4.3, 10.8)	
	Week 44	118	87.9 (25.8)	6.1	1.3	(3.5, 8.7)		118	9.1	1.7	(5.8, 12.4)	
	Week 48	116	87.8 (25.8)	4.1	1.3	(1.6, 6.7)		116	6.7	1.7	(3.4, 10.0)	
	Week 52	115	87.9 (26.1)	2.0	1.3	(-0.7, 4.6)		115	3.6	1.7	(0.2, 6.8)	

表 2.7.6.26－97　LDL-C のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	86.2 (28.1)	-0.3	1.2	(-2.7, 2.1)		160	0.6	1.5	(-2.4, 3.6)	
	Week 4	159	86.4 (28.1)	-0.3	1.2	(-2.7, 2.1)		159	0.6	1.5	(-2.4, 3.6)	
	Week 6	159	86.4 (28.1)	-0.4	1.2	(-2.8, 2.0)		159	0.5	1.5	(-2.5, 3.6)	
	Week 8	159	86.5 (28.2)	-2.2	1.2	(-4.6, 0.2)		158	-1.3	1.5	(-4.3, 1.7)	
	Week 10	157	86.5 (28.3)	-1.9	1.2	(-4.3, 0.5)		157	-1.1	1.5	(-4.2, 1.9)	
	Week 12	157	86.5 (28.3)	-1.4	1.2	(-3.8, 1.0)		157	-0.6	1.5	(-3.6, 2.4)	
	Week 16	156	86.6 (28.3)	-1.6	1.2	(-4.0, 0.8)		156	-0.7	1.5	(-3.8, 2.3)	
	Week 20	154	86.9 (28.4)	-1.4	1.2	(-3.8, 1.0)		154	-0.5	1.5	(-3.6, 2.5)	
	Week 24	152	87.1 (28.5)	-0.3	1.2	(-2.7, 2.2)		152	0.6	1.6	(-2.5, 3.6)	
	Week 28	150	86.9 (28.6)	0.9	1.2	(-1.6, 3.3)		150	1.8	1.6	(-1.2, 4.9)	
	Week 32	146	86.7 (28.6)	3.1	1.3	(0.6, 5.6)		146	4.9	1.6	(1.8, 8.0)	
	Week 36	142	86.8 (28.7)	1.5	1.3	(-0.9, 4.0)		142	3.4	1.6	(0.2, 6.5)	
	Week 40	141	87.0 (28.4)	2.5	1.3	(0.0, 5.0)		141	4.6	1.6	(1.5, 7.7)	
	Week 44	139	87.0 (28.6)	2.9	1.3	(0.4, 5.4)		139	4.5	1.6	(1.4, 7.6)	
	Week 48	133	87.2 (28.3)	1.3	1.3	(-1.2, 3.8)		133	2.7	1.6	(-0.5, 5.9)	
	Week 52	133	87.2 (28.3)	0.1	1.3	(-2.4, 2.6)		133	1.6	1.6	(-1.6, 4.7)	

表 2.7.6.26－97　LDL-C のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			-0.9	1.7	(-4.3, 2.5)	0.607		-1.1	2.2	(-5.4, 3.2)	0.613
	Week 4			-1.1	1.7	(-4.5, 2.3)	0.516		-1.4	2.2	(-5.7, 2.8)	0.507
	Week 6			-0.2	1.7	(-3.6, 3.2)	0.919		-0.1	2.2	(-4.3, 4.2)	0.978
	Week 8			1.3	1.7	(-2.1, 4.7)	0.451		1.3	2.2	(-3.0, 5.6)	0.565
	Week 10			1.1	1.7	(-2.4, 4.5)	0.544		1.3	2.2	(-3.0, 5.6)	0.563
	Week 12			1.7	1.8	(-1.8, 5.1)	0.345		1.8	2.2	(-2.5, 6.1)	0.408
	Week 16			2.4	1.8	(-1.1, 5.8)	0.176		2.7	2.2	(-1.7, 7.0)	0.224
	Week 20			5.2	1.8	(1.7, 8.6)	0.004		6.3	2.2	(1.9, 10.6)	0.005
	Week 24			2.0	1.8	(-1.5, 5.5)	0.270		2.5	2.2	(-1.8, 6.9)	0.255
	Week 28			3.4	1.8	(-0.1, 6.9)	0.057		4.2	2.2	(-0.2, 8.6)	0.060
	Week 32			3.1	1.8	(-0.4, 6.7)	0.083		4.1	2.3	(-0.3, 8.6)	0.067
	Week 36			4.2	1.8	(0.7, 7.8)	0.020		5.9	2.3	(1.5, 10.4)	0.009
	Week 40			2.4	1.8	(-1.2, 6.0)	0.186		3.0	2.3	(-1.5, 7.5)	0.196
	Week 44			3.2	1.8	(-0.4, 6.8)	0.080		4.6	2.3	(0.1, 9.1)	0.047
	Week 48			2.8	1.9	(-0.9, 6.4)	0.137		4.0	2.3	(-0.5, 8.6)	0.084
	Week 52			1.8	1.9	(-1.8, 5.5)	0.320		1.9	2.3	(-2.7, 6.5)	0.416

Note(s): LDL-C (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_13.sas

5.3.5.1—9 表 11.4.1—14 より引用

表 2.7.6.26－98　HDL-C のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	48.5 (15.6)	-2.9	0.6	(-4.0, -1.8)		160	-5.3	1.1	(-7.4, -3.1)	
	Week 4	157	48.3 (15.7)	-4.0	0.6	(-5.1, -2.9)		157	-7.2	1.1	(-9.4, -5.1)	
	Week 6	155	48.4 (15.7)	-4.1	0.6	(-5.2, -3.0)		155	-7.9	1.1	(-10.1, -5.7)	
	Week 8	151	48.6 (15.8)	-4.8	0.6	(-5.9, -3.6)		151	-8.7	1.1	(-10.9, -6.5)	
	Week 10	150	48.7 (15.8)	-5.0	0.6	(-6.1, -3.9)		150	-9.2	1.1	(-11.4, -7.0)	
	Week 12	147	48.6 (15.9)	-4.3	0.6	(-5.5, -3.2)		147	-7.8	1.1	(-10.0, -5.6)	
	Week 16	144	48.8 (16.0)	-3.2	0.6	(-4.3, -2.1)		144	-5.8	1.1	(-8.0, -3.5)	
	Week 20	140	48.9 (16.1)	-2.0	0.6	(-3.1, -0.9)		140	-3.2	1.1	(-5.5, -1.0)	
	Week 24	138	48.9 (16.0)	-1.5	0.6	(-2.6, -0.3)		138	-2.4	1.1	(-4.7, -0.2)	
	Week 28	132	48.5 (15.5)	-0.6	0.6	(-1.7, 0.6)		132	0.0	1.2	(-2.3, 2.3)	
	Week 32	131	48.7 (15.6)	-0.5	0.6	(-1.6, 0.7)		131	0.1	1.2	(-2.1, 2.4)	
	Week 36	127	48.6 (15.8)	0.4	0.6	(-0.7, 1.6)		127	1.7	1.2	(-0.6, 4.0)	
	Week 40	122	48.4 (15.7)	0.2	0.6	(-1.0, 1.4)		122	0.8	1.2	(-1.5, 3.1)	
	Week 44	118	48.3 (15.6)	0.1	0.6	(-1.1, 1.3)		118	0.9	1.2	(-1.4, 3.3)	
	Week 48	118	48.3 (15.6)	-1.8	0.6	(-3.0, -0.6)		118	-2.8	1.2	(-5.1, -0.4)	
	Week 52	115	48.3 (15.7)	-1.5	0.6	(-2.7, -0.3)		115	-2.7	1.2	(-5.0, -0.3)	

表 2.7.6.26－98　HDL-C のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	51.0 (16.1)	-0.2	0.6	(-1.3, 0.9)		160	0.6	1.1	(-1.6, 2.7)	
	Week 4	159	50.8 (16.0)	-0.9	0.6	(-1.9, 0.2)		159	-1.0	1.1	(-3.2, 1.1)	
	Week 6	159	50.8 (16.0)	-2.0	0.6	(-3.1, -1.0)		159	-3.2	1.1	(-5.4, -1.1)	
	Week 8	158	51.0 (16.0)	-1.5	0.6	(-2.6, -0.4)		158	-2.0	1.1	(-4.2, 0.1)	
	Week 10	157	50.8 (15.9)	-2.0	0.6	(-3.1, -0.9)		157	-3.4	1.1	(-5.6, -1.2)	
	Week 12	157	50.8 (15.9)	-0.7	0.6	(-1.8, 0.4)		157	-0.8	1.1	(-2.9, 1.4)	
	Week 16	156	50.7 (15.9)	0.1	0.6	(-1.0, 1.2)		156	0.8	1.1	(-1.4, 3.0)	
	Week 20	154	50.7 (15.9)	0.2	0.6	(-0.9, 1.3)		154	1.7	1.1	(-0.5, 3.8)	
	Week 24	152	50.8 (15.9)	2.1	0.6	(1.0, 3.2)		152	5.1	1.1	(3.0, 7.3)	
	Week 28	150	50.8 (16.0)	2.9	0.6	(1.8, 4.0)		150	7.0	1.1	(4.8, 9.2)	
	Week 32	146	50.7 (16.1)	3.1	0.6	(2.0, 4.2)		146	7.4	1.1	(5.2, 9.6)	
	Week 36	142	50.3 (16.1)	2.8	0.6	(1.7, 3.9)		142	6.9	1.1	(4.7, 9.1)	
	Week 40	141	50.1 (15.7)	3.6	0.6	(2.4, 4.7)		141	8.3	1.1	(6.1, 10.6)	
	Week 44	139	50.1 (15.8)	2.7	0.6	(1.5, 3.8)		139	6.7	1.1	(4.5, 8.9)	
	Week 48	133	50.2 (16.0)	1.9	0.6	(0.8, 3.0)		133	5.0	1.2	(2.8, 7.3)	
	Week 52	133	50.2 (16.0)	0.4	0.6	(-0.7, 1.5)		133	1.9	1.2	(-0.3, 4.2)	

表 2.7.6.26－98　HDL-C のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	Change from Baseline LSMean	SE	95% CI	p value	N	Percent Change from Baseline LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			-2.7	0.6	(-4.2, -1.2)	<0.001		-5.8	1.6	(-8.8, -2.7)	<0.001
	Week 4			-3.2	0.6	(-4.7, -1.6)	<0.001		-6.2	1.6	(-9.2, -3.1)	<0.001
	Week 6			-2.1	0.8	(-3.6, -0.5)	0.009		-4.6	1.6	(-7.7, -1.6)	0.003
	Week 8			-3.2	0.6	(-4.8, -1.7)	<0.001		-6.7	1.6	(-9.8, -3.6)	<0.001
	Week 10			-3.0	0.8	(-4.5, -1.4)	<0.001		-5.8	1.6	(-8.9, -2.7)	<0.001
	Week 12			-3.7	0.8	(-5.2, -2.1)	<0.001		-7.0	1.6	(-10.1, -3.9)	<0.001
	Week 16			-3.3	0.8	(-4.8, -1.7)	<0.001		-6.6	1.6	(-9.7, -3.5)	<0.001
	Week 20			-2.2	0.8	(-3.8, -0.6)	0.006		-4.9	1.6	(-8.0, -1.8)	0.002
	Week 24			-3.6	0.8	(-5.1, -2.0)	<0.001		-7.6	1.6	(-10.7, -4.4)	<0.001
	Week 28			-3.5	0.8	(-5.1, -1.8)	<0.001		-7.0	1.6	(-10.2, -3.9)	<0.001
	Week 32			-3.6	0.8	(-5.2, -2.0)	<0.001		-7.2	1.6	(-10.4, -4.1)	<0.001
	Week 36			-2.4	0.8	(-4.0, -0.7)	0.004		-5.2	1.6	(-8.4, -2.0)	0.001
	Week 40			-3.4	0.8	(-5.0, -1.8)	<0.001		-7.5	1.6	(-10.8, -4.3)	<0.001
	Week 44			-2.6	0.8	(-4.2, -0.9)	0.002		-5.8	1.7	(-9.0, -2.5)	<0.001
	Week 48			-3.7	0.8	(-5.3, -2.0)	<0.001		-7.8	1.7	(-11.1, -4.6)	<0.001
	Week 52			-1.9	0.8	(-3.6, -0.3)	0.024		-4.6	1.7	(-7.9, -1.3)	0.006

Note(s): HDL-C (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_14.sas

5.3.5.1—9 表 11.4.1—15 より引用

表 2.7.6.26－99　LDL-C／HDL-C 比のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	2.00 (0.82)	0.09	0.03	(0.01, 0.14)		160	6.05	1.85	(2.42, 9.69)	
	Week 4	157	2.00 (0.83)	0.13	0.03	(0.06, 0.19)		157	8.46	1.86	(4.80, 12.12)	
	Week 6	155	1.99 (0.83)	0.16	0.03	(0.09, 0.22)		155	10.30	1.87	(6.62, 13.97)	
	Week 8	151	1.97 (0.81)	0.17	0.03	(0.10, 0.23)		151	10.82	1.88	(7.12, 14.52)	
	Week 10	150	1.96 (0.81)	0.18	0.03	(0.12, 0.23)		150	11.94	1.89	(8.24, 15.65)	
	Week 12	147	1.97 (0.81)	0.16	0.03	(0.10, 0.23)		147	11.37	1.90	(7.65, 15.10)	
	Week 16	144	1.96 (0.81)	0.15	0.03	(0.08, 0.22)		144	9.69	1.91	(5.94, 13.43)	
	Week 20	140	1.96 (0.81)	0.17	0.03	(0.10, 0.23)		140	10.96	1.92	(7.19, 14.73)	
	Week 24	138	1.96 (0.81)	0.11	0.03	(0.04, 0.18)		138	8.03	1.93	(4.24, 11.81)	
	Week 28	132	1.97 (0.82)	0.12	0.03	(0.05, 0.19)		132	8.69	1.95	(4.86, 12.52)	
	Week 32	131	1.97 (0.82)	0.16	0.03	(0.09, 0.23)		131	11.39	1.96	(7.55, 15.23)	
	Week 36	127	1.98 (0.82)	0.13	0.04	(0.06, 0.20)		127	9.59	1.97	(5.72, 13.46)	
	Week 40	122	1.98 (0.83)	0.14	0.04	(0.07, 0.21)		122	8.95	1.99	(5.04, 12.87)	
	Week 44	119	1.99 (0.84)	0.16	0.04	(0.09, 0.23)		119	10.61	2.01	(6.66, 14.56)	
	Week 48	118	1.99 (0.84)	0.21	0.04	(0.14, 0.28)		118	13.43	2.01	(9.48, 17.37)	
	Week 52	116	2.00 (0.85)	0.17	0.04	(0.10, 0.24)		116	10.10	2.03	(6.12, 14.07)	

表 2.7.6.26－99　LDL-C／HDL-C 比のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	1.86 (0.81)	-0.01	0.03	(-0.07, 0.06)		160	0.54	1.85	(-3.09, 4.18)	
	Week 4	159	1.86 (0.80)	0.02	0.03	(-0.05, 0.08)		159	2.32	1.86	(-1.32, 5.96)	
	Week 6	159	1.86 (0.80)	0.04	0.03	(-0.02, 0.11)		159	4.85	1.86	(1.21, 8.49)	
	Week 8	158	1.86 (0.80)	-0.01	0.03	(-0.07, 0.06)		158	1.80	1.86	(-1.85, 5.45)	
	Week 10	157	1.86 (0.80)	0.03	0.03	(-0.04, 0.09)		157	3.43	1.86	(-0.22, 7.09)	
	Week 12	157	1.86 (0.80)	-0.01	0.03	(-0.07, 0.06)		157	1.51	1.86	(-2.14, 5.17)	
	Week 16	156	1.87 (0.80)	-0.04	0.03	(-0.11, 0.03)		156	-0.08	1.86	(-3.74, 3.58)	
	Week 20	154	1.87 (0.80)	-0.06	0.03	(-0.12, 0.01)		154	-0.72	1.87	(-4.40, 2.95)	
	Week 24	152	1.87 (0.81)	-0.08	0.03	(-0.14, -0.01)		152	-2.73	1.88	(-6.41, 0.96)	
	Week 28	150	1.87 (0.81)	-0.09	0.03	(-0.16, -0.03)		150	-3.46	1.88	(-7.16, 0.23)	
	Week 32	146	1.87 (0.81)	-0.04	0.03	(-0.11, 0.02)		146	-0.52	1.90	(-4.24, 3.20)	
	Week 36	142	1.89 (0.82)	-0.08	0.03	(-0.15, -0.02)		142	-2.13	1.91	(-5.88, 1.61)	
	Week 40	141	1.89 (0.79)	-0.08	0.03	(-0.15, -0.01)		141	-1.85	1.91	(-5.60, 1.90)	
	Week 44	139	1.89 (0.80)	-0.06	0.03	(-0.12, 0.01)		139	-0.37	1.92	(-4.14, 3.39)	
	Week 48	133	1.90 (0.80)	-0.05	0.03	(-0.12, 0.02)		133	-0.69	1.94	(-4.49, 3.12)	
	Week 52	133	1.90 (0.80)	-0.02	0.03	(-0.09, 0.05)		133	1.09	1.94	(-2.72, 4.89)	

表 2.7.6.26－99　LDL-C／HDL-C 比のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			0.09	0.05	(0.00, 0.18)	0.060		5.51	2.62	(0.36, 10.65)	0.036
	Week 4			0.11	0.05	(0.02, 0.20)	0.023		6.14	2.63	(0.97, 11.31)	0.020
	Week 6			0.11	0.05	(0.02, 0.20)	0.019		6.45	2.64	(1.27, 10.62)	0.039
	Week 8			0.17	0.05	(0.08, 0.26)	<0.001		9.02	2.65	(3.82, 14.22)	<0.001
	Week 10			0.16	0.05	(0.06, 0.25)	0.001		8.51	2.65	(3.30, 13.72)	0.001
	Week 12			0.17	0.05	(0.08, 0.26)	<0.001		9.86	2.66	(4.64, 15.08)	<0.001
	Week 16			0.19	0.05	(0.10, 0.28)	<0.001		9.77	2.67	(4.53, 15.01)	<0.001
	Week 20			0.22	0.05	(0.13, 0.32)	<0.001		11.69	2.68	(6.42, 16.95)	<0.001
	Week 24			0.19	0.05	(0.09, 0.28)	<0.001		10.75	2.69	(5.47, 16.04)	<0.001
	Week 28			0.21	0.05	(0.12, 0.31)	<0.001		12.15	2.71	(6.83, 17.46)	<0.001
	Week 32			0.20	0.05	(0.10, 0.30)	<0.001		11.91	2.73	(6.56, 17.26)	<0.001
	Week 36			0.22	0.05	(0.12, 0.31)	<0.001		12.12	2.75	(6.73, 17.51)	<0.001
	Week 40			0.22	0.05	(0.12, 0.31)	<0.001		10.81	2.76	(5.38, 16.23)	<0.001
	Week 44			0.22	0.05	(0.12, 0.32)	<0.001		10.98	2.78	(5.52, 16.44)	<0.001
	Week 48			0.25	0.05	(0.16, 0.35)	<0.001		14.11	2.80	(8.63, 19.60)	<0.001
	Week 52			0.19	0.05	(0.09, 0.29)	<0.001		9.01	2.81	(3.50, 14.52)	0.001

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visit as a fixed effect, baseline values as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_15.sas

5.3.5.1—9 表 11.4.1—16 より引用

表 2.7.6.26－100　中性脂肪のベースラインからの変化量（MMRM，FAS）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
MT-6548												
	Week 2	160	115.5 (69.4)	26.8	4.5	(17.4, 35.1)		160	26.5	3.9	(18.9, 34.0)	
	Week 4	157	116.2 (69.8)	22.2	4.5	(13.3, 31.2)		157	25.1	3.9	(17.4, 32.7)	
	Week 6	155	118.6 (70.0)	29.3	4.6	(19.3, 37.2)		155	27.5	3.9	(19.9, 35.1)	
	Week 8	151	114.1 (67.3)	32.8	4.6	(23.8, 41.9)		151	33.7	3.9	(26.0, 41.5)	
	Week 10	150	113.3 (66.8)	34.7	4.6	(25.6, 43.8)		150	34.8	3.9	(27.0, 42.5)	
	Week 12	147	114.2 (66.9)	38.1	4.7	(29.0, 47.2)		147	41.5	4.0	(33.7, 49.3)	
	Week 16	144	114.0 (67.0)	26.4	4.7	(17.2, 35.6)		144	30.3	4.0	(22.5, 38.2)	
	Week 20	140	114.5 (67.4)	29.1	4.7	(19.8, 38.4)		140	34.2	4.0	(26.2, 42.1)	
	Week 24	138	114.9 (67.6)	26.9	4.7	(17.6, 36.2)		138	30.4	4.1	(22.4, 38.3)	
	Week 28	132	117.1 (68.2)	26.1	4.8	(16.7, 35.6)		132	34.8	4.1	(26.7, 42.9)	
	Week 32	131	116.7 (68.6)	29.3	4.8	(19.8, 38.8)		131	35.1	4.1	(27.0, 43.2)	
	Week 36	127	117.7 (69.2)	22.1	4.9	(12.5, 31.6)		127	34.5	4.2	(26.4, 42.7)	
	Week 40	122	119.0 (70.1)	26.7	4.9	(17.0, 36.4)		122	37.9	4.2	(29.6, 46.1)	
	Week 44	118	120.2 (70.6)	20.2	5.0	(10.4, 30.0)		118	28.7	4.3	(20.4, 37.1)	
	Week 48	118	120.2 (70.6)	22.4	5.0	(12.6, 32.2)		118	30.5	4.3	(22.1, 38.8)	
	Week 52	115	121.0 (71.3)	17.6	5.0	(7.7, 27.5)		115	27.0	4.3	(18.6, 35.4)	

表 2.7.6.26－100　中性脂肪のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
darbepoetin												
	Week 2	160	112.0 (67.4)	-0.1	4.5	(-8.9, 8.8)		160	6.1	3.9	(-1.5, 13.6)	
	Week 4	159	112.2 (67.6)	4.0	4.5	(-4.8, 12.9)		159	11.6	3.9	(4.0, 19.2)	
	Week 6	159	112.2 (67.6)	5.2	4.5	(-3.6, 14.1)		159	14.7	3.9	(7.1, 22.3)	
	Week 8	158	112.4 (67.7)	4.4	4.5	(-4.5, 13.3)		158	13.0	3.9	(5.4, 20.6)	
	Week 10	157	112.5 (68.0)	9.2	4.5	(0.3, 18.1)		157	17.5	3.9	(9.8, 25.1)	
	Week 12	157	112.5 (68.0)	5.4	4.5	(-3.5, 14.3)		157	13.3	3.9	(5.7, 21.0)	
	Week 16	156	112.7 (68.1)	2.4	4.6	(-6.6, 11.3)		156	11.9	3.9	(4.3, 19.6)	
	Week 20	154	113.5 (68.2)	1.4	4.6	(-7.5, 10.4)		154	10.8	3.9	(3.1, 18.4)	
	Week 24	152	113.2 (68.4)	-1.9	4.6	(-10.9, 7.1)		152	8.4	3.9	(0.7, 16.1)	
	Week 28	150	113.8 (68.6)	-2.7	4.6	(-11.7, 6.4)		150	7.6	3.9	(-0.1, 15.4)	
	Week 32	146	113.4 (67.6)	2.7	4.6	(-6.5, 11.8)		146	13.0	4.0	(5.2, 20.8)	
	Week 36	142	114.5 (68.0)	0.7	4.7	(-8.5, 9.9)		142	9.6	4.0	(1.8, 17.5)	
	Week 40	141	115.0 (69.0)	-1.6	4.7	(-10.8, 7.6)		141	8.1	4.0	(0.2, 16.0)	
	Week 44	139	115.4 (69.4)	-3.9	4.7	(-13.1, 5.4)		139	9.7	4.0	(1.8, 17.6)	
	Week 48	133	114.6 (69.0)	-3.3	4.8	(-12.7, 6.1)		133	7.9	4.1	(-0.1, 16.0)	
	Week 52	133	114.6 (69.0)	-0.4	4.8	(-9.8, 9.0)		133	12.5	4.1	(4.5, 20.5)	

表 2.7.6.26－100　中性脂肪のベースラインからの変化量（MMRM，FAS）（続き）

				Change from Baseline					Percent Change from Baseline			
Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value	N	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin												
	Week 2			26.3	6.4	(13.8, 38.8)	<0.001		20.4	5.5	(9.7, 31.1)	<0.001
	Week 4			18.2	6.4	(5.6, 30.8)	0.005		18.5	5.5	(7.7, 29.2)	0.014
	Week 6			23.0	6.4	(10.4, 35.6)	<0.001		12.8	5.5	(2.0, 23.6)	0.020
	Week 8			28.4	6.5	(15.7, 41.1)	<0.001		20.8	5.5	(9.9, 31.6)	<0.001
	Week 10			25.5	6.5	(12.8, 38.3)	<0.001		17.3	5.5	(6.5, 28.2)	0.002
	Week 12			32.7	6.5	(20.0, 45.5)	<0.001		28.2	5.6	(17.3, 39.1)	<0.001
	Week 16			24.0	6.5	(11.2, 36.8)	<0.001		18.4	5.6	(7.4, 29.4)	0.001
	Week 20			27.6	6.6	(14.8, 40.5)	<0.001		23.4	5.6	(12.4, 34.4)	<0.001
	Week 24			28.8	6.6	(15.8, 41.7)	<0.001		22.0	5.6	(10.9, 33.1)	<0.001
	Week 28			28.8	6.7	(15.7, 41.9)	<0.001		27.2	5.7	(16.0, 38.3)	<0.001
	Week 32			26.7	6.7	(13.5, 39.8)	<0.001		22.1	5.7	(10.9, 33.3)	<0.001
	Week 36			21.4	6.8	(8.1, 34.7)	0.002		24.9	5.8	(13.6, 36.3)	<0.001
	Week 40			28.3	6.8	(14.9, 41.7)	<0.001		29.8	5.8	(18.3, 41.2)	<0.001
	Week 44			24.1	6.9	(10.6, 37.6)	<0.001		19.0	5.9	(7.5, 30.5)	0.001
	Week 48			25.7	6.9	(12.1, 39.2)	<0.001		22.5	5.9	(10.9, 34.1)	<0.001
	Week 52			18.0	6.9	(4.4, 31.6)	0.010		14.5	5.9	(2.9, 26.2)	0.015

Note(s): Triglyceride (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_3_16.sas

5.3.5.1—9 表 11.4.1—17 より引用

(10)　随時血糖

MMRM を用いた随時血糖のベースラインからの変化量を表 2.7.6.26－101 に示した．

MMRM を用いた随時血糖の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -2.5 mg/dL 及び -7.4～2.3 mg/dL，darbepoetin 群で 2.2 mg/dL 及び -2.4～6.8 mg/dL であった．MMRM を用いた随時血糖の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -4.8 mg/dL 及び -11.5～1.9 mg/dL であり，統計学的に有意な差は認められなかった．

表 2.7.6.26－101　随時血糖のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	121.0 (28.9)	-2.4	2.2	(-6.8, 1.9)	
	Week 4	157	121.2 (29.1)	-2.2	2.2	(-6.6, 2.1)	
	Week 6	155	121.1 (29.2)	-4.7	2.2	(-9.1, -0.3)	
	Week 8	151	120.8 (29.2)	-3.4	2.3	(-7.8, 1.0)	
	Week 10	150	120.8 (29.3)	-3.9	2.3	(-8.3, 0.6)	
	Week 12	147	120.5 (29.1)	-2.0	2.3	(-6.4, 2.5)	
	Week 16	144	120.5 (29.4)	-2.9	2.3	(-7.4, 1.6)	
	Week 20	140	120.3 (29.7)	-1.6	2.3	(-6.1, 3.0)	
	Week 24	138	120.0 (29.3)	-2.9	2.3	(-7.4, 1.7)	
	Week 28	132	120.6 (28.9)	-7.3	2.4	(-12.0, -2.7)	
	Week 32	131	121.2 (29.5)	-4.0	2.4	(-8.6, 0.7)	
	Week 36	127	121.0 (29.2)	-4.6	2.4	(-9.3, 0.1)	
	Week 40	122	122.2 (29.2)	-3.8	2.4	(-8.6, 0.9)	
	Week 44	118	122.0 (29.7)	-4.8	2.4	(-9.6, 0.0)	
	Week 48	118	122.0 (29.7)	0.7	2.4	(-4.1, 5.5)	
	Week 52	115	122.5 (29.9)	-2.5	2.5	(-7.4, 2.3)	
darbepoetin	Week 2	160	126.7 (39.8)	1.3	2.2	(-3.1, 5.6)	
	Week 4	159	126.6 (39.9)	-1.0	2.2	(-5.3, 3.4)	
	Week 6	159	126.6 (39.9)	0.4	2.2	(-3.9, 4.8)	
	Week 8	156	126.6 (40.0)	-3.2	2.2	(-7.6, 1.2)	
	Week 10	157	126.4 (40.1)	0.2	2.2	(-4.1, 4.6)	
	Week 12	157	126.4 (40.1)	-1.2	2.2	(-5.6, 3.2)	
	Week 16	156	126.5 (40.2)	2.6	2.2	(-1.8, 7.0)	
	Week 20	154	126.8 (40.3)	2.7	2.2	(-1.7, 7.1)	
	Week 24	152	126.4 (40.1)	0.8	2.2	(-3.6, 5.2)	
	Week 28	149	126.4 (40.3)	4.7	2.3	(0.3, 9.1)	
	Week 32	146	126.9 (40.6)	7.0	2.8	(2.5, 11.4)	
	Week 36	142	127.4 (40.9)	5.7	2.3	(1.2, 10.2)	
	Week 40	141	127.5 (41.0)	2.5	2.3	(-2.0, 7.0)	
	Week 44	139	127.7 (41.3)	0.4	2.3	(-4.1, 4.9)	
	Week 48	133	127.3 (40.9)	2.2	2.3	(-2.4, 6.8)	
	Week 52	133	127.3 (40.9)	2.2	2.3	(-2.4, 6.8)	

表 2.7.6.26－101　随時血糖のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference	Week 2			-3.7	3.1	(-9.8, 2.4)	0.235
MT-6548 - darbepoetin							
	Week 4			-1.3	3.1	(-7.4, 4.9)	0.681
	Week 6			-5.1	3.1	(-11.3, 1.1)	0.105
	Week 8			-0.2	3.2	(-6.4, 6.0)	0.948
	Week 10			-4.1	3.2	(-10.3, 2.1)	0.199
	Week 12			-0.9	3.2	(-7.0, 5.5)	0.803
	Week 16			-5.5	3.2	(-11.8, 0.8)	0.086
	Week 20			-4.3	3.2	(-10.6, 2.0)	0.183
	Week 24			-3.6	3.2	(-10.0, 2.7)	0.260
	Week 28			-12.0	3.3	(-18.5, -5.6)	<0.001
	Week 32			-10.9	3.3	(-17.4, -4.5)	<0.001
	Week 36			-10.3	3.3	(-16.8, -3.8)	0.002
	Week 40			-6.3	3.3	(-12.9, 0.2)	0.056
	Week 44			-5.2	3.4	(-11.8, 1.4)	0.125
	Week 48			-1.5	3.4	(-8.2, 5.1)	0.653
	Week 52			-4.8	3.4	(-11.5, 1.9)	0.160

Note(s): Blood Glucose (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_3.sas

5.3.5.1—9 表 11.4.1—18 より引用

(11)　血圧

MMRM を用いた収縮期血圧及び拡張期血圧のベースラインからの変化量を表 2.7.6.26－102 及び表 2.7.6.26－103 に示した.

MMRM を用いた収縮期血圧の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で-2.8 mmHg 及び -5.9～0.2 mmHg，darbepoetin 群で -1.8 mmHg 及び -4.6～1.1 mmHg であった．MMRM を用いた収縮期血圧の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群との差の LSMean 及びその 95%CI は -1.1 mmHg 及び -5.2～3.1 mmHg であり，統計学的に有意な差は認められなかった.

MMRM を用いた拡張期血圧の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -3.9 mmHg 及び -5.7～ -2.2 mmHg，darbepoetin 群で -1.5 mmHg 及び -3.2～0.1 mmHg であった．MMRM を用いた拡張期血圧の 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -2.4 mmHg 及び -4.8～0.0 mmHg であり，統計学的に有意な差が認められた（p=0.048）.

表 2.7.6.26－102　収縮期血圧のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	148.6 (19.8)	-2.4	1.4	(-5.1, 0.3)	
	Week 4	157	148.5 (19.9)	-3.1	1.4	(-5.8, -0.4)	
	Week 6	155	148.5 (19.9)	-2.6	1.4	(-5.3, 0.1)	
	Week 8	151	148.4 (19.9)	-3.4	1.4	(-6.1, -0.6)	
	Week 10	150	148.4 (20.0)	-4.5	1.4	(-7.2, -1.7)	
	Week 12	147	148.3 (20.1)	-2.2	1.4	(-5.0, 0.5)	
	Week 16	144	148.0 (20.1)	-3.9	1.4	(-6.6, -1.1)	
	Week 20	140	147.8 (20.1)	-0.2	1.4	(-3.1, 2.6)	
	Week 24	136	147.9 (20.0)	1.3	1.4	(-1.6, 4.1)	
	Week 28	132	147.9 (20.2)	1.1	1.5	(-1.8, 4.0)	
	Week 32	131	147.9 (20.1)	1.6	1.5	(-1.4, 4.4)	
	Week 36	127	148.1 (20.0)	-0.9	1.5	(-3.9, 2.1)	
	Week 40	122	147.2 (19.8)	0.3	1.5	(-2.7, 3.2)	
	Week 44	118	147.6 (20.0)	0.3	1.5	(-2.7, 3.3)	
	Week 48	116	147.6 (20.0)	-3.0	1.5	(-6.0, 0.0)	
	Week 52	115	147.8 (20.2)	-2.8	1.5	(-5.9, 0.2)	
darbepoetin	Week 2	160	146.4 (18.4)	-0.9	1.4	(-3.6, 1.7)	
	Week 4	159	146.4 (18.5)	-2.0	1.4	(-4.7, 0.7)	
	Week 6	159	146.4 (18.5)	-2.9	1.4	(-5.6, -0.2)	
	Week 8	158	146.4 (18.6)	-0.6	1.4	(-3.3, 2.1)	
	Week 10	157	146.3 (18.5)	-2.6	1.4	(-5.3, 0.1)	
	Week 12	157	146.3 (18.6)	-1.5	1.4	(-4.2, 1.2)	
	Week 16	156	146.3 (18.6)	-1.0	1.4	(-3.7, 1.8)	
	Week 20	154	146.2 (18.7)	1.1	1.4	(-1.6, 3.9)	
	Week 24	152	146.4 (18.7)	3.4	1.4	(0.7, 6.1)	
	Week 28	150	146.4 (18.8)	3.0	1.4	(0.3, 5.8)	
	Week 32	146	146.5 (18.9)	2.1	1.4	(-0.7, 4.9)	
	Week 36	142	146.3 (18.9)	1.7	1.4	(-1.1, 4.5)	
	Week 40	141	145.9 (18.9)	1.5	1.4	(-1.3, 4.3)	
	Week 44	139	145.9 (18.9)	1.8	1.4	(-1.0, 4.6)	
	Week 48	133	146.0 (18.4)	0.2	1.5	(-2.7, 3.1)	
	Week 52	133	146.0 (18.4)	-1.8	1.5	(-4.6, 1.1)	

表 2.7.6.26－102　収縮期血圧のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin	Week 2			-1.4	1.9	(-5.2, 2.4)	0.461
	Week 4			-1.1	1.9	(-4.9, 2.7)	0.576
	Week 6			0.2	2.0	(-3.6, 4.1)	0.900
	Week 8			-2.8	2.0	(-6.7, 1.0)	0.168
	Week 10			-1.9	2.0	(-5.7, 2.0)	0.351
	Week 12			-0.8	2.0	(-4.6, 3.1)	0.701
	Week 16			-2.9	2.0	(-6.8, 1.0)	0.145
	Week 20			-1.4	2.0	(-5.3, 2.5)	0.487
	Week 24			-2.1	2.0	(-6.1, 1.8)	0.288
	Week 28			-2.0	2.0	(-6.0, 2.0)	0.332
	Week 32			-0.7	2.0	(-4.7, 3.3)	0.747
	Week 36			-2.5	2.1	(-6.6, 1.5)	0.220
	Week 40			-1.2	2.1	(-5.3, 2.8)	0.550
	Week 44			-1.5	2.1	(-5.6, 2.6)	0.475
	Week 48			-3.2	2.1	(-7.3, 0.9)	0.130
	Week 52			-1.1	2.1	(-5.2, 3.1)	0.618

Note(s): Systolic Blood Pressure (mmHg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_1.sas

5.3.5.1—9 表 11.4.1—19 より引用

表 2.7.6.26－103　拡張期血圧のベースラインからの変化量（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	160	81.4 (11.8)	-2.2	0.8	(-3.7, -0.6)	
	Week 4	157	81.1 (11.6)	-2.6	0.8	(-4.1, -1.0)	
	Week 6	153	81.1 (11.6)	-2.7	0.8	(-4.3, -1.1)	
	Week 8	151	80.8 (11.6)	-3.2	0.8	(-4.8, -1.7)	
	Week 10	150	80.9 (11.6)	-3.3	0.8	(-4.9, -1.7)	
	Week 12	147	80.9 (11.5)	-1.8	0.8	(-3.4, -0.2)	
	Week 16	144	80.9 (11.6)	-2.6	0.8	(-4.2, -1.0)	
	Week 20	140	80.7 (11.7)	-1.4	0.8	(-3.1, 0.2)	
	Week 24	138	80.9 (11.6)	-0.5	0.8	(-2.1, 1.1)	
	Week 28	132	80.5 (11.6)	-1.2	0.8	(-2.9, 0.4)	
	Week 32	131	80.6 (11.6)	-0.4	0.8	(-2.1, 1.3)	
	Week 36	127	80.6 (11.5)	-1.0	0.9	(-2.7, 0.6)	
	Week 40	122	80.5 (11.4)	-1.2	0.9	(-2.9, 0.5)	
	Week 44	118	80.7 (11.4)	-1.6	0.9	(-3.3, 0.1)	
	Week 48	118	80.7 (11.4)	-3.2	0.9	(-5.0, -1.5)	
	Week 52	116	80.9 (11.4)	-3.9	0.9	(-5.7, -2.2)	
darbepoetin	Week 2	160	78.9 (12.6)	-0.7	0.8	(-2.3, 0.8)	
	Week 4	159	78.8 (12.6)	-1.0	0.8	(-2.6, 0.6)	
	Week 6	159	78.8 (12.6)	-1.0	0.8	(-2.5, 0.6)	
	Week 8	158	79.0 (12.4)	0.0	0.8	(-1.6, 1.5)	
	Week 10	157	79.0 (12.5)	-1.6	0.8	(-3.2, -0.1)	
	Week 12	157	79.0 (12.5)	-0.5	0.8	(-2.0, 1.1)	
	Week 16	156	78.9 (12.5)	-0.6	0.8	(-2.1, 1.0)	
	Week 20	154	78.9 (12.5)	0.1	0.8	(-1.4, 1.7)	
	Week 24	152	78.9 (12.5)	1.4	0.8	(-0.2, 2.9)	
	Week 28	150	79.0 (12.6)	1.1	0.8	(-0.5, 2.7)	
	Week 32	146	79.3 (12.2)	1.1	0.8	(-0.5, 2.7)	
	Week 36	142	79.3 (12.2)	0.6	0.8	(-1.0, 2.2)	
	Week 40	141	79.0 (12.6)	0.0	0.8	(-1.6, 1.6)	
	Week 44	139	78.9 (12.7)	-0.6	0.8	(-2.2, 1.1)	
	Week 48	133	79.1 (12.3)	-0.4	0.8	(-2.1, 1.2)	
	Week 52	133	79.1 (12.3)	-1.5	0.8	(-3.2, 0.1)	

表 2.7.6.26－103　拡張期血圧のベースラインからの変化量（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin	Week 2			-1.5	1.1	(-3.6, 0.7)	0.191
	Week 4			-1.6	1.1	(-3.7, 0.7)	0.175
	Week 6			-1.7	1.1	(-3.9, 0.6)	0.123
	Week 8			-3.2	1.1	(-5.4, -1.0)	0.005
	Week 10			-1.7	1.1	(-3.9, 0.5)	0.138
	Week 12			-1.3	1.1	(-3.5, 0.9)	0.251
	Week 16			-2.0	1.1	(-4.2, 0.2)	0.079
	Week 20			-1.6	1.1	(-3.8, 0.7)	0.166
	Week 24			-1.9	1.2	(-4.1, 0.4)	0.105
	Week 28			-2.3	1.2	(-4.6, 0.0)	0.045
	Week 32			-1.5	1.2	(-3.8, 0.8)	0.206
	Week 36			-1.6	1.2	(-4.0, 0.7)	0.165
	Week 40			-1.3	1.2	(-3.6, 1.1)	0.290
	Week 44			-1.0	1.2	(-3.4, 1.3)	0.389
	Week 48			-2.8	1.2	(-5.2, -0.4)	0.021
	Week 52			-2.4	1.2	(-4.8, 0.0)	0.048

Note(s): Diastolic Blood Pressure (mmHg).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.6
Source: t_14_2_3_11_2_2.sas

5.3.5.1—9 表 11.4.1—20 より引用

(12)　救済治療

ESA 製剤による救済治療を受けた被験者の割合を表 2.7.6.26－104 に，赤血球輸血による救済治療を受けた被験者の割合を表 2.7.6.26－105 に，瀉血による救済治療を受けた被験者の割合を表 2.7.6.26－106 に示した．

治療期間中に ESA 製剤による救済治療を受けた被験者の割合は，MT-6548 群で 6.8%，darbepoetin 群で 3.7%であった．治療期間中に赤血球輸血による救済治療を受けた被験者の割合は，MT-6548 群で 1.2%，darbepoetin 群で 0%であった．瀉血による救済治療を受けた被験者は両群で認められなかった．なお，中止日以降に初めて ESA 製剤による救済治療を受けた被験者は，MT-6548 群で 2 名，darbepoetin 群で 0 名であり，中止日以降に初めて赤血球輸血による救済治療を受けた被験者は MT-6548 群で 1 名，darbepoetin 群で 0 名，瀉血による救済治療を受けた被験者は両群で認められなかった．

表 2.7.6.26－104　ESA 製剤による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	161	0 (0.0)	(0.00, 2.27)	160	0 (0.0)	(0.00, 2.28)	-	(-, -)	-
Week 4 <= to < Week 6	157	1 (0.6)	(0.02, 3.50)	159	0 (0.0)	(0.00, 2.29)	0.6	(-10.5, 11.8)	0.497
Week 6 <= to < Week 8	155	2 (1.3)	(0.16, 4.58)	159	0 (0.0)	(0.00, 2.29)	1.3	(-9.9, 12.4)	0.243
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	1 (0.7)	(0.02, 3.66)	158	0 (0.0)	(0.00, 2.31)	0.7	(-10.5, 11.9)	0.487
Week 12 <= to < Week 16	148	0 (0.0)	(0.00, 2.46)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to < Week 24	140	0 (0.0)	(0.00, 2.60)	156	1 (0.6)	(0.02, 3.52)	-0.6	(-12.0, 10.8)	1.000
Week 24 <= to < Week 28	137	0 (0.0)	(0.00, 2.66)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 28 <= to < Week 32	133	1 (0.8)	(0.02, 4.12)	150	1 (0.7)	(0.02, 3.66)	0.1	(-11.5, 11.7)	1.000
Week 32 <= to < Week 36	132	1 (0.8)	(0.02, 4.15)	147	1 (0.7)	(0.02, 3.73)	0.1	(-11.6, 11.8)	1.000
Week 36 <= to < Week 40	129	3 (2.3)	(0.48, 6.65)	146	2 (1.4)	(0.17, 4.86)	1.0	(-10.9, 12.7)	0.668
Week 40 <= to < Week 44	127	4 (3.1)	(0.86, 7.87)	148	0 (0.0)	(0.00, 2.55)	3.1	(-8.8, 15.0)	0.048
Week 44 <= to < Week 48	126	1 (0.8)	(0.02, 4.34)	140	1 (0.7)	(0.02, 3.92)	0.1	(-12.0, 12.1)	1.000
Week 48 <= to <= Week 52	123	0 (0.0)	(0.00, 2.95)	135	0 (0.0)	(0.00, 2.70)	-	(-, -)	-
Baseline <= to <= Week 52	162	11 (6.8)	(3.44, 11.82)	161	6 (3.7)	(1.38, 7.93)	3.1	(-7.8, 13.9)	0.319

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.9
Source: t_14_2_3_2_1_1.sas

5.3.5.1―9 表 11.4.1―21 より引用

表 2.7.6.26－105　赤血球輸血による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	161	0 (0.0)	(0.00, 2.27)	160	0 (0.0)	(0.00, 2.28)	-	(-, -)	-
Week 4 <= to < Week 6	157	0 (0.0)	(0.00, 2.32)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 6 <= to < Week 8	155	0 (0.0)	(0.00, 2.35)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 12 <= to < Week 16	148	0 (0.0)	(0.00, 2.46)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to < Week 24	140	0 (0.0)	(0.00, 2.60)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 24 <= to < Week 28	137	0 (0.0)	(0.00, 2.66)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 28 <= to < Week 32	133	0 (0.0)	(0.00, 2.74)	150	0 (0.0)	(0.00, 2.43)	-	(-, -)	-
Week 32 <= to < Week 36	132	1 (0.8)	(0.02, 4.15)	147	0 (0.0)	(0.00, 2.48)	0.8	(-11.0, 12.5)	0.473
Week 36 <= to < Week 40	129	1 (0.8)	(0.02, 4.24)	146	0 (0.0)	(0.00, 2.49)	0.8	(-11.0, 12.6)	0.469
Week 40 <= to < Week 44	127	1 (0.8)	(0.02, 4.31)	143	0 (0.0)	(0.00, 2.55)	0.8	(-11.1, 12.7)	0.470
Week 44 <= to < Week 48	126	0 (0.0)	(0.00, 2.89)	140	0 (0.0)	(0.00, 2.60)	-	(-, -)	-
Week 48 <= to <= Week 52	123	0 (0.0)	(0.00, 2.95)	135	0 (0.0)	(0.00, 2.70)	-	(-, -)	-
Baseline <= to <= Week 52	162	2 (1.2)	(0.15, 4.39)	161	0 (0.0)	(0.00, 2.27)	1.2	(-9.6, 12.1)	0.498

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.10
Source: t_14_2_3_2_2_1.sas

5.3.5.1—9 表 11.4.1—22 より引用

表 2.7.6.26－106　瀉血による救済治療を受けた被験者数とその割合（FAS）

Period	MT-6548(N=162)			darbepoetin(N=161)			Difference of proportion (MT-6548 - darbepoetin)		
	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Baseline <= to < Week 2	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-
Week 2 <= to < Week 4	161	0 (0.0)	(0.00, 2.27)	160	0 (0.0)	(0.00, 2.28)	-	(-, -)	-
Week 4 <= to < Week 6	157	0 (0.0)	(0.00, 2.32)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 6 <= to < Week 8	155	0 (0.0)	(0.00, 2.35)	159	0 (0.0)	(0.00, 2.29)	-	(-, -)	-
Week 8 <= to < Week 10	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 10 <= to < Week 12	150	0 (0.0)	(0.00, 2.43)	158	0 (0.0)	(0.00, 2.31)	-	(-, -)	-
Week 12 <= to < Week 16	148	0 (0.0)	(0.00, 2.46)	157	0 (0.0)	(0.00, 2.32)	-	(-, -)	-
Week 16 <= to < Week 20	144	0 (0.0)	(0.00, 2.53)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 20 <= to < Week 24	140	0 (0.0)	(0.00, 2.60)	156	0 (0.0)	(0.00, 2.34)	-	(-, -)	-
Week 24 <= to < Week 28	137	0 (0.0)	(0.00, 2.66)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 28 <= to < Week 32	133	0 (0.0)	(0.00, 2.74)	150	0 (0.0)	(0.00, 2.43)	-	(-, -)	-
Week 32 <= to < Week 36	132	0 (0.0)	(0.00, 2.76)	147	0 (0.0)	(0.00, 2.48)	-	(-, -)	-
Week 36 <= to < Week 40	129	0 (0.0)	(0.00, 2.82)	146	0 (0.0)	(0.00, 2.49)	-	(-, -)	-
Week 40 <= to < Week 44	127	0 (0.0)	(0.00, 2.86)	143	0 (0.0)	(0.00, 2.55)	-	(-, -)	-
Week 44 <= to < Week 48	126	0 (0.0)	(0.00, 2.89)	140	0 (0.0)	(0.00, 2.60)	-	(-, -)	-
Week 48 <= to <= Week 52	123	0 (0.0)	(0.00, 2.95)	135	0 (0.0)	(0.00, 2.70)	-	(-, -)	-
Baseline <= to <= Week 52	162	0 (0.0)	(0.00, 2.25)	161	0 (0.0)	(0.00, 2.27)	-	(-, -)	-

Note(s): N*: number of subjects in each period.
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Note(s): 95%CI: 95% confidence interval of difference of proportion (MT-6548 - darbepoetin) is analyzed by Exact method.
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.2.11
Source: t_14_2_3_2_3_1.sas

5.3.5.1—9 表 14.2.3.2.3.1 より引用

(13)　QOL 指標

1)　QOL 指標（EQ-5D-5L）

MMRM を用いた EQ-5D-5L の Index Value 及び VAS スコアのベースラインからの変化量を表 2.7.6.26－107 に示した.

MMRM を用いた Index Value の 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は，MT-6548 群で -0.0144 及び -0.0329～0.0041，darbepoetin 群で -0.0323 及び -0.0497～ -0.0150 であった．MMRM を用いた 52 週後の Index Value の変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は 0.0179 及び -0.0074～0.0433 であり，統計学的に有意な差は認められなかった.

MMRM を用いた VAS スコアの 52 週後のベースラインからの変化量の LSMean 及びその 95%CI は MT-6548 群で -3.2 及び -5.7～ -0.7, darbepoetin 群で -2.0 及び -4.3～ 0.4 であった．MMRM を用いた VAS スコアの 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は -1.3 及び -4.7～2.2 であり，統計学的に有意な差は認められなかった.

表 2.7.6.26－107　EQ-5D-5L の Index Value 及び VAS スコアのベースラインからの変化量（MMRM，FAS）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Index value	MT-6548	Week 12	146	0.9127 (0.1266)	-0.0030	0.0086	(-0.0199, 0.0139)	
		Week 24	138	0.9060 (0.1315)	-0.0038	0.0088	(-0.0210, 0.0135)	
		Week 52	116	0.9088 (0.1291)	-0.0144	0.0094	(-0.0329, 0.0041)	
	darbepoetin	Week 12	157	0.9080 (0.1208)	-0.0139	0.0083	(-0.0302, 0.0024)	
		Week 24	152	0.9103 (0.1193)	-0.0244	0.0084	(-0.0409, -0.0079)	
		Week 52	133	0.9120 (0.1161)	-0.0323	0.0088	(-0.0497, -0.0150)	
	Difference MT-6548 - darbepoetin	Week 12			0.0109	0.0119	(-0.0126, 0.0344)	0.361
		Week 24			0.0207	0.0122	(-0.0032, 0.0445)	0.090
		Week 52			0.0179	0.0129	(-0.0074, 0.0433)	0.166
VAS score	MT-6548	Week 12	146	80.2 (15.5)	-1.6	1.2	(-3.9, 0.7)	
		Week 24	138	80.2 (15.8)	-1.0	1.2	(-3.3, 1.4)	
		Week 52	116	80.7 (16.0)	-3.2	1.3	(-5.7, -0.7)	
	darbepoetin	Week 12	156	79.6 (14.3)	-2.7	1.1	(-4.9, -0.5)	
		Week 24	151	80.1 (13.9)	-3.9	1.1	(-6.1, -1.6)	
		Week 52	132	79.8 (14.0)	-2.0	1.2	(-4.3, 0.4)	
	Difference MT-6548 - darbepoetin	Week 12			1.1	1.6	(-2.1, 4.3)	0.487
		Week 24			2.9	1.7	(-0.4, 6.1)	0.082
		Week 52			-1.3	1.8	(-4.7, 2.2)	0.474

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.7
Source: t_14_2_3_12_2_1.sas

5.3.5.1—9 表 11.4.1—23 より引用

2)　QOL 指標（KDQOL）

MMRM を用いた KDQOL のスコアのベースラインからの変化量を表 2.7.6.26－108 に示した.

MMRM を用いた KDQOL のスコアの 52 週後のベースラインからの変化量の MT-6548 群と darbepoetin 群の差について，特筆すべき差を認めたサブスケールはなかった.

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Physical Functioning	MT-6548	Week 12	144	83.70 (18.05)	-1.22	1.04	(-3.26, 0.83)	
		Week 24	136	84.10 (17.53)	-1.57	1.07	(-3.66, 0.53)	
		Week 52	114	84.56 (17.46)	-4.41	1.14	(-6.64, -2.18)	
	darbepoetin	Week 12	156	79.04 (19.18)	-2.82	1.00	(-4.79, -0.85)	
		Week 24	151	79.30 (19.17)	-2.17	1.02	(-4.17, -0.17)	
		Week 52	132	79.36 (17.68)	-3.51	1.06	(-5.60, -1.42)	
	Difference MT-6548 - darbepoetin	Week 12			1.60	1.45	(-1.25, 4.45)	0.270
		Week 24			0.60	1.48	(-2.30, 3.50)	0.683
		Week 52			-0.90	1.56	(-3.97, 2.16)	0.562
Role Functioning Physical	MT-6548	Week 12	144	78.47 (33.27)	-1.08	2.62	(-6.23, 4.07)	
		Week 24	136	79.68 (32.99)	-0.60	2.69	(-5.89, 4.69)	
		Week 52	114	78.51 (34.06)	-4.10	2.90	(-9.80, 1.60)	
	darbepoetin	Week 12	156	73.88 (35.17)	-1.94	2.52	(-6.89, 3.01)	
		Week 24	151	74.83 (34.70)	-3.94	2.56	(-8.96, 1.08)	
		Week 52	132	73.86 (35.34)	-0.82	2.71	(-6.14, 4.50)	
	Difference MT-6548 - darbepoetin	Week 12			0.86	3.64	(-6.29, 8.00)	0.814
		Week 24			3.34	3.71	(-3.96, 10.63)	0.370
		Week 52			-3.28	3.97	(-11.09, 4.52)	0.409

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Bodily Pain	MT-6548	Week 12	144	81.48 (20.96)	0.87	1.54	(-2.45, 3.89)	
		Week 24	136	80.94 (21.07)	-0.81	1.57	(-3.40, 2.78)	
		Week 52	114	81.51 (21.33)	-1.76	1.69	(-5.07, 1.57)	
	darbepoetin	Week 12	156	78.86 (20.37)	-1.64	1.48	(-4.54, 1.26)	
		Week 24	151	79.93 (19.51)	-4.27	1.60	(-7.21, -1.33)	
		Week 52	132	76.77 (19.75)	-2.98	1.58	(-6.09, 0.12)	
	Difference MT-6548 - darbepoetin	Week 12			2.21	2.13	(-1.98, 6.40)	0.301
		Week 24			3.96	2.17	(-0.31, 8.23)	0.069
		Week 52			1.23	2.32	(-3.32, 5.78)	0.595
General Health Perceptions	MT-6548	Week 12	144	56.19 (16.26)	-1.68	1.06	(-3.77, 0.41)	
		Week 24	136	56.41 (16.43)	-1.91	1.09	(-4.05, 0.22)	
		Week 52	114	56.89 (17.42)	-2.81	1.16	(-5.09, -0.54)	
	darbepoetin	Week 12	156	54.36 (16.60)	-0.39	1.02	(-2.40, 1.62)	
		Week 24	151	54.64 (16.77)	-3.47	1.04	(-5.51, -1.44)	
		Week 52	132	54.95 (17.33)	-2.77	1.09	(-4.90, -0.63)	
	Difference MT-6548 - darbepoetin	Week 12			-1.29	1.46	(-4.20, 1.61)	0.382
		Week 24			1.56	1.50	(-1.40, 4.51)	0.301
		Week 52			-0.05	1.59	(-3.17, 3.08)	0.977

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Vitality	MT-6548	Week 12	144	68.65 (18.78)	-2.65	1.29	(-5.16, -0.13)	
		Week 24	136	69.04 (19.07)	-1.70	1.31	(-4.27, 0.87)	
		Week 52	114	68.07 (19.49)	-3.15	1.39	(-5.88, -0.42)	
	darbepoetin	Week 12	156	65.83 (18.55)	-3.13	1.23	(-5.54, -0.71)	
		Week 24	151	66.32 (18.46)	-0.91	1.25	(-3.36, 1.54)	
		Week 52	132	65.87 (18.29)	-2.61	1.30	(-5.17, -0.05)	
	Difference MT-6548 - darbepoetin	Week 12			0.48	1.78	(-3.01, 3.97)	0.786
		Week 24			-0.79	1.81	(-4.34, 2.76)	0.662
		Week 52			-0.54	1.91	(-4.29, 3.21)	0.778
Social Functioning	MT-6548	Week 12	144	88.89 (16.99)	-1.05	1.45	(-3.91, 1.80)	
		Week 24	136	89.25 (16.68)	-1.32	1.49	(-4.24, 1.61)	
		Week 52	114	88.71 (17.20)	-2.13	1.61	(-5.29, 1.02)	
	darbepoetin	Week 12	156	86.14 (19.70)	-2.62	1.40	(-5.37, 0.22)	
		Week 24	151	87.17 (18.71)	-2.48	1.42	(-5.26, 0.30)	
		Week 52	132	86.55 (18.64)	-0.90	1.50	(-3.85, 2.04)	
	Difference MT-6548 - darbepoetin	Week 12			1.47	2.02	(-2.49, 5.44)	0.466
		Week 24			1.17	2.06	(-2.87, 5.21)	0.571
		Week 52			-1.28	2.20	(-5.55, 3.09)	0.575

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Role Functioning Emotional	MT-6548	Week 12	144	84.49 (32.49)	-6.36	2.65	(-11.56, -1.16)	
		Week 24	136	85.29 (32.65)	-0.01	2.71	(-5.34, 5.32)	
		Week 52	114	84.80 (33.23)	-2.15	2.91	(-7.87, 3.57)	
	darbepoetin	Week 12	156	82.05 (33.74)	-1.14	2.55	(-6.14, 3.86)	
		Week 24	151	82.56 (33.30)	-3.86	2.59	(-8.93, 1.21)	
		Week 52	132	82.07 (33.81)	-1.76	2.72	(-7.11, 3.59)	
	Difference MT-6548 - darbepoetin	Week 12			-5.22	3.68	(-12.44, 2.00)	0.156
		Week 24			3.84	3.75	(-3.52, 11.20)	0.306
		Week 52			-0.39	3.99	(-8.22, 7.44)	0.922
Mental Health	MT-6548	Week 12	144	78.47 (16.74)	-1.43	1.23	(-3.85, 0.99)	
		Week 24	136	78.88 (16.73)	-0.97	1.26	(-3.44, 1.49)	
		Week 52	114	79.39 (16.94)	-2.48	1.33	(-5.10, 0.14)	
	darbepoetin	Week 12	156	78.40 (16.26)	-1.38	1.19	(-3.72, 0.95)	
		Week 24	150	78.81 (16.26)	-0.43	1.20	(-2.79, 1.93)	
		Week 52	131	77.63 (16.66)	-0.79	1.26	(-3.25, 1.69)	
	Difference MT-6548 - darbepoetin	Week 12			-0.05	1.71	(-3.41, 3.31)	0.978
		Week 24			-0.54	1.74	(-3.96, 2.87)	0.755
		Week 52			-1.69	1.83	(-5.29, 1.91)	0.357

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Symptoms/Problems	MT-6548	Week 12	144	88.20 (10.36)	-0.35	0.66	(-1.65, 0.95)	
		Week 24	136	88.31 (10.37)	-1.00	0.68	(-2.34, 0.33)	
		Week 52	114	87.89 (10.74)	-1.34	0.73	(-2.77, 0.09)	
	darbepoetin	Week 12	156	86.99 (10.02)	-0.32	0.64	(-1.57, 0.93)	
		Week 24	151	87.14 (9.99)	-0.09	0.65	(-1.36, 1.18)	
		Week 52	132	87.06 (10.00)	-0.55	0.68	(-1.89, 0.78)	
	Difference MT-6548 - darbepoetin	Week 12			-0.03	0.92	(-1.83, 1.77)	0.975
		Week 24			-0.92	0.94	(-2.76, 0.92)	0.329
		Week 52			-0.78	1.00	(-2.74, 1.17)	0.432
Effect of kidney disease	MT-6548	Week 12	144	83.73 (18.64)	0.43	0.92	(-1.37, 2.23)	
		Week 24	136	83.82 (13.95)	0.91	0.94	(-0.93, 2.75)	
		Week 52	114	83.65 (14.11)	0.95	0.99	(-1.00, 2.91)	
	darbepoetin	Week 12	156	82.68 (14.38)	0.89	0.86	(-0.85, 2.62)	
		Week 24	151	82.98 (14.24)	0.68	0.89	(-1.07, 2.44)	
		Week 52	132	82.47 (14.68)	0.48	0.93	(-1.35, 2.31)	
	Difference MT-6548 - darbepoetin	Week 12			-0.46	1.27	(-2.96, 2.04)	0.719
		Week 24			0.22	1.30	(-2.32, 2.77)	0.862
		Week 52			0.48	1.36	(-2.20, 3.15)	0.727

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Burden of kidney disease	MT-6548	Week 12	144	48.18 (23.02)	-1.93	1.46	(-4.80, 0.94)	
		Week 24	136	47.33 (22.62)	0.36	1.49	(-2.57, 3.29)	
		Week 52	114	47.48 (23.16)	-0.24	1.58	(-3.34, 2.86)	
	darbepoetin	Week 12	155	47.78 (23.56)	-3.80	1.41	(-6.57, -1.03)	
		Week 24	150	48.17 (23.77)	-3.38	1.43	(-6.17, -0.56)	
		Week 52	131	47.90 (24.79)	-2.86	1.49	(-5.79, 0.06)	
	Difference MT-6548 - darbepoetin	Week 12			1.88	2.03	(-2.11, 5.87)	0.356
		Week 24			3.72	2.06	(-0.33, 7.78)	0.072
		Week 52			2.62	2.17	(-1.64, 6.89)	0.227
Work status	MT-6548	Week 12	144	59.03 (34.61)	-0.57	1.97	(-4.43, 3.30)	
		Week 24	136	59.09 (35.08)	-3.34	2.02	(-7.30, 0.62)	
		Week 52	118	59.73 (33.98)	-1.39	2.17	(-5.65, 2.88)	
	darbepoetin	Week 12	156	56.73 (34.59)	-0.21	1.89	(-3.93, 3.51)	
		Week 24	151	58.61 (33.55)	-0.92	1.92	(-4.69, 2.85)	
		Week 52	132	59.09 (34.88)	-2.68	2.02	(-6.65, 1.29)	
	Difference MT-6548 - darbepoetin	Week 12			-0.36	2.73	(-5.72, 5.01)	0.896
		Week 24			-2.42	2.78	(-7.89, 3.04)	0.385
		Week 52			1.30	2.97	(-4.53, 7.12)	0.662

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Cognitive function	MT-6548	Week 12	143	90.26 (13.37)	-1.09	0.86	(-2.78, 0.59)	
		Week 24	135	90.67 (13.44)	0.73	0.88	(-0.99, 2.45)	
		Week 52	118	90.50 (13.88)	-0.69	0.94	(-2.54, 1.16)	
	darbepoetin	Week 12	156	91.72 (12.28)	-0.67	0.82	(-2.29, 0.94)	
		Week 24	151	91.99 (11.90)	-0.17	0.83	(-1.80, 1.47)	
		Week 52	132	91.44 (12.45)	0.09	0.88	(-1.63, 1.81)	
	Difference MT-6548 - darbepoetin	Week 12			-0.42	1.19	(-2.75, 1.91)	0.723
		Week 24			0.90	1.21	(-1.48, 3.27)	0.459
		Week 52			-0.78	1.29	(-3.31, 1.75)	0.543
Quality of social interaction	MT-6548	Week 12	143	91.52 (13.29)	-1.13	0.90	(-2.89, 0.63)	
		Week 24	135	91.16 (13.79)	1.50	0.92	(-0.30, 3.30)	
		Week 52	118	91.09 (14.13)	0.25	0.98	(-1.67, 2.17)	
	darbepoetin	Week 12	156	91.67 (13.54)	-1.39	0.86	(-3.07, 0.30)	
		Week 24	151	91.57 (13.72)	-0.58	0.87	(-2.29, 1.12)	
		Week 52	132	90.86 (14.47)	-1.23	0.91	(-3.02, 0.56)	
	Difference MT-6548 - darbepoetin	Week 12			0.26	1.24	(-2.18, 2.69)	0.835
		Week 24			2.08	1.26	(-0.40, 4.56)	0.099
		Week 52			1.49	1.34	(-1.15, 4.10)	0.270

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Sexual function	MT-6548	Week 12	5	85.00 (10.46)	3.49	4.99	(-6.67, 13.66)	
		Week 24	4	87.50 (10.21)	7.63	5.56	(-3.67, 18.93)	
		Week 52	5	90.00 (10.46)	-0.49	4.98	(-10.64, 9.65)	
	darbepoetin	Week 12	10	90.00 (23.42)	3.60	3.53	(-3.58, 10.77)	
		Week 24	9	86.11 (24.56)	0.92	3.70	(-6.60, 8.44)	
		Week 52	10	90.00 (23.42)	-0.28	3.52	(-7.44, 6.89)	
	Difference MT-6548 - darbepoetin	Week 12			-0.10	6.12	(-12.56, 12.36)	0.987
		Week 24			6.71	6.68	(-6.95, 20.28)	0.322
		Week 52			-0.22	6.09	(-12.62, 12.19)	0.972
Sleep	MT-6548	Week 12	143	68.58 (16.49)	-1.59	1.11	(-3.76, 0.68)	
		Week 24	135	68.74 (16.64)	-1.32	1.13	(-3.55, 0.91)	
		Week 52	113	67.61 (17.16)	-1.56	1.22	(-3.95, 0.83)	
	darbepoetin	Week 12	156	70.29 (15.77)	-3.22	1.06	(-5.30, -1.14)	
		Week 24	151	70.30 (15.84)	-0.79	1.07	(-2.90, 1.32)	
		Week 52	132	70.88 (15.61)	1.13	1.13	(-1.10, 3.36)	
	Difference MT-6548 - darbepoetin	Week 12			1.63	1.53	(-1.38, 4.64)	0.288
		Week 24			-0.53	1.56	(-3.60, 2.54)	0.734
		Week 52			-2.69	1.67	(-5.96, 0.58)	0.107

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Social support	MT-6548	Week 12	144	79.63 (19.26)	-0.54	1.58	(-3.64, 2.55)	
		Week 24	135	79.26 (19.15)	-0.44	1.63	(-3.63, 2.75)	
		Week 52	114	79.38 (19.75)	0.36	1.75	(-3.07, 3.80)	
	darbepoetin	Week 12	156	76.60 (21.98)	-2.97	1.52	(-5.95, 0.00)	
		Week 24	151	76.49 (22.22)	-2.59	1.54	(-5.61, 0.44)	
		Week 52	132	75.75 (21.73)	-2.96	1.63	(-6.17, 0.24)	
	Difference MT-6548 - darbepoetin	Week 12			2.43	2.19	(-1.87, 6.73)	0.269
		Week 24			2.14	2.24	(-2.25, 6.54)	0.339
		Week 52			3.33	2.40	(-1.38, 8.03)	0.165
Dialysis staff encouragement	MT-6548	Week 12	142	84.60 (16.69)	1.50	1.44	(-1.34, 4.33)	
		Week 24	135	84.35 (16.99)	0.25	1.47	(-2.64, 3.15)	
		Week 52	114	86.51 (14.61)	-0.49	1.58	(-3.59, 2.61)	
	darbepoetin	Week 12	156	82.37 (16.88)	-2.25	1.38	(-4.96, 0.45)	
		Week 24	150	82.00 (19.02)	-3.64	1.40	(-6.39, -0.89)	
		Week 52	132	81.82 (19.31)	-4.52	1.47	(-7.42, -1.63)	
	Difference MT-6548 - darbepoetin	Week 12			3.75	2.00	(-0.17, 7.67)	0.061
		Week 24			3.89	2.03	(-0.10, 7.89)	0.056
		Week 52			4.03	2.16	(-0.22, 8.28)	0.063

表 2.7.6.26－108　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Subscale	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Patient satisfaction	MT-6548	Week 12	143	87.29 (12.66)	-0.26	1.05	(-2.33, 1.80)	
		Week 24	135	87.41 (12.63)	0.82	1.08	(-1.69, 2.64)	
		Week 52	114	88.30 (12.83)	-1.48	1.16	(-3.78, 0.79)	
	darbepoetin	Week 12	155	84.19 (14.81)	-2.07	1.01	(-4.05, -0.09)	
		Week 24	150	84.22 (14.68)	-0.28	1.02	(-2.29, 1.73)	
		Week 52	132	84.09 (14.83)	-1.94	1.08	(-4.06, 0.19)	
	Difference MT-6548 - darbepoetin	Week 12			1.80	1.46	(-1.06, 4.67)	0.217
		Week 24			0.81	1.49	(-2.12, 3.73)	0.589
		Week 52			0.46	1.58	(-2.66, 3.57)	0.771

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.10
Source: t_14_2_3_12_6_1.sas

5.3.5.1—9 表 11.4.1—24 より引用

(14)　部分集団の検討

部分集団の検討で用いた評価項目及びその結果を示した図表の一覧を表 2.7.6.26－109 に示した.

表 2.7.6.26－109　部分集団解析の評価項目

評価項目	結果を示した図表
被験者背景別の 52 週後の Hb 値（MMRM，FAS）	表 2.7.6.26－110
前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）	表 2.7.6.26－111
前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）	表 2.7.6.26－112
MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）	図 2.7.6.26－35
MT-6548 群の前治療 ESA 製剤（エポエチン製剤）の用量別の Hb 値の推移（FAS）	図 2.7.6.26－36
MT-6548 群の前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）	図 2.7.6.26－37
MT-6548 群の前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）	図 2.7.6.26－38
前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）	表 2.7.6.26－113
前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）	表 2.7.6.26－114
鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の記述統計量（FAS）	表 2.7.6.26－115
鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値（MMRM，FAS）	表 2.7.6.26－116
MT-6548 群の鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の推移（FAS）	図 2.7.6.26－39
MT-6548 群のベースラインの CRP と 52 週後の Hb 値の散布図（FAS）	図 2.7.6.26－40
被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）	表 2.7.6.26－117
前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－118
前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－41
前治療 ESA 製剤（エポエチン製剤）の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－42
前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－43
前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－44
前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－119
鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.26－120
鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量の推移（FAS）	図 2.7.6.26－45
ベースラインの CRP と 48 週から 52 週後の MT-6548 の 1 日平均投与量の散布図（FAS）	図 2.7.6.26－46

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Sex	Male	MT-6548	104	10.92 (0.73)	10.40	0.09	(10.22, 10.59)	
		darbepoetin	109	10.69 (0.67)	10.59	0.09	(10.42, 10.77)	
		Difference MT-6548 - darbepoetin			-0.19	0.13	(-0.44, 0.06)	0.136
	Female	MT-6548	56	10.61 (0.69)	10.36	0.13	(10.11, 10.61)	
		darbepoetin	51	10.83 (0.81)	10.69	0.12	(10.45, 10.93)	
		Difference MT-6548 - darbepoetin			-0.33	0.18	(-0.68, 0.01)	0.059
Age at Informed Consent (years)	<65	MT-6548	60	10.78 (0.72)	10.56	0.12	(10.32, 10.79)	
		darbepoetin	68	10.69 (0.72)	10.70	0.11	(10.49, 10.91)	
		Difference MT-6548 - darbepoetin			-0.14	0.16	(-0.46, 0.17)	0.374
	>=65	MT-6548	100	10.72 (0.73)	10.28	0.10	(10.10, 10.47)	
		darbepoetin	92	10.77 (0.72)	10.56	0.10	(10.37, 10.74)	
		Difference MT-6548 - darbepoetin			-0.27	0.14	(-0.54, 0.00)	0.047
	<75	MT-6548	122	10.76 (0.74)	10.40	0.09	(10.23, 10.57)	
		darbepoetin	129	10.76 (0.75)	10.60	0.09	(10.45, 10.76)	
		Difference MT-6548 - darbepoetin			-0.21	0.12	(-0.44, 0.02)	0.079
	>=75	MT-6548	38	10.68 (0.68)	10.33	0.16	(10.03, 10.64)	
		darbepoetin	31	10.65 (0.67)	10.71	0.16	(10.39, 11.02)	
		Difference MT-6548 - darbepoetin			-0.37	0.22	(-0.81, 0.07)	0.096

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Dry Weight (kg)	<60	MT-6548	98	10.71 (0.74)	10.33	0.10	(10.14, 10.52)	
		darbepoetin	91	10.79 (0.73)	10.62	0.09	(10.43, 10.80)	
		Difference MT-6548 - darbepoetin			-0.29	0.14	(-0.55, -0.02)	0.036
	>=60	MT-6548	62	10.80 (0.70)	10.49	0.12	(10.26, 10.72)	
		darbepoetin	69	10.67 (0.71)	10.63	0.11	(10.41, 10.84)	
		Difference MT-6548 - darbepoetin			-0.14	0.16	(-0.45, 0.18)	0.389
BMI (kg/m²)	<25	MT-6548	120	10.73 (0.71)	10.41	0.09	(10.24, 10.58)	
		darbepoetin	127	10.76 (0.78)	10.61	0.08	(10.46, 10.77)	
		Difference MT-6548 - darbepoetin			-0.20	0.12	(-0.43, 0.03)	0.089
	>=25	MT-6548	40	10.78 (0.78)	10.35	0.15	(10.05, 10.65)	
		darbepoetin	33	10.85 (0.68)	10.63	0.16	(10.32, 10.95)	
		Difference MT-6548 - darbepoetin			-0.28	0.22	(-0.72, 0.15)	0.202

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Etiology of CKD	Diabetes	MT-6548	29	10.92 (0.71)	10.10	0.17	(9.76, 10.43)	
		darbepoetin	39	10.76 (0.68)	10.77	0.13	(10.51, 11.02)	
		Difference			-0.67	0.22	(-1.09, -0.25)	0.002
		MT-6548 - darbepoetin						
	Hypertension	MT-6548	20	10.73 (0.82)	10.65	0.20	(10.26, 11.04)	
		darbepoetin	22	10.71 (0.77)	10.53	0.19	(10.17, 10.90)	
		Difference			0.11	0.27	(-0.42, 0.65)	0.682
		MT-6548 - darbepoetin						
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	62	10.71 (0.73)	10.41	0.12	(10.17, 10.64)	
		darbepoetin	64	10.76 (0.67)	10.56	0.11	(10.34, 10.77)	
		Difference			-0.15	0.16	(-0.47, 0.17)	0.358
		MT-6548 - darbepoetin						
	Interstitial Nephritis/Pyelonephritis	MT-6548	4	10.45 (0.54)	10.74	0.73	(9.63, 12.86)	
		darbepoetin	1	11.90 (-)				
		Difference						
		MT-6548 - darbepoetin						
	Cystic/Hereditary/Congenital Disease	MT-6548	17	10.54 (0.64)	10.43	0.29	(9.84, 11.01)	
		darbepoetin	10	10.39 (0.90)	10.57	0.37	(9.84, 11.31)	
		Difference			-0.15	0.47	(-1.09, 0.79)	0.757
		MT-6548 - darbepoetin						
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	1	10.00 (-)				
		Difference						
		MT-6548 - darbepoetin						

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Duration of Anemia from CKD (years)	<1	MT-6548	6	10.47 (0.79)	11.03	0.29	(10.45, 11.61)	
		darbepoetin	4	11.25 (0.44)	10.62	0.38	(9.87, 11.38)	
		Difference MT-6548 - darbepoetin			0.41	0.49	(-0.56, 1.37)	0.405
	1<= to <5	MT-6548	64	10.38 (0.75)	10.46	0.12	(10.23, 10.69)	
		darbepoetin	67	10.63 (0.76)	10.72	0.11	(10.50, 10.94)	
		Difference MT-6548 - darbepoetin			-0.26	0.16	(-0.58, 0.06)	0.106
	>=5	MT-6548	89	10.68 (0.70)	10.29	0.10	(10.09, 10.49)	
		darbepoetin	89	10.79 (0.69)	10.55	0.10	(10.36, 10.74)	
		Difference MT-6548 - darbepoetin			-0.26	0.14	(-0.54, 0.02)	0.068
Complications	Hypertension	MT-6548	150	10.74 (0.73)	10.38	0.05	(10.22, 10.53)	
		darbepoetin	147	10.74 (0.71)	10.63	0.07	(10.48, 10.77)	
		Difference MT-6548 - darbepoetin			-0.25	0.11	(-0.46, -0.04)	0.019
	Diabetes	MT-6548	85	10.38 (0.69)	10.29	0.16	(9.97, 10.60)	
		darbepoetin	48	10.67 (0.76)	10.81	0.12	(10.56, 11.05)	
		Difference MT-6548 - darbepoetin			-0.52	0.20	(-0.92, -0.12)	0.011
	Dyslipidaemia	MT-6548	57	10.72 (0.63)	10.56	0.11	(10.34, 10.77)	
		darbepoetin	79	10.79 (0.71)	10.67	0.09	(10.49, 10.86)	
		Difference MT-6548 - darbepoetin			-0.12	0.14	(-0.40, 0.16)	0.413

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline Hb (g/dL)	<10	MT-6548	23	9.66 (0.26)	10.36	0.19	(9.98, 10.74)	
		darbepoetin	24	9.61 (0.31)	10.62	0.19	(10.23, 11.00)	
		Difference MT-6548 - darbepoetin			-0.26	0.27	(-0.79, 0.28)	0.352
	10<= to <11	MT-6548	76	10.45 (0.27)	10.23	0.10	(10.03, 10.43)	
		darbepoetin	76	10.52 (0.27)	10.57	0.09	(10.39, 10.75)	
		Difference MT-6548 - darbepoetin			-0.33	0.14	(-0.61, -0.06)	0.016
	>=11	MT-6548	61	11.51 (0.33)	10.60	0.13	(10.35, 10.86)	
		darbepoetin	60	11.46 (0.40)	10.69	0.12	(10.45, 10.93)	
		Difference MT-6548 - darbepoetin			-0.09	0.17	(-0.44, 0.26)	0.596
Baseline Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	159	10.74 (0.72)	10.39	0.08	(10.24, 10.53)	
		darbepoetin	160	10.74 (0.72)	10.62	0.07	(10.48, 10.76)	
		Difference MT-6548 - darbepoetin			-0.23	0.10	(-0.44, -0.03)	0.024
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	1	11.40 (-)				
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						
	AST >80 or ALT >90	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline CRP (mg/dL)	<0.31	MT-6548	132	10.75 (0.73)	10.32	0.09	(10.16, 10.48)	
		darbepoetin	132	10.76 (0.69)	10.63	0.08	(10.46, 10.79)	
		Difference MT-6548 - darbepoetin			-0.31	0.11	(-0.53, -0.09)	0.006
	>=0.31	MT-6548	28	10.72 (0.72)	10.74	0.19	(10.37, 11.10)	
		darbepoetin	28	10.61 (0.87)	10.60	0.19	(10.23, 10.97)	
		Difference MT-6548 - darbepoetin			0.14	0.26	(-0.38, 0.65)	0.609
Baseline Serum Ferritin (ng/mL)	<82.7	MT-6548	55	10.79 (0.69)	10.37	0.12	(10.12, 10.61)	
		darbepoetin	52	10.83 (0.67)	10.62	0.12	(10.38, 10.86)	
		Difference MT-6548 - darbepoetin			-0.25	0.17	(-0.59, 0.09)	0.144
	82.7<= to <165	MT-6548	53	10.82 (0.84)	10.45	0.13	(10.19, 10.71)	
		darbepoetin	54	10.77 (0.74)	10.67	0.13	(10.42, 10.91)	
		Difference MT-6548 - darbepoetin			-0.21	0.18	(-0.57, 0.15)	0.245
	>=165	MT-6548	52	10.62 (0.61)	10.36	0.13	(10.09, 10.62)	
		darbepoetin	54	10.61 (0.74)	10.57	0.13	(10.33, 10.82)	
		Difference MT-6548 - darbepoetin			-0.22	0.18	(-0.58, 0.15)	0.241

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Baseline TSAT (%)	<23	MT-6548	48	10.73 (0.76)	10.45	0.15	(10.15, 10.75)	
		darbepoetin	53	10.67 (0.77)	10.60	0.13	(10.34, 10.86)	
		Difference MT-6548 - darbepoetin			-0.15	0.20	(-0.55, 0.24)	0.450
	23<= to <31	MT-6548	49	10.79 (0.67)	10.51	0.12	(10.28, 10.74)	
		darbepoetin	56	10.74 (0.70)	10.62	0.11	(10.40, 10.85)	
		Difference MT-6548 - darbepoetin			-0.12	0.16	(-0.44, 0.21)	0.486
	>=31	MT-6548	63	10.68 (0.74)	10.25	0.12	(10.00, 10.49)	
		darbepoetin	51	10.80 (0.70)	10.64	0.13	(10.39, 10.89)	
		Difference MT-6548 - darbepoetin			-0.39	0.18	(-0.74, -0.05)	0.026
Smoking Status	Never Smoked	MT-6548	73	10.61 (0.69)	10.34	0.11	(10.13, 10.55)	
		darbepoetin	73	10.83 (0.71)	10.59	0.10	(10.39, 10.79)	
		Difference MT-6548 - darbepoetin			-0.25	0.15	(-0.54, 0.05)	0.099
	Ex-Smoker	MT-6548	66	10.81 (0.72)	10.46	0.13	(10.22, 10.71)	
		darbepoetin	62	10.83 (0.69)	10.69	0.12	(10.45, 10.93)	
		Difference MT-6548 - darbepoetin			-0.22	0.18	(-0.57, 0.12)	0.203
	Current Smoker	MT-6548	21	11.00 (0.80)	10.36	0.19	(9.99, 10.73)	
		darbepoetin	25	10.22 (0.63)	10.58	0.17	(10.25, 10.91)	
		Difference MT-6548 - darbepoetin			-0.22	0.26	(-0.72, 0.29)	0.393

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	8	10.71 (0.44)	10.58	0.37	(9.78, 11.32)	
		darbepoetin	9	11.03 (0.53)	10.87	0.52	(9.80, 11.94)	
		Difference MT-6548 - darbepoetin			-0.32	0.65	(-1.66, 1.02)	0.628
	No	MT-6548	152	10.75 (0.74)	10.38	0.08	(10.23, 10.53)	
		darbepoetin	156	10.73 (0.73)	10.61	0.07	(10.47, 10.76)	
		Difference MT-6548 - darbepoetin			-0.23	0.11	(-0.44, -0.02)	0.029
Concomitant Medications of Oral Iron at Week 52	Yes	MT-6548	6	10.62 (0.47)	10.08	0.42	(9.23, 10.92)	
		darbepoetin	7	10.57 (0.81)	10.93	0.36	(10.21, 11.65)	
		Difference MT-6548 - darbepoetin			-0.85	0.55	(-1.97, 0.26)	0.130
	No	MT-6548	154	10.75 (0.73)	10.40	0.08	(10.25, 10.55)	
		darbepoetin	153	10.74 (0.72)	10.61	0.07	(10.46, 10.75)	
		Difference MT-6548 - darbepoetin			-0.20	0.11	(-0.41, 0.01)	0.056
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Baseline	Yes	MT-6548	59	10.95 (0.75)	10.22	0.13	(9.96, 10.47)	
		darbepoetin	51	10.75 (0.82)	10.70	0.14	(10.44, 10.97)	
		Difference MT-6548 - darbepoetin			-0.49	0.19	(-0.86, -0.12)	0.010
	No	MT-6548	101	10.68 (0.71)	10.50	0.09	(10.32, 10.68)	
		darbepoetin	109	10.73 (0.68)	10.58	0.08	(10.42, 10.75)	
		Difference MT-6548 - darbepoetin			-0.08	0.12	(-0.33, 0.16)	0.493

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 52	Yes	MT-6548	52	10.89 (0.76)	10.12	0.14	(9.85, 10.39)	
		darbepoetin	49	10.77 (0.84)	10.74	0.14	(10.47, 11.01)	
		Difference			-0.62	0.20	(-1.00, -0.24)	0.002
		MT-6548 - darbepoetin						
	No	MT-6548	108	10.67 (0.70)	10.52	0.09	(10.35, 10.70)	
		darbepoetin	111	10.72 (0.67)	10.57	0.09	(10.41, 10.73)	
		Difference			-0.05	0.12	(-0.28, 0.19)	0.709
		MT-6548 - darbepoetin						
Prior ESA Treatment: Medication	Epoetin	MT-6548	49	10.63 (0.76)	10.30	0.14	(10.01, 10.58)	
		darbepoetin	53	10.53 (0.80)	10.54	0.14	(10.27, 10.81)	
		Difference			-0.25	0.20	(-0.64, 0.15)	0.217
		MT-6548 - darbepoetin						
	Darbepoetin alfa	MT-6548	95	10.75 (0.70)	10.42	0.09	(10.24, 10.60)	
		darbepoetin	89	10.89 (0.66)	10.66	0.09	(10.48, 10.83)	
		Difference			-0.24	0.13	(-0.48, 0.01)	0.063
		MT-6548 - darbepoetin						
	Epoetin beta pegol	MT-6548	16	11.03 (0.75)	10.55	0.26	(10.05, 11.06)	
		darbepoetin	18	10.60 (0.67)	10.65	0.21	(10.23, 11.07)	
		Difference			-0.10	0.34	(-0.76, 0.56)	0.771
		MT-6548 - darbepoetin						
	Other	MT-6548	0					
		darbepoetin	0					
		Difference						
		MT-6548 - darbepoetin						

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Prior ESA Treatment: Weekly Dose (IU)	Epoetin, <3000	MT-6548	15	10.50 (0.69)	10.70	0.27	(10.17, 11.24)	
		darbepoetin	13	10.23 (0.89)	10.75	0.26	(10.24, 11.26)	
		Difference MT-6548 - darbepoetin			-0.04	0.37	(-0.79, 0.70)	0.905
	Epoetin, 3000<= to <4500	MT-6548	17	10.46 (0.75)	10.17	0.22	(9.73, 10.61)	
		darbepoetin	11	10.50 (0.68)	10.84	0.28	(10.28, 11.40)	
		Difference MT-6548 - darbepoetin			-0.67	0.36	(-1.38, 0.04)	0.065
	Epoetin, >=4500	MT-6548	17	10.93 (0.77)	10.02	0.23	(9.58, 10.47)	
		darbepoetin	29	10.68 (0.78)	10.38	0.18	(10.02, 10.74)	
		Difference MT-6548 - darbepoetin			-0.36	0.29	(-0.93, 0.22)	0.221
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	20	10.83 (0.56)	10.74	0.17	(10.41, 11.07)	
		darbepoetin	14	10.71 (0.73)	10.66	0.20	(10.27, 11.04)	
		Difference MT-6548 - darbepoetin			0.08	0.26	(-0.43, 0.59)	0.747
	Darbepoetin alfa, 10<= to <20	MT-6548	34	10.66 (0.75)	10.53	0.14	(10.26, 10.80)	
		darbepoetin	40	10.80 (0.67)	10.64	0.12	(10.40, 10.87)	
		Difference MT-6548 - darbepoetin			-0.11	0.18	(-0.46, 0.25)	0.549
	Darbepoetin alfa, >=20	MT-6548	41	10.80 (0.71)	10.16	0.15	(9.85, 10.46)	
		darbepoetin	35	11.06 (0.69)	10.70	0.15	(10.40, 10.99)	
		Difference MT-6548 - darbepoetin			-0.54	0.21	(-0.96, -0.12)	0.012

表 2.7.6.26－110　被験者背景別の 52 週後の Hb 値（MMRM，FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Prior ESA Treatment: Weekly Dose (ug)	Epoetin beta pegol, <12.5	MT-6548	3	10.80 (0.95)	11.30	0.35	(10.59, 12.01)	
		darbepoetin	4	10.83 (0.64)	10.56	0.30	(9.95, 11.18)	
		Difference MT-6548 - darbepoetin			0.74	0.46	(-0.20, 1.68)	0.119
	Epoetin beta pegol, 12.5<= to <25	MT-6548	7	10.80 (0.85)	10.34	0.37	(9.61, 11.07)	
		darbepoetin	6	10.28 (0.70)	10.61	0.41	(9.80, 11.42)	
		Difference MT-6548 - darbepoetin			-0.26	0.55	(-1.36, 0.84)	0.634
	Epoetin beta pegol, >=25	MT-6548	6	11.40 (0.83)	10.38	0.59	(9.20, 11.55)	
		darbepoetin	8	10.73 (0.65)	10.73	0.33	(10.07, 11.39)	
		Difference MT-6548 - darbepoetin			-0.35	0.69	(-1.71, 1.01)	0.612
Concomitant Medications of CYP2B6 Substrates	Yes	MT-6548	18	10.92 (0.68)	10.65	0.23	(10.20, 11.11)	
		darbepoetin	24	10.86 (0.77)	10.80	0.18	(10.45, 11.15)	
		Difference MT-6548 - darbepoetin			-0.15	0.29	(-0.72, 0.42)	0.609
	No	MT-6548	142	10.72 (0.78)	10.36	0.08	(10.20, 10.51)	
		darbepoetin	136	10.71 (0.71)	10.59	0.08	(10.44, 10.74)	
		Difference MT-6548 - darbepoetin			-0.23	0.11	(-0.45, -0.01)	0.039

Note(s): Hb (g/dL).
Note(s): N: number of subjects who was used in MMRM model (i.e. number of subjects with Hb at least one visit after baseline).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): Baseline Serum Ferritin, Baseline TSAT and each Prior ESA Treatment Total Weekly Dose are divided into three categories by the 3-quantiles.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.1
Source: t_14_2_5_1.sas

5.3.5.1—9 表 11.4.2—4 より引用

表 2.7.6.26－111　前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline						
Treatment Group	Prior ESA Treatment	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetin	Baseline	49	10.63	0.76	10.60	(9.4, 12.0)	(10.42, 10.85)							
		Week 2	49	10.51	0.83	10.60	(8.3, 12.5)	(10.27, 10.75)	49	-0.12	0.63	-0.10	(-1.6, 1.2)	(-0.30, 0.06)	0.193
		Week 4	48	10.37	0.98	10.25	(7.7, 12.4)	(10.08, 10.65)	48	-0.28	0.89	-0.20	(-2.2, 1.2)	(-0.54, -0.02)	0.033
		Week 6	47	10.24	1.16	10.10	(7.2, 13.2)	(9.90, 10.58)	47	-0.40	1.16	-0.20	(-2.7, 1.6)	(-0.74, -0.06)	0.022
		Week 8	47	10.25	1.14	10.30	(6.8, 13.0)	(9.91, 10.58)	47	-0.39	1.22	-0.20	(-3.1, 1.6)	(-0.75, -0.03)	0.034
		Week 10	47	10.31	1.28	10.30	(6.7, 12.8)	(9.93, 10.68)	47	-0.33	1.40	-0.20	(-3.2, 2.3)	(-0.74, 0.08)	0.112
		Week 12	46	10.54	1.26	10.45	(7.7, 13.3)	(10.17, 10.91)	46	-0.11	1.45	-0.15	(-2.8, 2.9)	(-0.54, 0.32)	0.599
		Week 16	46	10.73	1.08	10.95	(8.3, 12.9)	(10.41, 11.05)	46	0.07	1.32	0.30	(-3.1, 2.1)	(-0.32, 0.46)	0.714
		Week 20	46	10.84	1.06	10.85	(8.3, 13.1)	(10.53, 11.16)	46	0.19	1.29	0.10	(-2.8, 2.6)	(-0.20, 0.57)	0.332
		Week 24	46	10.80	1.08	10.85	(8.6, 13.3)	(10.48, 11.12)	46	0.14	1.19	0.30	(-3.1, 2.3)	(-0.21, 0.50)	0.416
		Week 28	43	10.71	1.00	10.70	(8.5, 12.8)	(10.40, 11.01)	43	0.07	1.16	0.10	(-3.2, 2.3)	(-0.28, 0.43)	0.676
		Week 32	43	10.64	1.00	10.70	(8.3, 13.0)	(10.34, 10.95)	43	0.01	1.22	0.10	(-3.4, 1.9)	(-0.36, 0.39)	0.950
		Week 36	40	10.41	1.02	10.65	(8.0, 12.1)	(10.08, 10.74)	40	-0.21	1.19	0.05	(-3.5, 1.6)	(-0.59, 0.17)	0.271
		Week 40	41	10.39	0.96	10.40	(8.6, 12.7)	(10.09, 10.69)	41	-0.24	1.24	-0.20	(-3.1, 3.1)	(-0.63, 0.15)	0.222
		Week 44	39	10.21	0.88	10.20	(8.3, 12.2)	(9.92, 10.50)	39	-0.43	1.10	-0.40	(-3.4, 1.6)	(-0.78, -0.07)	0.021
		Week 48	39	10.32	0.85	10.40	(8.3, 12.5)	(10.05, 10.60)	39	-0.32	1.12	-0.10	(-3.4, 1.4)	(-0.68, 0.05)	0.096
		Week 52	38	10.27	0.81	10.30	(8.1, 11.7)	(10.00, 10.53)	38	-0.39	1.17	-0.35	(-3.6, 1.7)	(-0.77, 0.00)	0.049
		Week 52(LOCF)	49	10.24	1.02	10.30	(6.6, 12.7)	(9.94, 10.53)	49	-0.40	1.22	-0.40	(-3.6, 1.7)	(-0.75, -0.05)	0.027
	Darbepoetin alfa	Baseline	97	10.74	0.70	10.70	(8.8, 12.1)	(10.60, 10.88)							
		Week 2	95	10.60	0.73	10.60	(8.8, 12.3)	(10.45, 10.75)	95	-0.16	0.52	0.00	(-1.7, 1.3)	(-0.26, -0.05)	0.005
		Week 4	93	10.32	0.81	10.30	(8.3, 11.9)	(10.15, 10.48)	93	-0.44	0.77	-0.40	(-2.3, 1.3)	(-0.60, -0.28)	<0.001
		Week 6	92	10.17	0.89	10.10	(7.8, 11.9)	(9.99, 10.35)	92	-0.59	0.87	-0.45	(-3.2, 1.3)	(-0.77, -0.41)	<0.001
		Week 8	87	10.15	0.94	10.20	(8.0, 12.5)	(9.95, 10.35)	87	-0.60	1.05	-0.60	(-3.3, 2.6)	(-0.82, -0.37)	<0.001
		Week 10	87	10.14	0.94	10.20	(7.7, 12.1)	(9.94, 10.34)	87	-0.63	1.10	-0.50	(-3.7, 2.0)	(-0.86, -0.39)	<0.001
		Week 12	85	10.33	0.95	10.40	(7.4, 12.5)	(10.12, 10.53)	85	-0.43	1.15	-0.50	(-3.9, 3.7)	(-0.68, -0.18)	<0.001
		Week 16	84	10.45	0.82	10.50	(8.5, 12.4)	(10.27, 10.63)	84	-0.30	1.09	-0.25	(-3.0, 2.6)	(-0.53, -0.06)	0.015
		Week 20	81	10.57	0.78	10.60	(8.7, 12.6)	(10.40, 10.75)	81	-0.15	1.00	0.00	(-2.9, 2.1)	(-0.38, 0.07)	0.170
		Week 24	79	10.53	0.82	10.60	(8.0, 12.2)	(10.34, 10.71)	79	-0.22	1.06	-0.20	(-3.6, 2.2)	(-0.45, 0.02)	0.071
		Week 28	76	10.51	0.94	10.60	(7.8, 12.1)	(10.30, 10.73)	76	-0.24	1.12	-0.20	(-3.1, 2.8)	(-0.49, 0.02)	0.070
		Week 32	76	10.55	0.92	10.70	(7.6, 13.5)	(10.34, 10.76)	76	-0.19	1.03	-0.20	(-2.6, 2.6)	(-0.43, 0.04)	0.103
		Week 36	74	10.48	0.81	10.55	(8.2, 12.9)	(10.29, 10.67)	74	-0.28	1.02	-0.20	(-3.4, 2.0)	(-0.52, -0.05)	0.020
		Week 40	71	10.57	0.85	10.60	(7.8, 12.5)	(10.37, 10.77)	71	-0.22	1.07	-0.20	(-3.6, 1.7)	(-0.47, 0.03)	0.089
		Week 44	69	10.62	0.88	10.70	(8.2, 12.6)	(10.41, 10.83)	69	-0.17	1.08	-0.10	(-3.4, 2.5)	(-0.43, 0.09)	0.190
		Week 48	69	10.51	0.96	10.60	(7.7, 12.4)	(10.28, 10.74)	69	-0.29	1.10	-0.30	(-3.9, 1.7)	(-0.55, -0.02)	0.034
		Week 52	67	10.54	0.85	10.60	(8.2, 12.6)	(10.33, 10.74)	67	-0.27	1.05	-0.30	(-2.8, 1.7)	(-0.52, -0.01)	0.042
		Week 52(LOCF)	96	10.25	1.03	10.35	(7.4, 12.6)	(10.04, 10.46)	96	-0.50	1.16	-0.40	(-3.9, 1.7)	(-0.73, -0.26)	<0.001

表 2.7.6.26－111　前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）（続き）

Treatment Group	Prior ESA Treatment	Visit	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Baseline N	Change from Baseline Mean	Change from Baseline SD	Change from Baseline Median	Change from Baseline Minimum, Maximum	Change from Baseline 95% CI	p value
	Epoetinbeta pegol	Baseline	16	11.03	0.75	10.65	(10.2, 12.6)	(10.62, 11.43)							
		Week 2	16	10.99	0.95	11.05	(9.6, 12.9)	(10.49, 11.50)	16	-0.03	0.42	-0.05	(-0.7, 0.6)	(-0.25, 0.19)	0.770
		Week 4	16	10.80	0.78	10.90	(9.4, 12.2)	(10.38, 11.22)	16	-0.23	0.69	-0.40	(-1.2, 1.3)	(-0.59, 0.14)	0.211
		Week 6	16	10.68	0.70	10.85	(9.2, 11.7)	(10.30, 11.05)	16	-0.35	0.89	-0.40	(-1.4, 1.2)	(-0.82, 0.12)	0.137
		Week 8	16	10.68	0.88	10.95	(9.1, 11.9)	(10.21, 11.14)	16	-0.35	1.16	-0.10	(-2.2, 1.3)	(-0.98, 0.28)	0.264
		Week 10	16	10.59	1.08	10.90	(8.6, 12.2)	(10.01, 11.16)	16	-0.44	1.47	-0.40	(-2.7, 2.0)	(-1.22, 0.34)	0.252
		Week 12	16	10.66	1.15	11.10	(8.4, 11.9)	(10.04, 11.27)	16	-0.37	1.60	-0.10	(-3.2, 1.6)	(-1.22, 0.48)	0.370
		Week 16	14	10.77	1.31	11.05	(7.5, 12.5)	(10.02, 11.53)	14	-0.20	1.80	0.30	(-4.1, 2.3)	(-1.24, 0.84)	0.684
		Week 20	13	10.85	0.90	10.90	(9.4, 12.0)	(10.30, 11.39)	13	-0.18	1.22	-0.20	(-2.1, 1.5)	(-0.92, 0.56)	0.612
		Week 24	13	10.90	0.76	10.60	(10.0, 12.4)	(10.44, 11.36)	13	-0.12	0.92	-0.30	(-1.4, 1.2)	(-0.68, 0.44)	0.640
		Week 28	13	10.61	0.98	10.40	(8.6, 12.5)	(10.02, 11.20)	13	-0.42	1.03	-0.20	(-3.0, 0.8)	(-1.04, 0.21)	0.172
		Week 32	12	10.71	0.99	10.65	(9.0, 12.5)	(10.08, 11.34)	12	-0.27	0.97	0.05	(-2.6, 0.6)	(-0.88, 0.35)	0.360
		Week 36	12	10.80	1.43	11.00	(7.8, 13.4)	(9.89, 11.71)	12	-0.18	1.42	0.35	(-3.8, 1.2)	(-1.08, 0.73)	0.678
		Week 40	10	10.83	0.49	10.90	(10.2, 11.6)	(10.48, 11.18)	10	0.01	0.71	0.10	(-1.1, 1.0)	(-0.50, 0.52)	0.966
		Week 44	10	11.31	0.41	11.35	(10.7, 11.8)	(11.02, 11.60)	10	0.49	0.89	0.70	(-1.6, 1.6)	(-0.14, 1.12)	0.113
		Week 48	10	11.12	0.70	11.00	(10.3, 12.5)	(10.62, 11.62)	10	0.30	0.63	0.35	(-0.9, 1.3)	(-0.15, 0.75)	0.166
		Week 52	10	10.75	1.22	10.30	(8.9, 13.4)	(9.88, 11.62)	10	-0.07	1.05	-0.30	(-1.8, 1.5)	(-0.82, 0.68)	0.837
		Week 52(LOCF)	16	10.22	1.41	10.20	(7.8, 13.4)	(9.47, 10.97)	16	-0.81	1.62	-0.45	(-3.8, 1.6)	(-1.67, 0.06)	0.065

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_5_1.sas

5.3.5.1—9 表 14.2.2.5.1 より引用

表 2.7.6.26－112　前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）

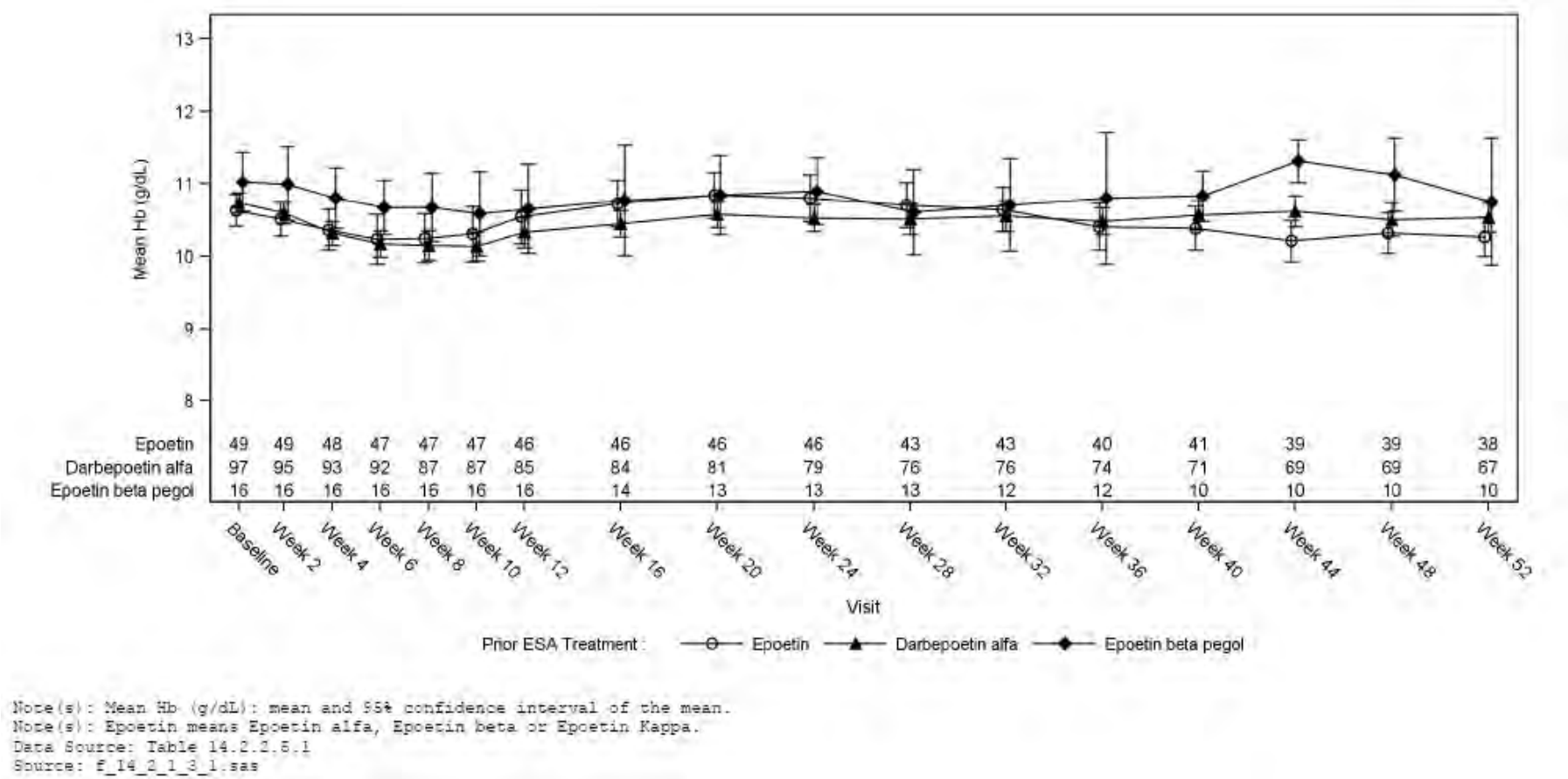
Treatment Group	Prior ESA Treatment	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Epoetin	Week 2	49	10.63 (0.76)	10.51	0.16	(10.20, 10.83)
		Week 4	48	10.65 (0.76)	10.35	0.16	(10.04, 10.66)
		Week 6	47	10.64 (0.76)	10.22	0.16	(9.91, 10.54)
		Week 8	47	10.64 (0.76)	10.23	0.16	(9.92, 10.55)
		Week 10	47	10.64 (0.76)	10.29	0.16	(9.97, 10.60)
		Week 12	46	10.65 (0.76)	10.46	0.16	(10.15, 10.78)
		Week 16	46	10.65 (0.76)	10.65	0.16	(10.33, 10.96)
		Week 20	46	10.65 (0.76)	10.76	0.16	(10.45, 11.08)
		Week 24	46	10.65 (0.76)	10.72	0.16	(10.41, 11.04)
		Week 28	43	10.63 (0.77)	10.63	0.16	(10.31, 10.95)
		Week 32	43	10.63 (0.77)	10.57	0.16	(10.25, 10.89)
		Week 36	40	10.62 (0.77)	10.42	0.16	(10.10, 10.75)
		Week 40	41	10.63 (0.76)	10.39	0.16	(10.07, 10.71)
		Week 44	39	10.64 (0.77)	10.26	0.16	(9.93, 10.58)
		Week 48	39	10.64 (0.77)	10.37	0.16	(10.04, 10.69)
		Week 52	38	10.65 (0.78)	10.30	0.17	(9.98, 10.63)
	Darbepoetin alfa	Week 2	95	10.75 (0.70)	10.60	0.09	(10.42, 10.78)
		Week 4	93	10.76 (0.70)	10.31	0.09	(10.13, 10.49)
		Week 6	92	10.76 (0.70)	10.16	0.09	(9.98, 10.34)
		Week 8	87	10.75 (0.70)	10.12	0.09	(9.93, 10.30)
		Week 10	87	10.76 (0.71)	10.10	0.09	(9.92, 10.28)
		Week 12	85	10.75 (0.70)	10.27	0.09	(10.09, 10.46)
		Week 16	84	10.75 (0.70)	10.38	0.09	(10.19, 10.56)
		Week 20	81	10.73 (0.70)	10.52	0.09	(10.33, 10.70)
		Week 24	79	10.74 (0.70)	10.46	0.10	(10.27, 10.65)
		Week 28	76	10.75 (0.71)	10.43	0.10	(10.24, 10.62)
		Week 32	76	10.75 (0.71)	10.47	0.10	(10.28, 10.66)
		Week 36	74	10.76 (0.72)	10.38	0.10	(10.20, 10.56)
		Week 40	71	10.75 (0.72)	10.47	0.10	(10.27, 10.66)
		Week 44	69	10.79 (0.73)	10.48	0.10	(10.28, 10.67)
		Week 48	69	10.79 (0.73)	10.37	0.10	(10.17, 10.56)
		Week 52	67	10.80 (0.73)	10.38	0.10	(10.20, 10.59)

表 2.7.6.26－112　前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）（続き）

Treatment Group	Prior ESA Treatment	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
	Epoetin beta pegol	Week 2	16	11.03 (0.75)	10.99	0.25	(10.49, 11.49)
		Week 4	16	11.03 (0.75)	10.80	0.25	(10.30, 11.29)
		Week 6	16	11.03 (0.75)	10.67	0.25	(10.17, 11.17)
		Week 8	16	11.03 (0.75)	10.67	0.25	(10.17, 11.17)
		Week 10	16	11.03 (0.75)	10.58	0.25	(10.09, 11.08)
		Week 12	16	11.03 (0.75)	10.65	0.25	(10.16, 11.15)
		Week 16	14	10.97 (0.78)	10.67	0.26	(10.15, 11.19)
		Week 20	13	11.02 (0.79)	10.78	0.27	(10.25, 11.31)
		Week 24	13	11.02 (0.79)	10.83	0.27	(10.30, 11.36)
		Week 28	13	11.02 (0.79)	10.54	0.27	(10.01, 11.07)
		Week 32	12	10.98 (0.80)	10.64	0.27	(10.10, 11.18)
		Week 36	12	10.98 (0.80)	10.73	0.27	(10.19, 11.27)
		Week 40	10	10.82 (0.79)	10.67	0.29	(10.09, 11.24)
		Week 44	10	10.82 (0.79)	11.15	0.29	(10.57, 11.72)
		Week 48	10	10.82 (0.79)	10.96	0.29	(10.38, 11.53)
		Week 52	10	10.82 (0.79)	10.55	0.29	(10.01, 11.16)

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_5_2.sas

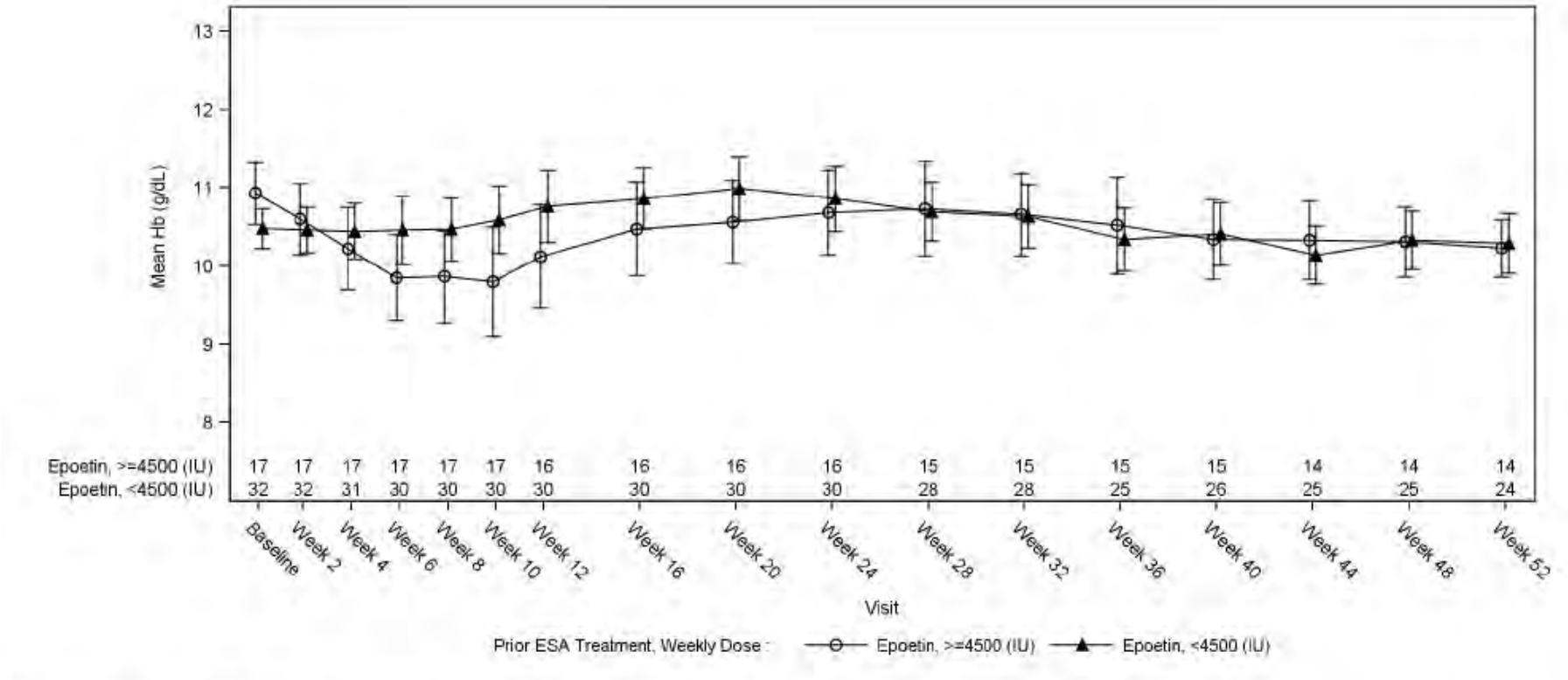
5.3.5.1—9 表 14.2.2.5.2 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_3_1.sas

図 2.7.6.26－35　MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）

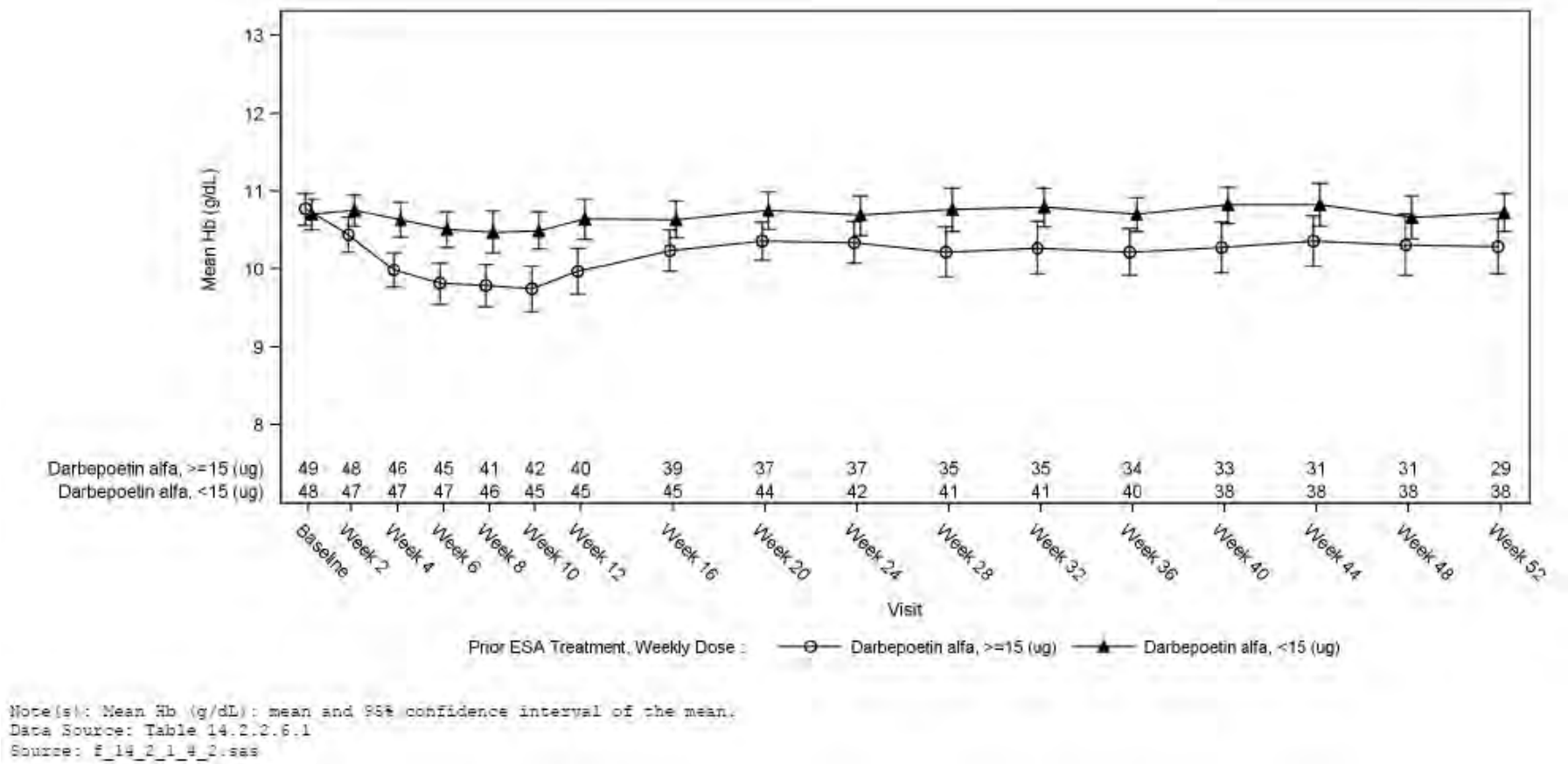
5.3.5.1—9 図 14.2.1.3.1 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_1.sas

図 2.7.6.26－36　MT-6548 群の前治療 ESA 製剤（エポエチン製剤）の用量別の Hb 値の推移（FAS）

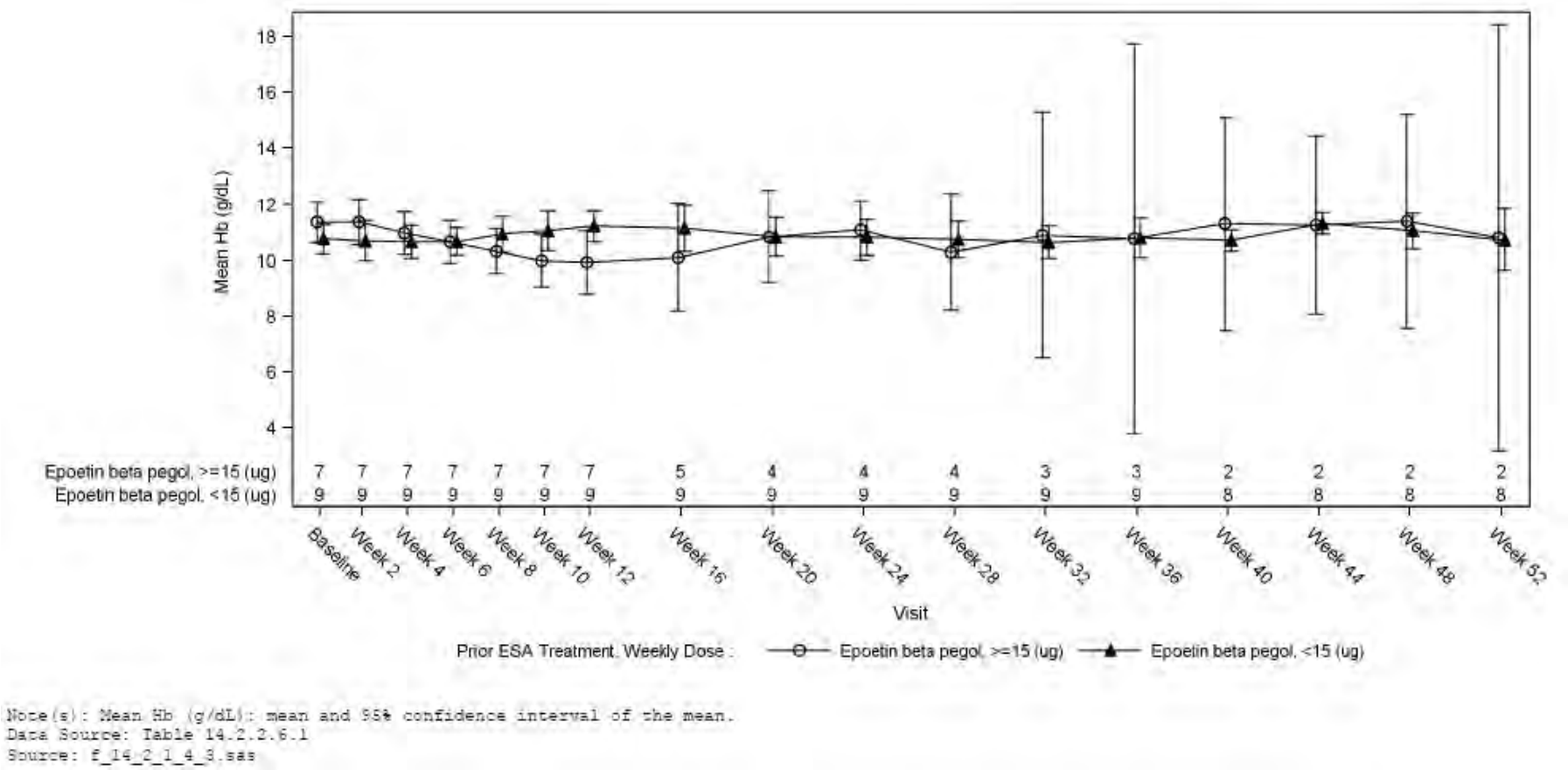
5.3.5.1—9 図 14.2.1.4.1 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_2.sas

図 2.7.6.26－37　MT-6548 群の前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）

5.3.5.1—9 図 14.2.1.4.2 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.6.1
Source: f_14_2_1_4_3.sas

図 2.7.6.26－38　MT-6548 群の前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の Hb 値の推移（FAS）

5.3.5.1—9 図 14.2.1.4.3 より引用

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline						
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetin, >=4500 (IU)	Baseline	17	10.93	0.77	10.90	(9.9, 12.0)	(10.53, 11.33)							
		Week 2	17	10.60	0.89	10.90	(8.3, 11.6)	(10.14, 11.06)	17	-0.33	0.59	-0.40	(-1.6, 0.6)	(-0.63, -0.03)	0.035
		Week 4	17	10.22	1.02	10.40	(7.7, 11.7)	(9.70, 10.75)	17	-0.71	0.79	-0.60	(-2.2, 0.5)	(-1.11, -0.30)	0.002
		Week 6	17	9.85	1.06	9.90	(7.2, 11.3)	(9.31, 10.40)	17	-1.08	1.02	-1.20	(-2.7, 0.9)	(-1.60, -0.55)	<0.001
		Week 8	17	9.86	1.15	10.00	(6.8, 11.7)	(9.28, 10.45)	17	-1.06	1.12	-1.30	(-3.1, 1.3)	(-1.64, -0.49)	0.001
		Week 10	17	9.80	1.37	9.80	(6.7, 11.9)	(9.10, 10.50)	17	-1.13	1.41	-1.50	(-3.2, 1.5)	(-1.86, -0.40)	0.005
		Week 12	16	10.13	1.24	9.90	(7.7, 12.3)	(9.47, 10.78)	16	-0.87	1.48	-1.40	(-2.6, 1.9)	(-1.66, -0.08)	0.033
		Week 16	16	10.48	1.11	10.35	(8.9, 12.4)	(9.88, 11.07)	16	-0.52	1.27	-0.65	(-2.5, 1.5)	(-1.19, 0.16)	0.122
		Week 20	16	10.56	1.00	10.50	(8.3, 11.9)	(10.03, 11.09)	16	-0.43	1.11	-0.65	(-2.3, 1.5)	(-1.02, 0.16)	0.140
		Week 24	16	10.68	1.02	10.90	(8.6, 11.9)	(10.14, 11.23)	16	-0.31	1.02	0.05	(-2.5, 1.0)	(-0.86, 0.23)	0.240
		Week 28	15	10.73	1.09	10.90	(8.5, 12.1)	(10.13, 11.34)	15	-0.21	1.03	0.10	(-2.4, 1.0)	(-0.78, 0.36)	0.437
		Week 32	15	10.66	0.95	10.70	(8.4, 11.9)	(10.14, 11.18)	15	-0.29	1.03	-0.40	(-2.0, 1.2)	(-0.86, 0.28)	0.299
		Week 36	15	10.52	1.11	10.90	(8.0, 11.7)	(9.90, 11.14)	15	-0.43	1.16	-0.30	(-2.5, 1.4)	(-1.07, 0.22)	0.177
		Week 40	15	10.34	0.92	10.50	(8.6, 11.8)	(9.83, 10.85)	15	-0.61	1.09	-0.90	(-1.9, 1.1)	(-1.21, 0.00)	0.049
		Week 44	14	10.33	0.87	10.35	(8.7, 12.2)	(9.83, 10.83)	14	-0.63	0.91	-0.70	(-2.0, 0.9)	(-1.21, -0.16)	0.014
		Week 48	14	10.31	0.78	10.40	(8.7, 11.4)	(9.86, 10.76)	14	-0.71	0.90	-0.85	(-2.2, 0.9)	(-1.23, -0.19)	0.011
		Week 52	14	10.23	0.64	10.20	(9.2, 11.7)	(9.86, 10.60)	14	-0.79	0.87	-1.15	(-1.7, 0.9)	(-1.29, -0.28)	0.005
		Week 52 (LOCF)	17	10.04	1.09	10.20	(6.6, 11.7)	(9.48, 10.59)	17	-0.89	1.14	-1.20	(-3.3, 1.1)	(-1.48, -0.31)	0.005

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

			Absolute						Change from Baseline					
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetin, <4500 (IU)	Baseline	32	10.48	0.71	10.35	(9.4, 11.7)	(10.22, 10.73)							
		Week 2	32	10.47	0.81	10.55	(9.0, 12.5)	(10.17, 10.76)	32	-0.01	0.64	0.10	(-1.3, 1.2)	(-0.24, 0.22)	0.913
		Week 4	31	10.45	0.97	10.20	(8.6, 12.4)	(10.09, 10.80)	31	-0.05	0.86	0.00	(-1.8, 1.2)	(-0.37, 0.27)	0.757
		Week 6	30	10.46	1.18	10.15	(8.6, 13.2)	(10.02, 10.90)	30	-0.02	1.06	0.10	(-2.3, 1.6)	(-0.41, 0.38)	0.932
		Week 8	30	10.47	1.09	10.40	(8.2, 13.0)	(10.06, 10.87)	30	-0.01	1.12	0.30	(-2.8, 1.6)	(-0.42, 0.41)	0.974
		Week 10	30	10.59	1.16	10.45	(8.1, 12.8)	(10.16, 11.03)	30	0.12	1.20	0.10	(-2.8, 2.3)	(-0.33, 0.57)	0.587
		Week 12	30	10.76	1.23	10.70	(8.1, 13.3)	(10.30, 11.22)	30	0.29	1.28	0.40	(-2.8, 2.9)	(-0.19, 0.77)	0.224
		Week 16	30	10.86	1.05	11.00	(8.3, 12.9)	(10.47, 11.25)	30	0.39	1.25	0.55	(-3.1, 2.1)	(-0.08, 0.85)	0.102
		Week 20	30	10.99	1.09	10.90	(8.7, 13.1)	(10.58, 11.40)	30	0.52	1.28	0.35	(-2.8, 2.6)	(0.04, 0.99)	0.035
		Week 24	30	10.86	1.12	10.80	(8.6, 13.3)	(10.44, 11.28)	30	0.39	1.21	0.50	(-3.1, 2.3)	(-0.07, 0.84)	0.091
		Week 28	28	10.69	0.97	10.60	(8.5, 12.8)	(10.32, 11.07)	28	0.23	1.21	0.35	(-3.2, 2.3)	(-0.24, 0.70)	0.328
		Week 32	28	10.64	1.04	10.75	(8.3, 13.0)	(10.23, 11.04)	28	0.17	1.29	0.20	(-3.4, 1.9)	(-0.33, 0.67)	0.489
		Week 36	25	10.34	0.97	10.60	(8.2, 12.1)	(9.94, 10.75)	25	-0.08	1.21	0.20	(-3.5, 1.6)	(-0.58, 0.42)	0.744
		Week 40	26	10.42	1.00	10.35	(8.6, 12.7)	(10.01, 10.82)	26	-0.03	1.30	0.05	(-3.1, 3.1)	(-0.56, 0.49)	0.905
		Week 44	25	10.14	0.90	10.20	(8.3, 12.1)	(9.77, 10.52)	25	-0.28	1.19	-0.40	(-3.4, 1.6)	(-0.77, 0.21)	0.250
		Week 48	25	10.33	0.90	10.40	(8.3, 12.5)	(9.96, 10.70)	25	-0.10	1.18	0.10	(-3.4, 1.4)	(-0.58, 0.39)	0.689
		Week 52	24	10.29	0.90	10.50	(8.1, 11.7)	(9.91, 10.67)	24	-0.15	1.27	0.15	(-3.6, 1.7)	(-0.69, 0.38)	0.559
		Week 52 (LOCF)	32	10.35	0.99	10.35	(8.1, 12.7)	(9.99, 10.70)	32	-0.13	1.18	0.15	(-3.6, 1.7)	(-0.56, 0.30)	0.536

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

			Absolute						Change from Baseline					
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Darbepoetin alfa, >=15 (ug)	Baseline	49	10.77	0.72	10.70	(9.4, 12.0)	(10.56, 10.98)							
		Week 2	48	10.44	0.76	10.40	(8.8, 11.9)	(10.22, 10.66)	49	-0.35	0.50	-0.35	(-1.7, 0.6)	(-0.49, -0.21)	<0.001
		Week 4	46	9.99	0.75	10.00	(8.3, 11.7)	(9.77, 10.21)	46	-0.81	0.76	-0.85	(-2.3, 0.9)	(-1.04, -0.59)	<0.001
		Week 6	45	9.82	0.88	9.80	(7.8, 11.9)	(9.55, 10.08)	45	-1.00	0.92	-0.90	(-3.2, 0.6)	(-1.28, -0.72)	<0.001
		Week 8	41	9.79	0.86	9.70	(8.0, 11.3)	(9.51, 10.06)	41	-1.01	1.10	-1.00	(-3.3, 1.4)	(-1.36, -0.66)	<0.001
		Week 10	42	9.76	0.94	9.70	(7.7, 12.1)	(9.46, 10.05)	42	-1.07	1.17	-1.00	(-3.7, 1.4)	(-1.43, -0.70)	<0.001
		Week 12	40	9.97	0.93	10.05	(7.4, 11.4)	(9.68, 10.27)	40	-0.83	1.21	-0.80	(-3.9, 1.5)	(-1.22, -0.45)	<0.001
		Week 16	39	10.24	0.81	10.20	(8.6, 12.1)	(9.97, 10.50)	39	-0.56	1.17	-0.50	(-3.0, 1.8)	(-0.93, -0.18)	0.005
		Week 20	37	10.36	0.72	10.40	(8.7, 12.5)	(10.12, 10.60)	37	-0.41	1.01	-0.10	(-2.9, 1.4)	(-0.74, -0.07)	0.020
		Week 24	37	10.34	0.80	10.40	(8.0, 11.8)	(10.08, 10.61)	37	-0.42	1.14	-0.50	(-3.6, 2.0)	(-0.80, -0.04)	0.030
		Week 28	35	10.22	0.93	10.40	(7.8, 11.7)	(9.90, 10.54)	35	-0.55	1.24	-0.70	(-3.1, 1.4)	(-0.98, -0.13)	0.012
		Week 32	35	10.27	0.97	10.30	(7.6, 12.9)	(9.94, 10.61)	35	-0.50	1.13	-0.60	(-2.6, 2.6)	(-0.89, -0.11)	0.014
		Week 36	34	10.22	0.86	10.35	(8.2, 12.3)	(9.92, 10.52)	34	-0.57	1.13	-0.55	(-3.4, 2.0)	(-0.96, -0.18)	0.006
		Week 40	33	10.28	0.91	10.40	(7.8, 11.7)	(9.95, 10.60)	33	-0.52	1.16	-0.50	(-3.6, 1.5)	(-0.93, -0.11)	0.015
		Week 44	31	10.36	0.88	10.40	(8.2, 12.0)	(10.04, 10.69)	31	-0.45	1.16	-0.70	(-3.4, 1.5)	(-0.88, -0.02)	0.040
		Week 48	31	10.31	1.06	10.30	(7.7, 12.4)	(9.92, 10.70)	31	-0.50	1.33	-0.60	(-3.9, 1.7)	(-0.99, -0.01)	0.045
		Week 52	29	10.29	0.92	10.30	(8.2, 11.5)	(9.94, 10.64)	29	-0.56	1.23	-0.60	(-2.8, 1.6)	(-1.02, -0.09)	0.021
		Week 52(LOCF)	48	9.91	1.08	10.00	(7.4, 11.5)	(9.60, 10.22)	48	-0.89	1.30	-0.85	(-3.9, 1.6)	(-1.26, -0.51)	<0.001

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

			Absolute						Change from Baseline					
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Darbepoetin alfa, <15 (ug)	Baseline	48	10.70	0.68	10.60	(8.8, 12.1)	(10.50, 10.90)							
		Week 2	47	10.75	0.68	10.80	(9.2, 12.3)	(10.55, 10.95)	47	0.04	0.47	0.10	(-1.0, 1.3)	(-0.10, 0.18)	0.540
		Week 4	47	10.64	0.75	10.80	(8.8, 11.9)	(10.42, 10.86)	47	-0.07	0.58	0.00	(-1.4, 1.3)	(-0.25, 0.10)	0.387
		Week 6	47	10.51	0.76	10.60	(8.7, 11.8)	(10.28, 10.73)	47	-0.20	0.60	-0.20	(-1.8, 1.3)	(-0.38, -0.03)	0.025
		Week 8	46	10.47	0.89	10.50	(8.2, 12.5)	(10.21, 10.74)	46	-0.23	0.85	-0.35	(-1.5, 2.6)	(-0.48, 0.03)	0.077
		Week 10	45	10.49	0.79	10.60	(8.3, 11.9)	(10.26, 10.73)	45	-0.22	0.86	-0.30	(-2.4, 2.0)	(-0.47, 0.04)	0.100
		Week 12	45	10.64	0.86	10.60	(8.5, 12.5)	(10.38, 10.90)	45	-0.07	0.98	0.00	(-2.0, 3.7)	(-0.36, 0.23)	0.650
		Week 16	45	10.64	0.79	10.80	(8.8, 12.4)	(10.40, 10.87)	45	-0.07	0.98	-0.10	(-1.7, 2.6)	(-0.37, 0.22)	0.619
		Week 20	44	10.75	0.80	10.90	(8.7, 12.4)	(10.51, 10.99)	44	0.06	0.96	0.20	(-1.9, 2.1)	(-0.23, 0.35)	0.695
		Week 24	42	10.69	0.82	10.80	(8.6, 12.2)	(10.43, 10.94)	42	-0.04	0.96	0.00	(-2.7, 2.2)	(-0.33, 0.26)	0.811
		Week 28	41	10.76	0.88	10.90	(8.6, 12.1)	(10.49, 11.04)	41	0.03	0.95	0.10	(-2.2, 2.8)	(-0.27, 0.34)	0.820
		Week 32	41	10.79	0.81	10.80	(9.2, 13.5)	(10.54, 11.05)	41	0.06	0.86	0.10	(-1.5, 1.9)	(-0.21, 0.34)	0.640
		Week 36	40	10.70	0.70	10.65	(9.1, 12.9)	(10.48, 10.93)	40	-0.04	0.85	0.05	(-2.6, 1.5)	(-0.31, 0.23)	0.782
		Week 40	38	10.82	0.71	10.80	(9.2, 12.5)	(10.59, 11.05)	38	0.04	0.91	0.10	(-2.1, 1.7)	(-0.25, 0.34)	0.763
		Week 44	38	10.83	0.84	10.80	(8.2, 12.6)	(10.55, 11.10)	38	0.05	0.97	0.05	(-2.2, 2.5)	(-0.27, 0.37)	0.740
		Week 48	38	10.66	0.84	10.70	(9.1, 12.3)	(10.39, 10.94)	38	-0.11	0.84	0.05	(-1.5, 1.4)	(-0.39, 0.17)	0.422
		Week 52	38	10.73	0.75	10.70	(9.0, 12.6)	(10.48, 10.97)	38	-0.05	0.85	0.10	(-1.8, 1.7)	(-0.33, 0.23)	0.734
		Week 52(LOCF)	48	10.59	0.86	10.55	(7.7, 12.6)	(10.34, 10.84)	48	-0.11	0.86	0.05	(-2.1, 1.7)	(-0.36, 0.14)	0.387

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

			Absolute					Change from Baseline					
Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Epoetinbeta pegol, >=15 (ug)	Baseline	7	11.36	0.77	11.60	(10.3, 12.6)	(10.65, 12.07)							
		Week 2	7	11.37	0.89	11.40	(9.9, 12.9)	(10.54, 12.20)	7	0.01	0.43	0.00	(-0.7, 0.6)	(-0.38, 0.41)	0.933
		Week 4	7	10.97	0.82	11.10	(9.7, 12.2)	(10.21, 11.73)	7	-0.39	0.80	-0.60	(-1.2, 1.3)	(-1.12, 0.35)	0.249
		Week 6	7	10.67	0.82	10.50	(9.6, 11.7)	(9.91, 11.43)	7	-0.69	0.97	-1.20	(-1.4, 1.2)	(-1.59, 0.21)	0.112
		Week 8	7	10.33	0.89	10.40	(9.3, 11.6)	(9.51, 11.15)	7	-1.03	1.26	-1.60	(-2.2, 1.3)	(-1.19, 0.13)	0.073
		Week 10	7	9.99	1.03	10.10	(8.6, 11.1)	(9.03, 10.94)	7	-1.37	1.29	-1.70	(-2.7, 0.8)	(-2.56, -0.18)	0.030
		Week 12	7	9.93	1.23	10.30	(8.4, 11.6)	(8.79, 11.07)	7	-1.43	1.66	-2.30	(-3.2, 1.3)	(-2.96, 0.10)	0.062
		Week 16	6	10.10	1.54	10.40	(7.5, 11.4)	(8.18, 12.02)	6	-1.24	2.14	-1.20	(-4.1, 1.1)	(-3.89, 1.41)	0.264
		Week 20	4	10.85	1.03	10.95	(9.5, 12.0)	(9.21, 12.49)	4	-0.75	1.55	-1.15	(-2.1, 1.4)	(-3.21, 1.71)	0.403
		Week 24	4	11.08	0.67	11.10	(10.4, 11.7)	(10.01, 12.14)	4	-0.53	1.09	-1.00	(-1.2, 1.1)	(-2.26, 1.21)	0.405
		Week 28	4	10.30	1.31	10.50	(8.6, 11.6)	(8.21, 12.39)	4	-1.30	1.41	-1.30	(-3.0, 0.4)	(-3.54, 0.94)	0.162
		Week 32	3	10.90	1.77	11.20	(9.0, 12.5)	(6.51, 15.29)	3	-0.70	1.68	-0.10	(-2.6, 0.6)	(-4.88, 3.48)	0.546
		Week 36	3	10.77	2.81	11.10	(7.8, 13.4)	(3.77, 17.76)	3	-0.83	2.57	0.50	(-3.8, 0.8)	(-7.23, 5.56)	0.631
		Week 40	2	11.30	0.42	11.30	(11.0, 11.6)	(7.49, 15.11)	2	-0.80	0.99	-0.30	(-1.0, 0.4)	(-9.19, 8.59)	0.742
		Week 44	2	11.25	0.35	11.25	(11.0, 11.5)	(8.07, 14.43)	2	-0.35	1.77	-0.35	(-1.6, 0.9)	(-16.23, 15.53)	0.826
		Week 48	2	11.40	0.42	11.40	(11.1, 11.7)	(7.59, 15.21)	2	-0.20	0.99	-0.20	(-0.9, 0.5)	(-9.09, 8.69)	0.823
		Week 52	2	10.80	0.85	10.80	(10.2, 11.4)	(3.18, 18.42)	2	-0.80	0.57	-0.80	(-1.2, -0.4)	(-5.88, 4.28)	0.295
		Week 52 (LOCF)	7	9.59	1.43	8.90	(7.8, 11.4)	(8.27, 10.90)	7	-1.77	1.70	-2.30	(-3.8, 1.1)	(-3.35, -0.20)	0.033

表 2.7.6.26－113　前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	Absolute N	Absolute Mean	Absolute SD	Absolute Median	Absolute Minimum, Maximum	Absolute 95% CI	Change from Baseline N	Change from Baseline Mean	Change from Baseline SD	Change from Baseline Median	Change from Baseline Minimum, Maximum	Change from Baseline 95% CI	Change from Baseline p value
MT-6548	Epoetinbeta pegol, <15 (ug)	Baseline	9	10.77	0.67	10.60	(10.2, 11.9)	(10.25, 11.28)							
		Week 2	9	10.70	0.94	10.30	(9.6, 12.1)	(9.98, 11.42)	9	-0.07	0.43	-0.10	(-0.6, 0.6)	(-0.40, 0.27)	0.656
		Week 4	9	10.67	0.77	10.80	(9.4, 11.8)	(10.07, 11.26)	9	-0.10	0.61	-0.10	(-1.2, 0.8)	(-0.57, 0.37)	0.636
		Week 6	9	10.68	0.65	10.90	(9.2, 11.4)	(10.18, 11.18)	9	-0.09	0.77	0.10	(-1.4, 0.9)	(-0.68, 0.51)	0.739
		Week 8	9	10.94	0.82	11.10	(9.1, 11.9)	(10.32, 11.57)	9	0.18	0.85	0.20	(-1.5, 1.1)	(-0.47, 0.83)	0.546
		Week 10	9	11.06	0.91	11.00	(9.1, 12.2)	(10.36, 11.75)	9	0.29	1.20	0.30	(-1.5, 2.0)	(-0.63, 1.21)	0.491
		Week 12	9	11.22	0.71	11.40	(9.5, 11.9)	(10.67, 11.77)	9	0.46	0.99	0.70	(-1.1, 1.6)	(-0.30, 1.21)	0.204
		Week 16	9	11.14	1.07	11.40	(8.8, 12.5)	(10.32, 11.97)	9	0.38	1.38	0.40	(-1.8, 2.3)	(-0.68, 1.44)	0.436
		Week 20	9	10.84	0.91	10.90	(9.4, 12.0)	(10.15, 11.54)	9	0.08	1.06	0.00	(-1.2, 1.5)	(-0.73, 0.89)	0.831
		Week 24	9	10.82	0.82	10.50	(10.0, 12.4)	(10.19, 11.45)	9	0.06	0.85	0.00	(-1.4, 1.2)	(-0.60, 0.71)	0.849
		Week 28	9	10.74	0.85	10.40	(9.7, 12.6)	(10.09, 11.40)	9	-0.02	0.84	-0.10	(-0.9, 0.8)	(-0.43, 0.39)	0.904
		Week 32	9	10.64	0.75	10.60	(9.7, 12.1)	(10.07, 11.22)	9	-0.12	0.70	0.10	(-1.2, 0.6)	(-0.66, 0.41)	0.613
		Week 36	9	10.81	0.90	10.90	(9.7, 12.2)	(10.12, 11.51)	9	0.04	0.95	0.30	(-1.4, 1.2)	(-0.68, 0.77)	0.892
		Week 40	8	10.71	0.45	10.65	(10.2, 11.2)	(10.34, 11.08)	8	0.09	0.69	0.10	(-1.1, 1.0)	(-0.49, 0.67)	0.731
		Week 44	8	11.33	0.44	11.35	(10.7, 11.8)	(10.96, 11.69)	8	0.70	0.55	0.70	(-0.1, 1.6)	(0.24, 1.16)	0.009
		Week 48	8	11.05	0.76	10.80	(10.3, 12.5)	(10.41, 11.69)	8	0.43	0.53	0.40	(-0.2, 1.3)	(-0.02, 0.87)	0.059
		Week 52	8	10.74	1.34	10.30	(8.9, 13.4)	(9.62, 11.86)	8	0.11	1.08	0.00	(-1.8, 1.5)	(-0.79, 1.02)	0.777
		Week 52(LOCF)	9	10.71	1.26	10.40	(8.9, 13.4)	(9.75, 11.68)	9	-0.06	1.13	-0.20	(-1.8, 1.5)	(-0.93, 0.81)	0.887

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): p value is analyzed by paired t-test from baseline value.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_6_1.sas

5.3.5.1—9 表 14.2.2.6.1 より引用

表 2.7.6.26－114　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Epoetin, >=4500 (IU)	Week 2	17	10.93 (0.77)	10.62	0.27	(10.08, 11.16)
		Week 4	17	10.93 (0.77)	10.24	0.27	(9.70, 10.79)
		Week 6	17	10.93 (0.77)	9.87	0.27	(9.33, 10.41)
		Week 8	17	10.93 (0.77)	9.88	0.27	(9.34, 10.43)
		Week 10	17	10.93 (0.77)	9.82	0.27	(9.28, 10.36)
		Week 12	16	10.99 (0.75)	9.99	0.27	(9.44, 10.53)
		Week 16	16	10.99 (0.75)	10.34	0.27	(9.79, 10.88)
		Week 20	16	10.99 (0.75)	10.42	0.27	(9.88, 10.97)
		Week 24	16	10.99 (0.75)	10.54	0.27	(9.99, 11.09)
		Week 28	15	10.95 (0.75)	10.55	0.27	(10.00, 11.11)
		Week 32	15	10.95 (0.75)	10.48	0.27	(9.92, 11.03)
		Week 36	15	10.95 (0.75)	10.34	0.27	(9.78, 10.89)
		Week 40	15	10.95 (0.75)	10.16	0.27	(9.60, 10.71)
		Week 44	14	11.01 (0.73)	10.17	0.28	(9.61, 10.73)
		Week 48	14	11.01 (0.73)	10.15	0.28	(9.59, 10.71)
		Week 52	14	11.01 (0.73)	10.07	0.28	(9.51, 10.63)
	Epoetin, <4500 (IU)	Week 2	32	10.48 (0.71)	10.46	0.19	(10.09, 10.84)
		Week 4	31	10.49 (0.72)	10.42	0.19	(10.04, 10.79)
		Week 6	30	10.47 (0.72)	10.42	0.19	(10.04, 10.81)
		Week 8	30	10.47 (0.72)	10.43	0.19	(10.05, 10.82)
		Week 10	30	10.47 (0.72)	10.56	0.19	(10.18, 10.94)
		Week 12	30	10.47 (0.72)	10.73	0.19	(10.35, 11.11)
		Week 16	30	10.47 (0.72)	10.83	0.19	(10.45, 11.21)
		Week 20	30	10.47 (0.72)	10.96	0.19	(10.58, 11.34)
		Week 24	30	10.47 (0.72)	10.83	0.19	(10.45, 11.21)
		Week 28	28	10.46 (0.74)	10.69	0.19	(10.30, 11.07)
		Week 32	28	10.46 (0.74)	10.63	0.19	(10.24, 11.01)
		Week 36	25	10.42 (0.73)	10.47	0.20	(10.08, 10.87)
		Week 40	26	10.45 (0.72)	10.52	0.20	(10.13, 10.91)
		Week 44	25	10.42 (0.73)	10.31	0.20	(9.92, 10.71)
		Week 48	25	10.42 (0.73)	10.50	0.20	(10.10, 10.89)
		Week 52	24	10.44 (0.74)	10.44	0.20	(10.04, 10.84)

表 2.7.6.26－114　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
	Darbepoetin alfa, >=15 (ug)	Week 2	48	10.79 (0.71)	10.44	0.13	(10.19, 10.70)
		Week 4	46	10.80 (0.72)	9.98	0.13	(9.72, 10.24)
		Week 6	45	10.82 (0.72)	9.80	0.13	(9.54, 10.06)
		Week 8	41	10.80 (0.72)	9.72	0.14	(9.46, 9.99)
		Week 10	42	10.82 (0.72)	9.69	0.14	(9.42, 9.95)
		Week 12	40	10.81 (0.70)	9.88	0.14	(9.61, 10.15)
		Week 16	39	10.79 (0.71)	10.11	0.14	(9.84, 10.38)
		Week 20	37	10.77 (0.71)	10.27	0.14	(9.99, 10.54)
		Week 24	37	10.77 (0.71)	10.25	0.14	(9.97, 10.52)
		Week 28	35	10.77 (0.73)	10.10	0.14	(9.82, 10.39)
		Week 32	35	10.77 (0.73)	10.16	0.14	(9.88, 10.44)
		Week 36	34	10.79 (0.73)	10.11	0.14	(9.83, 10.40)
		Week 40	33	10.80 (0.74)	10.15	0.15	(9.87, 10.44)
		Week 44	31	10.81 (0.76)	10.17	0.15	(9.88, 10.46)
		Week 48	31	10.81 (0.76)	10.12	0.15	(9.83, 10.41)
		Week 52	29	10.84 (0.77)	10.10	0.15	(9.81, 10.40)
	Darbepoetin alfa, <15 (ug)	Week 2	47	10.71 (0.69)	10.76	0.11	(10.55, 10.98)
		Week 4	47	10.71 (0.69)	10.64	0.11	(10.43, 10.86)
		Week 6	47	10.71 (0.69)	10.52	0.11	(10.30, 10.73)
		Week 8	46	10.70 (0.69)	10.50	0.11	(10.28, 10.71)
		Week 10	45	10.71 (0.70)	10.51	0.11	(10.29, 10.72)
		Week 12	45	10.71 (0.70)	10.66	0.11	(10.44, 10.87)
		Week 16	45	10.71 (0.70)	10.65	0.11	(10.43, 10.87)
		Week 20	44	10.69 (0.70)	10.77	0.11	(10.55, 10.99)
		Week 24	42	10.72 (0.70)	10.68	0.11	(10.46, 10.90)
		Week 28	41	10.73 (0.71)	10.75	0.11	(10.52, 10.97)
		Week 32	41	10.73 (0.71)	10.78	0.11	(10.56, 11.00)
		Week 36	40	10.74 (0.71)	10.66	0.11	(10.44, 10.89)
		Week 40	38	10.77 (0.70)	10.78	0.12	(10.55, 11.01)
		Week 44	38	10.77 (0.70)	10.78	0.12	(10.56, 11.02)
		Week 48	38	10.77 (0.70)	10.62	0.12	(10.39, 10.85)
		Week 52	38	10.77 (0.70)	10.69	0.12	(10.46, 10.92)

表 2.7.6.26－114　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
	Epoetin beta pegol, >=15 (ug)	Week 2	7	11.36 (0.77)	11.37	0.46	(10.40, 12.34)
		Week 4	7	11.36 (0.77)	10.97	0.46	(10.00, 11.94)
		Week 6	7	11.36 (0.77)	10.67	0.46	(9.70, 11.64)
		Week 8	7	11.36 (0.77)	10.33	0.46	(9.36, 11.29)
		Week 10	7	11.36 (0.77)	9.98	0.46	(9.02, 10.96)
		Week 12	7	11.36 (0.77)	9.93	0.46	(8.96, 10.89)
		Week 16	5	11.34 (0.92)	9.88	0.51	(8.83, 10.94)
		Week 20	4	11.60 (0.82)	10.78	0.55	(9.66, 11.91)
		Week 24	4	11.60 (0.82)	11.01	0.55	(9.89, 12.13)
		Week 28	4	11.60 (0.82)	10.23	0.55	(9.11, 11.36)
		Week 32	3	11.60 (1.00)	10.88	0.61	(9.65, 12.11)
		Week 36	3	11.60 (1.00)	10.75	0.61	(9.52, 11.98)
		Week 40	2	11.60 (1.41)	10.79	0.71	(9.36, 12.22)
		Week 44	2	11.60 (1.41)	10.74	0.71	(9.31, 12.17)
		Week 48	2	11.60 (1.41)	10.89	0.71	(9.46, 12.32)
		Week 52	2	11.60 (1.41)	10.29	0.71	(8.86, 11.72)
	Epoetin beta pegol, <15 (ug)	Week 2	9	10.77 (0.67)	10.69	0.27	(10.13, 11.24)
		Week 4	9	10.77 (0.67)	10.65	0.27	(10.10, 11.21)
		Week 6	9	10.77 (0.67)	10.66	0.27	(10.11, 11.22)
		Week 8	9	10.77 (0.67)	10.93	0.27	(10.38, 11.48)
		Week 10	9	10.77 (0.67)	11.04	0.27	(10.49, 11.60)
		Week 12	9	10.77 (0.67)	11.21	0.27	(10.66, 11.76)
		Week 16	9	10.77 (0.67)	11.13	0.27	(10.58, 11.68)
		Week 20	9	10.77 (0.67)	10.83	0.27	(10.28, 11.38)
		Week 24	9	10.77 (0.67)	10.81	0.27	(10.26, 11.36)
		Week 28	9	10.77 (0.67)	10.73	0.27	(10.18, 11.28)
		Week 32	9	10.77 (0.67)	10.63	0.27	(10.08, 11.18)
		Week 36	9	10.77 (0.67)	10.80	0.27	(10.24, 11.35)
		Week 40	8	10.63 (0.55)	10.72	0.28	(10.15, 11.29)
		Week 44	8	10.63 (0.55)	11.33	0.28	(10.76, 11.90)
		Week 48	8	10.63 (0.55)	11.06	0.28	(10.49, 11.63)
		Week 52	8	10.63 (0.55)	10.75	0.28	(10.17, 11.32)

Note(s): Hb (g/dL).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_6_2.sas

5.3.5.1—9 表 14.2.2.6.2 より引用

表 2.7.6.26－115　鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の記述統計量（FAS）

			Absolute						Change from Baseline						
Treatment Group	Iron or Iron-containing Phosphorus	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	User	Baseline	43	10.95	0.69	10.90	(9.6, 12.0)	(10.74, 11.16)							
		Week 2	42	10.71	0.77	10.75	(9.2, 12.1)	(10.47, 10.95)	42	-0.27	0.43	-0.30	(-1.3, 0.5)	(-0.41, -0.14)	<0.001
		Week 4	41	10.36	0.79	10.30	(8.8, 11.9)	(10.11, 10.61)	41	-0.64	0.69	-0.60	(-2.1, 0.6)	(-0.86, -0.43)	<0.001
		Week 6	39	10.08	0.92	10.10	(8.4, 11.7)	(9.79, 10.38)	39	-0.94	0.89	-0.70	(-3.1, 0.4)	(-1.23, -0.65)	<0.001
		Week 8	38	10.00	1.09	10.25	(8.0, 12.0)	(9.64, 10.36)	38	-1.01	1.09	-1.05	(-3.3, 0.8)	(-1.37, -0.65)	<0.001
		Week 10	38	10.05	1.19	10.10	(7.7, 12.1)	(9.66, 10.45)	38	-0.96	1.25	-0.85	(-3.6, 1.2)	(-1.37, -0.54)	<0.001
		Week 12	38	10.14	1.17	10.25	(7.4, 12.1)	(9.76, 10.53)	38	-0.87	1.29	-0.95	(-3.9, 1.5)	(-1.29, -0.44)	<0.001
		Week 16	36	10.54	1.09	10.50	(8.3, 12.4)	(10.17, 10.91)	36	-0.46	1.23	-0.35	(-3.1, 1.8)	(-0.88, -0.04)	0.031
		Week 20	35	10.67	0.97	10.70	(8.7, 12.5)	(10.34, 11.01)	35	-0.30	1.11	0.00	(-2.8, 1.5)	(-0.68, 0.09)	0.115
		Week 24	34	10.43	0.99	10.45	(8.6, 12.3)	(10.09, 10.77)	34	-0.57	1.06	-0.60	(-3.1, 1.2)	(-0.94, -0.20)	0.004
		Week 28	33	10.37	1.02	10.40	(8.5, 12.1)	(10.01, 10.73)	33	-0.65	1.14	-0.50	(-3.2, 1.4)	(-1.05, -0.24)	0.003
		Week 32	32	10.35	1.10	10.60	(8.3, 13.5)	(9.96, 10.75)	32	-0.68	1.18	-0.75	(-3.4, 1.9)	(-1.09, -0.26)	0.002
		Week 36	31	10.48	1.15	10.60	(8.2, 12.9)	(10.06, 10.90)	31	-0.57	1.27	-0.50	(-3.5, 2.0)	(-1.04, -0.11)	0.018
		Week 40	29	10.64	1.18	10.80	(7.8, 12.5)	(10.20, 11.09)	29	-0.40	1.35	-0.20	(-3.1, 1.6)	(-0.91, 0.12)	0.124
		Week 44	28	10.60	1.07	10.80	(8.3, 12.6)	(10.19, 11.02)	28	-0.45	1.27	-0.45	(-3.4, 1.5)	(-0.94, 0.04)	0.069
		Week 48	28	10.60	1.12	10.70	(8.3, 12.5)	(10.17, 11.04)	28	-0.45	1.25	-0.45	(-3.4, 1.7)	(-0.94, 0.03)	0.065
		Week 52	28	10.41	1.03	10.40	(8.1, 12.6)	(10.01, 10.81)	28	-0.65	1.22	-0.80	(-3.6, 1.4)	(-1.12, -0.17)	0.009
		Week 52(LOCF)	42	10.06	1.15	10.10	(7.4, 12.6)	(9.70, 10.42)	42	-0.93	1.29	-1.00	(-3.9, 1.4)	(-1.33, -0.53)	<0.001

表 2.7.6.26－115　鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の記述統計量（FAS）（続き）

			Absolute						Change from Baseline					
Treatment Group	Iron or Iron-containing Phosphorus	Visit	N	Mean	SD	Median	Minimum, Maximum	95% CI	N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Non-user	Baseline	17	10.71	0.66	10.80	(9.8, 12.0)	(10.36, 11.05)							
		Week 2	17	10.86	0.82	10.80	(8.3, 11.6)	(10.14, 10.98)	17	-0.15	0.69	0.10	(-1.6, 1.0)	(-0.50, 0.21)	0.391
		Week 4	15	10.35	1.16	10.50	(7.7, 12.1)	(9.71, 11.00)	15	-0.37	1.06	-0.10	(-2.3, 1.1)	(-0.96, 0.22)	0.195
		Week 6	15	10.01	1.22	10.00	(7.2, 12.3)	(9.34, 10.69)	15	-0.71	1.18	-0.40	(-3.2, 1.3)	(-1.37, -0.06)	0.034
		Week 8	15	9.90	1.23	9.80	(6.8, 12.4)	(9.22, 10.58)	15	-0.83	1.25	-0.90	(-3.1, 1.4)	(-1.52, -0.13)	0.023
		Week 10	15	9.87	1.43	10.00	(6.7, 12.4)	(9.08, 10.66)	15	-0.86	1.45	-0.60	(-3.7, 1.4)	(-1.66, -0.06)	0.037
		Week 12	12	10.57	1.29	10.35	(8.8, 13.3)	(9.74, 11.39)	12	-0.17	1.28	-0.40	(-2.8, 2.3)	(-0.98, 0.65)	0.661
		Week 16	11	10.67	1.12	10.80	(8.5, 12.7)	(9.92, 11.43)	11	0.03	0.90	-0.10	(-1.3, 1.7)	(-0.58, 0.63)	0.922
		Week 20	10	10.93	1.25	10.95	(8.7, 12.9)	(10.03, 11.83)	10	0.30	1.04	0.25	(-1.1, 1.9)	(-0.44, 1.04)	0.386
		Week 24	9	10.99	0.91	10.70	(9.9, 12.7)	(10.29, 11.69)	9	0.27	0.87	0.10	(-1.0, 1.7)	(-0.40, 0.94)	0.386
		Week 28	8	10.98	0.42	10.95	(10.4, 11.6)	(10.62, 11.33)	8	0.29	0.49	0.25	(-0.4, 1.1)	(-0.12, 0.70)	0.140
		Week 32	8	11.06	0.27	11.15	(10.6, 11.4)	(10.83, 11.29)	8	0.38	0.42	0.40	(-0.4, 0.9)	(0.03, 0.72)	0.038
		Week 36	7	10.56	0.45	10.70	(9.7, 10.9)	(10.14, 10.98)	7	-0.09	0.81	0.20	(-1.2, 0.9)	(-0.83, 0.66)	0.788
		Week 40	8	10.24	0.81	10.25	(9.4, 11.1)	(9.81, 10.67)	8	-0.45	0.91	-0.40	(-1.8, 0.7)	(-1.21, 0.31)	0.205
		Week 44	8	10.23	0.45	10.15	(9.6, 11.1)	(9.85, 10.60)	8	-0.46	0.83	-0.30	(-1.7, 0.6)	(-1.16, 0.23)	0.160
		Week 48	8	10.15	0.59	10.20	(9.3, 11.1)	(9.66, 10.64)	8	-0.54	1.01	-0.25	(-2.2, 0.6)	(-1.38, 0.30)	0.174
		Week 52	8	10.18	0.74	10.20	(9.0, 11.2)	(9.55, 10.80)	8	-0.51	1.17	-0.80	(-1.8, 1.2)	(-1.49, 0.47)	0.256
		Week 52 (LOCF)	17	9.66	1.43	9.60	(6.6, 12.7)	(8.92, 10.39)	17	-1.05	1.51	-1.30	(-3.6, 1.7)	(-1.82, -0.27)	0.011

Note(s): Hb (g/dL).
Note(s): p value is analyzed by paired t-test from baseline value.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_1_1.sas

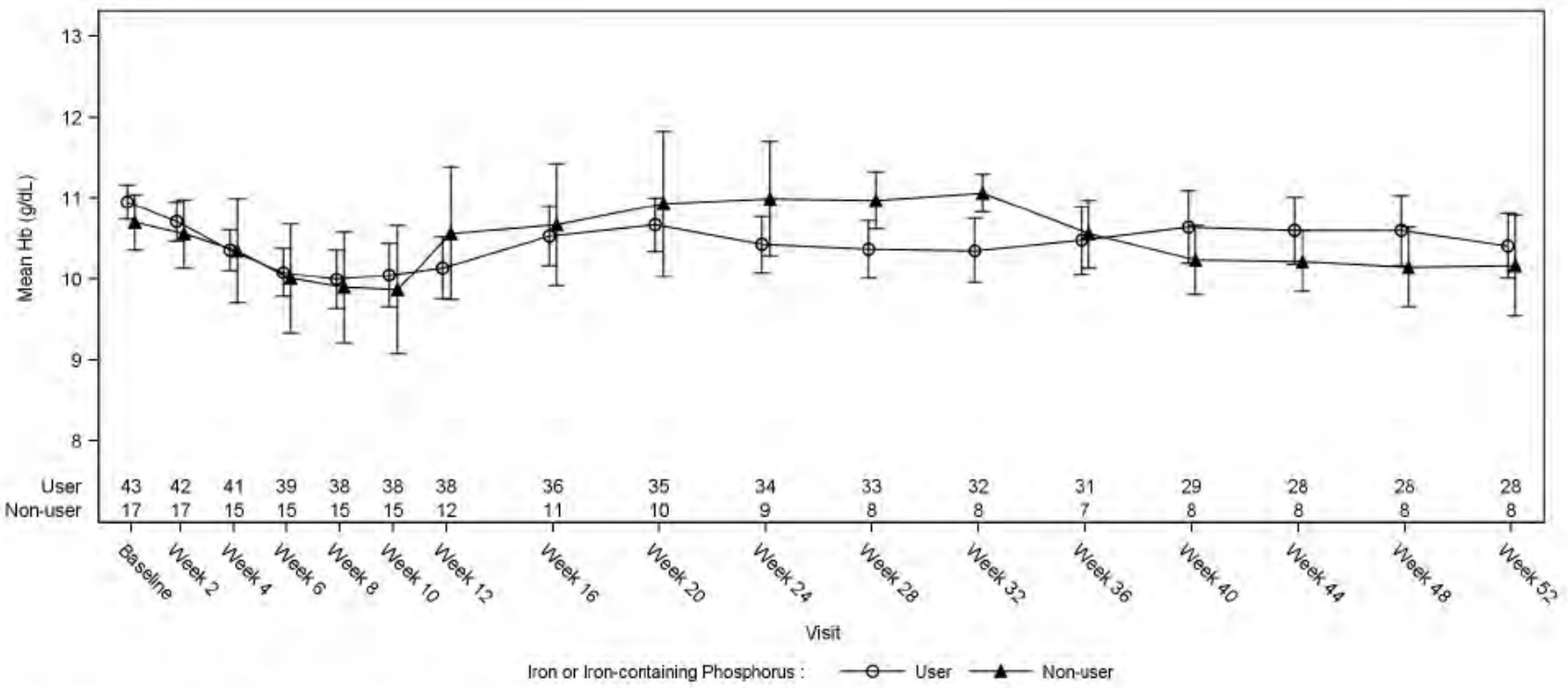
5.3.5.1—9 表 14.2.2.8.1.1 より引用

表 2.7.6.26－116　鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値（MMRM，FAS）

Treatment Group	Iron or Iron-containing Phosphorus	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	User	Week 2	42	10.98 (0.67)	10.72	0.16	(10.41, 11.04)
		Week 4	41	11.01 (0.66)	10.35	0.16	(10.04, 10.67)
		Week 6	39	11.02 (0.66)	10.06	0.16	(9.74, 10.38)
		Week 8	38	11.01 (0.67)	9.95	0.16	(9.63, 10.27)
		Week 10	38	11.01 (0.67)	10.00	0.16	(9.68, 10.32)
		Week 12	38	11.01 (0.67)	10.09	0.16	(9.77, 10.41)
		Week 16	36	11.00 (0.68)	10.43	0.16	(10.11, 10.76)
		Week 20	35	10.98 (0.68)	10.58	0.16	(10.26, 10.91)
		Week 24	34	11.00 (0.68)	10.34	0.17	(10.01, 10.67)
		Week 28	33	11.01 (0.69)	10.25	0.17	(9.92, 10.58)
		Week 32	32	11.03 (0.69)	10.24	0.17	(9.91, 10.58)
		Week 36	31	11.05 (0.69)	10.34	0.17	(10.01, 10.68)
		Week 40	29	11.04 (0.69)	10.50	0.17	(10.16, 10.84)
		Week 44	28	11.06 (0.70)	10.39	0.17	(10.05, 10.74)
		Week 48	28	11.06 (0.70)	10.39	0.17	(10.05, 10.74)
		Week 52	28	11.06 (0.70)	10.20	0.17	(9.86, 10.54)
	Non-user	Week 2	17	10.71 (0.66)	10.56	0.28	(9.97, 11.14)
		Week 4	16	10.73 (0.70)	10.27	0.29	(9.67, 10.86)
		Week 6	15	10.73 (0.70)	9.93	0.29	(9.33, 10.54)
		Week 8	15	10.73 (0.70)	9.82	0.29	(9.22, 10.42)
		Week 10	15	10.73 (0.70)	9.79	0.29	(9.18, 10.39)
		Week 12	12	10.73 (0.63)	10.13	0.31	(9.50, 10.75)
		Week 16	11	10.65 (0.57)	10.20	0.31	(9.56, 10.83)
		Week 20	10	10.63 (0.60)	10.46	0.32	(9.82, 11.11)
		Week 24	9	10.72 (0.56)	10.37	0.32	(9.72, 11.03)
		Week 28	8	10.69 (0.59)	10.86	0.33	(9.98, 11.23)
		Week 32	8	10.69 (0.59)	10.64	0.33	(9.97, 11.32)
		Week 36	7	10.64 (0.62)	10.21	0.34	(9.52, 10.90)
		Week 40	8	10.69 (0.59)	9.92	0.33	(9.15, 10.49)
		Week 44	8	10.69 (0.59)	9.81	0.33	(9.13, 10.48)
		Week 48	8	10.69 (0.59)	9.73	0.33	(9.06, 10.40)
		Week 52	8	10.69 (0.59)	9.76	0.33	(9.08, 10.43)

Note(s): Hb (g/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, interaction of treatment group and visits as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_2_1.sas

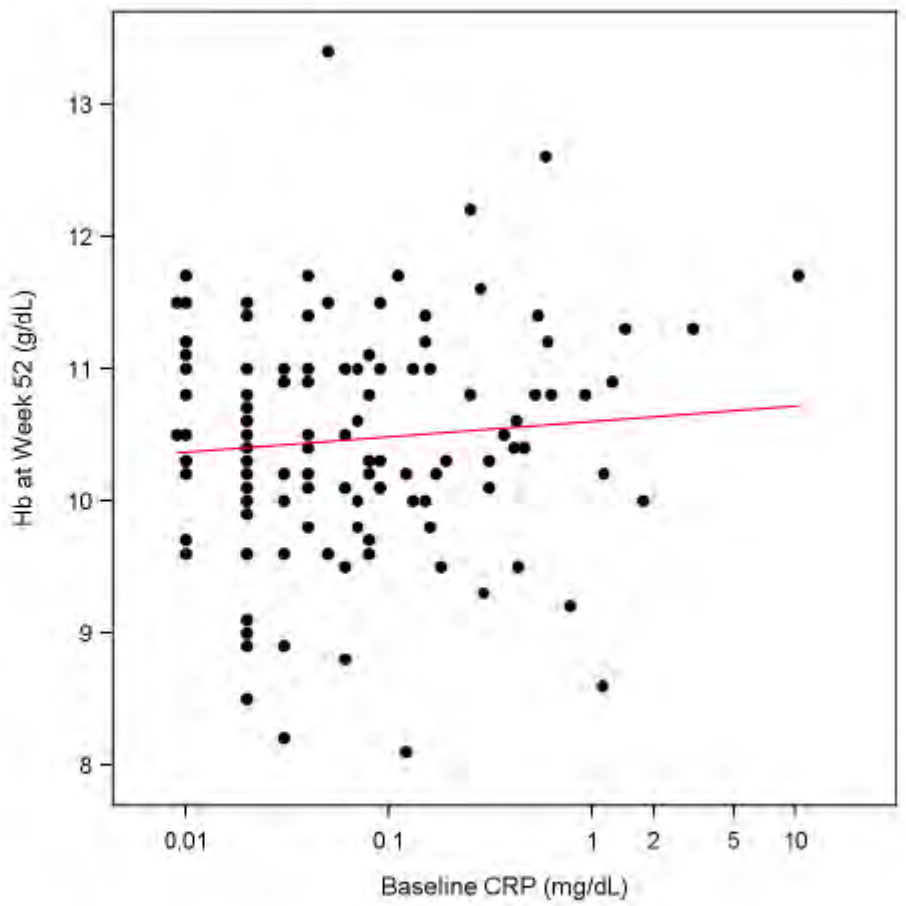
5.3.5.1—9 表 14.2.2.8.2.1 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Table 14.2.2.6.1.1
Source: f_14_2_1_6_1_1.sas

図 2.7.6.26－39　MT-6548 群の鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値の推移（FAS）

5.3.5.1—9 図 14.2.1.6.1.1 より引用



Note(s): linear regression model: Y=aX + b; Y: Hb at Week 52; X: baseline CRP.
Data Source: Listing 16.2.4.1, Listing 16.2.6.4
Source: f_14_2_1_8_1.sas

図 2.7.6.26－40　MT-6548 群のベースラインの CRP と 52 週後の Hb 値の散布図（FAS）

5.3.5.1—9 図 14.2.1.8.1 より引用

表 2.7.6.26－117　被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Sex	Male	MT-6548	76	346.46	189.63	300.00	(0.0, 600.0)	(303.13, 389.79)
		darbepoetin	91	25.60	32.68	15.00	(2.5, 180.0)	(18.80, 32.41)
	Female	MT-6548	42	405.99	203.80	468.75	(42.9, 600.0)	(342.49, 469.50)
		darbepoetin	42	21.00	20.18	15.00	(5.0, 106.7)	(14.71, 27.29)
Age at Informed Consent (years)	<65	MT-6548	46	350.19	193.91	300.00	(0.0, 600.0)	(292.61, 407.78)
		darbepoetin	61	20.42	27.98	10.00	(2.5, 160.0)	(13.25, 27.58)
	>=65	MT-6548	72	378.80	197.90	358.93	(75.0, 600.0)	(332.30, 425.31)
		darbepoetin	72	27.31	30.23	18.75	(5.0, 180.0)	(20.21, 34.41)
	<75	MT-6548	94	375.41	199.49	318.75	(0.0, 600.0)	(334.55, 416.27)
		darbepoetin	109	22.72	26.82	15.00	(2.5, 160.0)	(17.63, 27.81)
	>=75	MT-6548	24	337.28	182.62	300.00	(150.0, 600.0)	(260.16, 414.39)
		darbepoetin	24	30.63	38.73	16.88	(5.0, 180.0)	(14.27, 46.98)
Dry Weight (kg)	<60	MT-6548	69	381.91	190.80	337.50	(42.9, 600.0)	(336.07, 427.75)
		darbepoetin	75	25.18	28.65	15.00	(2.5, 180.0)	(18.63, 31.77)
	>=60	MT-6548	49	347.67	203.43	300.00	(0.0, 600.0)	(289.14, 406.01)
		darbepoetin	58	22.91	30.35	10.00	(5.0, 160.0)	(14.93, 30.79)
BMI (kg/m²)	<25	MT-6548	86	355.69	193.06	300.00	(42.9, 600.0)	(314.30, 397.08)
		darbepoetin	103	22.84	26.91	15.00	(2.5, 180.0)	(17.58, 28.10)
	>=25	MT-6548	32	399.80	203.38	466.07	(0.0, 600.0)	(326.47, 473.12)
		darbepoetin	30	28.64	36.58	15.00	(5.0, 160.0)	(14.99, 42.30)

表 2.7.6.26－117　被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Etiology of CKD	Diabetes	MT-6548	20	396.16	187.97	375.00	(150.0, 600.0)	(308.19, 484.14)
		darbepoetin	37	30.35	41.06	15.00	(5.0, 180.0)	(16.66, 44.04)
	Hypertension	MT-6548	16	448.33	164.03	450.00	(75.0, 600.0)	(360.92, 535.73)
		darbepoetin	17	23.42	27.17	10.00	(2.5, 106.7)	(9.45, 37.38)
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	45	377.74	212.17	300.00	(0.0, 600.0)	(313.99, 441.48)
		darbepoetin	88	20.12	17.59	15.00	(5.0, 80.0)	(16.27, 24.97)
	Interstitial Nephritis/Pyelonephritis	MT-6548	3	362.50	226.04	337.50	(150.0, 600.0)	(-199.01, 924.01)
		darbepoetin	0					
	Cystic/Hereditary/Congenital Disease	MT-6548	12	291.07	191.33	225.00	(42.9, 600.0)	(169.51, 412.63)
		darbepoetin	8	9.69	5.78	6.88	(5.0, 20.0)	(4.86, 14.52)
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	1	7.50	-	7.50	(7.5, 7.5)	-
Duration of Anemia from CKD (years)	<1	MT-6548	6	425.00	178.36	450.00	(150.0, 600.0)	(240.97, 609.03)
		darbepoetin	3	8.33	5.77	5.00	(5.0, 15.0)	(-6.01, 22.68)
	1<= to <5	MT-6548	45	354.54	201.01	300.00	(42.9, 600.0)	(294.15, 414.93)
		darbepoetin	53	24.72	27.78	15.00	(5.0, 120.0)	(17.07, 32.37)
	>=5	MT-6548	66	374.68	195.87	300.00	(0.0, 600.0)	(326.60, 422.75)
		darbepoetin	77	24.37	30.50	15.00	(2.5, 180.0)	(17.36, 31.38)

表 2.7.6.26－117　被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Complications	Hypertension	MT-6548	110	369.64	194.87	300.00	(0.0, 600.0)	(333.02, 406.67)
		darbepoetin	125	24.41	29.92	15.00	(2.5, 180.0)	(19.12, 29.71)
	Diabetes	MT-6548	24	411.38	181.90	450.00	(150.0, 600.0)	(334.57, 488.19)
		darbepoetin	43	29.37	40.82	15.00	(5.0, 180.0)	(16.81, 41.93)
	Dyslipidaemia	MT-6548	46	367.43	197.45	415.28	(0.0, 600.0)	(308.80, 426.06)
		darbepoetin	66	24.33	29.46	16.88	(2.5, 180.0)	(17.09, 31.57)
Baseline Hb (g/dL)	<10	MT-6548	18	360.42	199.74	319.75	(150.0, 600.0)	(261.09, 459.74)
		darbepoetin	17	28.17	28.80	15.00	(5.0, 90.0)	(13.62, 42.72)
	10<= to <11	MT-6548	56	389.94	196.00	393.75	(42.9, 600.0)	(337.45, 442.43)
		darbepoetin	66	21.61	26.49	15.00	(5.0, 160.0)	(14.99, 28.02)
	>=11	MT-6548	44	342.25	195.74	300.00	(0.0, 600.0)	(282.74, 401.76)
		darbepoetin	50	26.27	33.21	15.00	(2.5, 180.0)	(16.83, 35.71)
Baseline Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	117	369.51	195.82	300.00	(0.0, 600.0)	(333.66, 405.37)
		darbepoetin	133	24.15	29.31	15.00	(2.5, 180.0)	(19.12, 29.18)
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	1	150.00	-	150.00	(150.0, 150.0)	-
		darbepoetin	0					
	AST >80 or ALT >90	MT-6548	0					
		darbepoetin	0					
Baseline CRP (mg/dL)	<0.31	MT-6548	97	388.32	187.10	380.36	(42.9, 600.0)	(350.61, 426.03)
		darbepoetin	113	20.02	22.86	15.00	(2.5, 160.0)	(15.76, 24.28)
	>=0.31	MT-6548	21	272.19	212.43	150.00	(0.0, 600.0)	(175.50, 368.89)
		darbepoetin	20	47.47	47.09	30.63	(5.0, 180.0)	(25.44, 69.50)

表 2.7.6.26－117　被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Baseline Serum Ferritin (ng/mL)	<82.7	MT-6548	39	349.04	196.16	300.00	(42.9, 600.0)	(285.45, 412.63)
		darbepoetin	49	27.33	38.92	13.75	(2.5, 180.0)	(15.35, 39.30)
	82.7<= to <165	MT-6548	40	376.09	201.82	318.75	(75.0, 600.0)	(311.54, 440.63)
		darbepoetin	46	21.28	29.04	12.50	(5.0, 120.0)	(13.84, 28.72)
	>=165	MT-6548	39	377.61	193.64	300.00	(0.0, 600.0)	(314.84, 440.38)
		darbepoetin	44	24.04	21.97	18.84	(5.0, 106.7)	(17.36, 30.72)
Baseline TSAT (%)	<23	MT-6548	32	320.59	214.12	225.00	(0.0, 600.0)	(243.39, 397.79)
		darbepoetin	44	34.20	38.79	16.25	(5.0, 180.0)	(22.41, 46.00)
	23<= to <31	MT-6548	41	379.05	183.30	360.36	(150.0, 600.0)	(321.20, 436.91)
		darbepoetin	43	16.61	15.54	15.00	(2.5, 80.0)	(13.83, 23.39)
	>=31	MT-6548	45	390.73	192.50	300.00	(150.0, 600.0)	(332.90, 448.56)
		darbepoetin	46	19.70	26.63	10.00	(5.0, 160.0)	(11.80, 27.61)
Smoking Status	Never Smoked	MT-6548	55	392.16	196.47	337.50	(150.0, 600.0)	(339.04, 445.27)
		darbepoetin	61	19.83	21.76	13.33	(5.0, 120.0)	(14.26, 25.40)
	Ex-Smoker	MT-6548	46	349.26	192.23	300.00	(0.0, 600.0)	(292.18, 406.35)
		darbepoetin	51	31.87	38.31	20.00	(5.0, 180.0)	(21.10, 42.65)
	Current Smoker	MT-6548	17	338.13	206.93	300.00	(42.9, 600.0)	(231.74, 444.52)
		darbepoetin	21	17.92	18.24	10.00	(2.5, 80.0)	(9.61, 26.22)
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	6	325.00	175.36	300.00	(150.0, 600.0)	(140.97, 509.03)
		darbepoetin	3	38.89	58.70	5.00	(5.0, 106.7)	(-106.92, 184.70)
	No	MT-6548	112	369.94	197.52	300.00	(0.0, 600.0)	(332.95, 406.92)
		darbepoetin	130	23.81	28.65	15.00	(2.5, 180.0)	(18.84, 28.78)

表 2.7.6.26－117 被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Concomitant Medications of Oral Iron at Week 52	Yes	MT-6548	4	337.50	188.75	300.00	(150.0, 600.0)	(37.16, 637.84)
		darbepoetin	6	23.33	28.75	12.50	(5.0, 80.0)	(-6.84, 53.51)
	No	MT-6548	114	368.71	196.99	300.00	(0.0, 600.0)	(332.16, 405.26)
		darbepoetin	127	24.19	29.45	15.00	(2.5, 180.0)	(19.01, 29.36)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Baseline	Yes	MT-6548	45	387.99	208.63	450.00	(0.0, 600.0)	(325.31, 450.67)
		darbepoetin	42	21.65	22.73	15.00	(5.0, 106.7)	(14.57, 28.73)
	No	MT-6548	73	355.11	188.21	300.00	(42.9, 600.0)	(311.20, 399.03)
		darbepoetin	91	25.30	31.95	15.00	(2.5, 180.0)	(18.65, 31.95)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 52	Yes	MT-6548	38	384.16	210.74	450.00	(0.0, 600.0)	(314.89, 453.43)
		darbepoetin	40	20.19	21.25	15.00	(5.0, 106.7)	(13.40, 26.99)
	No	MT-6548	80	359.81	189.61	300.00	(42.9, 600.0)	(317.63, 401.98)
		darbepoetin	93	25.85	32.12	15.00	(2.5, 180.0)	(19.23, 32.46)
Prior ESA Treatment: Medication	Epoetin	MT-6548	39	368.82	185.35	300.00	(150.0, 600.0)	(309.73, 428.90)
		darbepoetin	42	17.44	17.13	10.00	(2.5, 80.0)	(12.10, 22.78)
	Darbepoetin alfa	MT-6548	69	386.11	200.19	450.00	(0.0, 600.0)	(338.02, 434.20)
		darbepoetin	75	26.15	30.22	15.00	(5.0, 180.0)	(18.19, 32.10)
	Epoetin beta pegol	MT-6548	10	235.71	172.39	150.00	(75.0, 600.0)	(112.39, 359.04)
		darbepoetin	16	[redacted]				
	Other	MT-6548	0					
		darbepoetin	0					

表 2.7.6.26－117 被験者背景別の 48 週～52 週後の治験薬の平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Prior ESA Treatment: Weekly Dose (IU)	Epoetin, <3000	MT-6548	9	338.10	190.70	300.00	(150.0, 600.0)	(191.51, 484.68)
		darbepoetin	12	7.29	4.05	5.00	(2.5, 15.0)	(4.72, 9.87)
	Epoetin, 3000<= to <4500	MT-6548	16	412.50	185.74	375.00	(150.0, 600.0)	(313.53, 511.47)
		darbepoetin	9	14.31	7.48	15.00	(5.0, 25.0)	(8.56, 20.05)
	Epoetin, >=4500	MT-6548	14	338.65	185.08	300.00	(150.0, 600.0)	(231.78, 445.51)
		darbepoetin	21	24.58	21.23	20.00	(5.0, 80.0)	(14.92, 34.25)
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	16	260.49	177.21	150.00	(0.0, 600.0)	(166.06, 354.92)
		darbepoetin	12	10.31	6.79	6.25	(5.0, 21.3)	(6.00, 14.62)
	Darbepoetin alfa, 10<= to <20	MT-6548	25	396.81	195.39	450.00	(150.0, 600.0)	(306.16, 487.47)
		darbepoetin	34	15.81	12.46	14.38	(5.0, 50.0)	(11.47, 20.16)
	Darbepoetin alfa, >=20	MT-6548	28	457.27	186.95	600.00	(42.9, 600.0)	(384.78, 529.76)
		darbepoetin	29	42.23	41.36	30.00	(5.0, 180.0)	(26.49, 57.96)
Prior ESA Treatment: Weekly Dose (ug)	Epoetin beta pegol, <12.5	MT-6548	3	200.00	86.60	150.00	(150.0, 300.0)	(-15.13, 415.13)
		darbepoetin	4	[redacted]				
	Epoetin beta pegol, 12.5<= to <25	MT-6548	5	306.43	218.21	150.00	(150.0, 600.0)	(35.46, 577.38)
		darbepoetin	4	[redacted]				
	Epoetin beta pegol, >=25	MT-6548	2	112.50	53.03	112.50	(75.0, 150.0)	(-363.98, 588.98)
		darbepoetin	8	[redacted]				
Concomitant Medications of CYP2B6 Substrates	Yes	MT-6548	12	337.50	203.62	300.00	(0.0, 600.0)	(208.19, 466.81)
		darbepoetin	20	26.32	29.88	16.96	(5.0, 110.0)	(12.34, 40.30)
	No	MT-6548	106	371.06	195.86	300.00	(42.9, 600.0)	(333.34, 408.79)
		darbepoetin	113	23.76	29.33	15.00	(2.5, 180.0)	(18.30, 29.23)

Note(s): average dose: MT-6548: average daily dose (mg); darbepoetin: average weekly dose (ug).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Note(s): Baseline Serum Ferritin, Baseline TSAT and each Prior ESA Treatment Total Weekly Dose are divided into three categories by the 3-quantiles.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_5_2.sas

5.3.5.1—9 表 14.2.5.2 より引用

表 2.7.6.26－118　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）

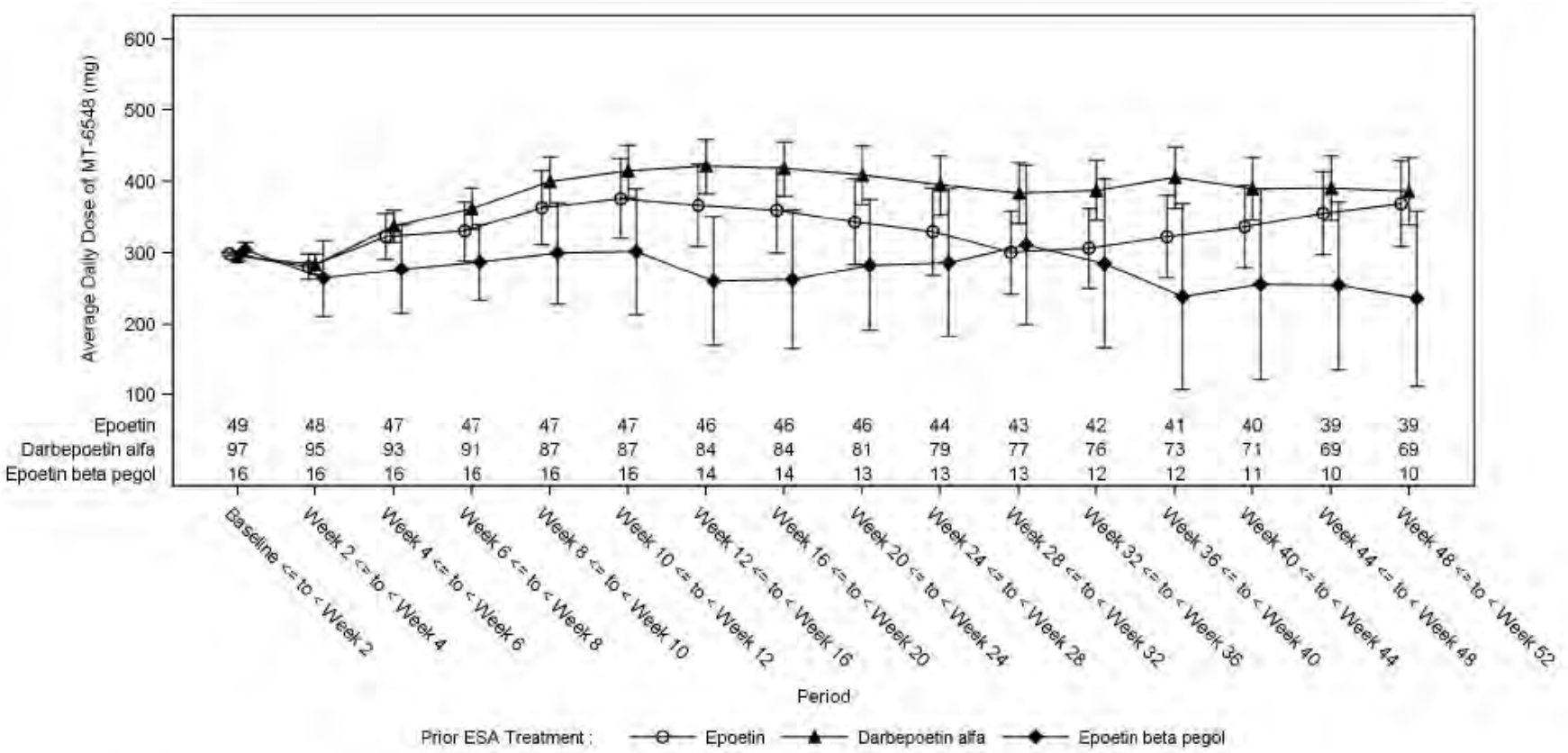
Treatment Group	Prior ESA Treatment	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Epoetin	Baseline <= to < Week 2	49	298.69	6.79	300.00	(257.1, 300.0)	(296.74, 300.64)
		Week 2 <= to < Week 4	48	280.58	63.35	300.00	(42.9, 450.0)	(262.18, 298.98)
		Week 4 <= to < Week 6	47	322.80	109.58	300.00	(150.0, 600.0)	(290.62, 354.97)
		Week 6 <= to < Week 8	47	330.09	141.96	300.00	(0.0, 600.0)	(286.41, 371.77)
		Week 8 <= to < Week 10	47	362.92	175.31	300.00	(0.0, 600.0)	(311.45, 414.39)
		Week 10 <= to < Week 12	47	376.37	190.22	385.71	(0.0, 600.0)	(320.52, 432.22)
		Week 12 <= to < Week 16	46	366.27	194.46	356.25	(0.0, 600.0)	(308.52, 424.01)
		Week 16 <= to < Week 20	46	359.51	200.22	300.00	(0.0, 600.0)	(300.05, 418.97)
		Week 20 <= to < Week 24	46	343.18	200.56	300.00	(0.0, 600.0)	(283.63, 402.74)
		Week 24 <= to < Week 28	44	329.10	202.29	300.00	(0.0, 600.0)	(267.60, 390.60)
		Week 28 <= to < Week 32	43	300.25	189.46	235.71	(0.0, 600.0)	(241.94, 358.56)
		Week 32 <= to < Week 36	42	306.12	181.15	300.00	(0.0, 600.0)	(249.67, 362.57)
		Week 36 <= to < Week 40	41	322.34	183.58	300.00	(0.0, 600.0)	(264.40, 380.29)
		Week 40 <= to < Week 44	40	336.56	178.55	300.00	(107.1, 600.0)	(279.46, 393.67)
		Week 44 <= to < Week 48	39	355.36	180.13	300.00	(150.0, 600.0)	(296.57, 413.75)
		Week 48 <= to < Week 52	39	368.82	185.35	300.00	(150.0, 600.0)	(308.73, 428.90)
	Darbepoetin alfa	Baseline <= to < Week 2	97	295.14	30.85	300.00	(42.9, 364.3)	(288.92, 301.36)
		Week 2 <= to < Week 4	95	283.87	73.52	300.00	(0.0, 514.3)	(268.90, 298.85)
		Week 4 <= to < Week 6	93	337.10	112.32	300.00	(0.0, 600.0)	(313.96, 360.23)
		Week 6 <= to < Week 8	91	361.70	140.35	417.86	(0.0, 600.0)	(332.46, 390.93)
		Week 8 <= to < Week 10	87	400.25	164.47	450.00	(96.4, 600.0)	(365.19, 435.30)
		Week 10 <= to < Week 12	87	414.33	173.54	450.00	(0.0, 600.0)	(377.35, 451.32)
		Week 12 <= to < Week 16	84	420.98	176.83	450.00	(0.0, 600.0)	(382.72, 459.25)
		Week 16 <= to < Week 20	84	417.49	175.64	450.00	(37.5, 600.0)	(379.37, 455.60)
		Week 20 <= to < Week 24	81	408.47	184.60	450.00	(0.0, 600.0)	(367.65, 449.28)
		Week 24 <= to < Week 28	79	394.88	186.75	450.00	(37.5, 600.0)	(353.09, 436.71)
		Week 28 <= to < Week 32	77	383.77	188.05	342.86	(0.0, 600.0)	(341.08, 426.45)
		Week 32 <= to < Week 36	76	387.76	187.59	369.64	(0.0, 600.0)	(344.85, 430.62)
		Week 36 <= to < Week 40	73	405.37	184.10	450.00	(150.0, 600.0)	(362.42, 448.33)
		Week 40 <= to < Week 44	71	389.26	188.54	450.00	(0.0, 600.0)	(344.63, 433.89)
		Week 44 <= to < Week 48	69	390.94	188.25	439.29	(150.0, 600.0)	(345.62, 436.06)
		Week 48 <= to < Week 52	69	386.11	200.19	450.00	(0.0, 600.0)	(338.02, 434.20)

表 2.7.6.26－118　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）（続き）

Treatment Group	Prior ESA Treatment	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
	Epoetin beta pegol	Baseline <= to < Week 2	16	304.69	18.75	300.00	(300.0, 375.0)	(294.70, 314.68)
		Week 2 <= to < Week 4	16	263.84	98.89	300.00	(21.4, 450.0)	(211.15, 316.53)
		Week 4 <= to < Week 6	16	276.56	115.26	300.00	(0.0, 450.0)	(215.14, 337.99)
		Week 6 <= to < Week 8	16	286.61	99.17	300.00	(150.0, 450.0)	(233.76, 339.45)
		Week 8 <= to < Week 10	16	299.33	183.39	300.00	(0.0, 450.0)	(228.26, 370.41)
		Week 10 <= to < Week 12	16	301.34	164.40	300.00	(0.0, 600.0)	(213.73, 388.94)
		Week 12 <= to < Week 16	14	260.20	157.21	249.11	(0.0, 600.0)	(169.43, 350.97)
		Week 16 <= to < Week 20	14	262.50	168.99	168.75	(112.5, 600.0)	(164.93, 360.07)
		Week 20 <= to < Week 24	13	282.69	152.41	294.64	(128.2, 600.0)	(190.59, 374.79)
		Week 24 <= to < Week 28	13	285.99	171.21	300.00	(85.7, 600.0)	(182.53, 389.45)
		Week 28 <= to < Week 32	13	311.13	183.90	300.00	(150.0, 600.0)	(200.00, 422.26)
		Week 32 <= to < Week 36	12	285.27	186.21	281.25	(0.0, 600.0)	(166.96, 403.58)
		Week 36 <= to < Week 40	12	238.39	205.61	150.00	(0.0, 600.0)	(107.76, 369.03)
		Week 40 <= to < Week 44	11	255.68	199.01	150.00	(0.0, 600.0)	(121.96, 389.38)
		Week 44 <= to < Week 48	10	253.98	164.60	150.00	(150.0, 600.0)	(136.18, 371.68)
		Week 48 <= to < Week 52	10	235.71	172.39	150.00	(75.0, 600.0)	(112.39, 359.04)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Listing 16.2.8.1, Listing 16.2.8.2
Source: t_14_2_3_3_4_1.sas

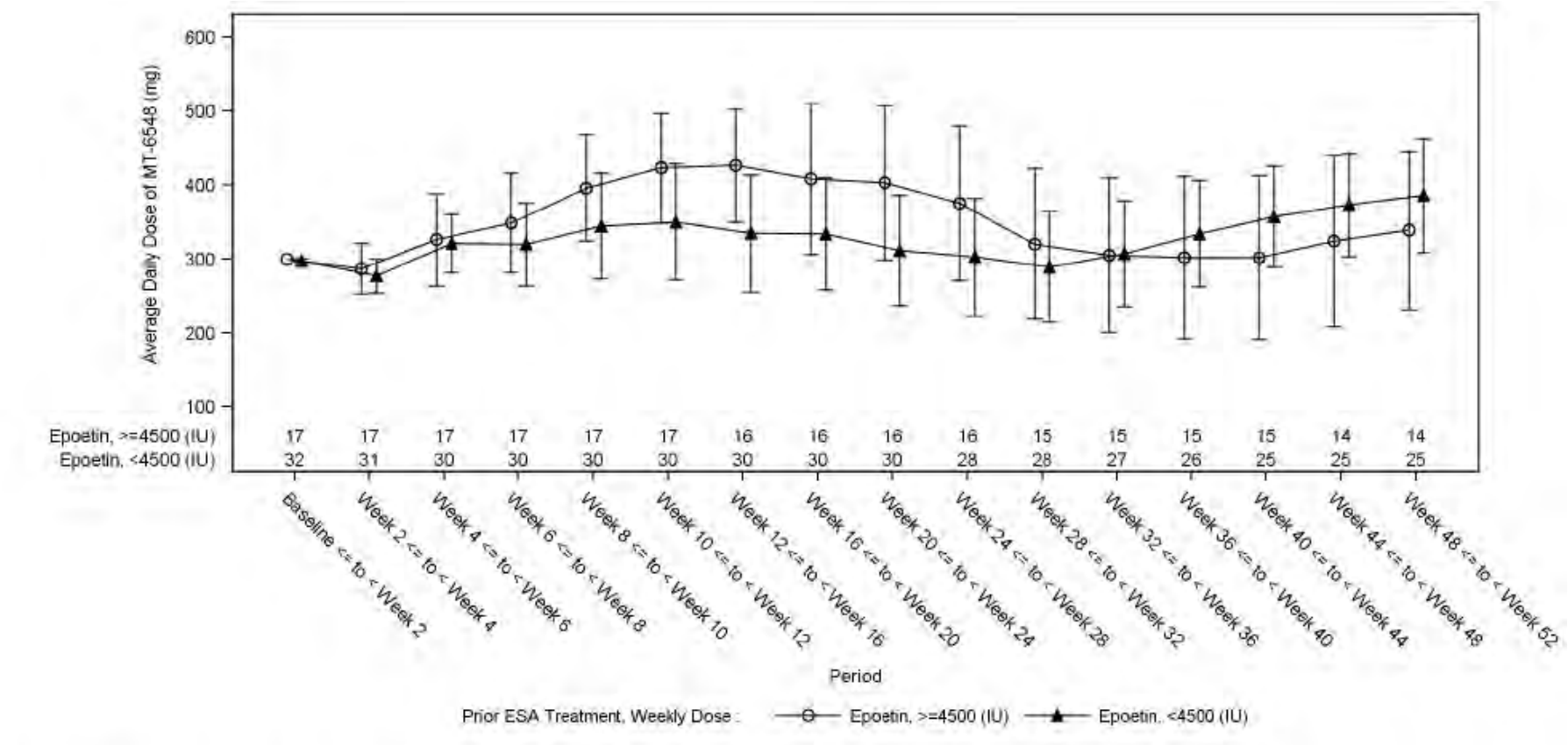
5.3.5.1—9 表 14.2.3.3.4.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.3.3.4.1
Source: f_14_2_3_4_1.sas

図 2.7.6.26－41　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量の推移（FAS）

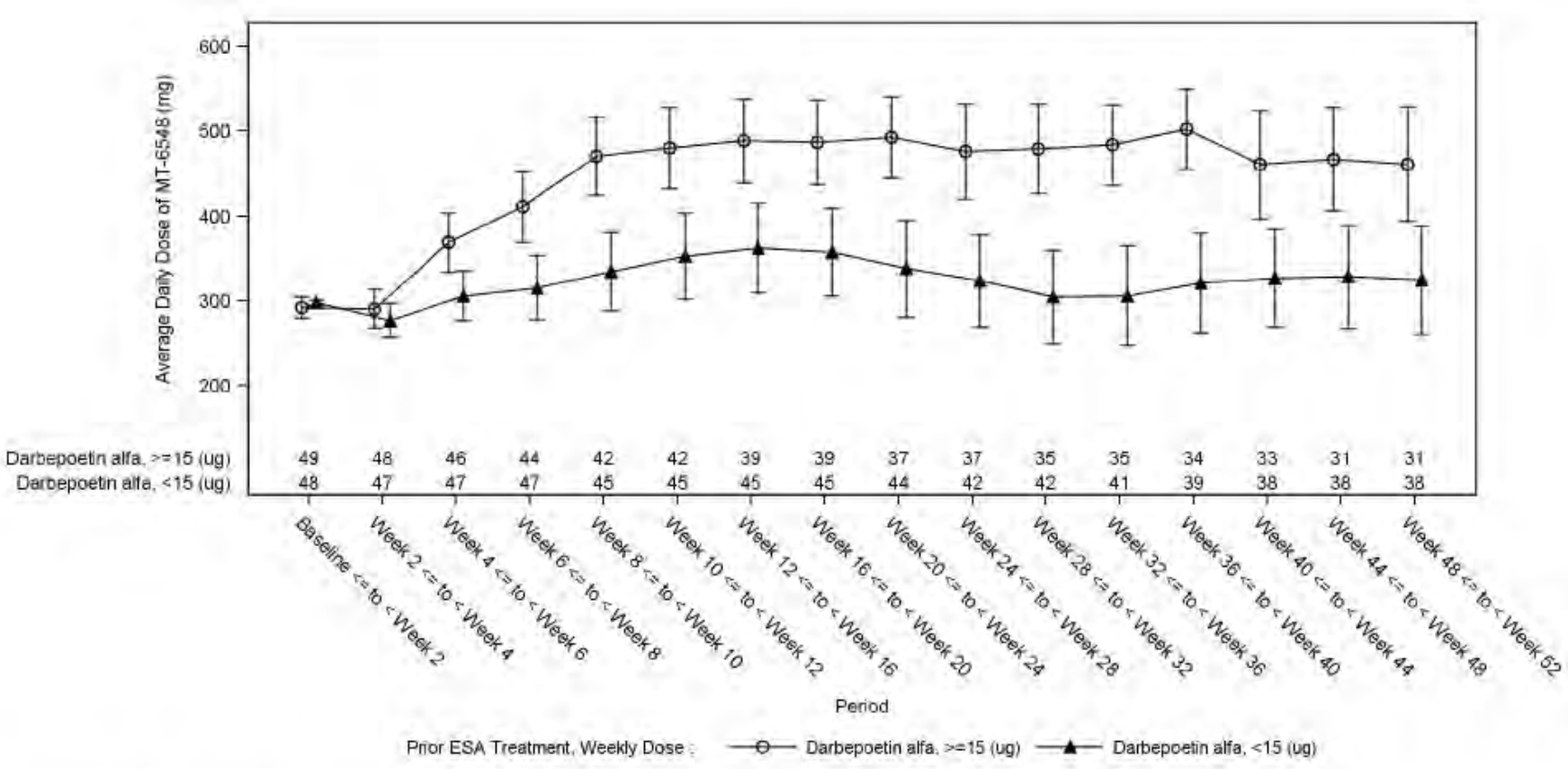
5.3.5.1—9 図 14.2.3.4.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Table 14.2.3.3.5.1
Source: f_14_2_3_5_1.sas

図 2.7.6.26－42　前治療 ESA 製剤（エポエチン製剤）の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

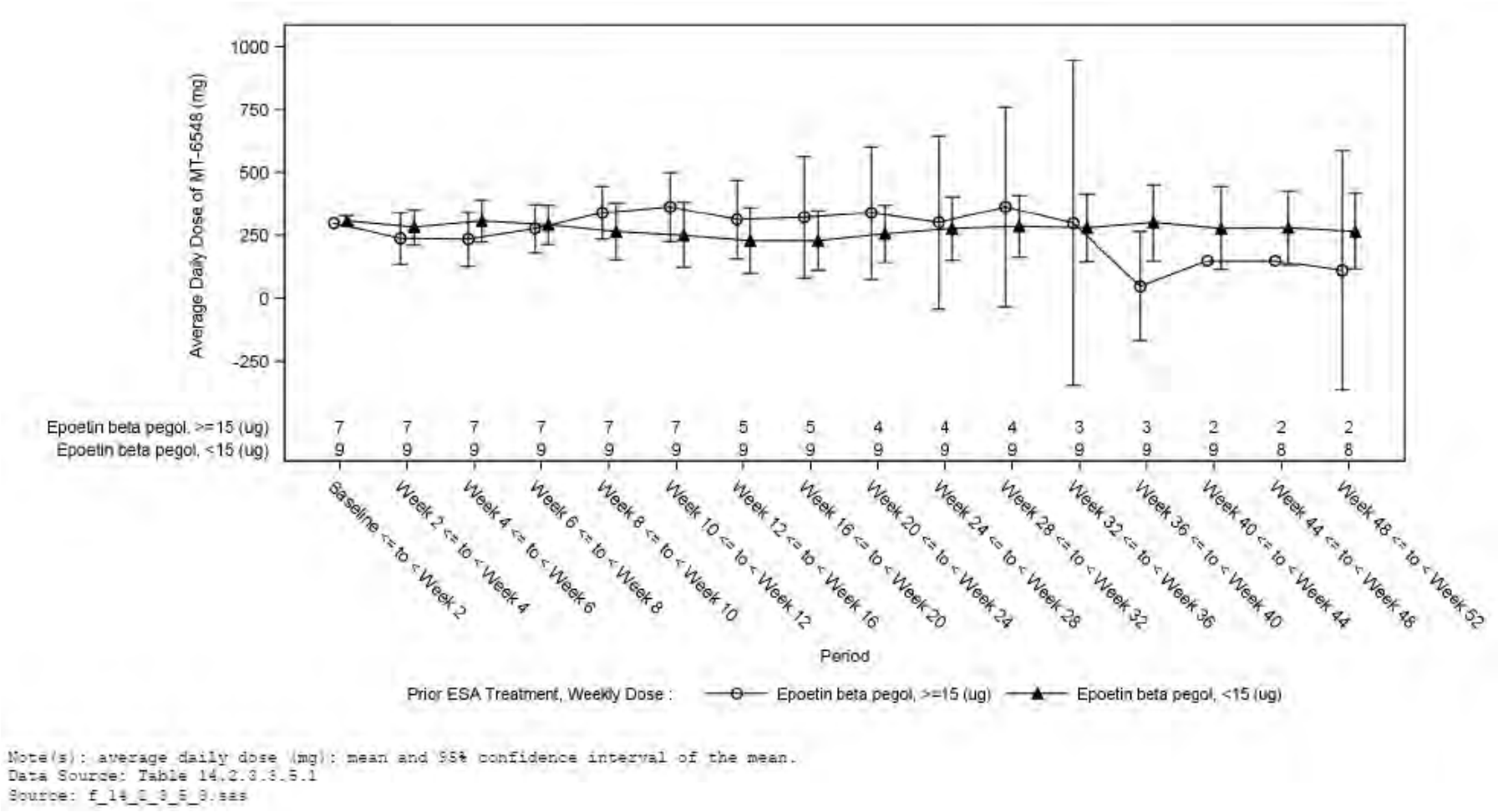
5.3.5.1—9 図 14.2.3.5.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.5.1
Source: f_14_2_3_5_2.sas

図 2.7.6.26－43　前治療 ESA 製剤｛ダルベポエチンアルファ（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—9 図 14.2.3.5.2 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.3.5.1
Source: f_14_2_3_5_3.sas

図 2.7.6.26－44　前治療 ESA 製剤｛エポエチンベータペゴル（遺伝子組換え）｝の用量別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—9 図 14.2.3.5.3 より引用

表 2.7.6.26－119　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Epoetin, >=4500 (IU)	Baseline <= to < Week 2	17	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	17	286.76	66.21	300.00	(150.0, 450.0)	(252.72, 320.81)
		Week 4 <= to < Week 6	17	325.84	120.81	300.00	(150.0, 600.0)	(263.73, 387.95)
		Week 6 <= to < Week 8	17	348.53	129.74	375.00	(150.0, 600.0)	(281.82, 415.24)
		Week 8 <= to < Week 10	17	395.90	140.34	450.00	(150.0, 600.0)	(323.64, 467.96)
		Week 10 <= to < Week 12	17	422.90	144.00	450.00	(150.0, 600.0)	(348.86, 496.94)
		Week 12 <= to < Week 16	16	426.23	143.03	450.00	(150.0, 600.0)	(350.01, 502.44)
		Week 16 <= to < Week 20	16	408.48	152.38	450.00	(85.7, 600.0)	(305.97, 510.99)
		Week 20 <= to < Week 24	16	403.13	155.34	450.00	(150.0, 600.0)	(299.04, 507.21)
		Week 24 <= to < Week 28	16	375.33	155.85	450.00	(150.0, 600.0)	(270.37, 479.70)
		Week 28 <= to < Week 32	15	320.36	184.40	285.71	(150.0, 600.0)	(218.24, 422.48)
		Week 32 <= to < Week 36	15	305.00	189.03	150.00	(150.0, 600.0)	(200.32, 409.68)
		Week 36 <= to < Week 40	15	301.79	198.42	155.36	(150.0, 600.0)	(191.91, 411.67)
		Week 40 <= to < Week 44	15	301.48	199.78	150.00	(107.1, 600.0)	(190.79, 412.07)
		Week 44 <= to < Week 48	14	324.11	200.39	243.75	(150.0, 600.0)	(208.41, 439.81)
		Week 48 <= to < Week 52	14	338.65	185.08	300.00	(150.0, 600.0)	(231.79, 445.51)
	Epoetin, <4500 (IU)	Baseline <= to < Week 2	32	297.99	8.36	300.00	(257.1, 300.0)	(294.98, 301.01)
		Week 2 <= to < Week 4	31	277.15	62.58	300.00	(42.9, 300.0)	(254.23, 300.14)
		Week 4 <= to < Week 6	30	321.07	104.91	300.00	(150.0, 450.0)	(281.94, 360.21)
		Week 6 <= to < Week 8	30	319.64	149.56	300.00	(0.0, 600.0)	(263.80, 375.49)
		Week 8 <= to < Week 10	30	344.29	192.07	300.00	(0.0, 600.0)	(272.57, 416.01)
		Week 10 <= to < Week 12	30	350.00	209.68	300.00	(0.0, 600.0)	(271.70, 428.30)
		Week 12 <= to < Week 16	30	334.29	212.27	300.00	(0.0, 600.0)	(255.02, 413.55)
		Week 16 <= to < Week 20	30	333.39	202.57	300.00	(0.0, 600.0)	(257.75, 409.03)
		Week 20 <= to < Week 24	30	311.21	199.08	300.00	(0.0, 600.0)	(236.87, 385.55)
		Week 24 <= to < Week 28	28	302.68	204.62	300.00	(0.0, 600.0)	(223.34, 382.02)
		Week 28 <= to < Week 32	28	289.48	194.58	262.50	(0.0, 600.0)	(214.03, 364.93)
		Week 32 <= to < Week 36	27	306.75	180.30	300.00	(0.0, 600.0)	(235.42, 378.07)
		Week 36 <= to < Week 40	26	334.20	177.41	300.00	(0.0, 600.0)	(262.55, 405.86)
		Week 40 <= to < Week 44	25	357.64	165.19	300.00	(150.0, 600.0)	(289.45, 425.83)
		Week 44 <= to < Week 48	25	372.86	169.51	300.00	(150.0, 600.0)	(302.89, 442.83)
		Week 48 <= to < Week 52	25	385.71	187.12	300.00	(150.0, 600.0)	(308.48, 462.95)

表 2.7.6.26－119　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
	Darbepoetin alfa, >=15 (ug)	Baseline <= to < Week 2	49	292.13	42.34	300.00	(42.9, 364.3)	(279.97, 304.29)
		Week 2 <= to < Week 4	48	290.85	78.35	300.00	(0.0, 514.3)	(268.09, 313.61)
		Week 4 <= to < Week 6	46	368.71	117.75	401.79	(0.0, 600.0)	(333.74, 403.68)
		Week 6 <= to < Week 8	44	410.80	136.19	450.00	(0.0, 600.0)	(369.39, 452.20)
		Week 8 <= to < Week 10	42	470.41	147.68	525.00	(150.0, 600.0)	(424.39, 516.43)
		Week 10 <= to < Week 12	42	480.46	153.60	600.00	(150.0, 600.0)	(432.59, 528.32)
		Week 12 <= to < Week 16	39	488.32	158.24	600.00	(150.0, 600.0)	(438.65, 538.00)
		Week 16 <= to < Week 20	39	486.71	158.48	600.00	(150.0, 600.0)	(436.96, 536.46)
		Week 20 <= to < Week 24	37	492.28	143.99	600.00	(150.0, 600.0)	(444.27, 540.29)
		Week 24 <= to < Week 28	37	475.94	167.09	600.00	(54.5, 600.0)	(420.23, 531.65)
		Week 28 <= to < Week 32	35	479.08	159.78	600.00	(150.0, 600.0)	(426.26, 531.91)
		Week 32 <= to < Week 36	35	483.52	138.52	557.14	(150.0, 600.0)	(435.94, 531.10)
		Week 36 <= to < Week 40	34	501.98	134.25	597.32	(150.0, 600.0)	(455.14, 548.82)
		Week 40 <= to < Week 44	33	460.71	190.31	562.50	(0.0, 600.0)	(396.76, 524.66)
		Week 44 <= to < Week 48	31	467.11	165.05	600.00	(150.0, 600.0)	(406.57, 527.65)
		Week 48 <= to < Week 52	31	461.41	183.36	600.00	(42.9, 600.0)	(394.15, 528.66)
	Darbepoetin alfa, <15 (ug)	Baseline <= to < Week 2	48	298.21	9.72	300.00	(235.7, 300.0)	(295.39, 301.04)
		Week 2 <= to < Week 4	47	276.75	66.29	300.00	(21.4, 450.0)	(256.70, 296.80)
		Week 4 <= to < Week 6	47	306.16	98.45	300.00	(0.0, 450.0)	(277.25, 335.06)
		Week 6 <= to < Week 8	47	315.73	129.46	300.00	(0.0, 600.0)	(277.72, 353.74)
		Week 8 <= to < Week 10	45	334.76	153.17	300.00	(96.4, 600.0)	(288.74, 380.78)
		Week 10 <= to < Week 12	45	352.62	169.73	300.00	(0.0, 600.0)	(301.63, 403.61)
		Week 12 <= to < Week 16	45	362.62	175.70	300.00	(0.0, 600.0)	(309.83, 415.41)
		Week 16 <= to < Week 20	45	357.50	172.97	300.00	(37.5, 600.0)	(305.53, 409.47)
		Week 20 <= to < Week 24	44	337.99	186.85	300.00	(0.0, 600.0)	(281.18, 394.79)
		Week 24 <= to < Week 28	42	323.47	175.17	300.00	(37.5, 600.0)	(266.88, 378.06)
		Week 28 <= to < Week 32	42	304.34	178.10	300.00	(0.0, 600.0)	(248.84, 359.84)
		Week 32 <= to < Week 36	41	306.01	186.54	300.00	(0.0, 600.0)	(247.13, 364.89)
		Week 36 <= to < Week 40	39	321.15	181.48	262.50	(150.0, 600.0)	(262.33, 379.96)
		Week 40 <= to < Week 44	38	327.21	175.00	300.00	(150.0, 600.0)	(269.69, 384.73)
		Week 44 <= to < Week 48	38	328.62	184.91	300.00	(150.0, 600.0)	(267.84, 389.40)
		Week 48 <= to < Week 52	38	324.69	194.35	300.00	(0.0, 600.0)	(260.81, 388.57)

表 2.7.6.26－119　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（続き）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
	Epoetin beta pegol, >=18 (ug)	Baseline <= to < Week 2	7	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	7	238.78	110.95	300.00	(21.4, 300.0)	(136.16, 341.39)
		Week 4 <= to < Week 6	7	235.71	118.02	300.00	(0.0, 300.0)	(126.56, 344.86)
		Week 6 <= to < Week 8	7	278.57	103.51	300.00	(150.0, 450.0)	(182.84, 374.30)
		Week 8 <= to < Week 10	7	341.33	111.76	300.00	(150.0, 450.0)	(237.96, 444.69)
		Week 10 <= to < Week 12	7	364.29	146.39	300.00	(150.0, 600.0)	(228.90, 499.67)
		Week 12 <= to < Week 16	5	313.93	125.84	332.14	(150.0, 450.0)	(157.68, 470.18)
		Week 16 <= to < Week 20	5	322.50	194.13	225.00	(150.0, 600.0)	(81.45, 563.55)
		Week 20 <= to < Week 24	4	340.18	165.78	375.00	(123.2, 487.5)	(76.38, 603.98)
		Week 24 <= to < Week 28	4	301.34	215.37	300.00	(85.7, 519.6)	(-41.36, 644.04)
		Week 28 <= to < Week 32	4	365.63	249.45	356.25	(150.0, 600.0)	(-31.31, 762.56)
		Week 32 <= to < Week 36	3	300.00	259.81	150.00	(150.0, 600.0)	(-345.40, 945.40)
		Week 36 <= to < Week 40	3	50.00	86.60	0.00	(0.0, 150.0)	(-165.13, 265.13)
		Week 40 <= to < Week 44	2	150.00	0.00	150.00	(150.0, 150.0)	(-, -)
		Week 44 <= to < Week 48	2	150.00	0.00	150.00	(150.0, 150.0)	(-, -)
		Week 48 <= to < Week 52	2	112.50	53.03	112.50	(75.0, 150.0)	(-363.98, 588.98)
	Epoetin beta pegol, <15 (ug)	Baseline <= to < Week 2	9	308.33	25.00	300.00	(300.0, 375.0)	(289.12, 327.55)
		Week 2 <= to < Week 4	9	283.33	90.14	300.00	(150.0, 450.0)	(214.05, 352.62)
		Week 4 <= to < Week 6	9	308.33	108.97	300.00	(150.0, 450.0)	(224.57, 392.10)
		Week 6 <= to < Week 8	9	292.86	101.50	300.00	(150.0, 450.0)	(214.83, 370.88)
		Week 8 <= to < Week 10	9	266.67	145.77	300.00	(0.0, 450.0)	(154.62, 378.72)
		Week 10 <= to < Week 12	9	252.38	168.65	300.00	(0.0, 600.0)	(122.74, 382.02)
		Week 12 <= to < Week 16	9	230.36	171.57	225.00	(0.0, 600.0)	(98.47, 362.24)
		Week 16 <= to < Week 20	9	229.17	155.12	150.00	(112.5, 600.0)	(109.93, 348.40)
		Week 20 <= to < Week 24	9	257.14	148.62	187.50	(150.0, 600.0)	(142.75, 371.54)
		Week 24 <= to < Week 28	9	279.17	162.50	300.00	(112.5, 600.0)	(154.26, 404.08)
		Week 28 <= to < Week 32	9	286.90	168.90	300.00	(150.0, 600.0)	(164.76, 409.04)
		Week 32 <= to < Week 36	9	280.36	175.20	300.00	(0.0, 600.0)	(145.69, 415.02)
		Week 36 <= to < Week 40	9	301.19	196.23	278.57	(75.0, 600.0)	(150.36, 452.02)
		Week 40 <= to < Week 44	9	279.17	214.69	150.00	(0.0, 600.0)	(114.14, 444.20)
		Week 44 <= to < Week 48	8	279.91	176.00	198.21	(150.0, 600.0)	(132.77, 427.05)
		Week 48 <= to < Week 52	8	266.52	179.96	150.00	(150.0, 600.0)	(116.06, 416.97)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): Epoetin means Epoetin alfa, Epoetin beta or Epoetin Kappa.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_3_5_1.sas

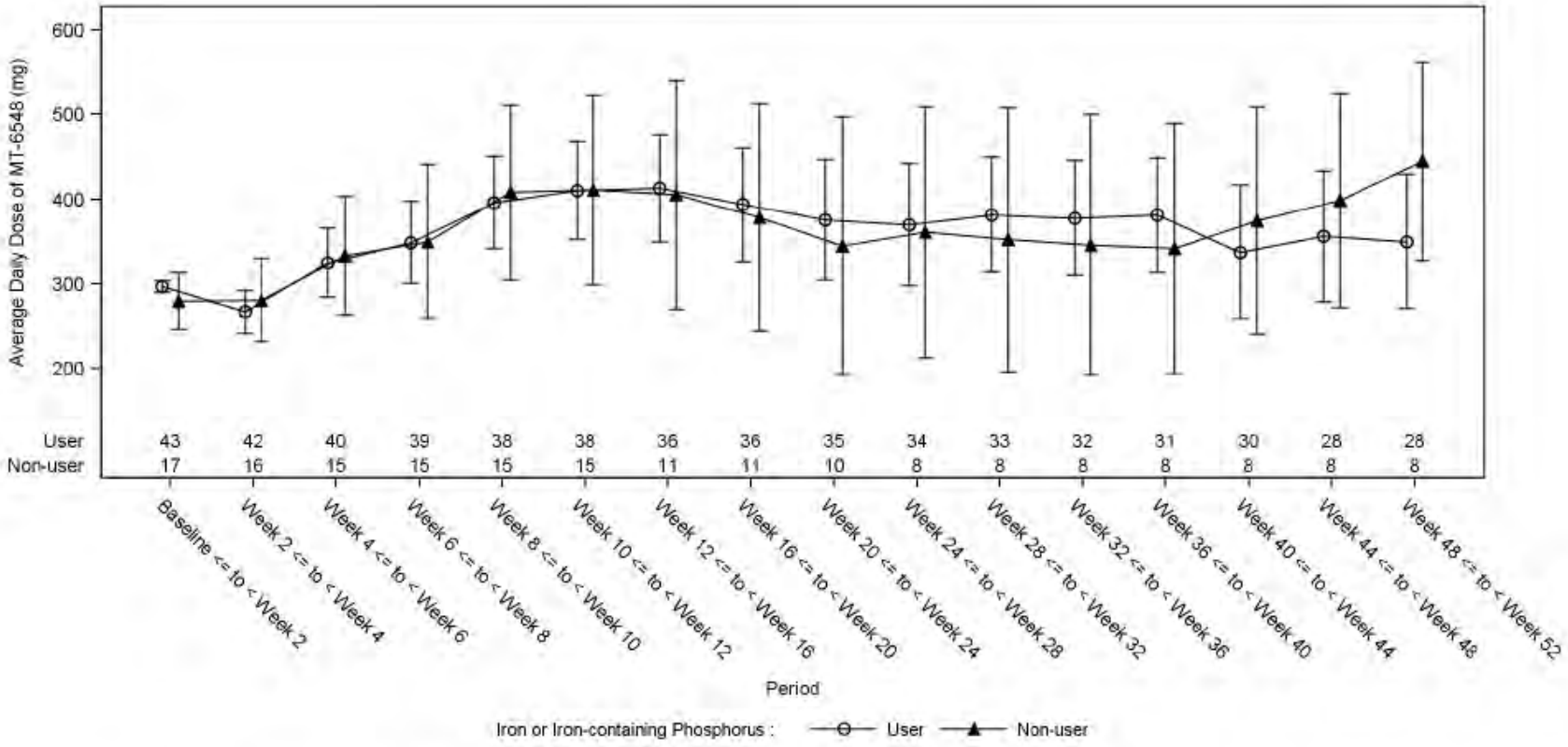
5.3.5.1—9 表 14.2.3.3.5.1 より引用

表 2.7.6.26－120　鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量（FAS）

Treatment Group	Iron or Iron-containing Phosphorus	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	User	Baseline <= to < Week 2	43	297.26	22.56	300.00	(192.9, 375.0)	(290.32, 304.20)
		Week 2 <= to < Week 4	42	267.09	81.82	300.00	(0.0, 450.0)	(241.60, 292.59)
		Week 4 <= to < Week 6	40	325.18	127.87	300.00	(0.0, 525.0)	(284.28, 366.07)
		Week 6 <= to < Week 8	39	348.18	149.23	375.00	(0.0, 600.0)	(300.50, 397.85)
		Week 8 <= to < Week 10	38	396.15	164.91	450.00	(150.0, 600.0)	(341.94, 450.35)
		Week 10 <= to < Week 12	38	410.53	175.88	450.00	(0.0, 600.0)	(352.72, 468.34)
		Week 12 <= to < Week 16	36	413.24	186.28	450.00	(0.0, 600.0)	(350.22, 476.27)
		Week 16 <= to < Week 20	36	393.93	198.02	377.68	(37.5, 600.0)	(326.93, 460.93)
		Week 20 <= to < Week 24	35	375.61	207.13	300.00	(0.0, 600.0)	(304.46, 446.77)
		Week 24 <= to < Week 28	34	370.14	205.53	300.00	(37.5, 600.0)	(298.43, 441.86)
		Week 28 <= to < Week 32	33	381.49	190.71	300.00	(150.0, 600.0)	(313.87, 449.12)
		Week 32 <= to < Week 36	32	378.01	187.69	332.14	(37.5, 600.0)	(310.34, 445.68)
		Week 36 <= to < Week 40	31	381.03	185.20	300.00	(150.0, 600.0)	(313.10, 448.96)
		Week 40 <= to < Week 44	30	337.68	211.39	300.00	(0.0, 600.0)	(258.75, 416.61)
		Week 44 <= to < Week 48	28	356.25	195.64	300.00	(150.0, 600.0)	(279.22, 433.28)
		Week 48 <= to < Week 52	28	349.94	203.91	300.00	(0.0, 600.0)	(270.87, 429.00)
	Non-user	Baseline <= to < Week 2	17	279.83	64.50	300.00	(42.9, 300.0)	(246.67, 312.99)
		Week 2 <= to < Week 4	16	281.25	92.87	300.00	(0.0, 450.0)	(231.76, 330.74)
		Week 4 <= to < Week 6	15	333.57	126.44	300.00	(150.0, 600.0)	(263.55, 403.59)
		Week 6 <= to < Week 8	15	350.00	164.18	300.00	(10.7, 600.0)	(259.09, 440.92)
		Week 8 <= to < Week 10	15	407.96	186.39	450.00	(0.0, 600.0)	(304.64, 511.08)
		Week 10 <= to < Week 12	15	411.00	202.82	450.00	(0.0, 600.0)	(298.68, 523.32)
		Week 12 <= to < Week 16	11	405.68	201.06	450.00	(0.0, 600.0)	(270.61, 540.76)
		Week 16 <= to < Week 20	11	378.41	200.08	417.86	(0.0, 600.0)	(244.00, 512.82)
		Week 20 <= to < Week 24	10	345.00	212.72	300.00	(0.0, 600.0)	(192.93, 497.17)
		Week 24 <= to < Week 28	8	360.94	176.96	318.75	(150.0, 600.0)	(213.00, 508.86)
		Week 28 <= to < Week 32	8	352.23	186.23	337.50	(150.0, 600.0)	(196.54, 507.93)
		Week 32 <= to < Week 36	8	346.21	183.96	300.00	(150.0, 600.0)	(192.41, 500.00)
		Week 36 <= to < Week 40	8	342.19	176.89	300.00	(150.0, 600.0)	(194.72, 489.65)
		Week 40 <= to < Week 44	8	375.00	160.36	300.00	(150.0, 600.0)	(240.94, 509.06)
		Week 44 <= to < Week 48	8	398.44	151.25	375.00	(187.5, 600.0)	(271.99, 524.89)
		Week 48 <= to < Week 52	8	444.64	139.70	428.57	(300.0, 600.0)	(327.85, 561.43)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Listing 16.2.3.1
Source: t_14_2_3_3_7_1_1.sas

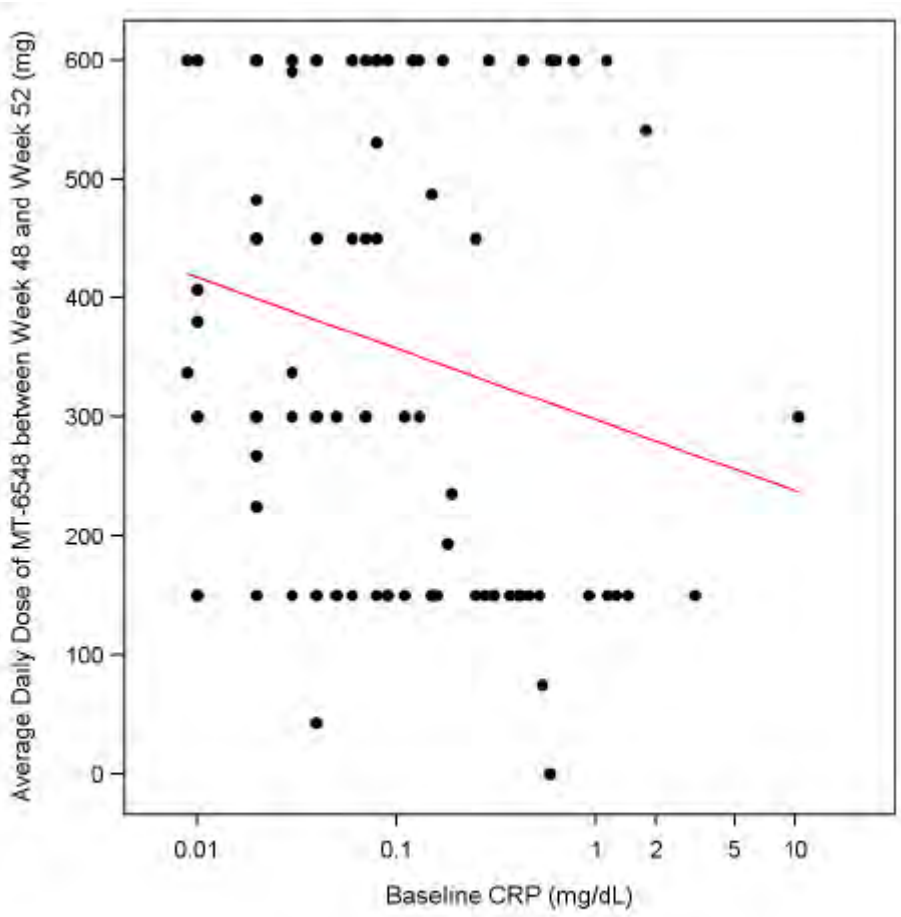
5.3.5.1—9 表 14.2.3.3.7.1.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Note(s): User: subjects who used iron or iron containing phosphorus throughout the study; Non-user: subjects who did not use iron or iron containing phosphorus throughout the study.
Note(s): Subjects who used Saccharated Ferric Oxide even once are excluded from this analysis.
Data Source: Table 14.2.3.3.7.1.1
Source: f_14_2_3_7_1_1.sas

図 2.7.6.26－45　鉄剤及び鉄含有リン吸着剤の併用有無別の MT-6548 の 1 日平均投与量の推移（FAS）

5.3.5.1—9 図 14.2.3.7.1.1 より引用



Note(s): linear regression model: Y=aX + b; Y: average daily dose; X: baseline CRP.
Data Source: Listing 16.2.3.1, Listing 16.2.6.4
Source: f_14_2_3_9_1.sas

図 2.7.6.26－46　ベースラインの CRP と 48 週から 52 週後の MT-6548 の 1 日平均投与量の散布図（FAS）

5.3.5.1—9 図 14.2.3.9.1 より引用

2.7.6.26.3.1.4　安全性

(1)　治験薬投与期間及び累積投与量

安全性解析対象集団の治験薬投与期間の記述統計量を表 2.7.6.26－121 に示した．治験薬投与期間の平均値±SD は MT-6548 群で 307.5±108.9 日，darbepoetin 群で 337.9±70.2 日であった．

治験薬の累積投与量の記述統計量を表 2.7.6.26－122 に示した．治験薬の累積投与量の平均値±SD は MT-6548 群で 110166.7± 62484.2 mg，darbepoetin 群で 977.1± 938.9 μg であった．

表 2.7.6.26－121　治験薬投与期間の記述統計量（安全性解析対象集団）

Duration of Exposure (days)	MT-6548 (N=162)	darbepoetin (N=161)
Mean	307.5	337.9
SD	108.9	70.2
Median	364.0	364.0
Minimum, Maximum	(9, 366)	(4, 364)

Data Source: Listing 16.2.3.3
Source: t_14_1_4_4_1.sas

5.3.5.1—9 表 12.1—1 より引用

表 2.7.6.26－122　治験薬の累積投与量の記述統計量（安全性解析対象集団）

Cumulative Dose	MT-6548 (N=162) (mg)	darbepoetin (N=161) (ug)
Mean	110166.7	977.1
SD	62484.2	938.9
Median	100875.0	660.0
Minimum, Maximum	(600, 210000)	(20, 6300)

Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_1_4_5_2.sas

5.3.5.1—9 表 12.1—2 より引用

(2)　有害事象

1)　有害事象の簡潔な要約

有害事象の要約を表 2.7.6.26－123 に示した．有害事象の発現割合は，MT-6548 群で 95.1%（154／162 名），darbepoetin 群で 98.1%（158／161 名）であった．副作用は MT-6548 群で 11.1%（18 名），darbepoetin 群で 3.7%（6 名）であった．

重篤な有害事象の発現割合は，MT-6548 群で 25.3%（41 名），darbepoetin 群で 27.3%（44 名）であった．重篤な副作用は両群で認められなかった．

中止に至った有害事象の発現割合は，MT-6548 群で 9.9%（16 名），darbepoetin 群で 8.7%（14 名）であった．

治験薬の休薬又は減量に至った有害事象の発現割合は，MT-6548 群で 8.0%（13 名），darbepoetin 群で 2.5%（4 名）であった．

救済治療に至った有害事象の発現割合は，MT-6548 群で 3.7%（6 名），darbepoetin 群で 1.2%（2 名）であった．

死亡に至った有害事象は，MT-6548 群で 1.2%（2 名），darbepoetin 群で 0.6%（1 名）であった．

表 2.7.6.26－123　有害事象の要約（安全性解析対象集団）

	MT-6548 (N=162) n (%)	darbepoetin (N=161) n (%)
Subjects with at least one adverse event	154 (95.1)	158 (98.1)
Subjects with at least one adverse drug reaction	18 (11.1)	6 (3.7)
Subjects with at least one serious adverse event	41 (25.3)	44 (27.3)
Subjects with at least one serious adverse drug reaction	0 (0.0)	0 (0.0)
Subjects with at least one adverse event leading to study discontinuation	16 (9.9)	14 (8.7)
Subjects who had dose reduction or interruption of study drug due to adverse event	13 (8.0)	4 (2.5)
Subjects with at least one adverse event leading to rescue therapy	6 (3.7)	2 (1.2)
Deaths due to adverse event	2 (1.2)	1 (0.6)

Data Source: Listing 16.2.9.1
Source: t_14_3_1_1_1.sas

5.3.5.1—9 表 12.2.1—1 より引用

2)　有害事象及び副作用

有害事象及び副作用を表 2.7.6.26－124 及び表 2.7.6.26－125 に示した．

有害事象のうち，MT-6548 群で発現割合が 20%以上の SOC は，「感染症および寄生虫症」｛MT-6548 群：66.0%（107 名），darbepoetin 群：68.9%（111 名）（以下，同順で記載）｝，「傷害、中毒および処置合併症」｛46.3%（75 名），54.0%（87 名）｝，「胃腸障害」｛40.7%（66 名），50.3%（81 名）｝，「筋骨格系および結合組織障害」｛40.7%（66 名），34.8%（56 名）｝，「皮膚および皮下組織障害」｛34.6%（56 名），23.0%（37 名）｝，「神経系障害」｛22.2%（36 名），14.9%（24 名）｝及び「眼障害」｛21.6%（35 名），21.7%（35 名）｝であった．これらの SOC のうち，darbepoetin 群と比較して 10%以上高かった SOC は，「皮膚および皮下組織障害」であった．副作用のうち，MT-6548 群で発現割合が 20%以上の SOC は認められなかった．MT-6548 群で発現割合が最も高い副作用の SOC は，「胃腸障害」｛6.2%（10 名），1.2%（2 名）｝であった．

SOC「皮膚および皮下組織障害」は MT-6548 群で darbepoetin 群と比較して発現割合が高かったが，MT-6548 群で発現した SOC「皮膚および皮下組織障害」の有害事象の内訳の発現割合に，特定の傾向は認められなかった．

MT-6548 群で発現割合が 5%以上の有害事象は，「上咽頭炎」｛MT-6548 群：45.7%（74 名），darbepoetin 群：45.3%（73 名）（以下，同順で記載）｝，「下痢」｛15.4%（25 名），14.9%（24 名）｝，「シャント狭窄」｛14.2%（23 名），16.1%（26 名）｝，「挫傷」｛13.0%（21 名），11.8%（19 名）｝，「網膜出血」｛9.9%（16 名），6.2%（10 名）｝，「背部痛」｛9.3%（15 名），6.8%（11 名）｝，「頭痛」｛8.0%（13 名），3.1%（5 名）｝，「四肢痛」｛8.0%（13 名），2.5%（4 名）｝，「そう痒症」｛7.4%（12 名），5.6%（9 名）｝，「胃腸炎」｛7.4%（12 名），0.6%（1 名）｝，「結膜炎」｛6.8%（11 名），2.5%（4 名）｝，「嘔吐」｛6.2%（10 名），10.6%（17 名）｝，「関節痛」｛6.2%（10 名），6.8%（11 名）｝，「湿疹」｛6.2%（10 名），5.0%（8 名）｝，「創傷」｛6.2%（10 名），4.3%（7 名）｝，「悪心」｛6.2%（10 名），1.2%（2 名）｝，「皮膚擦過傷」｛5.6%（9 名），9.3%（15 名）｝，「インフルエンザ」｛5.6%（9 名），7.5%（12 名）｝，「筋肉痛」｛5.6%（9 名），3.1%（5 名）｝及び「食欲減退」｛5.6%（9 名），2.5%（4 名）｝であった．これらの事象のうち，darbepoetin 群と比較して 3%以上高かった有害事象は，「胃腸炎」，「四肢痛」，「悪心」，「頭痛」，「結膜炎」，「網膜出血」及び「食欲減退」であった．MT-6548 群で発現割合が 5%以上の副作用は認められなかった．MT-6548 群で発現割合が最も高かった副作用は，「下痢」｛2.5%（4 名），1.2%（2 名）｝続いて「悪心」｛1.9%（3 名），0%｝であった．

MT-6548 群で副作用として最も発現割合が高かった「下痢」，MT-6548 群で「下痢」に次いで発現割合の高かった副作用かつ darbepoetin 群と比較して発現割合の高かった有害事象「悪心」，darbepoetin 群と比較して発現割合の高かった有害事象「胃腸炎」，「四肢痛」，「頭痛」，「結膜炎」，「網膜出血」及び「食欲減退」に関して，下記に詳細を示した．

「下痢」は有害事象の発現割合が 10%以上であり，副作用の発現割合が最も高い事象

であったが，有害事象及び副作用の発現割合は両群で同程度であった．MT-6548 群で発現した「下痢」のうち 3 名は中等度，それ以外の 22 名は軽度であり，4 名は因果関係が合理的な可能性ありと判断された．転帰は 25 名すべてが回復であった．「下痢」に次いで MT-6548 群で副作用の発現割合が高かった「悪心」の有害事象の発現割合は MT-6548 群で darbepoetin 群よりも高かったが，副作用の発現割合は両群で同程度であった．MT-6548 群で発現した「悪心」のうち 1 名は中等度，それ以外の 9 名は軽度であり，3 名は因果関係が合理的な可能性ありと判断された．転帰は 1 名が軽快，それ以外の 9 名はすべて回復であった．darbepoetin 群と比較して発現割合の高かった有害事象「胃腸炎」は 1 名が中等度，それ以外の 11 名は軽度であり，1 名は因果関係が合理的な可能性ありと判断された．転帰は 12 名すべてが回復であった．「四肢痛」は 1 名が中等度，それ以外の 12 名は軽度であり，因果関係が合理的な可能性ありのものは認められなかった．転帰は 13 名すべてが回復であった．「頭痛」は 13 名すべて軽度であり，因果関係が合理的な可能性ありと判断された事象は認められなかった．転帰は 13 名すべてが回復であった．「結膜炎」は 11 名すべて軽度であり，因果関係が合理的な可能性ありと判断された事象は認められなかった．転帰は 1 名が未回復，それ以外の 10 名はすべて回復であった．「網膜出血」は 16 名すべてが軽度であり，因果関係が合理的な可能性ありと判断された事象は認められなかった．転帰は 8 名が未回復，2 名が軽快，6 名が回復であった．「網膜出血」は半数で転帰が未回復であったが，4 名は 48 週～52 週時，1 名は中止時の眼底検査の際に発現していた．なお，MT-6548 群で「網膜出血」が発現した被験者の血管内皮成長因子（以下，VEGF）に顕著な変動は認められなかった．「食欲減退」は 2 名が中等度，それ以外の 7 名は軽度であり，因果関係が合理的な可能性ありと判断された事象は認められなかった．転帰は 1 名が未回復，1 名が軽快，それ以外の 7 名が回復であった．

表 2.7.6.26－124　有害事象（安全性解析対象集団）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Subjects with at least one adverse event		154(95.1)	158(98.1)
Infections and infestations	感染症および寄生虫症	107(66.0)	111(68.9)
Nasopharyngitis	上咽頭炎	74(45.7)	73(45.3)
Gastroenteritis	胃腸炎	12(7.4)	1(0.6)
Conjunctivitis	結膜炎	11(6.8)	4(2.5)
Influenza	インフルエンザ	9(5.6)	12(7.5)
Upper respiratory tract infection	上気道感染	7(4.3)	8(5.0)
Pneumonia	肺炎	7(4.3)	2(1.2)
Bronchitis	気管支炎	5(3.1)	6(3.7)
Hordeolum	麦粒腫	4(2.5)	1(0.6)
Pharyngitis	咽頭炎	3(1.9)	7(4.3)
Periodontitis	歯周炎	3(1.9)	5(3.1)
Cystitis	膀胱炎	3(1.9)	1(0.6)
Tinea pedis	足部白癬	2(1.2)	6(3.7)
Shunt infection	シャント感染	2(1.2)	5(3.1)
Dermatophytosis of nail	爪の皮膚糸状菌症	2(1.2)	2(1.2)
Herpes zoster	帯状疱疹	2(1.2)	2(1.2)
Skin infection	皮膚感染	2(1.2)	1(0.6)
Infected dermal cyst	感染性皮膚嚢腫	2(1.2)	1(0.6)
Otitis media	中耳炎	2(1.2)	0(0.0)
Enteritis infectious	感染性腸炎	2(1.2)	0(0.0)
Oral herpes	口腔ヘルペス	1(0.6)	3(1.9)
Angular cheilitis	口角口唇炎	1(0.6)	2(1.2)
Chronic sinusitis	慢性副鼻腔炎	1(0.6)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Pyelonephritis	腎盂腎炎	1(0.6)	1(0.6)
Cellulitis	蜂巣炎	1(0.6)	0(0.0)
Dermatitis infected	感染性皮膚炎	1(0.6)	0(0.0)
Furuncle	せつ	1(0.6)	0(0.0)
Gastroenteritis viral	ウイルス性胃腸炎	1(0.6)	0(0.0)
Hydrocele male infected	感染性陰嚢水瘤	1(0.6)	0(0.0)
Osteomyelitis	骨髄炎	1(0.6)	0(0.0)
Otitis media chronic	慢性中耳炎	1(0.6)	0(0.0)
Paronychia	爪囲炎	1(0.6)	0(0.0)
Sinusitis	副鼻腔炎	1(0.6)	0(0.0)
Hepatic cyst infection	肝嚢胞感染	1(0.6)	0(0.0)
Upper respiratory tract infection bacterial	細菌性上気道感染	1(0.6)	0(0.0)
Bacterial infection	細菌感染	1(0.6)	0(0.0)
Device related infection	医療機器関連感染	1(0.6)	0(0.0)
Folliculitis	毛包炎	0(0.0)	2(1.2)
Gingivitis	歯肉炎	0(0.0)	2(1.2)
Pericoronitis	歯冠周囲炎	0(0.0)	2(1.2)
Catheter site infection	カテーテル留置部位感染	0(0.0)	2(1.2)
Vessel puncture site infection	血管穿刺部位感染	0(0.0)	2(1.2)
Acute sinusitis	急性副鼻腔炎	0(0.0)	1(0.6)
Chronic tonsillitis	慢性扁桃炎	0(0.0)	1(0.6)
Diverticulitis	憩室炎	0(0.0)	1(0.6)
Otitis media acute	急性中耳炎	0(0.0)	1(0.6)
Peritonitis	腹膜炎	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Pulpitis dental	歯髄炎	0(0.0)	1(0.6)
Rash pustular	膿疱性皮疹	0(0.0)	1(0.6)
Subcutaneous abscess	皮下組織膿瘍	0(0.0)	1(0.6)
Tinea cruris	股部白癬	0(0.0)	1(0.6)
Urinary tract infection	尿路感染	0(0.0)	1(0.6)
Urinary tract infection fungal	真菌性尿路感染	0(0.0)	1(0.6)
Gingival abscess	歯肉膿瘍	0(0.0)	1(0.6)
Skin bacterial infection	皮膚細菌感染	0(0.0)	1(0.6)
Abdominal infection	腹部感染	0(0.0)	1(0.6)
Staphylococcal infection	ブドウ球菌感染	0(0.0)	1(0.6)
Pneumonia bacterial	細菌性肺炎	0(0.0)	1(0.6)
Purulence	化膿	0(0.0)	1(0.6)
Mycotic endophthalmitis	真菌性眼内炎	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	7(4.3)	9(5.6)
Breast cancer	乳癌	1(0.6)	1(0.6)
Gastric cancer	胃癌	1(0.6)	1(0.6)
Seborrhoeic keratosis	脂漏性角化症	1(0.6)	1(0.6)
Cholesteatoma	真珠腫	1(0.6)	0(0.0)
Laryngeal papilloma	喉頭乳頭腫	1(0.6)	0(0.0)
Squamous cell carcinoma of skin	皮膚有棘細胞癌	1(0.6)	0(0.0)
Uterine leiomyoma	子宮平滑筋腫	1(0.6)	0(0.0)
Pyogenic granuloma	化膿性肉芽腫	0(0.0)	1(0.6)
Thymoma	胸腺腫	0(0.0)	1(0.6)
Prostate cancer	前立腺癌	0(0.0)	1(0.6)
Pancreatic neoplasm	膵新生物	0(0.0)	1(0.6)
Urethral neoplasm	尿道新生物	0(0.0)	1(0.6)
Renal cell carcinoma	腎細胞癌	0(0.0)	1(0.6)
Gastrointestinal submucosal tumour	消化管粘膜下腫瘍	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Blood and lymphatic system disorders	血液およびリンパ系障害	9(5.6)	2(1.2)
Anaemia	貧血	2(1.2)	0(0.0)
Anaemia macrocytic	大球性貧血	1(0.6)	0(0.0)
Eosinophilia	好酸球増加症	1(0.6)	0(0.0)
Lymphadenitis	リンパ節炎	1(0.6)	0(0.0)
Lymphadenopathy	リンパ節症	1(0.6)	0(0.0)
Polycythaemia	赤血球増加症	1(0.6)	0(0.0)
Haemorrhagic anaemia	出血性貧血	1(0.6)	0(0.0)
Nephrogenic anaemia	腎性貧血	1(0.6)	0(0.0)
Aplastic anaemia	再生不良性貧血	0(0.0)	1(0.6)
Iron deficiency anaemia	鉄欠乏性貧血	0(0.0)	1(0.6)
Immune system disorders	免疫系障害	4(2.5)	14(8.7)
Seasonal allergy	季節性アレルギー	4(2.5)	12(7.5)
Drug hypersensitivity	薬物過敏症	0(0.0)	1(0.6)
Dialysis amyloidosis	透析アミロイドーシス	0(0.0)	1(0.6)
Endocrine disorders	内分泌障害	3(1.9)	4(2.5)
Hyperparathyroidism secondary	続発性副甲状腺機能亢進症	2(1.2)	2(1.2)
Hypothyroidism	甲状腺機能低下症	1(0.6)	2(1.2)
Goitre	甲状腺腫	0(0.0)	1(0.6)
Hyperparathyroidism	副甲状腺機能亢進症	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6848(N=162) n (%)	darbepoetin(N=161) n (%)
Metabolism and nutrition disorders	代謝および栄養障害	19(11.7)	21(13.0)
Decreased appetite	食欲減退	9(5.6)	4(2.5)
Hypocarnitinaemia	低カルニチン血症	4(2.5)	2(1.2)
Hyperphosphataemia	高リン酸塩血症	2(1.2)	2(1.2)
Hypoglycaemia	低血糖	1(0.6)	2(1.2)
Hypercalcaemia	高カルシウム血症	1(0.6)	1(0.6)
Hyperkalaemia	高カリウム血症	1(0.6)	1(0.6)
Hypoalbuminaemia	低アルブミン血症	1(0.6)	1(0.6)
Dyslipidaemia	脂質異常症	1(0.6)	0(0.0)
Zinc deficiency	亜鉛欠乏	0(0.0)	3(1.9)
Type 2 diabetes mellitus	2型糖尿病	0(0.0)	2(1.2)
Dehydration	脱水	0(0.0)	1(0.6)
Diabetes mellitus inadequate control	コントロール不良の糖尿病	0(0.0)	1(0.6)
Hyperuricaemia	高尿酸血症	0(0.0)	1(0.6)
Hypophosphataemia	低リン酸血症	0(0.0)	1(0.6)
Psychiatric disorders	精神障害	7(4.3)	7(4.3)
Insomnia	不眠症	6(3.7)	6(3.7)
Depression	うつ病	1(0.6)	0(0.0)
Abnormal behaviour	異常行動	1(0.6)	0(0.0)
Sleep disorder	睡眠障害	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Nervous system disorders	神経系障害	36(22.2)	24(14.9)
Headache	頭痛	13(8.0)	5(3.1)
Dizziness	浮動性めまい	8(4.9)	5(3.1)
Carpal tunnel syndrome	手根管症候群	2(1.2)	0(0.0)
Facial paralysis	顔面麻痺	2(1.2)	0(0.0)
Cerebral infarction	脳梗塞	1(0.6)	5(3.1)
Carotid artery stenosis	頸動脈狭窄	1(0.6)	1(0.6)
Cerebellar infarction	小脳梗塞	1(0.6)	1(0.6)
Neuralgia	神経痛	1(0.6)	1(0.6)
Dizziness postural	体位性めまい	1(0.6)	0(0.0)
Hypoaesthesia	感覚鈍麻	1(0.6)	0(0.0)
Intracranial aneurysm	頭蓋内動脈瘤	1(0.6)	0(0.0)
Myelopathy	脊髄症	1(0.6)	0(0.0)
Myoclonus	ミオクローヌス	1(0.6)	0(0.0)
Sciatica	坐骨神経痛	1(0.6)	0(0.0)
Somnolence	傾眠	1(0.6)	0(0.0)
Tremor	振戦	1(0.6)	0(0.0)
Intercostal neuralgia	肋間神経痛	1(0.6)	0(0.0)
Cervical radiculopathy	頸髄神経根障害	1(0.6)	0(0.0)
Lacunar infarction	ラクナ梗塞	1(0.6)	0(0.0)
Restless legs syndrome	下肢静止不能症候群	1(0.6)	0(0.0)
Thrombotic cerebral infarction	血栓性脳梗塞	1(0.6)	0(0.0)
Loss of consciousness	意識消失	0(0.0)	2(1.2)
Trigeminal neuralgia	三叉神経痛	0(0.0)	2(1.2)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Cervicobrachial syndrome	頚腕症候群	0 (0.0)	1 (0.6)
Dysgeusia	味覚異常	0 (0.0)	1 (0.6)
Head discomfort	頭部不快感	0 (0.0)	1 (0.6)
Seizure	痙攣発作	0 (0.0)	1 (0.6)
Tension headache	緊張性頭痛	0 (0.0)	1 (0.6)
Vocal cord paralysis	声帯麻痺	0 (0.0)	1 (0.6)
Cervicogenic headache	頚原性頭痛	0 (0.0)	1 (0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Eye disorders	眼障害	35(21.6)	35(21.7)
Retinal haemorrhage	網膜出血	16(9.9)	10(6.2)
Conjunctival haemorrhage	結膜出血	4(2.5)	3(1.9)
Diabetic retinopathy	糖尿病網膜症	2(1.2)	1(0.6)
Dry eye	眼乾燥	2(1.2)	1(0.6)
Cataract	白内障	1(0.6)	3(1.9)
Conjunctivitis allergic	アレルギー性結膜炎	1(0.6)	3(1.9)
Macular oedema	黄斑浮腫	1(0.6)	3(1.9)
Blepharitis	眼瞼炎	1(0.6)	2(1.2)
Glaucoma	緑内障	1(0.6)	1(0.6)
Ocular hyperaemia	眼充血	1(0.6)	1(0.6)
Optic disc haemorrhage	視神経乳頭出血	1(0.6)	1(0.6)
Eye pruritus	眼そう痒症	1(0.6)	1(0.6)
Diplopia	複視	1(0.6)	0(0.0)
Keratitis	角膜炎	1(0.6)	0(0.0)
Punctate keratitis	点状角膜炎	1(0.6)	0(0.0)
Retinal oedema	網膜浮腫	1(0.6)	0(0.0)
Retinal vein occlusion	網膜静脈閉塞	1(0.6)	0(0.0)
Trichiasis	睫毛乱生	1(0.6)	0(0.0)
Vitreous floaters	硝子体浮遊物	1(0.6)	0(0.0)
Cystoid macular oedema	嚢胞様黄斑浮腫	1(0.6)	0(0.0)
Chorioretinopathy	網脈絡膜症	1(0.6)	0(0.0)
Eyelid haematoma	眼瞼血腫	1(0.6)	0(0.0)
Chalazion	霰粒腫	0(0.0)	1(0.6)

表 2.7.6.26－124　有害事象（安全性解析対象集団）（続き）

System Organ Class Preferred Term (MedDRA)	System Organ Class Preferred Term (MedDRA/J)	MT-6548(N=162) n (%)	darbepoetin(N=161) n (%)
Eye discharge	眼脂	0(0.0)	1(0.6)
Eyelid oedema	眼瞼浮腫	0(0.0)	1(0.6)
Posterior capsule opacification	後嚢部混濁	0(0.0)	1(0.6)
Retinal detachment	網膜剥離	0(0.0)	1(0.6)
Retinal vascular disorder	網膜血管障害	0(0.0)	1(0.6)
Vitreous detachment	硝子体剥離	0(0.0)	1(0.6)
Vitreous haemorrhage	硝子体出血	0(0.0)	1(0.6)
Conjunctival hyperaemia	結膜充血	0(0.0)	1(0.6)
Retinal aneurysm	網膜血管瘤	0(0.0)	1(0.6)
Age-related macular degeneration	加齢黄斑変性	0(0.0)	1(0.6)
Ear and labyrinth disorders	耳および迷路障害	8(4.9)	6(3.7)
Vertigo	回転性めまい	5(3.1)	2(1.2)
Vertigo positional	頭位性回転性めまい	1(0.6)	1(0.6)
Deafness	難聴	1(0.6)	0(0.0)
Sudden hearing loss	突発性難聴	1(0.6)	0(0.0)
Eustachian tube stenosis	耳管狭窄	1(0.6)	0(0.0)
Tinnitus	耳鳴	0(0.0)	2(1.2)
Ear pruritus	耳そう痒症	0(0.0)	1(0.6)