表 2.7.6.25－60　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	151	54.5 (16.8)	-4.4	0.7	(-5.7, -3.1)		151	-7.9	1.2	(-10.2, -5.6)	
	Week 4	149	54.2 (16.7)	-4.4	0.7	(-5.7, -3.1)		149	-7.6	1.2	(-9.9, -5.3)	
	Week 6	148	54.3 (16.7)	-5.3	0.7	(-6.6, -4.0)		148	-9.3	1.2	(-11.6, -7.0)	
	Week 8	145	54.3 (16.8)	-5.2	0.7	(-6.5, -3.9)		145	-8.4	1.2	(-10.7, -6.1)	
	Week 10	145	53.9 (16.6)	-5.1	0.7	(-6.4, -3.8)		145	-7.8	1.2	(-10.1, -5.5)	
	Week 12	145	53.9 (16.5)	-4.8	0.7	(-6.1, -3.5)		145	-7.3	1.2	(-9.6, -5.0)	
	Week 16	143	54.1 (16.5)	-4.5	0.7	(-5.8, -3.2)		143	-6.1	1.2	(-8.4, -3.8)	
	Week 20	139	54.1 (15.7)	-2.8	0.7	(-4.1, -1.5)		139	-3.6	1.2	(-5.9, -1.3)	
	Week 24	132	54.4 (15.5)	-1.6	0.7	(-2.9, -0.2)		132	-1.1	1.2	(-3.5, 1.2)	
darbepoetin												
	Week 2	153	56.4 (18.7)	-0.6	0.7	(-1.9, 0.7)		153	-0.7	1.2	(-3.0, 1.5)	
	Week 4	152	56.5 (18.7)	-0.7	0.7	(-2.0, 0.5)		152	-1.0	1.2	(-3.3, 1.3)	
	Week 6	152	56.5 (18.7)	-0.7	0.7	(-2.0, 0.6)		152	-0.6	1.2	(-2.9, 1.6)	
	Week 8	151	56.6 (18.8)	-0.6	0.7	(-1.9, 0.7)		151	-0.1	1.2	(-2.3, 2.2)	
	Week 10	150	56.7 (18.8)	-0.2	0.7	(-1.5, 1.1)		150	0.8	1.2	(-1.5, 3.1)	
	Week 12	148	56.6 (18.8)	0.3	0.7	(-1.0, 1.6)		148	1.9	1.2	(-0.4, 4.1)	
	Week 16	148	56.6 (18.7)	0.2	0.7	(-1.1, 1.5)		148	2.0	1.2	(-0.3, 4.3)	
	Week 20	144	55.8 (16.7)	1.9	0.7	(0.6, 3.2)		144	4.9	1.2	(2.5, 7.2)	
	Week 24	140	56.4 (18.9)	3.4	0.7	(2.1, 4.7)		140	7.7	1.2	(5.3, 10.0)	
Difference MT-6548 - darbepoetin												
	Week 2			-3.8	0.9	(-5.6, -2.0)	<0.001		-7.2	1.6	(-10.4, -4.0)	<0.001
	Week 4			-3.6	0.9	(-5.5, -1.8)	<0.001		-6.6	1.6	(-9.8, -3.4)	<0.001
	Week 6			-4.6	0.9	(-6.4, -2.8)	<0.001		-8.7	1.6	(-11.9, -5.5)	<0.001
	Week 8			-4.7	0.9	(-6.5, -2.8)	<0.001		-8.3	1.6	(-11.6, -5.1)	<0.001
	Week 10			-4.9	0.9	(-6.7, -3.1)	<0.001		-8.6	1.6	(-11.9, -5.4)	<0.001
	Week 12			-5.1	0.9	(-6.9, -3.2)	<0.001		-9.2	1.7	(-12.4, -5.9)	<0.001
	Week 16			-4.7	0.9	(-6.5, -2.9)	<0.001		-8.1	1.7	(-11.3, -4.8)	<0.001
	Week 20			-4.7	0.9	(-6.6, -2.9)	<0.001		-8.5	1.7	(-11.7, -5.2)	<0.001
	Week 24			-4.9	1.0	(-6.8, -3.1)	<0.001		-8.8	1.7	(-12.1, -5.5)	<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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_3_14.sas

5.3.5.1—6 表 11.4.1—20 より引用

表 2.7.6.25－61　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	151	2.00 (0.82)	0.16	0.04	(0.09, 0.23)		151	8.93	1.77	(5.45, 12.41)	
	Week 4	149	2.01 (0.82)	0.12	0.04	(0.05, 0.19)		149	6.58	1.78	(3.08, 10.08)	
	Week 6	148	2.01 (0.82)	0.12	0.04	(0.05, 0.19)		148	7.90	1.79	(4.39, 11.40)	
	Week 8	145	2.00 (0.82)	0.15	0.04	(0.08, 0.22)		145	10.23	1.80	(6.70, 13.76)	
	Week 10	145	2.02 (0.83)	0.15	0.04	(0.08, 0.22)		145	10.07	1.80	(6.55, 13.60)	
	Week 12	145	2.02 (0.83)	0.16	0.04	(0.09, 0.23)		145	10.93	1.80	(7.40, 14.46)	
	Week 16	143	2.01 (0.83)	0.17	0.04	(0.10, 0.24)		143	11.21	1.80	(7.67, 14.75)	
	Week 20	139	2.01 (0.81)	0.10	0.04	(0.03, 0.17)		139	7.24	1.82	(3.68, 10.81)	
	Week 24	132	2.00 (0.82)	0.07	0.04	(0.00, 0.15)		132	6.22	1.84	(2.61, 9.83)	
darbepoetin												
	Week 2	153	1.83 (0.74)	0.02	0.03	(-0.05, 0.09)		153	1.82	1.76	(-1.64, 5.28)	
	Week 4	152	1.83 (0.74)	0.00	0.03	(-0.06, 0.07)		152	0.92	1.77	(-2.54, 4.39)	
	Week 6	152	1.83 (0.74)	0.01	0.03	(-0.05, 0.08)		152	1.86	1.77	(-1.60, 5.33)	
	Week 8	151	1.83 (0.75)	-0.02	0.03	(-0.09, 0.05)		151	0.77	1.77	(-2.71, 4.24)	
	Week 10	150	1.81 (0.73)	-0.01	0.03	(-0.08, 0.06)		150	0.97	1.77	(-2.52, 4.45)	
	Week 12	148	1.81 (0.73)	-0.02	0.04	(-0.09, 0.05)		148	0.01	1.78	(-3.48, 3.50)	
	Week 16	148	1.82 (0.73)	-0.04	0.04	(-0.11, 0.03)		148	0.31	1.78	(-3.18, 3.80)	
	Week 20	144	1.81 (0.72)	-0.03	0.04	(-0.10, 0.04)		144	0.60	1.79	(-2.92, 4.12)	
	Week 24	140	1.82 (0.73)	-0.08	0.04	(-0.15, -0.01)		140	-2.54	1.80	(-6.08, 1.00)	
Difference MT-6548 - darbepoetin												
	Week 2			0.14	0.05	(0.04, 0.24)	0.005		7.11	2.50	(2.19, 12.02)	0.005
	Week 4			0.12	0.05	(0.02, 0.21)	0.020		5.66	2.51	(0.72, 10.59)	0.025
	Week 6			0.10	0.05	(0.01, 0.20)	0.036		6.03	2.51	(1.10, 10.97)	0.017
	Week 8			0.17	0.05	(0.07, 0.27)	<0.001		9.46	2.52	(4.51, 14.42)	<0.001
	Week 10			0.16	0.05	(0.06, 0.25)	0.002		9.11	2.53	(4.15, 14.07)	<0.001
	Week 12			0.18	0.05	(0.09, 0.28)	<0.001		10.92	2.53	(5.95, 15.88)	<0.001
	Week 16			0.21	0.05	(0.11, 0.31)	<0.001		10.90	2.53	(5.93, 15.88)	<0.001
	Week 20			0.13	0.05	(0.03, 0.22)	0.013		6.64	2.55	(1.63, 11.66)	0.009
	Week 24			0.15	0.05	(0.05, 0.25)	0.003		8.76	2.58	(3.70, 13.82)	<0.001

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_3_15.sas

5.3.5.1—6 表 11.4.1—21 より引用

表 2.7.6.25－62　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	151	142.4 (78.3)	23.0	5.4	(12.4, 33.6)		151	23.5	3.5	(16.6, 30.3)	
	Week 4	149	142.9 (78.7)	17.0	5.4	(6.3, 27.6)		149	17.2	3.5	(10.2, 24.1)	
	Week 6	148	142.8 (78.9)	26.8	5.4	(16.1, 37.5)		148	24.4	3.5	(17.5, 31.4)	
	Week 8	145	142.2 (79.6)	28.7	5.5	(17.9, 39.4)		145	25.8	3.6	(18.8, 32.8)	
	Week 10	145	141.7 (79.2)	25.7	5.5	(15.0, 36.5)		145	25.2	3.6	(18.3, 32.2)	
	Week 12	145	142.6 (79.6)	22.5	5.5	(11.7, 33.3)		145	22.2	3.6	(15.2, 29.2)	
	Week 16	143	142.5 (79.9)	30.4	5.5	(19.5, 41.2)		143	31.1	3.6	(24.1, 38.1)	
	Week 20	139	143.6 (80.7)	19.3	5.6	(8.4, 30.2)		139	21.3	3.6	(14.2, 28.4)	
	Week 24	132	143.4 (82.1)	27.0	5.7	(15.9, 38.1)		132	25.1	3.7	(17.9, 32.3)	
darbepoetin												
	Week 2	153	143.2 (81.5)	-0.6	5.4	(-11.2, 9.9)		153	6.2	3.5	(-0.6, 13.1)	
	Week 4	152	143.0 (81.7)	-4.8	5.4	(-15.4, 5.7)		152	3.3	3.5	(-3.6, 10.1)	
	Week 6	152	143.0 (81.7)	-1.2	5.4	(-11.7, 9.4)		152	2.8	3.5	(-4.1, 9.6)	
	Week 8	151	143.4 (81.8)	5.1	5.4	(-5.5, 15.7)		151	9.5	3.5	(2.7, 16.4)	
	Week 10	150	140.0 (73.8)	-0.5	5.4	(-11.1, 10.1)		150	3.5	3.5	(-3.4, 10.4)	
	Week 12	148	143.7 (82.6)	-5.8	5.4	(-16.5, 4.9)		148	3.4	3.5	(-3.6, 10.3)	
	Week 16	148	143.7 (82.6)	2.1	5.4	(-8.5, 12.8)		148	8.3	3.5	(1.4, 15.2)	
	Week 20	144	141.2 (73.9)	0.4	5.5	(-10.4, 11.2)		144	7.7	3.6	(0.7, 14.7)	
	Week 24	140	142.2 (74.3)	-0.9	5.5	(-11.8, 9.9)		140	4.9	3.6	(-2.2, 11.9)	
Difference MT-6548 - darbepoetin												
	Week 2			23.6	7.6	(8.7, 38.6)	0.002		17.2	4.9	(7.5, 26.9)	<0.001
	Week 4			21.8	7.6	(6.8, 36.8)	0.004		13.9	5.0	(4.2, 23.7)	0.005
	Week 6			28.0	7.6	(12.9, 43.0)	<0.001		21.6	5.0	(11.9, 31.4)	<0.001
	Week 8			23.6	7.7	(8.5, 38.7)	0.002		16.2	5.0	(6.4, 26.0)	0.001
	Week 10			26.2	7.7	(11.1, 41.3)	<0.001		21.7	5.0	(11.9, 31.6)	<0.001
	Week 12			28.3	7.7	(13.2, 43.5)	<0.001		18.9	5.0	(9.0, 28.7)	<0.001
	Week 16			28.2	7.7	(13.0, 43.4)	<0.001		22.8	5.0	(12.9, 32.6)	<0.001
	Week 20			18.9	7.8	(3.6, 34.3)	0.016		13.6	5.1	(3.7, 23.6)	0.007
	Week 24			27.9	7.9	(12.4, 43.5)	<0.001		20.3	5.1	(10.2, 30.3)	<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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_3_16.sas

5.3.5.1—6 表 11.4.1—22 より引用

(13)　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 2.7.6.25－63 に示した．随時血糖は，全集団を対象に記載した．

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 -9.3 mg/dL 及び -14.7～ -3.8 mg/dL，darbepoetin 群で -4.6 mg/dL 及び -9.9～0.7 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，-4.7 mg/dL 及び -12.3～2.9 mg/dL であり，統計学的に有意な差が認められなかった（p = 0.228）．

表 2.7.6.25－63　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	151	120.2 (38.9)	-3.8	2.7	(-9.1, 1.4)	
	Week 4	149	120.3 (39.1)	-1.7	2.7	(-7.0, 3.5)	
	Week 6	148	120.5 (39.2)	-1.8	2.7	(-7.1, 3.4)	
	Week 8	145	120.2 (39.1)	-1.5	2.7	(-6.8, 3.8)	
	Week 10	145	120.3 (39.2)	-1.4	2.7	(-6.7, 3.9)	
	Week 12	145	120.8 (39.4)	1.2	2.7	(-4.1, 6.5)	
	Week 16	143	121.0 (39.5)	-1.2	2.7	(-6.5, 4.1)	
	Week 20	139	120.8 (40.0)	-1.2	2.7	(-6.5, 4.2)	
	Week 24	132	119.0 (38.0)	-9.3	2.8	(-14.7, -3.8)	
darbepoetin	Week 2	153	122.0 (33.2)	-0.6	2.6	(-5.8, 4.6)	
	Week 4	152	121.9 (33.3)	2.8	2.7	(-2.4, 8.0)	
	Week 6	152	121.9 (33.3)	3.1	2.7	(-2.2, 8.3)	
	Week 8	151	122.0 (33.4)	7.2	2.7	(2.0, 12.5)	
	Week 10	150	122.0 (33.5)	4.4	2.7	(-0.8, 9.6)	
	Week 12	148	121.4 (32.8)	3.7	2.7	(-1.5, 9.0)	
	Week 16	148	121.0 (32.3)	5.3	2.7	(0.1, 10.6)	
	Week 20	144	121.5 (32.5)	2.6	2.7	(-2.7, 7.9)	
	Week 24	140	121.5 (32.9)	-4.6	2.7	(-9.9, 0.7)	
Difference MT-6548 - darbepoetin	Week 2			-3.2	3.8	(-10.6, 4.1)	0.389
	Week 4			-4.5	3.8	(-11.9, 2.8)	0.228
	Week 6			-4.9	3.8	(-12.3, 2.5)	0.196
	Week 8			-8.7	3.8	(-16.1, -1.3)	0.022
	Week 10			-5.8	3.8	(-13.3, 1.6)	0.124
	Week 12			-2.5	3.8	(-10.0, 4.9)	0.506
	Week 16			-6.6	3.8	(-14.0, 0.9)	0.085
	Week 20			-3.8	3.8	(-11.3, 3.7)	0.321
	Week 24			-4.7	3.9	(-12.3, 2.9)	0.228

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_3.sas

5.3.5.1—6 表 11.4.1—23 より引用

(14)　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 2.7.6.25－64 及び表 2.7.6.25－65 に示した．血圧は全集団を対象に記載した．

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 0.8 mmHg 及び -1.6～3.3 mmHg，darbepoetin 群で 1.6 mmHg 及び -0.7～4.0 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 群の差の LSMean 及びその 95%CI は，-0.8 mmHg 及び -4.2～2.6 mmHg であり，統計学的に有意な差が認められなかった（p = 0.641）．

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 0.1 mmHg 及び -1.4～1.6 mmHg，darbepoetin 群で 1.4 mmHg 及び -0.1～2.8 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，-1.3 mmHg 及び -3.4～0.8 mmHg であり，統計学的に有意な差が認められなかった（p = 0.228）．

表 2.7.6.25－64　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	151	132.6 (15.6)	-3.8	1.2	(-6.1, -1.4)	
	Week 4	149	132.8 (15.6)	-3.2	1.2	(-5.6, -0.9)	
	Week 6	148	132.9 (15.6)	-5.1	1.2	(-7.4, -2.7)	
	Week 8	145	133.0 (15.6)	-3.8	1.2	(-6.1, -1.4)	
	Week 10	145	133.0 (15.5)	-4.3	1.2	(-6.7, -2.0)	
	Week 12	145	133.2 (15.6)	-3.8	1.2	(-6.2, -1.5)	
	Week 16	143	133.0 (15.6)	-3.1	1.2	(-5.4, -0.7)	
	Week 20	139	132.9 (15.4)	-1.6	1.2	(-3.9, 0.8)	
	Week 24	132	133.2 (14.8)	0.8	1.2	(-1.6, 3.3)	
darbepoetin	Week 2	153	133.3 (17.9)	-0.6	1.2	(-2.9, 1.7)	
	Week 4	152	133.0 (17.7)	0.0	1.2	(-2.3, 2.3)	
	Week 6	152	133.0 (17.7)	-2.7	1.2	(-5.0, -0.4)	
	Week 8	151	133.0 (17.7)	-0.2	1.2	(-2.6, 2.1)	
	Week 10	150	132.9 (17.4)	-0.8	1.2	(-3.1, 1.5)	
	Week 12	148	133.0 (17.3)	-1.7	1.2	(-4.1, 0.6)	
	Week 16	148	132.6 (17.5)	-0.1	1.2	(-2.4, 2.3)	
	Week 20	145	132.5 (17.5)	0.1	1.2	(-2.3, 2.4)	
	Week 24	140	132.4 (17.7)	1.6	1.2	(-0.7, 4.0)	
Difference MT-6548 - darbepoetin	Week 2			-3.2	1.7	(-6.4, 0.1)	0.057
	Week 4			-3.2	1.7	(-6.5, 0.1)	0.054
	Week 6			-2.4	1.7	(-5.7, 0.9)	0.154
	Week 8			-3.5	1.7	(-6.8, -0.2)	0.037
	Week 10			-3.5	1.7	(-6.8, -0.2)	0.036
	Week 12			-2.1	1.7	(-5.4, 1.2)	0.215
	Week 16			-3.0	1.7	(-6.3, 0.3)	0.076
	Week 20			-1.6	1.7	(-5.0, 1.7)	0.340
	Week 24			-0.8	1.7	(-4.2, 2.6)	0.641

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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—6 表 11.4.1—24 より引用

表 2.7.6.25－65　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	151	71.0 (11.2)	-2.1	0.7	(-3.6, -0.7)	
	Week 4	149	71.0 (11.3)	-2.0	0.7	(-3.5, -0.6)	
	Week 6	148	71.1 (11.3)	-2.5	0.7	(-3.9, -1.0)	
	Week 8	145	71.1 (11.4)	-2.9	0.7	(-4.4, -1.5)	
	Week 10	145	71.1 (11.4)	-1.9	0.7	(-3.4, -0.5)	
	Week 12	145	71.1 (11.4)	-1.8	0.7	(-3.2, -0.3)	
	Week 16	143	71.1 (11.4)	-1.3	0.7	(-2.7, 0.2)	
	Week 20	139	71.2 (11.4)	-0.5	0.7	(-1.9, 1.0)	
	Week 24	132	71.5 (11.4)	0.1	0.8	(-1.4, 1.6)	
darbepoetin	Week 2	153	71.1 (11.4)	-0.3	0.7	(-1.7, 1.1)	
	Week 4	152	70.9 (11.3)	-0.8	0.7	(-2.2, 0.7)	
	Week 6	152	70.9 (11.3)	-0.1	0.7	(-1.5, 1.3)	
	Week 8	151	70.9 (11.3)	1.1	0.7	(-0.3, 2.5)	
	Week 10	150	70.8 (11.3)	2.4	0.7	(1.0, 3.8)	
	Week 12	148	70.9 (11.3)	1.2	0.7	(-0.3, 2.6)	
	Week 16	148	70.8 (11.3)	1.0	0.7	(-0.5, 2.4)	
	Week 20	145	70.7 (11.4)	1.1	0.7	(-0.3, 2.6)	
	Week 24	140	70.7 (11.4)	1.4	0.7	(-0.1, 2.8)	
Difference MT-6548 - darbepoetin	Week 2			-1.9	1.0	(-3.9, 0.1)	0.069
	Week 4			-1.3	1.0	(-3.3, 0.7)	0.210
	Week 6			-2.3	1.0	(-4.4, -0.3)	0.022
	Week 8			-4.1	1.0	(-6.1, -2.0)	<0.001
	Week 10			-4.3	1.0	(-6.4, -2.3)	<0.001
	Week 12			-2.9	1.0	(-5.0, -0.9)	0.004
	Week 16			-2.2	1.0	(-4.3, -0.2)	0.032
	Week 20			-1.6	1.0	(-3.7, 0.4)	0.123
	Week 24			-1.3	1.1	(-3.4, 0.8)	0.228

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_2.sas

5.3.5.1—6 表 11.4.1—25 より引用

(15)　腎機能関連評価項目

MMRM を用いた eGFR，血清クレアチニン及び尿中アルブミン／クレアチニン比のベースラインからの変化量の推移を表 2.7.6.25－66，表 2.7.6.25－67 及び表 2.7.6.25－68 に示した．また，24 週後に eGFR がベースラインから 30%以上減少した被験者の割合を表 2.7.6.25－69，24 週後に eGFR がベースラインから 40%以上減少した被験者の割合を表 2.7.6.25－70，24 週後に血清クレアチニンがベースラインから 2 倍以上になった被験者の割合を表 2.7.6.25－71 に示した．腎機能関連評価項目は，全集団を対象に記載した．

MMRM を用いた eGFR 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 -1.46 mL/min/1.73m^2 及び -2.03～ -0.89 mL/min/1.73m^2，darbepoetin 群で -0.91 mL/min/1.73m^2 及び -1.47～ -0.35 mL/min/1.73m^2 であった．MMRM を用いた eGFR 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，-0.55 mL/min/1.73m^2 及び -1.35～0.25 mL/min/1.73m^2 であり，統計学的に有意な差が認められなかった（p = 0.175）．

MMRM を用いた血清クレアチニンの 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 0.292 mg/dL 及び 0.210～0.374 mg/dL，darbepoetin 群で 0.343 mg/dL 及び 0.263～0.424 mg/dL であった．MMRM を用いた血清クレアチニンの 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，-0.051 mg/dL 及び -0.167～0.064 mg/dL であり，統計学的に有意な差が認められなかった（p = 0.382）．

MMRM を用いた尿中アルブミン／クレアチニン比の 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 265.47 mg/g Cr 及び 129.44～401.51 mg/g Cr ，darbepoetin 群で 316.24 mg/g Cr 及び 183.37～449.12 mg/g Cr であった．MMRM を用いた尿中アルブミン／クレアチニン比の 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，-50.77 mg/g Cr 及び -240.87～139.33 mg/g Cr であり，統計学的に有意な差が認められなかった（p = 0.600）．

24 週後に eGFR がベースラインから 30%以上減少した被験者の割合は，MT-6548 群で 3.8%，darbepoetin 群で 7.9%であった．24 週後に eGFR がベースラインから 30%以上減少した被験者の MT-6548 群と darbepoetin 群の差及びその 95%CI は，-4.1%及び -15.9%～7.9%であり，統計学的に有意な差が認められなかった（p = 0.200）．

24 週後に eGFR がベースラインから 40%以上減少した被験者の割合は，MT-6548 群で 1.5%，darbepoetin 群で 2.1%であった．24 週後に eGFR がベースラインから 40%以上減少した被験者の MT-6548 群と darbepoetin 群の差及びその 95%CI は，-0.6%及び -12.5%～11.3%であり，統計学的に有意な差が認められなかった（p = 1.000）．

表 2.7.6.25－66　eGFR 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	151	21.28 (11.66)	-1.36	0.28	(-1.91, -0.80)		151	-5.13	1.19	(-7.47, -2.79)	
	Week 4	149	21.22 (11.60)	-0.68	0.28	(-1.24, -0.12)		149	-2.82	1.20	(-5.17, -0.47)	
	Week 6	148	21.28 (11.63)	-1.24	0.28	(-1.80, -0.68)		148	-4.53	1.20	(-6.88, -2.17)	
	Week 8	145	21.34 (11.59)	-1.33	0.28	(-1.89, -0.77)		145	-5.22	1.20	(-7.59, -2.86)	
	Week 10	145	21.25 (11.63)	-1.48	0.29	(-2.04, -0.92)		145	-5.47	1.20	(-7.83, -3.10)	
	Week 12	145	21.25 (11.63)	-1.43	0.28	(-1.99, -0.87)		145	-5.15	1.20	(-7.52, -2.79)	
	Week 16	143	21.35 (11.68)	-1.60	0.29	(-2.16, -1.04)		143	-6.97	1.21	(-9.35, -4.60)	
	Week 20	139	21.67 (11.67)	-1.47	0.29	(-2.03, -0.90)		139	-6.91	1.21	(-9.29, -4.52)	
	Week 24	132	21.96 (11.69)	-1.46	0.29	(-2.03, -0.89)		132	-7.04	1.23	(-9.45, -4.63)	
darbepoetin												
	Week 2	153	22.60 (11.60)	-0.07	0.28	(-0.62, 0.49)		153	0.04	1.18	(-2.29, 2.36)	
	Week 4	152	22.69 (11.58)	0.00	0.28	(-0.55, 0.55)		152	0.23	1.19	(-2.10, 2.56)	
	Week 6	152	22.69 (11.58)	-0.21	0.28	(-0.77, 0.34)		152	-0.50	1.19	(-2.83, 1.83)	
	Week 8	151	22.73 (11.61)	0.04	0.28	(-0.51, 0.60)		151	-0.41	1.19	(-2.74, 1.93)	
	Week 10	150	22.79 (11.63)	0.00	0.28	(-0.55, 0.55)		150	-1.11	1.19	(-3.44, 1.23)	
	Week 12	148	22.75 (11.44)	-0.37	0.28	(-0.92, 0.19)		148	-2.76	1.19	(-5.10, -0.41)	
	Week 16	148	22.68 (11.50)	-0.16	0.28	(-0.71, 0.40)		148	-2.87	1.19	(-5.21, -0.52)	
	Week 20	144	22.72 (11.62)	-0.50	0.28	(-1.06, 0.06)		144	-4.79	1.20	(-7.15, -2.43)	
	Week 24	140	23.16 (11.52)	-0.91	0.29	(-1.47, -0.35)		140	-6.32	1.21	(-8.69, -3.95)	
Difference MT-6548 - darbepoetin												
	Week 2			-1.29	0.40	(-2.07, -0.51)	0.001		-5.16	1.68	(-8.46, -1.86)	0.002
	Week 4			-0.68	0.40	(-1.46, 0.10)	0.088		-3.05	1.69	(-6.36, 0.26)	0.070
	Week 6			-1.03	0.40	(-1.81, -0.24)	0.010		-4.03	1.69	(-7.34, -0.72)	0.017
	Week 8			-1.38	0.40	(-2.16, -0.59)	<0.001		-4.81	1.69	(-8.13, -1.49)	0.005
	Week 10			-1.48	0.40	(-2.27, -0.70)	<0.001		-4.36	1.69	(-7.69, -1.04)	0.010
	Week 12			-1.06	0.40	(-1.85, -0.27)	0.009		-2.40	1.70	(-5.73, 0.93)	0.158
	Week 16			-1.44	0.40	(-2.23, -0.65)	<0.001		-4.11	1.70	(-7.44, -0.77)	0.016
	Week 20			-0.97	0.40	(-1.76, -0.17)	0.017		-2.12	1.71	(-5.47, 1.23)	0.215
	Week 24			-0.55	0.41	(-1.35, 0.25)	0.175		-0.72	1.72	(-4.10, 2.67)	0.677

Note(s): eGFR (mL/min/1.73m2).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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 16.2.6.2
Source: t_14_2_3_13_1_3.sas

5.3.5.1—6 表 14.2.3.13.1.3 より引用

表 2.7.6.25－67　血清クレアチニ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	151	2.830 (1.492)	0.139	0.040	(0.059, 0.218)	
	Week 4	149	2.839 (1.494)	0.095	0.041	(0.016, 0.175)	
	Week 6	148	2.833 (1.498)	0.121	0.041	(0.041, 0.201)	
	Week 8	145	2.820 (1.497)	0.150	0.041	(0.070, 0.230)	
	Week 10	145	2.837 (1.505)	0.153	0.041	(0.073, 0.233)	
	Week 12	145	2.841 (1.504)	0.141	0.041	(0.060, 0.221)	
	Week 16	143	2.830 (1.510)	0.247	0.041	(0.167, 0.328)	
	Week 20	139	2.780 (1.494)	0.292	0.041	(0.211, 0.373)	
	Week 24	132	2.723 (1.407)	0.292	0.042	(0.210, 0.374)	
darbepoetin	Week 2	153	2.616 (1.441)	0.025	0.040	(-0.053, 0.104)	
	Week 4	152	2.598 (1.428)	0.031	0.040	(-0.048, 0.110)	
	Week 6	152	2.598 (1.428)	0.046	0.040	(-0.033, 0.125)	
	Week 8	151	2.596 (1.432)	0.069	0.040	(-0.010, 0.148)	
	Week 10	150	2.590 (1.433)	0.110	0.040	(0.031, 0.189)	
	Week 12	148	2.577 (1.413)	0.164	0.041	(0.085, 0.244)	
	Week 16	148	2.582 (1.413)	0.226	0.041	(0.147, 0.306)	
	Week 20	144	2.583 (1.430)	0.297	0.041	(0.217, 0.377)	
	Week 24	140	2.497 (1.323)	0.343	0.041	(0.263, 0.424)	
Difference MT-6548 - darbepoetin	Week 2			0.113	0.057	(0.002, 0.225)	0.047
	Week 4			0.065	0.057	(-0.047, 0.177)	0.257
	Week 6			0.074	0.057	(-0.038, 0.187)	0.194
	Week 8			0.081	0.057	(-0.032, 0.193)	0.160
	Week 10			0.043	0.057	(-0.070, 0.156)	0.455
	Week 12			-0.024	0.058	(-0.137, 0.089)	0.681
	Week 16			0.021	0.058	(-0.092, 0.134)	0.718
	Week 20			-0.005	0.058	(-0.119, 0.109)	0.929
	Week 24			-0.051	0.059	(-0.167, 0.064)	0.382

Note(s): Serum Creatinine (mg/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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 16.2.6.2
Source: t_14_2_3_13_2_2.sas

5.3.5.1—6 表 14.2.3.13.2.2 より引用

表 2.7.6.25－68　尿中アルブミン／クレアチニン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 12	145	1018.25 (1236.06)	75.63	67.36	(-56.82, 208.07)		145	40.96	20.04	(1.53, 80.39)	
	Week 24	132	901.30 (1057.88)	265.47	69.20	(129.44, 401.51)		132	71.25	20.60	(30.74, 111.76)	
darbepoetin												
	Week 12	148	932.58 (1323.58)	123.20	66.48	(-7.51, 253.91)		148	54.68	19.78	(15.76, 93.60)	
	Week 24	140	877.61 (1298.36)	316.24	67.59	(183.37, 449.12)		140	83.78	20.12	(44.21, 123.34)	
Difference MT-6548 - darbepoetin												
	Week 12			-47.57	94.53	(-233.44, 138.30)	0.615		-13.72	28.13	(-69.06, 41.62)	0.626
	Week 24			-50.77	96.70	(-240.67, 139.33)	0.600		-12.53	28.79	(-69.14, 44.08)	0.664

Note(s): Urin Albumin/Creatinine Ratio (mg/g Cr).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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 16.2.6.4
Source: t_14_2_3_13_1_4.sas

5.3.5.1—6 表 14.2.3.13.1.4 より引用

表 2.7.6.25－69　24 週後に eGFR がベースラインから 30%以上減少した被験者の割合（FAS）

	MT-6548(N=151)			darbepoetin(N=153)			Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Week 24	132	5 (3.8)	(1.24, 8.62)	140	11 (7.9)	(3.99, 13.62)	-4.1	(-15.9, 7.9)	0.200

Note(s): N*: number of subjects at Week 24.
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 16.2.6.2
Source: t_14_2_3_13_3_1.sas

5.3.5.1—6 表 14.2.3.13.3.1 より引用

表 2.7.6.25－70　24 週後に eGFR がベースラインから 40%以上減少した被験者の割合（FAS）

	MT-6548(N=151)			darbepoetin(N=153)			Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Week 24	132	2 (1.5)	(0.18, 5.37)	140	3 (2.1)	(0.44, 6.13)	-0.6	(-12.5, 11.3)	1.000

Note(s): N*: number of subjects at Week 24.
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 16.2.6.2
Source: t_14_2_3_13_3_2.sas

5.3.5.1—6 表 14.2.3.13.3.2 より引用

表 2.7.6.25－71　24 週後に血清クレアチニンがベースラインから 2 倍以上になった被験者の割合（FAS）

	MT-6548(N=151)			darbepoetin(N=153)			Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Week 24	132	0 (0.0)	(0.00, 2.76)	140	0 (0.0)	(0.00, 2.60)	-	-	-

Note(s): N*: number of subjects at Week 24.
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 16.2.6.2
Source: t_14_2_3_13_3_3.sas

5.3.5.1—6 表 14.2.3.13.3.3 より引用

(16)　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 2.7.6.25－72, 赤血球輸血による救済治療を受けた被験者の割合を表 2.7.6.25－73, 瀉血による救済治療を受けた被験者の割合を表 2.7.6.25－74 に示した．救済治療は，全集団を対象に記載した．

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 1.3%，darbepoetin 群では認められなかった．治療期間 I 期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 群で認められず，darbepoetin 群で 0.7%であった．治療期間 I 期中に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，赤血球輸血又は瀉血による救済治療を受けた被験者は認められなかった．

表 2.7.6.25－72　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=151) N*	MT-6548(N=151) n (%)	MT-6548(N=151) 95% CI of proportion	darbepoetin(N=153) N*	darbepoetin(N=153) n (%)	darbepoetin(N=153) 95% CI of proportion	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Baseline <= to < Week 2	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 2 <= to < Week 4	150	0 (0.0)	(0.00, 2.43)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 4 <= to < Week 6	149	1 (0.7)	(0.02, 3.68)	153	0 (0.0)	(0.00, 2.38)	0.7	(-10.7, 12.0)	0.493
Week 6 <= to < Week 8	147	0 (0.0)	(0.00, 2.48)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 8 <= to < Week 10	146	0 (0.0)	(0.00, 2.49)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 10 <= to < Week 12	146	0 (0.0)	(0.00, 2.49)	151	0 (0.0)	(0.00, 2.41)	-	(-, -)	-
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	149	0 (0.0)	(0.00, 2.45)	-	(-, -)	-
Week 16 <= to < Week 20	141	1 (0.7)	(0.02, 3.89)	147	0 (0.0)	(0.00, 2.48)	0.7	(-10.9, 12.3)	0.490
Week 20 <= to <= Week 24	136	0 (0.0)	(0.00, 2.68)	145	0 (0.0)	(0.00, 2.51)	-	(-, -)	-
Baseline <= to <= Week 24	151	2 (1.3)	(0.16, 4.70)	153	0 (0.0)	(0.00, 2.38)	1.3	(-10.1, 12.7)	0.246

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 16.2.2.6
Source: t_14_2_3_3_1_1.sas

5.3.5.1—6 表 14.2.3.3.1.1 より引用

表 2.7.6.25－73　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=151) N*	MT-6548(N=151) n (%)	MT-6548(N=151) 95% CI of proportion	darbepoetin(N=153) N*	darbepoetin(N=153) n (%)	darbepoetin(N=153) 95% CI of proportion	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Baseline <= to < Week 2	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 2 <= to < Week 4	150	0 (0.0)	(0.00, 2.43)	153	1 (0.7)	(0.02, 3.59)	-0.7	(-11.9, 10.6)	1.000
Week 4 <= to < Week 6	149	0 (0.0)	(0.00, 2.45)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 6 <= to < Week 8	147	0 (0.0)	(0.00, 2.48)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 8 <= to < Week 10	146	0 (0.0)	(0.00, 2.49)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 10 <= to < Week 12	146	0 (0.0)	(0.00, 2.49)	151	0 (0.0)	(0.00, 2.41)	-	(-, -)	-
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	149	0 (0.0)	(0.00, 2.45)	-	(-, -)	-
Week 16 <= to < Week 20	141	0 (0.0)	(0.00, 2.58)	147	0 (0.0)	(0.00, 2.48)	-	(-, -)	-
Week 20 <= to <= Week 24	136	0 (0.0)	(0.00, 2.68)	145	0 (0.0)	(0.00, 2.51)	-	(-, -)	-
Baseline <= to <= Week 24	151	0 (0.0)	(0.00, 2.41)	153	1 (0.7)	(0.02, 3.59)	-0.7	(-12.0, 10.7)	1.000

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 16.2.2.7
Source: t_14_2_3_3_2_1.sas

5.3.5.1—6 表 14.2.3.3.2.1 より引用

表 2.7.6.25－74　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=151) N*	MT-6548(N=151) n (%)	MT-6548(N=151) 95% CI of proportion	darbepoetin(N=153) N*	darbepoetin(N=153) n (%)	darbepoetin(N=153) 95% CI of proportion	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Baseline <= to < Week 2	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 2 <= to < Week 4	150	0 (0.0)	(0.00, 2.43)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 4 <= to < Week 6	149	0 (0.0)	(0.00, 2.45)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-
Week 6 <= to < Week 8	147	0 (0.0)	(0.00, 2.48)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 8 <= to < Week 10	146	0 (0.0)	(0.00, 2.49)	152	0 (0.0)	(0.00, 2.40)	-	(-, -)	-
Week 10 <= to < Week 12	146	0 (0.0)	(0.00, 2.49)	151	0 (0.0)	(0.00, 2.41)	-	(-, -)	-
Week 12 <= to < Week 16	144	0 (0.0)	(0.00, 2.53)	149	0 (0.0)	(0.00, 2.45)	-	(-, -)	-
Week 16 <= to < Week 20	141	0 (0.0)	(0.00, 2.58)	147	0 (0.0)	(0.00, 2.48)	-	(-, -)	-
Week 20 <= to <= Week 24	136	0 (0.0)	(0.00, 2.68)	145	0 (0.0)	(0.00, 2.51)	-	(-, -)	-
Baseline <= to <= Week 24	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)	-	(-, -)	-

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 16.2.2.8
Source: t_14_2_3_3_3_1.sas

5.3.5.1—6 表 14.2.3.3.3.1 より引用

(17)　QOL 指標

QOL 指標は，全集団を対象に記載した．

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 2.7.6.25－75 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 -0.0164 及び -0.0357～0.0029，darbepoetin 群で -0.0288 及び -0.0476～ -0.0100 であった．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 MT-6548 群と darbepoetin 群の差の LSMean 及びその 95%CI は, 0.0124 及び -0.0145～0.0393 であり，統計学的に有意な差が認められなかった（p = 0.366）．

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 -2.6 及び -4.7～ -0.4，darbepoetin 群で -0.7 及び -2.8～1.5 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, -1.9 及び -4.9～1.1 であり，統計学的に有意な差が認められなかった（p = 0.220）．

表 2.7.6.25－75　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	145	0.8995 (0.1138)	-0.0011	0.0095	(-0.0198, 0.0176)	
		Week 24	132	0.9052 (0.1095)	-0.0164	0.0098	(-0.0357, 0.0029)	
	darbepoetin	Week 12	148	0.8967 (0.1122)	-0.0111	0.0094	(-0.0296, 0.0074)	
		Week 24	140	0.9041 (0.1019)	-0.0288	0.0096	(-0.0476, -0.0100)	
	Difference MT-6548 - darbepoetin	Week 12			0.0100	0.0133	(-0.0162, 0.0363)	0.453
		Week 24			0.0124	0.0137	(-0.0145, 0.0393)	0.366
VAS score	MT-6548	Week 12	145	76.9 (14.0)	-1.1	1.1	(-3.2, 1.0)	
		Week 24	132	76.9 (13.8)	-2.6	1.1	(-4.7, -0.4)	
	darbepoetin	Week 12	148	77.2 (14.3)	-1.2	1.1	(-3.2, 0.9)	
		Week 24	140	77.1 (14.4)	-0.7	1.1	(-2.8, 1.5)	
	Difference MT-6548 - darbepoetin	Week 12			0.1	1.5	(-2.9, 3.0)	0.966
		Week 24			-1.9	1.5	(-4.9, 1.1)	0.220

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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 16.2.4.8
Source: t_14_2_3_14_2_1.sas

5.3.5.1—6 表 11.4.1—26 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 2.7.6.25－76 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 2.7.6.25－76　KDQOL の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
Physical Functioning	MT-6548	Week 12	145	77.61 (20.64)	-1.74	1.08	(-3.86, 0.38)	
		Week 24	131	79.61 (18.11)	-0.97	1.12	(-3.16, 1.22)	
	darbepoetin	Week 12	148	77.47 (19.42)	-2.71	1.07	(-4.80, -0.61)	
		Week 24	140	78.61 (18.74)	-1.40	1.09	(-3.54, 0.73)	
	Difference MT-6548 - darbepoetin	Week 12			0.97	1.51	(-2.01, 3.94)	0.522
		Week 24			0.43	1.56	(-2.62, 3.49)	0.781
Role Functioning Physical	MT-6548	Week 12	145	82.59 (31.09)	-4.02	2.49	(-8.90, 0.86)	
		Week 24	131	83.21 (31.08)	-5.84	2.60	(-10.95, -0.74)	
	darbepoetin	Week 12	148	78.38 (34.71)	-10.63	2.46	(-15.46, -5.79)	
		Week 24	140	79.29 (34.18)	-3.78	2.52	(-8.73, 1.17)	
	Difference MT-6548 - darbepoetin	Week 12			6.61	3.50	(-0.26, 13.47)	0.059
		Week 24			-2.07	3.62	(-9.18, 5.05)	0.568
Bodily Pain	MT-6548	Week 12	145	80.97 (20.23)	-3.91	1.48	(-6.83, -0.99)	
		Week 24	131	81.41 (19.94)	-1.36	1.55	(-4.41, 1.69)	
	darbepoetin	Week 12	148	77.52 (20.67)	-2.00	1.47	(-4.89, 0.89)	
		Week 24	140	77.79 (19.91)	-1.57	1.51	(-4.53, 1.39)	
	Difference MT-6548 - darbepoetin	Week 12			-1.91	2.09	(-6.02, 2.19)	0.360
		Week 24			0.21	2.17	(-4.05, 4.46)	0.924
General Health Perceptions	MT-6548	Week 12	145	52.83 (14.37)	-1.48	1.00	(-3.45, 0.49)	
		Week 24	131	53.40 (13.98)	-2.19	1.04	(-4.24, -0.14)	
	darbepoetin	Week 12	148	51.08 (17.66)	0.44	0.99	(-1.51, 2.39)	
		Week 24	140	51.50 (17.95)	0.61	1.01	(-1.39, 2.60)	
	Difference MT-6548 - darbepoetin	Week 12			-1.93	1.41	(-4.70, 0.85)	0.173
		Week 24			-2.79	1.46	(-5.65, 0.07)	0.056

表 2.7.6.25－76　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Vitality	MT-6548	Week 12	145	66.23 (18.69)	-1.43	1.41	(-4.20, 1.34)	
		Week 24	131	67.35 (18.26)	-0.71	1.47	(-3.58, 2.17)	
	darbepoetin	Week 12	148	63.92 (19.83)	-0.95	1.40	(-3.69, 1.80)	
		Week 24	140	63.64 (19.83)	-1.07	1.42	(-3.87, 1.73)	
	Difference MT-6548 - darbepoetin	Week 12			-0.48	1.98	(-4.38, 3.42)	0.809
		Week 24			0.36	2.05	(-3.66, 4.38)	0.859
Social Functioning	MT-6548	Week 12	145	90.26 (16.96)	-1.03	1.44	(-3.86, 1.79)	
		Week 24	131	91.13 (15.46)	0.55	1.51	(-2.42, 3.52)	
	darbepoetin	Week 12	148	89.70 (16.67)	-3.61	1.43	(-6.41, -0.81)	
		Week 24	140	89.91 (16.49)	-2.90	1.46	(-5.77, -0.02)	
	Difference MT-6548 - darbepoetin	Week 12			2.57	2.02	(-1.40, 6.55)	0.204
		Week 24			3.45	2.10	(-0.68, 7.58)	0.102
Role Functioning Emotional	MT-6548	Week 12	145	85.06 (32.85)	-0.25	2.54	(-5.24, 4.74)	
		Week 24	131	85.75 (32.30)	-2.80	2.66	(-8.04, 2.43)	
	darbepoetin	Week 12	148	82.21 (34.87)	-10.73	2.52	(-15.67, -5.78)	
		Week 24	140	82.62 (34.27)	-5.25	2.58	(-10.32, -0.17)	
	Difference MT-6548 - darbepoetin	Week 12			10.48	3.57	(3.45, 17.50)	0.004
		Week 24			2.44	3.71	(-4.85, 9.73)	0.511
Mental Health	MT-6548	Week 12	145	81.13 (14.55)	-0.81	1.21	(-3.19, 1.58)	
		Week 24	131	81.86 (13.77)	-4.27	1.27	(-6.77, -1.78)	
	darbepoetin	Week 12	148	78.32 (16.13)	-2.18	1.20	(-4.55, 0.18)	
		Week 24	140	78.80 (15.94)	-4.05	1.23	(-6.47, -1.63)	
	Difference MT-6548 - darbepoetin	Week 12			1.38	1.71	(-1.98, 4.73)	0.421
		Week 24			-0.22	1.77	(-3.70, 3.26)	0.900

表 2.7.6.25－76　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Symptoms/Problems	MT-6548	Week 12	145	87.51 (10.47)	0.09	0.64	(-1.17, 1.35)	
		Week 24	131	87.84 (10.33)	-0.33	0.67	(-1.64, 0.98)	
	darbepoetin	Week 12	148	87.38 (9.65)	0.21	0.63	(-1.04, 1.45)	
		Week 24	140	87.70 (9.25)	0.70	0.65	(-0.58, 1.97)	
	Difference MT-6548 - darbepoetin	Week 12			-0.12	0.90	(-1.89, 1.65)	0.896
		Week 24			-1.02	0.93	(-2.85, 0.80)	0.272
Effect of kidney disease	MT-6548	Week 12	145	93.28 (7.93)	-1.34	0.68	(-2.67, -0.01)	
		Week 24	131	93.50 (7.85)	-1.24	0.70	(-2.63, 0.14)	
	darbepoetin	Week 12	148	92.81 (9.08)	-1.97	0.67	(-3.28, -0.65)	
		Week 24	140	93.26 (8.49)	-0.72	0.68	(-2.06, 0.63)	
	Difference MT-6548 - darbepoetin	Week 12			0.63	0.95	(-1.24, 2.50)	0.509
		Week 24			-0.53	0.98	(-2.46, 1.40)	0.590
Burden of kidney disease	MT-6548	Week 12	145	67.61 (23.95)	0.51	1.51	(-2.47, 3.48)	
		Week 24	131	69.12 (23.33)	-1.11	1.57	(-4.19, 1.98)	
	darbepoetin	Week 12	148	67.31 (23.11)	-3.63	1.50	(-6.58, -0.69)	
		Week 24	140	67.68 (23.31)	-1.70	1.53	(-4.70, 1.30)	
	Difference MT-6548 - darbepoetin	Week 12			4.14	2.13	(-0.04, 8.32)	0.052
		Week 24			0.60	2.19	(-3.70, 4.90)	0.785
Work status	MT-6548	Week 12	140	65.36 (31.10)	-1.22	1.57	(-4.30, 1.86)	
		Week 24	128	64.84 (30.97)	-2.67	1.63	(-5.86, 0.53)	
	darbepoetin	Week 12	138	59.78 (29.51)	-1.89	1.58	(-4.99, 1.22)	
		Week 24	132	60.23 (28.13)	-3.55	1.61	(-6.71, -0.39)	
	Difference MT-6548 - darbepoetin	Week 12			0.67	2.23	(-3.71, 5.05)	0.764
		Week 24			0.88	2.29	(-3.62, 5.39)	0.700

表 2.7.6.25－76　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Cognitive function	MT-6548	Week 12	145	91.72 (12.23)	1.38	0.84	(-0.28, 3.04)	
		Week 24	131	92.42 (10.15)	1.27	0.87	(-0.45, 2.99)	
	darbepoetin	Week 12	148	92.48 (11.25)	-1.61	0.83	(-3.25, 0.03)	
		Week 24	140	92.81 (11.02)	-0.98	0.85	(-2.65, 0.69)	
	Difference MT-6548 - darbepoetin	Week 12			2.99	1.18	(0.66, 5.32)	0.012
		Week 24			2.25	1.22	(-0.14, 4.65)	0.065
Quality of social interaction	MT-6548	Week 12	145	93.75 (8.93)	0.09	0.75	(-1.39, 1.56)	
		Week 24	131	93.94 (8.85)	-0.33	0.78	(-1.86, 1.21)	
	darbepoetin	Week 12	148	94.59 (8.42)	-1.47	0.74	(-2.92, -0.01)	
		Week 24	140	94.95 (8.27)	0.18	0.76	(-1.31, 1.67)	
	Difference MT-6548 - darbepoetin	Week 12			1.55	1.05	(-0.52, 3.63)	0.141
		Week 24			-0.51	1.09	(-2.65, 1.63)	0.641
Sexual function	MT-6548	Week 12	9	79.17 (26.52)	-0.05	9.10	(-19.49, 19.39)	
		Week 24	6	83.33 (20.41)	1.84	10.08	(-19.46, 23.14)	
	darbepoetin	Week 12	5	70.00 (40.12)	-5.30	13.02	(-33.35, 22.76)	
		Week 24	4	68.75 (46.21)	-6.32	13.90	(-35.90, 23.26)	
	Difference MT-6548 - darbepoetin	Week 12			5.24	15.98	(-29.06, 39.55)	0.748
		Week 24			8.16	17.50	(-28.95, 45.27)	0.647
Sleep	MT-6548	Week 12	145	71.03 (16.73)	-2.24	1.07	(-4.35, -0.13)	
		Week 24	131	70.90 (16.57)	-3.01	1.12	(-5.20, -0.81)	
	darbepoetin	Week 12	148	69.24 (17.22)	-0.38	1.06	(-2.46, 1.71)	
		Week 24	140	69.55 (17.22)	-0.24	1.08	(-2.37, 1.89)	
	Difference MT-6548 - darbepoetin	Week 12			-1.86	1.51	(-4.82, 1.10)	0.218
		Week 24			-2.76	1.56	(-5.82, 0.30)	0.076

表 2.7.6.25－76　KDQOL のスコアのベースラインからの変化量（MMRM，FAS）（続き）

Parameter	Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Social support	MT-6548	Week 12	145	81.15 (21.72)	0.36	1.61	(-2.81, 3.52)	
		Week 24	131	80.28 (22.25)	-0.76	1.69	(-4.07, 2.55)	
	darbepoetin	Week 12	148	80.29 (19.83)	-0.80	1.60	(-3.93, 2.34)	
		Week 24	140	81.19 (19.06)	-0.07	1.64	(-3.28, 3.14)	
	Difference MT-6548 - darbepoetin	Week 12			1.16	2.27	(-3.30, 5.61)	0.610
		Week 24			-0.69	2.35	(-5.30, 3.92)	0.769

Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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 16.2.4.11
Source: t_14_2_3_14_6_1.sas

5.3.5.1—6 表 11.4.1—27 より引用

(18)　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 2.7.6.25－77 に示した.

表 2.7.6.25－77　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 2.7.6.25－78
前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）（Conversion 集団）	表 2.7.6.25－79
前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）（Conversion 集団）	表 2.7.6.25－80
MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）（Conversion 集団）	図 2.7.6.25－26
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）（Conversion 集団）	図 2.7.6.25－27
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）（Conversion 集団）	図 2.7.6.25－28
前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（Conversion 集団）	表 2.7.6.25－81
前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（Conversion 集団）	表 2.7.6.25－82
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 2.7.6.25－83
鉄剤及び鉄含有リン吸着剤の併用有無別の Hb 値（MMRM，FAS）	表 2.7.6.25－84
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 2.7.6.25－29
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 2.7.6.25－30
被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）	表 2.7.6.25－85
前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）（Conversion 集団）	表 2.7.6.25－86
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）（Conversion 集団）	図 2.7.6.25－31
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）（Conversion 集団）	図 2.7.6.25－32
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）（Conversion 集団）	図 2.7.6.25－33
前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（Conversion 集団）	表 2.7.6.25－87
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 2.7.6.25－88
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 2.7.6.25－34
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 2.7.6.25－35

表 2.7.6.25－78　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	75	10.44 (0.92)	11.54	0.12	(11.31, 11.77)	
		darbepoetin	73	10.48 (0.85)	11.92	0.12	(11.69, 12.15)	
		Difference MT-6548 - darbepoetin			-0.38	0.16	(-0.71, -0.06)	0.020
	Female	MT-6548	76	10.44 (0.91)	11.79	0.10	(11.59, 11.99)	
		darbepoetin	80	10.56 (0.91)	11.94	0.09	(11.76, 12.13)	
		Difference MT-6548 - darbepoetin			-0.15	0.14	(-0.42, 0.12)	0.277
Age at Informed Consent (years)	<65	MT-6548	33	10.42 (0.94)	11.90	0.16	(11.59, 12.21)	
		darbepoetin	28	10.68 (0.92)	11.99	0.17	(11.65, 12.34)	
		Difference MT-6548 - darbepoetin			-0.09	0.24	(-0.56, 0.37)	0.695
	>=65	MT-6548	118	10.44 (0.91)	11.60	0.09	(11.43, 11.77)	
		darbepoetin	125	10.49 (0.87)	11.91	0.08	(11.74, 12.07)	
		Difference MT-6548 - darbepoetin			-0.31	0.12	(-0.54, -0.07)	0.010
	<75	MT-6548	81	10.46 (0.86)	11.91	0.10	(11.71, 12.10)	
		darbepoetin	79	10.60 (0.77)	11.89	0.10	(11.69, 12.09)	
		Difference MT-6548 - darbepoetin			0.02	0.14	(-0.27, 0.30)	0.912
	>=75	MT-6548	70	10.41 (0.98)	11.37	0.12	(11.14, 11.59)	
		darbepoetin	74	10.44 (0.99)	11.95	0.11	(11.74, 12.17)	
		Difference MT-6548 - darbepoetin			-0.59	0.16	(-0.90, -0.28)	<0.001

表 2.7.6.25－78　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
Weight (kg)	<60	MT-6548	95	10.46 (0.91)	11.61	0.10	(11.42, 11.79)	
		darbepoetin	92	10.56 (0.88)	11.93	0.10	(11.74, 12.12)	
		Difference MT-6548 - darbepoetin			-0.32	0.13	(-0.59, -0.06)	0.017
	>=60	MT-6548	56	10.40 (0.92)	11.78	0.13	(11.53, 12.03)	
		darbepoetin	61	10.46 (0.89)	11.90	0.12	(11.67, 12.14)	
		Difference MT-6548 - darbepoetin			-0.13	0.17	(-0.47, 0.22)	0.472
BMI (kg/m^2)	<25	MT-6548	100	10.41 (0.88)	11.63	0.09	(11.45, 11.82)	
		darbepoetin	111	10.53 (0.88)	11.89	0.09	(11.72, 12.06)	
		Difference MT-6548 - darbepoetin			-0.26	0.13	(-0.51, -0.01)	0.045
	>=25	MT-6548	51	10.50 (0.98)	11.76	0.13	(11.49, 12.02)	
		darbepoetin	42	10.50 (0.90)	12.02	0.15	(11.73, 12.31)	
		Difference MT-6548 - darbepoetin			-0.27	0.20	(-0.66, 0.13)	0.183

表 2.7.6.25－78　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	43	10.42 (0.79)	11.98	0.15	(11.69, 12.27)	
		darbepoetin	48	10.48 (0.92)	12.02	0.14	(11.75, 12.30)	
		Difference MT-6548 - darbepoetin			-0.04	0.21	(-0.44, 0.36)	0.845
	Hypertension	MT-6548	52	10.49 (1.00)	11.43	0.13	(11.17, 11.69)	
		darbepoetin	60	10.48 (0.92)	11.96	0.12	(11.72, 12.20)	
		Difference MT-6548 - darbepoetin			-0.53	0.18	(-0.88, -0.17)	0.004
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	20	10.38 (0.88)	11.39	0.20	(10.99, 11.79)	
		darbepoetin	31	10.70 (0.79)	11.74	0.15	(11.44, 12.05)	
		Difference MT-6548 - darbepoetin			-0.35	0.25	(-0.86, 0.15)	0.165
	Interstitial Nephritis/Pyelonephritis	MT-6548	4	10.48 (0.46)	11.38	0.49	(10.37, 12.40)	
		darbepoetin	2	10.75 (0.92)	12.06	1.09	(9.81, 14.32)	
		Difference MT-6548 - darbepoetin			-0.68	1.29	(-3.36, 2.00)	0.605
	Cystic/Hereditary/Congenital Disease	MT-6548	13	10.29 (0.74)	11.79	0.32	(11.16, 12.43)	
		darbepoetin	9	10.93 (0.85)	11.54	0.38	(10.77, 12.31)	
		Difference MT-6548 - darbepoetin			0.25	0.50	(-0.76, 1.27)	0.617
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						

表 2.7.6.25－78　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	50	10.50 (0.90)	11.52	0.14	(11.25, 11.79)	
		darbepoetin	51	10.51 (0.84)	11.99	0.13	(11.72, 12.25)	
		Difference MT-6548 - darbepoetin			-0.47	0.19	(-0.84, -0.09)	0.015
	1<= to <5	MT-6548	78	10.44 (0.95)	11.87	0.10	(11.66, 12.07)	
		darbepoetin	80	10.54 (0.96)	12.00	0.10	(11.80, 12.20)	
		Difference MT-6548 - darbepoetin			-0.14	0.15	(-0.42, 0.15)	0.345
	>=5	MT-6548	23	10.30 (0.82)	11.30	0.20	(10.91, 11.68)	
		darbepoetin	22	10.48 (0.65)	11.61	0.20	(11.22, 12.01)	
		Difference MT-6548 - darbepoetin			-0.32	0.28	(-0.88, 0.24)	0.265
Complications	Hypertension	MT-6548	147	10.44 (0.91)	11.66	0.08	(11.51, 11.81)	
		darbepoetin	145	10.51 (0.89)	11.92	0.08	(11.77, 12.07)	
		Difference MT-6548 - darbepoetin			-0.26	0.11	(-0.48, -0.05)	0.017
	Diabetes	MT-6548	57	10.38 (0.84)	11.88	0.13	(11.62, 12.14)	
		darbepoetin	62	10.47 (0.86)	11.92	0.12	(11.68, 12.17)	
		Difference MT-6548 - darbepoetin			-0.04	0.18	(-0.40, 0.32)	0.817
	Dyslipidaemia	MT-6548	94	10.44 (0.97)	11.75	0.09	(11.57, 11.93)	
		darbepoetin	100	10.55 (0.87)	11.95	0.09	(11.78, 12.12)	
		Difference MT-6548 - darbepoetin			-0.20	0.13	(-0.45, 0.05)	0.115

表 2.7.6.25－78　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)	<9	MT-6548	8	8.44 (0.50)	11.54	0.49	(10.55, 12.53)	
		darbepoetin	7	8.37 (0.19)	11.54	0.48	(10.55, 12.53)	
		Difference MT-6548 - darbepoetin			0.00	0.55	(-1.12, 1.11)	0.995
	9<= to <11	MT-6548	96	10.10 (0.49)	11.59	0.10	(11.39, 11.78)	
		darbepoetin	96	10.19 (0.49)	11.88	0.10	(11.68, 12.07)	
		Difference MT-6548 - darbepoetin			-0.29	0.14	(-0.57, -0.02)	0.036
	>=11	MT-6548	47	11.48 (0.36)	11.85	0.12	(11.61, 12.09)	
		darbepoetin	50	11.45 (0.42)	12.05	0.13	(11.80, 12.30)	
		Difference MT-6548 - darbepoetin			-0.20	0.15	(-0.50, 0.10)	0.195
Baseline eGFR (mL/min/1.73m^2)	<15	MT-6548	60	10.25 (0.82)	11.62	0.13	(11.36, 11.89)	
		darbepoetin	50	10.48 (0.96)	11.91	0.14	(11.63, 12.20)	
		Difference MT-6548 - darbepoetin			-0.29	0.19	(-0.67, 0.09)	0.140
	15<= to <30	MT-6548	54	10.57 (1.01)	11.69	0.12	(11.45, 11.92)	
		darbepoetin	70	10.57 (0.90)	11.92	0.11	(11.71, 12.13)	
		Difference MT-6548 - darbepoetin			-0.23	0.16	(-0.54, 0.08)	0.145
	30<= to <60	MT-6548	37	10.55 (0.88)	11.74	0.15	(11.44, 12.04)	
		darbepoetin	32	10.46 (0.73)	12.04	0.16	(11.73, 12.35)	
		Difference MT-6548 - darbepoetin			-0.30	0.21	(-0.72, 0.12)	0.161
	>=60	MT-6548	0					
		darbepoetin	1	11.20 (-)				
		Difference MT-6548 - darbepoetin						

表 2.7.6.25－78　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 Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	146	10.46 (0.92)	11.66	0.08	(11.50, 11.81)	
		darbepoetin	151	10.52 (0.88)	11.94	0.07	(11.80, 12.09)	
		Difference MT-6548 - darbepoetin			-0.29	0.11	(-0.50, -0.08)	0.008
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	4	9.95 (0.68)				
		darbepoetin	1	10.10 (-)				
		Difference MT-6548 - darbepoetin						
	AST >80 or ALT >90	MT-6548	1	9.80 (-)				
		darbepoetin	1	11.10 (-)				
		Difference MT-6548 - darbepoetin						
Baseline CRP (mg/dL)	<0.31	MT-6548	128	10.48 (0.90)	11.66	0.08	(11.50, 11.83)	
		darbepoetin	133	10.58 (0.84)	11.95	0.08	(11.79, 12.10)	
		Difference MT-6548 - darbepoetin			-0.28	0.11	(-0.51, -0.06)	0.012
	>=0.31	MT-6548	23	10.18 (0.98)	11.70	0.22	(11.27, 12.14)	
		darbepoetin	20	10.16 (1.06)	11.79	0.23	(11.33, 12.24)	
		Difference MT-6548 - darbepoetin			-0.09	0.32	(-0.71, 0.54)	0.789

表 2.7.6.25－78　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 Serum Ferritin (ng/mL)	<82	MT-6548	48	10.39 (0.66)	11.65	0.13	(11.40, 11.90)	
		darbepoetin	53	10.61 (0.81)	11.96	0.12	(11.72, 12.19)	
		Difference MT-6548 - darbepoetin			-0.31	0.18	(-0.65, 0.04)	0.081
	82<= to <155	MT-6548	49	10.73 (0.86)	11.75	0.14	(11.48, 12.02)	
		darbepoetin	52	10.62 (0.88)	12.01	0.13	(11.77, 12.26)	
		Difference MT-6548 - darbepoetin			-0.26	0.18	(-0.62, 0.10)	0.159
	>=155	MT-6548	54	10.22 (1.08)	11.61	0.13	(11.35, 11.87)	
		darbepoetin	48	10.32 (0.93)	11.76	0.14	(11.48, 12.03)	
		Difference MT-6548 - darbepoetin			-0.15	0.19	(-0.53, 0.23)	0.450
Baseline TSAT (%)	<25	MT-6548	44	10.41 (0.93)	11.67	0.14	(11.39, 11.94)	
		darbepoetin	53	10.44 (0.89)	12.01	0.13	(11.75, 12.26)	
		Difference MT-6548 - darbepoetin			-0.34	0.19	(-0.71, 0.03)	0.073
	25<= to <34	MT-6548	53	10.47 (0.86)	11.80	0.12	(11.56, 12.04)	
		darbepoetin	47	10.54 (0.96)	11.91	0.13	(11.66, 12.16)	
		Difference MT-6548 - darbepoetin			-0.11	0.18	(-0.45, 0.24)	0.540
	>=34	MT-6548	54	10.44 (0.96)	11.49	0.14	(11.22, 11.76)	
		darbepoetin	53	10.59 (0.81)	11.79	0.14	(11.52, 12.06)	
		Difference MT-6548 - darbepoetin			-0.30	0.19	(-0.67, 0.08)	0.119

表 2.7.6.25－78　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
Smoking Status	Never Smoked	MT-6548	87	10.46 (0.92)	11.83	0.09	(11.65, 12.02)	
		darbepoetin	86	10.55 (0.91)	11.92	0.09	(11.74, 12.10)	
		Difference MT-6548 - darbepoetin			-0.09	0.13	(-0.35, 0.17)	0.499
	Ex-Smoker	MT-6548	53	10.39 (0.94)	11.32	0.14	(11.04, 11.59)	
		darbepoetin	49	10.50 (0.81)	11.92	0.15	(11.63, 12.20)	
		Difference MT-6548 - darbepoetin			-0.60	0.20	(-1.00, -0.21)	0.003
	Current Smoker	MT-6548	11	10.50 (0.76)	12.25	0.37	(11.53, 12.98)	
		darbepoetin	18	10.47 (0.96)	11.96	0.24	(11.48, 12.44)	
		Difference MT-6548 - darbepoetin			0.29	0.46	(-0.62, 1.20)	0.528
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	34	10.67 (0.94)	11.86	0.15	(11.55, 12.16)	
		darbepoetin	29	10.40 (0.90)	11.95	0.17	(11.62, 12.29)	
		Difference MT-6548 - darbepoetin			-0.10	0.23	(-0.55, 0.35)	0.670
	No	MT-6548	117	10.37 (0.90)	11.61	0.09	(11.44, 11.78)	
		darbepoetin	124	10.55 (0.88)	11.91	0.08	(11.75, 12.07)	
		Difference MT-6548 - darbepoetin			-0.30	0.12	(-0.54, -0.07)	0.012
Concomitant Medications of Oral Iron at Week 24	Yes	MT-6548	54	10.40 (0.94)	11.83	0.13	(11.59, 12.08)	
		darbepoetin	49	10.32 (0.83)	12.24	0.13	(11.98, 12.50)	
		Difference MT-6548 - darbepoetin			-0.40	0.18	(-0.76, -0.04)	0.028
	No	MT-6548	97	10.46 (0.90)	11.57	0.10	(11.38, 11.76)	
		darbepoetin	104	10.62 (0.89)	11.77	0.09	(11.59, 11.94)	
		Difference MT-6548 - darbepoetin			-0.20	0.13	(-0.46, 0.06)	0.129

表 2.7.6.25－78　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 Baseline	Yes	MT-6548	1	9.60 (-)				
		darbepoetin	2	11.05 (0.35)				
		Difference MT-6548 - darbepoetin						
	No	MT-6548	150	10.44 (0.91)	11.67	0.08	(11.52, 11.82)	
		darbepoetin	151	10.52 (0.88)	11.92	0.08	(11.77, 12.07)	
		Difference MT-6548 - darbepoetin			-0.25	0.11	(-0.46, -0.04)	0.018
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 24	Yes	MT-6548	1	9.60 (-)				
		darbepoetin	2	11.05 (0.35)				
		Difference MT-6548 - darbepoetin						
	No	MT-6548	150	10.44 (0.91)	11.67	0.08	(11.52, 11.82)	
		darbepoetin	151	10.52 (0.88)	11.92	0.08	(11.77, 12.07)	
		Difference MT-6548 - darbepoetin			-0.25	0.11	(-0.46, -0.04)	0.018

表 2.7.6.25－78　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: Medication	Epoetin	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						
	Darbepoetin alfa	MT-6548	47	10.61 (0.82)	11.51	0.13	(11.26, 11.76)	
		darbepoetin	45	10.92 (0.89)	11.79	0.13	(11.54, 12.04)	
		Difference MT-6548 - darbepoetin			-0.28	0.18	(-0.64, 0.07)	0.116
	Epoetin beta pegol	MT-6548	33	10.77 (0.99)	11.20	0.18	(10.85, 11.55)	
		darbepoetin	37	10.85 (0.69)	11.87	0.16	(11.55, 12.18)	
		Difference MT-6548 - darbepoetin			-0.67	0.24	(-1.13, -0.20)	0.005
	Other	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	15	10.82 (0.91)	11.81	0.20	(11.41, 12.21)	
		darbepoetin	15	11.20 (0.78)	11.70	0.20	(11.30, 12.10)	
		Difference MT-6548 - darbepoetin			0.11	0.29	(-0.46, 0.68)	0.714
	Darbepoetin alfa, 10<= to <15	MT-6548	5	10.46 (0.65)	11.80	0.31	(11.05, 12.56)	
		darbepoetin	1	10.00 (-)	12.68	0.71	(10.94, 14.41)	
		Difference MT-6548 - darbepoetin			-0.87	0.78	(-2.79, 1.05)	0.307
	Darbepoetin alfa, >=15	MT-6548	27	10.51 (0.80)	11.24	0.18	(10.89, 11.59)	
		darbepoetin	29	10.81 (0.93)	11.83	0.16	(11.51, 12.15)	
		Difference MT-6548 - darbepoetin			-0.59	0.24	(-1.07, -0.11)	0.016

表 2.7.6.25－78　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, <6.25	MT-6548	0					
		darbepoetin	0					
		Difference MT-6548 - darbepoetin						
	Epoetin beta pegol, 6.25<= to <12.5	MT-6548	9	10.66 (0.87)	11.54	0.27	(11.00, 12.08)	
		darbepoetin	16	11.06 (0.64)	11.65	0.20	(11.25, 12.05)	
		Difference MT-6548 - darbepoetin			-0.11	0.34	(-0.79, 0.57)	0.746
	Epoetin beta pegol, >=12.5	MT-6548	24	10.82 (1.05)	11.06	0.22	(10.62, 11.50)	
		darbepoetin	21	10.69 (0.71)	12.07	0.23	(11.62, 12.52)	
		Difference MT-6548 - darbepoetin			-1.01	0.32	(-1.64, -0.38)	0.002
Concomitant Medications of CYP2B6 Substrates	Yes	MT-6548	11	10.05 (0.63)				
		darbepoetin	6	10.87 (0.92)				
		Difference MT-6548 - darbepoetin						
	No	MT-6548	140	10.47 (0.93)	11.69	0.08	(11.53, 11.84)	
		darbepoetin	147	10.51 (0.88)	11.93	0.08	(11.78, 12.08)	
		Difference MT-6548 - darbepoetin			-0.25	0.11	(-0.46, -0.03)	0.024

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 or Epoetin beta.
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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Note(s): p value is analyzed by MMRM model.
Note(s): Subjects only in conversion group are included in analysis of 'Prior ESA Treatment'.
Data Source: Listing 16.2.4.1
Source: c_001_1_1_1.sas

5.3.5.1—6 表 11.4.2—4 より引用

表 2.7.6.25－79 前治療 ESA 製剤の種類別の Hb 値の記述統計量（FAS）（Conversion 集団）

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
MT-6548	Darbepoetin alfa	Baseline	47	10.61	0.82	10.60	(8.9, 12.1)	(10.37, 10.85)							
		Week 2	47	10.66	1.03	10.70	(8.5, 13.8)	(10.36, 10.96)	47	0.05	0.55	0.10	(-1.1, 1.7)	(-0.11, 0.22)	0.512
		Week 4	47	10.70	1.06	11.00	(8.0, 12.8)	(10.39, 11.02)	47	0.10	0.69	0.10	(-1.5, 1.6)	(-0.11, 0.30)	0.337
		Week 6	46	10.77	1.09	10.85	(8.2, 13.5)	(10.44, 11.09)	46	0.13	0.83	0.05	(-1.8, 1.6)	(-0.12, 0.38)	0.292
		Week 8	46	11.10	1.09	11.25	(8.4, 13.7)	(10.77, 11.42)	46	0.46	0.92	0.55	(-1.6, 2.6)	(0.19, 0.74)	0.001
		Week 10	46	11.17	1.03	11.35	(9.2, 13.6)	(10.86, 11.48)	46	0.53	0.93	0.55	(-1.6, 2.5)	(0.26, 0.81)	<0.001
		Week 12	46	11.30	1.01	11.40	(9.1, 13.4)	(11.00, 11.60)	46	0.67	1.04	0.75	(-1.5, 3.2)	(0.36, 0.98)	<0.001
		Week 16	45	11.46	1.01	11.50	(9.1, 13.4)	(11.16, 11.77)	45	0.81	1.12	0.90	(-1.3, 3.1)	(0.47, 1.14)	<0.001
		Week 20	43	11.61	0.95	11.70	(8.3, 13.6)	(11.32, 11.91)	43	0.93	1.14	0.90	(-1.7, 3.4)	(0.58, 1.28)	<0.001
		Week 24	41	11.52	1.03	11.70	(7.4, 13.2)	(11.19, 11.85)	41	0.85	1.13	0.90	(-2.6, 3.2)	(0.49, 1.21)	<0.001
		Week 24 (LOCF)	47	11.41	1.17	11.70	(7.4, 13.2)	(11.06, 11.75)	47	0.80	1.16	0.80	(-2.6, 3.2)	(0.46, 1.14)	<0.001
	Epoetinbeta pegol	Baseline	33	10.77	0.99	10.90	(9.1, 12.5)	(10.42, 11.12)							
		Week 2	33	10.78	1.03	10.90	(8.4, 12.6)	(10.41, 11.15)	33	0.01	0.59	-0.20	(-0.8, 1.3)	(-0.20, 0.22)	0.953
		Week 4	33	10.67	1.16	10.80	(8.0, 12.6)	(10.25, 11.08)	33	-0.11	0.87	-0.10	(-1.7, 1.6)	(-0.42, 0.20)	0.491
		Week 6	33	10.80	1.08	10.70	(8.3, 12.2)	(10.41, 11.18)	33	0.02	1.00	-0.10	(-1.8, 2.4)	(-0.33, 0.38)	0.890
		Week 8	31	10.94	1.15	11.00	(9.1, 12.9)	(10.52, 11.36)	31	0.14	1.17	0.30	(-2.4, 2.6)	(-0.29, 0.57)	0.513
		Week 10	32	11.13	0.97	11.20	(9.4, 13.0)	(10.78, 11.48)	32	0.32	1.22	0.45	(-2.4, 3.0)	(-0.12, 0.76)	0.147
		Week 12	31	11.19	1.12	11.40	(9.0, 13.1)	(10.78, 11.60)	31	0.42	1.30	0.40	(-2.2, 2.9)	(-0.06, 0.89)	0.084
		Week 16	31	11.07	1.01	11.10	(8.6, 12.5)	(10.71, 11.44)	31	0.30	1.40	0.60	(-2.6, 2.7)	(-0.21, 0.81)	0.242
		Week 20	29	11.26	1.23	11.40	(8.5, 13.3)	(10.80, 11.73)	29	0.49	1.45	0.60	(-3.2, 2.9)	(-0.07, 1.04)	0.082
		Week 24	25	11.25	1.17	11.20	(8.2, 13.2)	(10.77, 11.73)	25	0.42	1.36	0.70	(-2.6, 2.7)	(-0.14, 0.98)	0.139
		Week 24 (LOCF)	33	11.08	1.24	11.20	(8.2, 13.2)	(10.64, 11.52)	33	0.30	1.46	0.60	(-3.2, 2.8)	(-0.21, 0.82)	0.242

Note(s): Hb (g/dL).
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
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

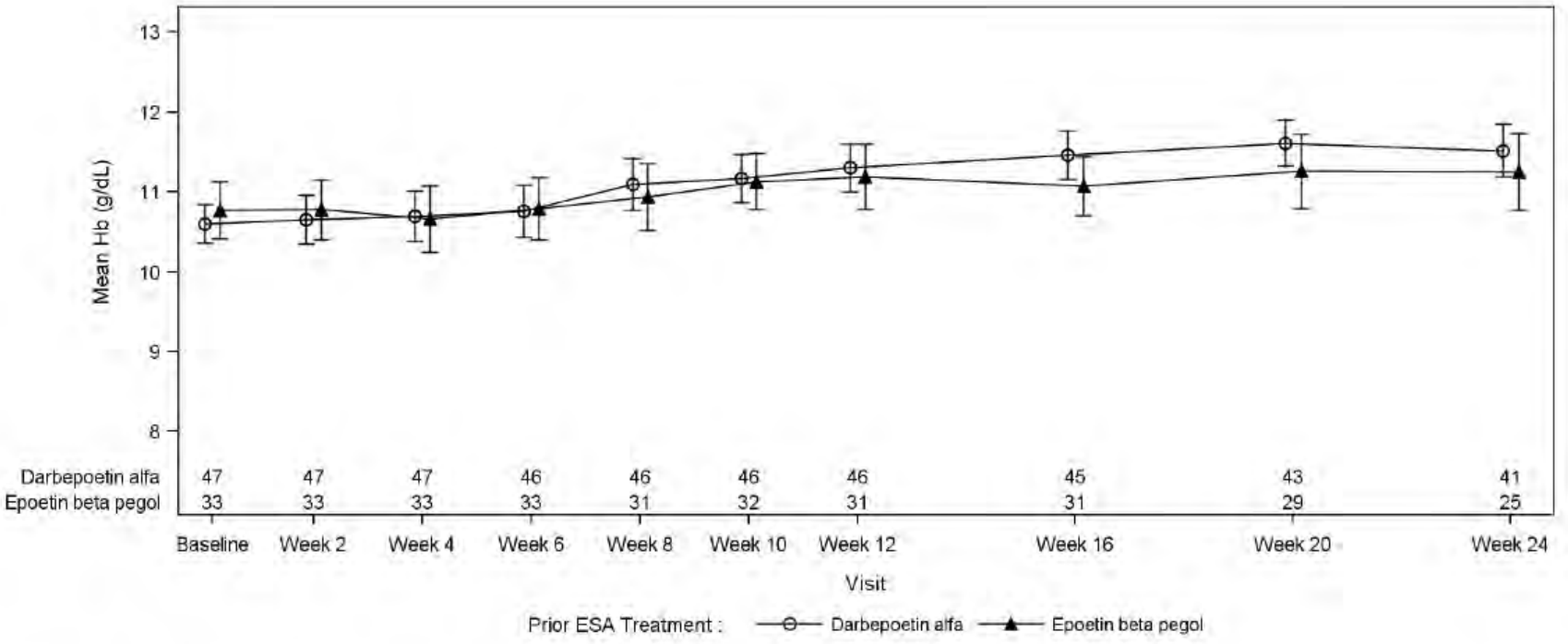
5.3.5.1—6 表 14.2.2.5.1 より引用

表 2.7.6.25－80　前治療 ESA 製剤の種類別の Hb 値（MMRM，FAS）（Conversion 集団）

Treatment Group	Prior ESA Treatment	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Darbepoetin alfa	Week 2	47	10.61 (0.82)	10.68	0.13	(10.42, 10.94)
		Week 4	47	10.61 (0.82)	10.73	0.13	(10.46, 10.99)
		Week 6	46	10.63 (0.80)	10.76	0.13	(10.49, 11.02)
		Week 8	46	10.63 (0.80)	11.09	0.13	(10.83, 11.35)
		Week 10	46	10.63 (0.80)	11.16	0.13	(10.90, 11.42)
		Week 12	46	10.63 (0.80)	11.29	0.13	(11.03, 11.56)
		Week 16	45	10.66 (0.80)	11.42	0.13	(11.15, 11.68)
		Week 20	43	10.68 (0.80)	11.54	0.14	(11.27, 11.81)
		Week 24	41	10.67 (0.81)	11.43	0.14	(11.15, 11.70)
	Epoetin beta pegol	Week 2	33	10.77 (0.99)	10.78	0.18	(10.43, 11.14)
		Week 4	33	10.77 (0.99)	10.67	0.18	(10.32, 11.03)
		Week 6	33	10.77 (0.99)	10.80	0.18	(10.45, 11.16)
		Week 8	31	10.80 (1.00)	10.92	0.18	(10.56, 11.28)
		Week 10	32	10.81 (0.98)	11.10	0.18	(10.75, 11.46)
		Week 12	31	10.77 (0.98)	11.17	0.18	(10.80, 11.53)
		Week 16	31	10.77 (0.98)	11.05	0.18	(10.69, 11.41)
		Week 20	29	10.78 (1.00)	11.22	0.18	(10.85, 11.58)
		Week 24	25	10.84 (0.99)	11.18	0.19	(10.80, 11.56)

Note(s): Hb (g/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
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_4.sas

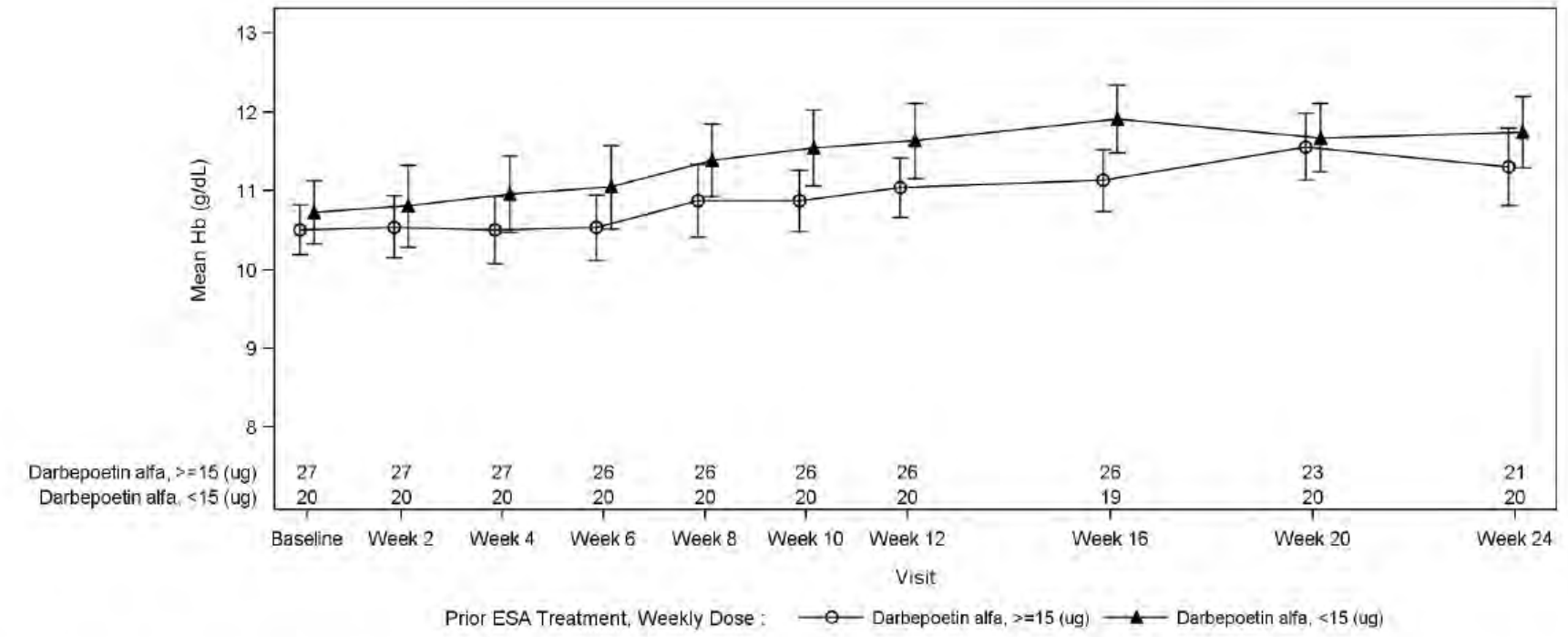
5.3.5.1—6 表 14.2.2.5.4 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.5.1
Source: f_14_2_1_3_1.sas

図 2.7.6.25－26　MT-6548 群の前治療 ESA 製剤の種類別の Hb 値の推移（FAS）（Conversion 集団）

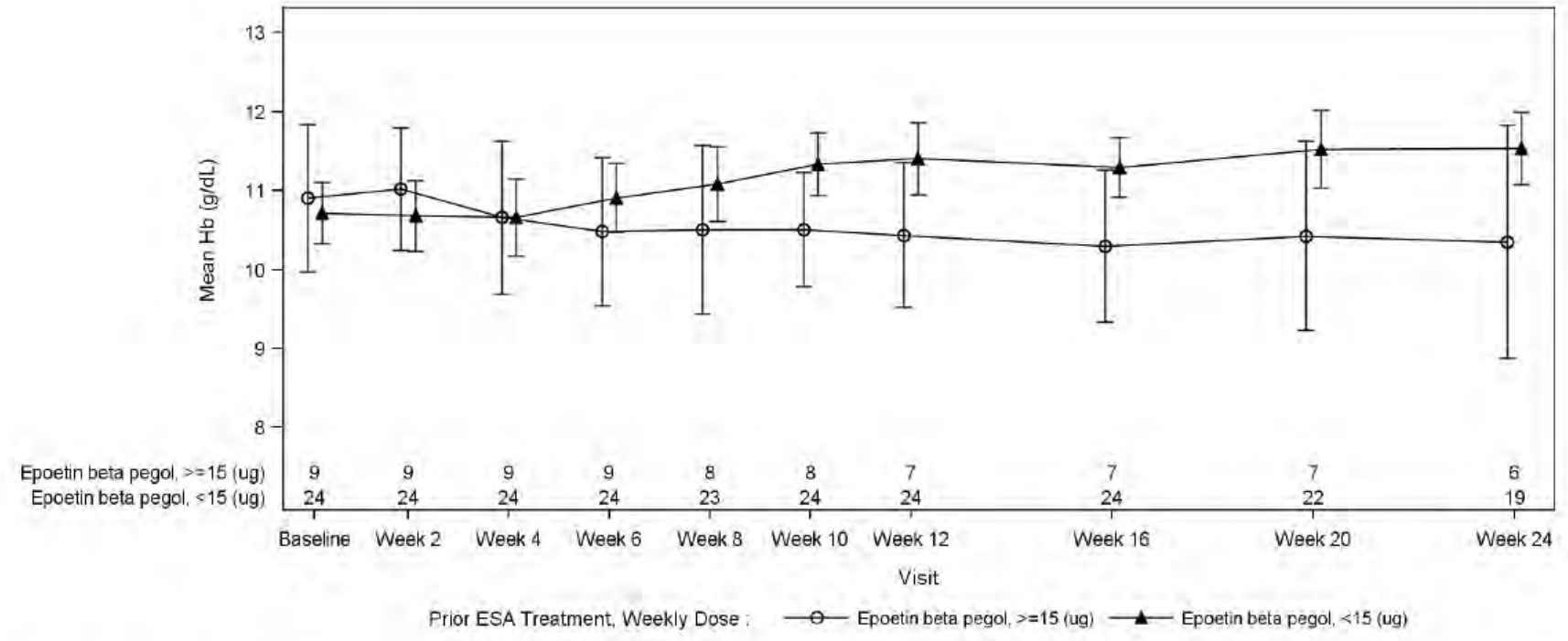
5.3.5.1—6 図 14.2.1.3.1 より引用



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_1.sas

図 2.7.6.25－27　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）
（Conversion 集団）

5.3.5.1—6 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_4.sas

図 2.7.6.25－28　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）
（Conversion 集団）

5.3.5.1—6 図 14.2.1.4.4 より引用

表 2.7.6.25－81 前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（Conversion 集団）

			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	27	10.51	0.80	10.50	(8.9, 12.0)	(10.20, 10.83)							
		Week 2	27	10.55	0.99	10.60	(8.5, 12.1)	(10.16, 10.94)	27	0.03	0.57	0.20	(-1.1, 1.1)	(-0.19, 0.26)	0.765
		Week 4	27	10.51	1.07	10.70	(8.0, 12.1)	(10.09, 10.93)	27	0.00	0.77	0.00	(-1.5, 1.6)	(-0.31, 0.30)	0.980
		Week 6	26	10.54	1.02	10.90	(8.2, 12.0)	(10.13, 10.96)	26	-0.02	0.90	-0.05	(-1.8, 1.6)	(-0.38, 0.34)	0.914
		Week 8	26	10.87	1.14	11.20	(8.4, 12.5)	(10.41, 11.33)	26	0.31	1.04	0.15	(-1.6, 2.6)	(-0.11, 0.73)	0.139
		Week 10	26	10.88	0.95	10.70	(9.2, 12.6)	(10.49, 11.26)	26	0.32	0.98	0.40	(-1.6, 2.5)	(-0.08, 0.71)	0.115
		Week 12	26	11.04	0.94	11.15	(9.1, 13.1)	(10.66, 11.42)	26	0.48	1.11	0.25	(-1.5, 3.2)	(0.03, 0.93)	0.036
		Week 16	26	11.13	0.98	11.20	(9.1, 13.0)	(10.74, 11.53)	26	0.57	1.05	0.45	(-1.1, 3.1)	(0.15, 1.00)	0.010
		Week 20	23	11.56	0.98	11.70	(8.3, 13.0)	(11.14, 11.98)	23	0.92	1.15	0.90	(-1.7, 3.4)	(0.42, 1.42)	<0.001
		Week 24	21	11.30	1.08	11.70	(7.4, 12.4)	(10.81, 11.80)	21	0.69	1.12	0.70	(-2.6, 2.4)	(0.18, 1.20)	0.010
		Week 24(LOCF)	27	11.16	1.27	11.70	(7.4, 12.4)	(10.65, 11.66)	27	0.64	1.16	0.70	(-2.6, 2.6)	(0.18, 1.10)	0.008
	Darbepoetin alfa, <15 (ug)	Baseline	20	10.73	0.85	10.90	(9.3, 12.1)	(10.33, 11.13)							
		Week 2	20	10.81	1.09	10.75	(8.9, 13.8)	(10.30, 11.32)	20	0.08	0.53	0.10	(-0.7, 1.7)	(-0.17, 0.33)	0.511
		Week 4	20	10.97	1.03	11.10	(8.7, 12.8)	(10.48, 11.45)	20	0.24	0.55	0.35	(-0.9, 0.9)	(-0.02, 0.49)	0.073
		Week 6	20	11.06	1.13	10.80	(8.5, 13.5)	(10.53, 11.58)	20	0.33	0.70	0.20	(-1.1, 1.5)	(0.00, 0.65)	0.053
		Week 8	20	11.39	0.97	11.30	(8.9, 13.7)	(10.93, 11.85)	20	0.66	0.72	0.75	(-0.7, 1.8)	(0.32, 1.00)	<0.001
		Week 10	20	11.55	1.03	11.70	(9.3, 13.6)	(11.07, 12.03)	20	0.82	0.79	0.70	(-0.4, 2.3)	(0.45, 1.19)	<0.001
		Week 12	20	11.64	1.02	11.55	(9.1, 13.4)	(11.16, 12.12)	20	0.91	0.92	0.85	(-0.8, 2.5)	(0.48, 1.34)	<0.001
		Week 16	19	11.92	0.89	12.00	(9.5, 13.4)	(11.49, 12.35)	19	1.13	1.15	1.20	(-1.3, 3.0)	(0.57, 1.68)	<0.001
		Week 20	20	11.68	0.93	11.70	(9.9, 13.6)	(11.24, 12.11)	20	0.95	1.16	0.95	(-1.3, 2.8)	(0.40, 1.49)	0.002
		Week 24	20	11.75	0.96	11.90	(10.0, 13.2)	(11.30, 12.19)	20	1.02	1.15	1.10	(-1.5, 3.2)	(0.47, 1.56)	<0.001
		Week 24(LOCF)	20	11.75	0.96	11.90	(10.0, 13.2)	(11.30, 12.19)	20	1.02	1.15	1.10	(-1.5, 3.2)	(0.47, 1.56)	<0.001

表 2.7.6.25－81 前治療 ESA 製剤の用量別の Hb 値の記述統計量（FAS）（Conversion 集団）（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	p value
	Epoetinbeta pegol, >=15 (ug)	Baseline	9	10.91	1.21	11.60	(9.4, 12.1)	(9.98, 11.84)							
		Week 2	9	11.02	1.00	11.20	(9.5, 12.6)	(10.25, 11.79)	9	0.11	0.65	-0.20	(-0.6, 1.3)	(-0.39, 0.61)	0.623
		Week 4	9	10.67	1.26	10.60	(8.9, 12.6)	(9.70, 11.63)	9	-0.24	1.05	-0.10	(-1.5, 1.6)	(-1.05, 0.56)	0.505
		Week 6	9	10.49	1.22	10.60	(8.3, 11.9)	(9.55, 11.42)	9	-0.42	0.92	-0.80	(-1.5, 1.2)	(-1.13, 0.29)	0.208
		Week 8	8	10.51	1.28	10.55	(9.1, 12.9)	(9.44, 11.58)	8	-0.56	1.23	-0.60	(-2.4, 1.2)	(-1.59, 0.47)	0.238
		Week 10	8	10.51	0.86	10.30	(9.4, 11.9)	(9.79, 11.24)	8	-0.56	1.42	-0.70	(-2.4, 2.1)	(-1.75, 0.62)	0.299
		Week 12	7	10.44	0.99	10.20	(9.0, 11.9)	(9.53, 11.36)	7	-0.51	1.44	-0.80	(-2.2, 2.0)	(-1.84, 0.81)	0.380
		Week 16	7	10.30	1.05	10.30	(8.6, 11.7)	(9.33, 11.27)	7	-0.66	1.74	-1.20	(-2.6, 2.3)	(-2.26, 0.95)	0.356
		Week 20	7	10.43	1.30	10.70	(8.5, 12.1)	(9.22, 11.64)	7	-0.53	1.83	-0.90	(-3.2, 2.7)	(-2.22, 1.17)	0.474
		Week 24	6	10.35	1.41	10.60	(8.2, 12.1)	(8.87, 11.83)	6	-0.42	1.93	-1.00	(-2.6, 2.7)	(-2.44, 1.61)	0.620
		Week 24(LOCF)	9	10.11	1.48	10.40	(8.2, 12.1)	(8.97, 11.25)	9	-0.80	1.80	-1.20	(-3.2, 2.7)	(-2.18, 0.58)	0.219
	Epoetinbeta pegol, <15 (ug)	Baseline	24	10.72	0.92	10.75	(9.1, 12.5)	(10.33, 11.11)							
		Week 2	24	10.69	1.05	10.85	(8.4, 12.4)	(10.24, 11.13)	24	-0.03	0.58	-0.15	(-0.8, 1.1)	(-0.28, 0.21)	0.779
		Week 4	24	10.67	1.15	10.90	(8.0, 12.3)	(10.18, 11.15)	24	-0.05	0.82	-0.10	(-1.7, 1.5)	(-0.40, 0.29)	0.748
		Week 6	24	10.91	1.03	10.85	(8.7, 12.2)	(10.48, 11.35)	24	0.19	0.99	0.00	(-1.8, 2.4)	(-0.23, 0.61)	0.354
		Week 8	23	11.09	1.09	11.20	(9.3, 12.7)	(10.62, 11.56)	23	0.38	1.07	0.40	(-1.9, 2.6)	(-0.08, 0.84)	0.099
		Week 10	24	11.34	0.94	11.35	(9.4, 13.0)	(10.94, 11.73)	24	0.62	1.02	0.65	(-1.6, 3.0)	(0.19, 1.05)	0.007
		Week 12	24	11.41	1.07	11.50	(9.4, 13.1)	(10.96, 11.86)	24	0.69	1.15	0.80	(-1.6, 2.9)	(0.20, 1.17)	0.007
		Week 16	24	11.30	0.89	11.40	(9.7, 12.5)	(10.92, 11.68)	24	0.58	1.19	0.70	(-1.9, 2.7)	(0.08, 1.08)	0.025
		Week 20	22	11.53	1.10	11.45	(9.3, 13.3)	(11.04, 12.02)	22	0.81	1.18	0.75	(-1.2, 2.9)	(0.28, 1.33)	0.004
		Week 24	19	11.54	0.95	11.30	(9.9, 13.2)	(11.08, 12.00)	19	0.68	1.06	0.70	(-1.0, 2.7)	(0.17, 1.19)	0.012
		Week 24(LOCF)	24	11.44	0.94	11.25	(9.9, 13.2)	(11.04, 11.83)	24	0.72	1.09	0.70	(-1.0, 2.8)	(0.26, 1.18)	0.004

Note(s): Hb (g/dL).
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
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—6 表 14.2.2.6.1 より引用

表 2.7.6.25－82　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（Conversion 集団）

Treatment Group	Prior ESA Treatment, Weekly Dose	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Darbepoetin alfa, >=15 (ug)	Week 2	27	10.51 (0.80)	10.58	0.18	(10.22, 10.94)
		Week 4	27	10.51 (0.80)	10.54	0.18	(10.18, 10.90)
		Week 6	26	10.56 (0.78)	10.52	0.18	(10.16, 10.88)
		Week 8	26	10.56 (0.78)	10.85	0.18	(10.49, 11.21)
		Week 10	26	10.56 (0.78)	10.86	0.18	(10.50, 11.22)
		Week 12	26	10.56 (0.78)	11.02	0.18	(10.66, 11.38)
		Week 16	26	10.56 (0.78)	11.11	0.18	(10.75, 11.47)
		Week 20	23	10.64 (0.77)	11.45	0.19	(11.08, 11.82)
		Week 24	21	10.61 (0.79)	11.16	0.19	(10.79, 11.54)
	Darbepoetin alfa, <15 (ug)	Week 2	20	10.73 (0.85)	10.81	0.19	(10.43, 11.19)
		Week 4	20	10.73 (0.85)	10.97	0.19	(10.59, 11.35)
		Week 6	20	10.73 (0.85)	11.06	0.19	(10.68, 11.44)
		Week 8	20	10.73 (0.85)	11.39	0.19	(11.01, 11.77)
		Week 10	20	10.73 (0.85)	11.55	0.19	(11.17, 11.93)
		Week 12	20	10.73 (0.85)	11.64	0.19	(11.26, 12.02)
		Week 16	19	10.79 (0.83)	11.82	0.19	(11.44, 12.21)
		Week 20	20	10.73 (0.85)	11.68	0.19	(11.30, 12.06)
		Week 24	20	10.73 (0.85)	11.75	0.19	(11.37, 12.13)

表 2.7.6.25－82　前治療 ESA 製剤の用量別の Hb 値（MMRM，FAS）（Conversion 集団）（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	9	10.91 (1.21)	11.04	0.37	(10.26, 11.82)
		Week 4	9	10.91 (1.21)	10.68	0.37	(9.90, 11.46)
		Week 6	9	10.91 (1.21)	10.50	0.37	(9.72, 11.28)
		Week 8	8	11.08 (1.18)	10.40	0.38	(9.60, 11.20)
		Week 10	8	11.08 (1.18)	10.40	0.38	(9.60, 11.20)
		Week 12	7	10.96 (1.23)	10.35	0.40	(9.53, 11.18)
		Week 16	7	10.96 (1.23)	10.21	0.40	(9.39, 11.04)
		Week 20	7	10.96 (1.23)	10.34	0.40	(9.51, 11.17)
		Week 24	6	10.77 (1.22)	10.23	0.42	(9.37, 11.08)
	Epoetin beta pegol, <15 (ug)	Week 2	24	10.72 (0.92)	10.69	0.19	(10.31, 11.07)
		Week 4	24	10.72 (0.92)	10.67	0.19	(10.29, 11.05)
		Week 6	24	10.72 (0.92)	10.92	0.19	(10.54, 11.30)
		Week 8	23	10.70 (0.94)	11.10	0.19	(10.72, 11.49)
		Week 10	24	10.72 (0.92)	11.34	0.19	(10.96, 11.72)
		Week 12	24	10.72 (0.92)	11.41	0.19	(11.03, 11.79)
		Week 16	24	10.72 (0.92)	11.31	0.19	(10.93, 11.68)
		Week 20	22	10.72 (0.95)	11.50	0.19	(11.11, 11.88)
		Week 24	19	10.86 (0.94)	11.48	0.20	(11.08, 11.88)

Note(s): Hb (g/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
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_4.sas

5.3.5.1—6 表 14.2.2.6.4 より引用

表 2.7.6.25－83 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	23	10.62	1.04	10.70	(8.0, 12.1)	(10.17, 11.07)							
		Week 2	23	10.98	1.14	11.00	(8.4, 13.8)	(10.49, 11.47)	23	0.36	0.77	0.20	(-1.0, 1.7)	(0.03, 0.69)	0.035
		Week 4	23	11.11	1.14	11.30	(8.0, 12.8)	(10.62, 11.60)	23	0.49	0.75	0.50	(-1.1, 1.9)	(0.17, 0.82)	0.005
		Week 6	23	11.30	1.18	11.50	(8.3, 13.5)	(10.79, 11.81)	23	0.68	1.09	0.60	(-1.3, 2.9)	(0.21, 1.15)	0.007
		Week 8	22	11.49	0.80	11.55	(9.5, 13.7)	(11.14, 11.85)	22	0.83	0.87	0.85	(-0.5, 3.2)	(0.44, 1.21)	<0.001
		Week 10	22	11.77	0.82	11.65	(10.0, 13.6)	(11.41, 12.13)	22	1.10	1.15	1.05	(-1.7, 4.1)	(0.60, 1.61)	<0.001
		Week 12	22	11.81	0.64	11.75	(10.4, 12.9)	(11.53, 12.09)	22	1.15	1.32	1.15	(-1.3, 4.9)	(0.56, 1.73)	<0.001
		Week 16	22	11.98	0.73	12.00	(10.3, 13.8)	(11.65, 12.30)	22	1.31	1.51	1.30	(-1.8, 4.6)	(0.64, 1.98)	<0.001
		Week 20	22	12.09	0.84	12.20	(10.9, 14.6)	(11.72, 12.46)	22	1.43	1.41	1.30	(-1.2, 4.8)	(0.80, 2.05)	<0.001
		Week 24	19	12.03	0.56	12.10	(10.8, 13.1)	(11.76, 12.30)	19	1.22	0.92	1.40	(-0.8, 3.3)	(0.77, 1.66)	<0.001
		Week 24(LOCF)	23	11.88	0.94	12.10	(8.3, 13.1)	(11.47, 12.28)	23	1.26	1.16	1.40	(-1.3, 3.6)	(0.76, 1.76)	<0.001
MT-6548	Non-user	Baseline	69	10.45	0.96	10.40	(8.2, 12.5)	(10.22, 10.68)							
		Week 2	69	10.54	0.96	10.70	(8.4, 12.6)	(10.31, 10.77)	69	0.09	0.63	0.10	(-1.1, 1.4)	(-0.06, 0.24)	0.228
		Week 4	67	10.64	1.13	10.90	(8.0, 13.1)	(10.37, 10.92)	67	0.19	0.96	0.20	(-1.7, 2.8)	(-0.05, 0.42)	0.116
		Week 6	66	10.84	1.07	10.90	(8.2, 12.8)	(10.58, 11.10)	66	0.37	1.00	0.40	(-1.8, 2.6)	(0.12, 0.61)	0.004
		Week 8	65	11.10	1.12	11.30	(8.4, 13.1)	(10.83, 11.38)	65	0.64	1.13	0.70	(-1.9, 3.0)	(0.36, 0.92)	<0.001
		Week 10	65	11.31	1.07	11.50	(8.3, 13.3)	(11.05, 11.58)	65	0.84	1.21	0.80	(-2.4, 4.0)	(0.54, 1.14)	<0.001
		Week 12	65	11.40	1.10	11.60	(8.3, 13.4)	(11.12, 11.67)	65	0.94	1.27	0.90	(-2.2, 3.7)	(0.63, 1.26)	<0.001
		Week 16	64	11.37	1.03	11.40	(8.6, 13.4)	(11.11, 11.63)	64	0.90	1.29	1.00	(-2.6, 4.0)	(0.57, 1.22)	<0.001
		Week 20	62	11.41	1.13	11.55	(8.5, 13.6)	(11.12, 11.70)	62	0.91	1.39	1.00	(-3.2, 4.4)	(0.56, 1.26)	<0.001
		Week 24	60	11.41	1.16	11.55	(8.2, 14.1)	(11.10, 11.71)	60	0.93	1.42	0.90	(-2.6, 4.3)	(0.56, 1.30)	<0.001
		Week 24(LOCF)	69	11.27	1.23	11.50	(8.2, 14.1)	(10.97, 11.56)	69	0.82	1.46	0.90	(-3.2, 4.3)	(0.46, 1.17)	<0.001

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_7_16_2.sas

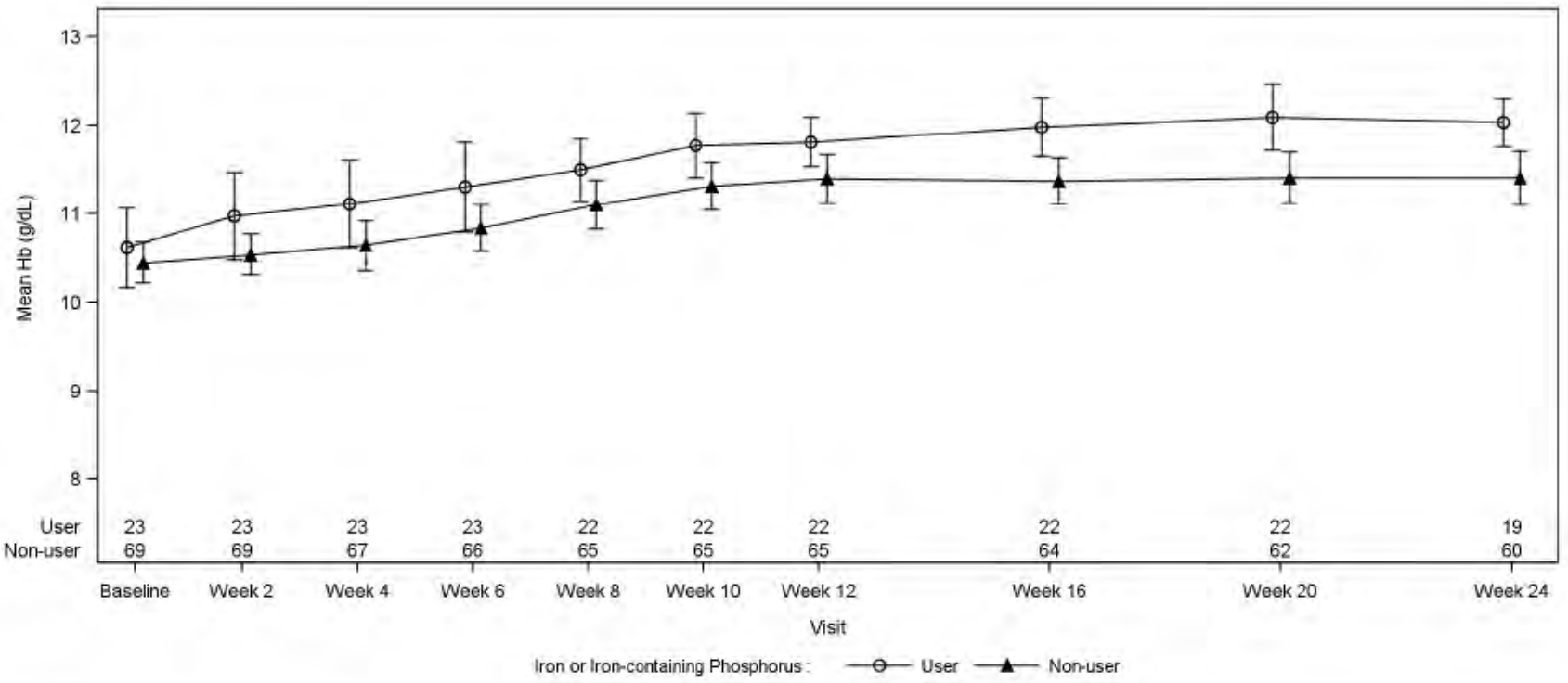
5.3.5.1—8 表 14.2.2.7.16.2 より引用

表 2.7.6.25－84　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	23	10.62 (1.04)	11.00	0.18	(10.65, 11.35)
		Week 4	23	10.62 (1.04)	11.15	0.18	(10.80, 11.50)
		Week 6	23	10.62 (1.04)	11.35	0.18	(11.00, 11.70)
		Week 8	22	10.66 (1.04)	11.48	0.18	(11.12, 11.84)
		Week 10	22	10.66 (1.04)	11.77	0.18	(11.42, 12.13)
		Week 12	22	10.66 (1.04)	11.83	0.18	(11.47, 12.19)
		Week 16	22	10.66 (1.04)	11.99	0.18	(11.63, 12.34)
		Week 20	22	10.66 (1.04)	12.10	0.18	(11.74, 12.45)
		Week 24	19	10.82 (0.87)	12.01	0.19	(11.63, 12.38)
	Non-user	Week 2	69	10.45 (0.96)	10.55	0.12	(10.32, 10.79)
		Week 4	67	10.46 (0.97)	10.67	0.12	(10.44, 10.91)
		Week 6	66	10.48 (0.97)	10.85	0.12	(10.61, 11.09)
		Week 8	65	10.47 (0.97)	11.12	0.12	(10.88, 11.36)
		Week 10	65	10.47 (0.98)	11.33	0.12	(11.09, 11.57)
		Week 12	65	10.45 (0.96)	11.41	0.12	(11.17, 11.65)
		Week 16	64	10.48 (0.95)	11.40	0.12	(11.16, 11.64)
		Week 20	62	10.50 (0.96)	11.38	0.12	(11.14, 11.62)
		Week 24	60	10.48 (0.95)	11.38	0.12	(11.13, 11.62)

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_7_21_2.sas

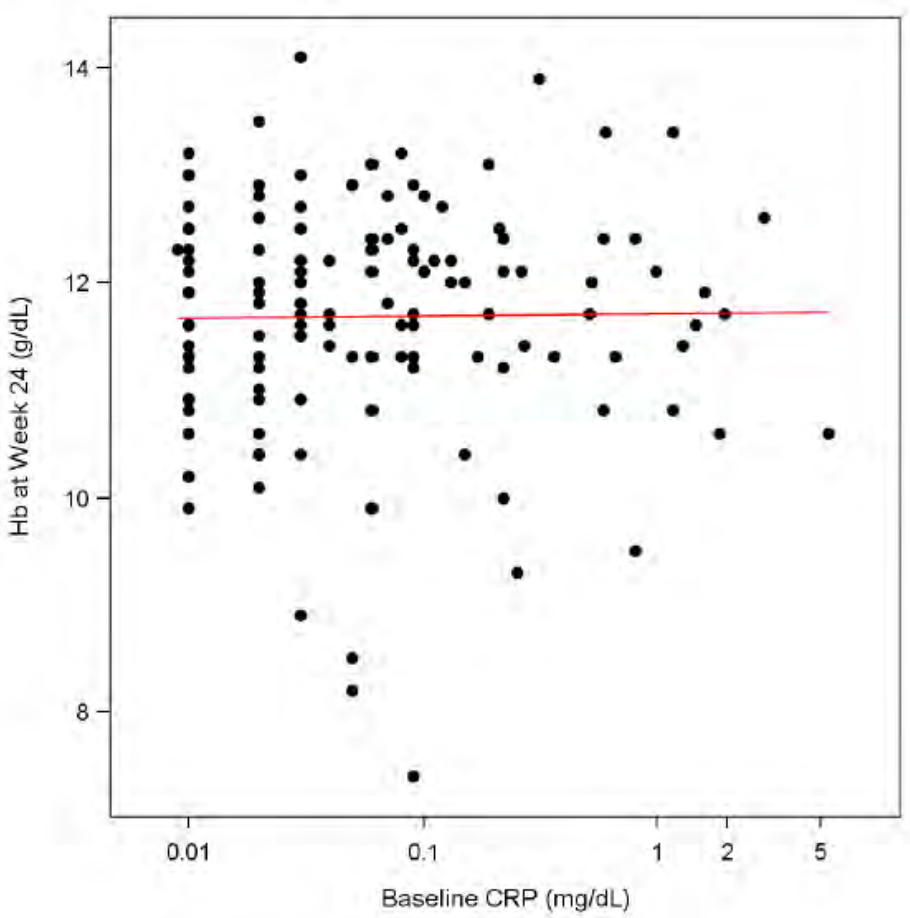
5.3.5.1—8 表 14.2.2.7.21.2 より引用



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 14.2.2.7.16.2
Source: f_14_2_1_6_1_2.sas

図 2.7.6.25－29　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—8 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 2.7.6.25－30　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—6 図 14.2.1.8.1 より引用

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Sex	Male	MT-6548	66	392.37	188.19	450.00	(0.0, 600.0)	(346.11, 438.63)
		darbepoetin	67	31.88	30.03	22.50	(0.0, 180.0)	(24.56, 39.21)
	Female	MT-6548	70	365.50	188.49	300.00	(0.0, 600.0)	(320.55, 410.44)
		darbepoetin	78	19.97	22.74	15.00	(0.0, 174.2)	(14.84, 25.10)
Age at Informed Consent (years)	<65	MT-6548	31	389.37	192.44	305.36	(0.0, 600.0)	(318.78, 459.96)
		darbepoetin	25	20.25	14.60	15.00	(3.8, 52.5)	(14.22, 26.28)
	>=65	MT-6548	105	375.34	187.65	300.00	(0.0, 600.0)	(339.03, 411.66)
		darbepoetin	120	26.56	28.77	15.00	(0.0, 180.0)	(21.36, 31.76)
	<75	MT-6548	75	389.36	191.85	305.36	(0.0, 600.0)	(345.22, 433.50)
		darbepoetin	76	22.68	19.23	15.00	(0.0, 90.0)	(18.28, 27.07)
	>=75	MT-6548	61	365.24	184.15	300.00	(0.0, 600.0)	(318.07, 412.40)
		darbepoetin	69	28.56	33.31	15.00	(0.0, 180.0)	(20.55, 36.56)
Weight (kg)	<60	MT-6548	87	368.19	195.15	300.00	(0.0, 600.0)	(326.60, 409.78)
		darbepoetin	88	22.15	18.40	15.00	(0.0, 90.0)	(18.25, 26.04)
	>=60	MT-6548	49	396.91	175.40	450.00	(112.5, 600.0)	(346.53, 447.29)
		darbepoetin	57	30.61	35.98	15.00	(0.0, 180.0)	(21.07, 40.16)
BMI (kg/m^2)	<25	MT-6548	92	372.42	195.59	300.00	(0.0, 600.0)	(331.91, 412.92)
		darbepoetin	107	24.46	24.68	15.00	(0.0, 180.0)	(19.72, 29.19)
	>=25	MT-6548	44	391.34	172.94	377.68	(90.0, 600.0)	(338.77, 443.92)
		darbepoetin	38	28.34	32.65	15.00	(0.0, 174.2)	(17.61, 39.08)

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Etiology of CKD	Diabetes	MT-6548	40	375.15	189.13	300.00	(0.0, 600.0)	(314.66, 435.64)
		darbepoetin	45	30.73	30.62	30.00	(3.8, 180.0)	(21.53, 39.93)
	Hypertension	MT-6548	46	390.98	182.98	450.00	(0.0, 600.0)	(336.64, 445.32)
		darbepoetin	55	23.46	28.10	15.00	(0.0, 174.2)	(15.86, 31.06)
	Autoimmune/Glomerulonephritis/Vasculitis	MT-6548	18	481.40	157.16	597.58	(150.0, 600.0)	(403.25, 559.56)
		darbepoetin	31	22.52	19.68	15.00	(0.0, 90.0)	(15.30, 29.74)
	Interstitial Nephritis/Pyelonephritis	MT-6548	4	374.95	195.05	374.91	(150.0, 600.0)	(64.58, 685.32)
		darbepoetin	1	7.50	-	7.50	(7.5, 7.5)	-
	Cystic/Hereditary/Congenital Disease	MT-6548	13	262.50	187.50	150.00	(0.0, 600.0)	(149.19, 375.81)
		darbepoetin	9	22.83	15.13	15.00	(7.5, 45.0)	(11.21, 34.46)
	Neoplasms/Tumors	MT-6548	0					
		darbepoetin	0					
Duration of Anemia from CKD (years)	<1	MT-6548	46	377.78	189.04	372.41	(0.0, 600.0)	(321.64, 433.91)
		darbepoetin	48	24.24	21.36	15.00	(0.0, 90.0)	(18.04, 30.44)
	1<= to <5	MT-6548	69	360.05	185.28	300.00	(0.0, 600.0)	(315.55, 404.56)
		darbepoetin	76	25.65	31.07	15.00	(0.0, 180.0)	(18.55, 32.75)
	>=5	MT-6548	21	440.95	191.05	564.71	(0.0, 600.0)	(353.98, 527.91)
		darbepoetin	21	27.67	22.83	30.00	(0.0, 75.0)	(17.28, 38.07)

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Complications	Hypertension	MT-6548	133	376.06	188.44	300.00	(0.0, 600.0)	(343.74, 408.39)
		darbepoetin	137	25.32	27.15	15.00	(0.0, 180.0)	(20.73, 29.91)
	Diabetes	MT-6548	49	401.14	189.69	450.00	(0.0, 600.0)	(346.66, 455.63)
		darbepoetin	57	28.86	29.05	22.50	(0.0, 180.0)	(21.15, 36.57)
	Dyslipidaemia	MT-6548	87	415.94	169.38	450.00	(0.0, 600.0)	(379.84, 452.04)
		darbepoetin	93	25.09	28.22	15.00	(0.0, 180.0)	(19.28, 30.91)
Baseline Hb (g/dL)	<9	MT-6548	8	422.48	214.82	522.32	(90.0, 600.0)	(242.88, 602.07)
		darbepoetin	7	14.82	15.28	11.48	(0.0, 45.0)	(0.69, 28.95)
	9<= to <11	MT-6548	84	394.99	193.46	450.00	(0.0, 600.0)	(353.00, 436.97)
		darbepoetin	88	28.15	31.84	15.00	(0.0, 180.0)	(21.40, 34.90)
	>=11	MT-6548	44	339.15	169.95	300.00	(0.0, 600.0)	(287.48, 390.82)
		darbepoetin	50	22.26	16.22	15.00	(0.0, 75.0)	(17.65, 26.87)
Baseline eGFR (mL/min/1.73m²)	<15	MT-6548	52	364.13	191.79	300.00	(0.0, 600.0)	(310.74, 417.53)
		darbepoetin	47	33.17	31.32	30.00	(3.8, 174.2)	(23.97, 42.36)
	15<= to <30	MT-6548	49	376.48	189.00	450.00	(0.0, 600.0)	(322.19, 430.76)
		darbepoetin	66	23.72	26.02	15.00	(0.0, 180.0)	(17.32, 30.12)
	30<= to <60	MT-6548	35	402.83	184.36	444.83	(150.0, 600.0)	(339.50, 466.16)
		darbepoetin	31	18.13	18.55	15.00	(0.0, 77.5)	(11.32, 24.93)
	>=60	MT-6548	0					
		darbepoetin	1	7.50	-	7.50	(7.5, 7.5)	-

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Baseline Liver Function Test (U/L)	AST <=40 and ALT <=45	MT-6548	132	379.78	189.60	300.00	(0.0, 600.0)	(347.14, 412.43)
		darbepoetin	143	24.68	26.24	15.00	(0.0, 180.0)	(20.34, 29.01)
	'AST >40 or ALT >45' and 'AST <=80 and ALT <=90'	MT-6548	3	400.00	86.60	450.00	(300.0, 450.0)	(184.87, 615.13)
		darbepoetin	1	90.00	-	90.00	(90.0, 90.0)	-
	AST >80 or ALT >90	MT-6548	1	150.00	-	150.00	(150.0, 150.0)	-
		darbepoetin	1	75.00	-	75.00	(75.0, 75.0)	-
Baseline CRP (mg/dL)	<0.31	MT-6548	116	381.83	189.35	305.36	(0.0, 600.0)	(347.00, 416.65)
		darbepoetin	127	23.21	19.87	15.00	(0.0, 90.0)	(19.72, 26.70)
	>=0.31	MT-6548	20	359.46	184.41	300.00	(150.0, 600.0)	(273.16, 445.77)
		darbepoetin	18	41.42	53.95	16.32	(0.0, 180.0)	(14.59, 68.25)
Baseline Serum Ferritin (ng/mL)	<82	MT-6548	45	398.22	201.25	450.00	(0.0, 600.0)	(337.76, 458.68)
		darbepoetin	50	22.26	18.32	15.00	(0.0, 90.0)	(17.05, 27.46)
	82<= to <155	MT-6548	42	404.48	169.29	450.00	(150.0, 600.0)	(351.73, 457.24)
		darbepoetin	50	24.78	21.94	15.00	(3.6, 90.0)	(18.55, 31.02)
	>=155	MT-6548	49	338.23	187.94	300.00	(0.0, 600.0)	(284.24, 392.21)
		darbepoetin	45	29.82	37.85	15.00	(0.0, 180.0)	(18.45, 41.19)
Baseline TSAT (%)	<25	MT-6548	41	344.85	184.47	300.00	(0.0, 600.0)	(286.63, 403.08)
		darbepoetin	49	24.35	31.10	15.00	(0.0, 180.0)	(15.42, 33.28)
	25<= to <34	MT-6548	45	396.87	197.30	450.00	(0.0, 600.0)	(337.59, 456.14)
		darbepoetin	46	24.17	16.74	20.07	(3.8, 77.5)	(19.20, 29.14)
	>=34	MT-6548	50	389.67	182.73	447.41	(0.0, 600.0)	(337.74, 441.60)
		darbepoetin	50	27.77	30.31	15.00	(0.0, 174.2)	(19.16, 36.39)

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Smoking Status	Never Smoked	MT-6548	80	384.94	178.57	300.00	(0.0, 600.0)	(345.20, 424.67)
		darbepoetin	84	23.54	29.28	15.00	(0.0, 180.0)	(17.18, 29.89)
	Ex-Smoker	MT-6548	48	391.12	196.61	447.41	(0.0, 600.0)	(334.03, 448.21)
		darbepoetin	45	28.71	23.65	22.50	(0.0, 90.0)	(21.60, 35.81)
	Current Smoker	MT-6548	8	239.06	198.37	150.00	(0.0, 600.0)	(73.22, 404.90)
		darbepoetin	16	26.55	22.89	18.75	(7.5, 84.3)	(14.35, 38.75)
Concomitant Medications of Oral Iron at Baseline	Yes	MT-6548	33	298.01	170.50	300.00	(0.0, 600.0)	(237.55, 358.47)
		darbepoetin	27	17.00	19.73	7.50	(0.0, 90.0)	(9.20, 24.81)
	No	MT-6548	103	404.34	186.95	450.00	(0.0, 600.0)	(367.80, 440.88)
		darbepoetin	118	27.41	28.03	15.00	(0.0, 180.0)	(22.30, 32.52)
Concomitant Medications of Oral Iron at Week 24	Yes	MT-6548	53	351.77	191.37	300.00	(0.0, 600.0)	(299.02, 404.52)
		darbepoetin	47	27.45	31.23	15.00	(0.0, 174.2)	(18.28, 36.62)
	No	MT-6548	83	395.63	185.16	444.83	(0.0, 600.0)	(355.20, 436.06)
		darbepoetin	98	24.53	24.73	15.00	(0.0, 180.0)	(19.57, 29.48)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Baseline	Yes	MT-6548	0					
		darbepoetin	2	33.39	37.64	33.39	(6.8, 60.0)	(-304.76, 371.54)
	No	MT-6548	136	378.54	188.13	300.00	(0.0, 600.0)	(346.64, 410.44)
		darbepoetin	143	25.36	26.92	15.00	(0.0, 180.0)	(20.91, 29.81)
Concomitant Medications of Iron-Containing Phosphorus Adsorbent at Week 24	Yes	MT-6548	0					
		darbepoetin	2	33.39	37.64	33.39	(6.8, 60.0)	(-304.76, 371.54)
	No	MT-6548	136	378.54	188.13	300.00	(0.0, 600.0)	(346.64, 410.44)
		darbepoetin	143	25.36	26.92	15.00	(0.0, 180.0)	(20.91, 29.81)

表 2.7.6.25－85 被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Prior ESA Treatment: Medication	Epoetin	MT-6548	0					
		darbepoetin	0					
	Darbepoetin alfa	MT-6548	43	397.67	175.92	300.00	(0.0, 600.0)	(343.54, 451.81)
		darbepoetin	45	34.54	34.60	30.00	(3.8, 180.0)	(24.14, 44.93)
	Epoetin beta pegol	MT-6548	26	456.97	166.44	510.03	(150.0, 600.0)	(389.74, 524.19)
		darbepoetin	35	[redacted]				
	Other	MT-6548	0					
		darbepoetin	0					
Prior ESA Treatment: Weekly Dose (ug)	Darbepoetin alfa, <10	MT-6548	15	310.00	154.92	300.00	(0.0, 600.0)	(224.21, 395.79)
		darbepoetin	15	18.75	12.60	15.00	(3.8, 45.0)	(11.77, 25.73)
	Darbepoetin alfa, 10<= to <15	MT-6548	5	480.00	125.50	450.00	(300.0, 600.0)	(324.17, 635.83)
		darbepoetin	1	22.50	-	22.50	(22.5, 22.5)	-
	Darbepoetin alfa, >=15	MT-6548	23	436.96	180.41	450.00	(150.0, 600.0)	(358.94, 514.97)
		darbepoetin	29	43.12	39.84	45.00	(3.8, 180.0)	(27.96, 58.27)
Prior ESA Treatment: Weekly Dose (ug)	Epoetin beta pegol, <6.25	MT-6548	0					
		darbepoetin	0					
	Epoetin beta pegol, 6.25<= to <12.5	MT-6548	9	448.94	147.48	452.68	(178.6, 600.0)	(325.64, 572.24)
		darbepoetin	15	[redacted]				
	Epoetin beta pegol, >=12.5	MT-6548	18	460.54	178.15	600.00	(150.0, 600.0)	(371.94, 549.13)
		darbepoetin	20	[redacted]				

表 2.7.6.25－85　被験者背景別の 20 週～24 週後の MT-6548 の 1 日平均投与量（FAS）（続き）

Stratification Factor (unit)	Category	Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
Concomitant Medications of CYP2B6 Substrates	Yes	MT-6548	8	506.25	137.42	600.00	(300.0, 600.0)	(391.37, 621.13)
		darbepoetin	5	32.25	21.48	30.00	(3.8, 60.0)	(5.58, 58.92)
	No	MT-6548	128	370.56	188.38	300.00	(0.0, 600.0)	(337.61, 403.51)
		darbepoetin	140	25.23	27.14	15.00	(0.0, 180.0)	(20.70, 29.77)

Note(s): average dose: MT-6548: average daily dose (mg); darbepoetin: average weekly dose (ug).
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
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): Subjects only in conversion group are included in analysis of 'Prior ESA Treatment'.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: c_001_1_2_1.sas

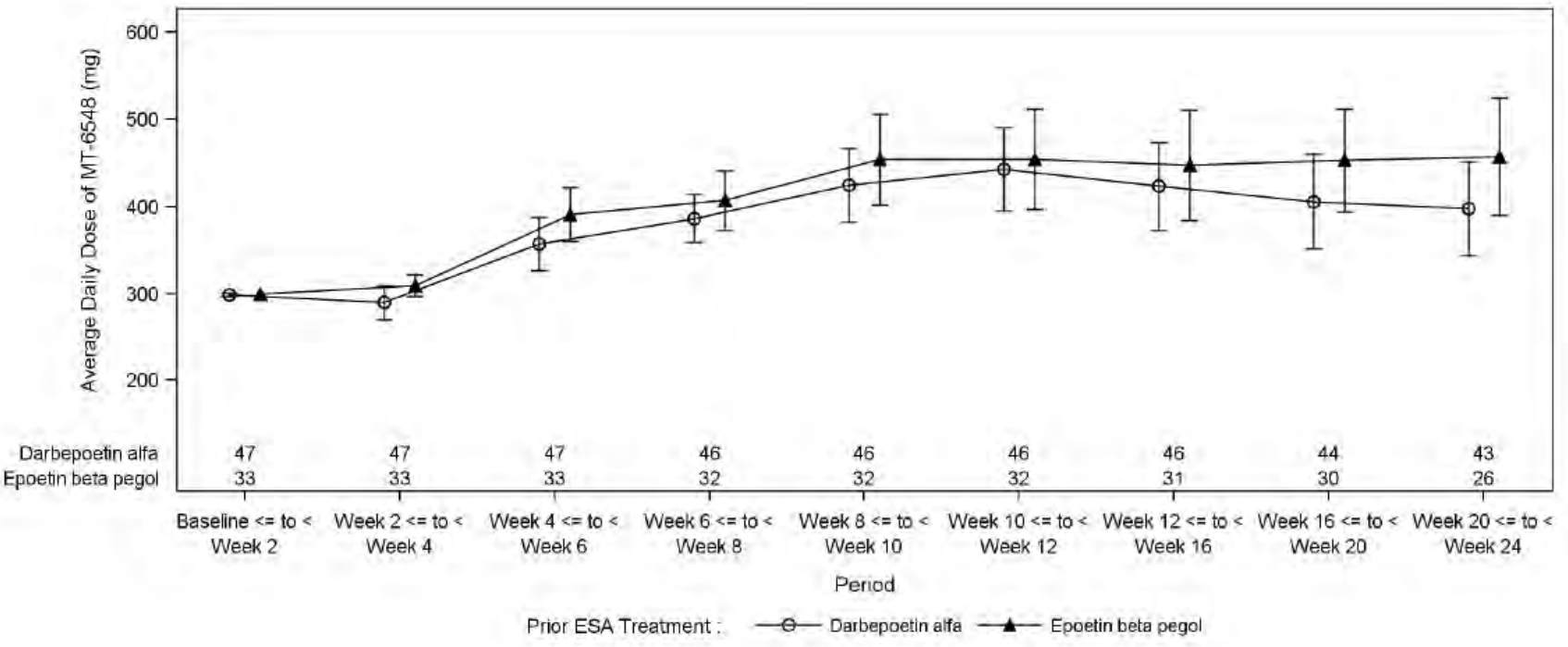
5.3.5.1—6 表 14.2.5.2 より引用

表 2.7.6.25－86　前治療 ESA 製剤の種類別の MT-6548 の 1 日平均投与量（FAS）（Conversion 集団）

Treatment Group	Prior ESA Treatment	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Darbepoetin alfa	Baseline <= to < Week 2	47	299.09	6.25	300.00	(257.1, 300.0)	(297.25, 300.92)
		Week 2 <= to < Week 4	47	289.97	66.66	300.00	(0.0, 450.0)	(270.40, 309.54)
		Week 4 <= to < Week 6	47	357.45	103.70	417.86	(0.0, 450.0)	(327.00, 387.89)
		Week 6 <= to < Week 8	46	386.41	91.76	450.00	(150.0, 460.7)	(359.16, 413.66)
		Week 8 <= to < Week 10	46	424.84	142.54	450.00	(10.7, 600.0)	(382.52, 467.17)
		Week 10 <= to < Week 12	46	442.78	160.06	450.00	(0.0, 600.0)	(395.25, 490.31)
		Week 12 <= to < Week 16	46	423.21	169.93	450.00	(150.0, 664.3)	(372.75, 473.68)
		Week 16 <= to < Week 20	44	405.80	177.54	441.96	(10.7, 600.0)	(351.83, 459.78)
		Week 20 <= to < Week 24	43	397.67	175.92	300.00	(0.0, 600.0)	(343.54, 451.81)
	Epoetin beta pegol	Baseline <= to < Week 2	33	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	33	309.42	33.96	300.00	(300.0, 439.3)	(297.37, 321.46)
		Week 4 <= to < Week 6	33	390.58	86.68	439.29	(150.0, 589.3)	(359.85, 421.32)
		Week 6 <= to < Week 8	32	406.81	94.21	450.00	(150.0, 600.0)	(372.84, 440.78)
		Week 8 <= to < Week 10	32	454.02	145.07	450.00	(150.0, 600.0)	(401.71, 506.32)
		Week 10 <= to < Week 12	32	454.35	159.03	450.00	(139.3, 600.0)	(397.02, 511.69)
		Week 12 <= to < Week 16	31	447.93	172.51	450.00	(85.7, 600.0)	(384.65, 511.20)
		Week 16 <= to < Week 20	30	452.87	158.37	468.75	(144.6, 600.0)	(393.74, 512.01)
		Week 20 <= to < Week 24	26	456.97	166.44	510.03	(150.0, 600.0)	(389.74, 524.19)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_4_4_1.sas

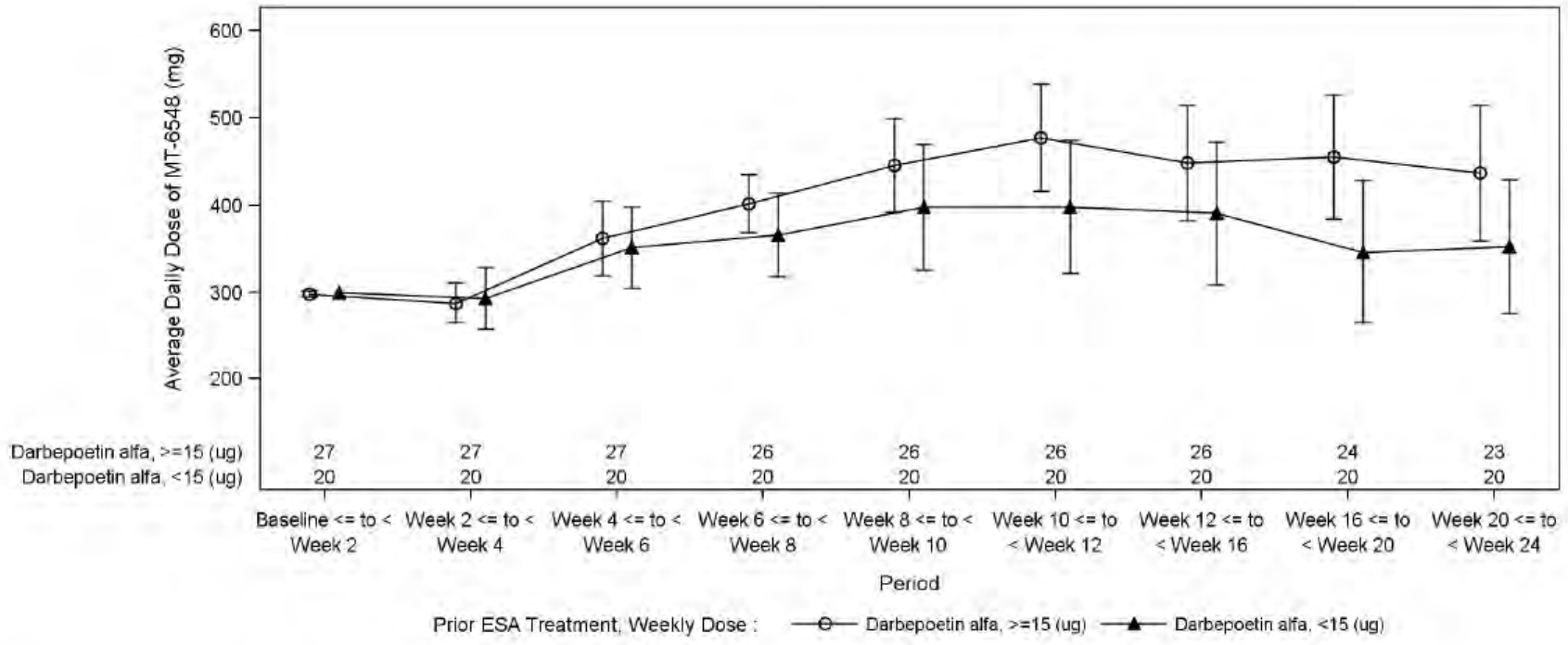
5.3.5.1—6 表 14.2.3.4.4.1 より引用




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Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.4.4.1
Source: f_14_2_4_4_1.sas
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図 2.7.6.25－31　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）（Conversion 集団）

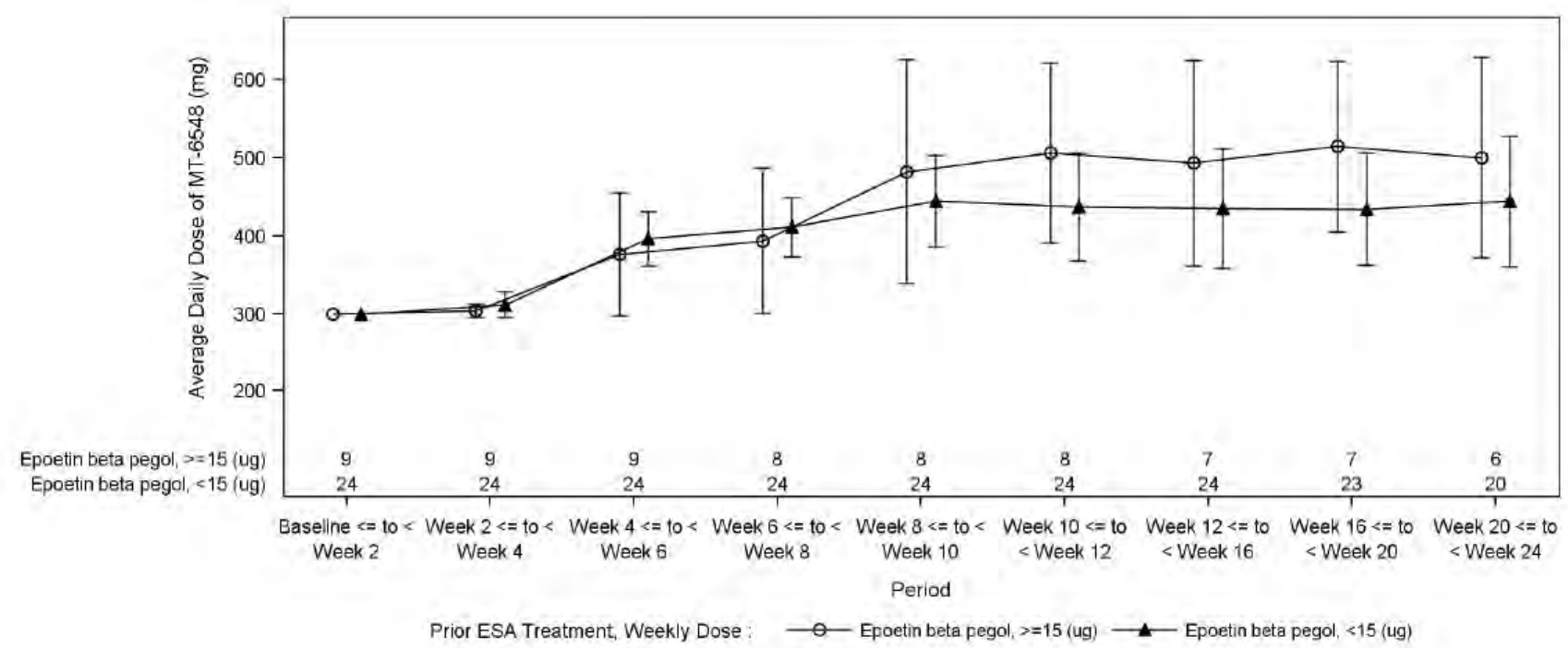
5.3.5.1—6 図 14.2.4.4.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.4.5.1
Source: f_14_2_4_5_1.sas

図 2.7.6.25－32　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）（Conversion 集団）

5.3.5.1—6 図 14.2.4.5.1 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.4.5.1
Source: f_14_2_4_5_4.sas

図 2.7.6.25－33　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）（Conversion 集団）

5.3.5.1—6 図 14.2.4.5.4 より引用

表 2.7.6.25－87　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（Conversion 集団）

Treatment Group	Prior ESA Treatment, Weekly Dose	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Darbepoetin alfa, >=15 (ug)	Baseline <= to < Week 2	27	298.41	8.25	300.00	(257.1, 300.0)	(295.15, 301.68)
		Week 2 <= to < Week 4	27	287.70	59.63	300.00	(0.0, 321.4)	(264.11, 311.29)
		Week 4 <= to < Week 6	27	361.90	108.30	417.86	(0.0, 450.0)	(319.06, 404.75)
		Week 6 <= to < Week 8	26	401.79	81.44	450.00	(150.0, 450.0)	(368.89, 434.68)
		Week 8 <= to < Week 10	26	445.88	132.76	450.00	(150.0, 600.0)	(392.26, 499.50)
		Week 10 <= to < Week 12	26	477.20	151.86	578.57	(150.0, 600.0)	(415.86, 538.54)
		Week 12 <= to < Week 16	26	448.35	164.53	450.00	(150.0, 600.0)	(381.90, 514.81)
		Week 16 <= to < Week 20	24	455.36	167.94	525.00	(150.0, 600.0)	(384.44, 526.27)
		Week 20 <= to < Week 24	23	436.96	180.41	450.00	(150.0, 600.0)	(358.94, 514.97)
	Darbepoetin alfa, <15 (ug)	Baseline <= to < Week 2	20	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	20	293.04	76.66	300.00	(0.0, 450.0)	(257.16, 328.91)
		Week 4 <= to < Week 6	20	351.43	99.58	300.00	(150.0, 450.0)	(304.82, 398.03)
		Week 6 <= to < Week 8	20	366.43	102.33	433.93	(150.0, 460.7)	(318.54, 414.32)
		Week 8 <= to < Week 10	20	397.50	153.42	450.00	(10.7, 600.0)	(325.70, 469.30)
		Week 10 <= to < Week 12	20	398.04	163.09	450.00	(0.0, 600.0)	(321.71, 474.37)
		Week 12 <= to < Week 16	20	390.54	175.44	450.00	(150.0, 664.3)	(308.43, 472.65)
		Week 16 <= to < Week 20	20	346.34	174.28	300.00	(10.7, 600.0)	(264.77, 427.90)
		Week 20 <= to < Week 24	20	352.50	163.41	300.00	(0.0, 600.0)	(276.02, 428.98)

表 2.7.6.25－87　前治療 ESA 製剤の用量別の MT-6548 の 1 日平均投与量（FAS）（Conversion 集団）（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	9	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	9	303.57	10.71	300.00	(300.0, 332.1)	(295.34, 311.81)
		Week 4 <= to < Week 6	9	376.19	103.11	439.29	(150.0, 450.0)	(296.93, 455.45)
		Week 6 <= to < Week 8	8	393.75	111.60	450.00	(150.0, 450.0)	(300.45, 487.05)
		Week 8 <= to < Week 10	8	482.14	170.85	589.29	(150.0, 600.0)	(339.31, 624.98)
		Week 10 <= to < Week 12	8	506.25	137.42	600.00	(300.0, 600.0)	(391.37, 621.13)
		Week 12 <= to < Week 16	7	492.86	142.68	600.00	(300.0, 600.0)	(360.90, 624.81)
		Week 16 <= to < Week 20	7	514.29	118.02	600.00	(300.0, 600.0)	(405.14, 623.44)
		Week 20 <= to < Week 24	6	500.00	122.47	525.00	(300.0, 600.0)	(371.47, 628.53)
	Epoetin beta pegol, <15 (ug)	Baseline <= to < Week 2	24	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	24	311.61	39.32	300.00	(300.0, 439.3)	(295.00, 328.21)
		Week 4 <= to < Week 6	24	395.98	81.50	439.29	(300.0, 589.3)	(361.57, 430.40)
		Week 6 <= to < Week 8	24	411.16	89.97	450.00	(300.0, 600.0)	(373.17, 449.15)
		Week 8 <= to < Week 10	24	444.64	138.26	450.00	(203.6, 600.0)	(386.26, 503.03)
		Week 10 <= to < Week 12	24	437.05	164.60	450.00	(139.3, 600.0)	(367.55, 506.56)
		Week 12 <= to < Week 16	24	434.82	180.87	450.00	(85.7, 600.0)	(358.45, 511.20)
		Week 16 <= to < Week 20	23	434.18	166.42	450.00	(144.6, 600.0)	(362.21, 506.15)
		Week 20 <= to < Week 24	20	444.06	178.16	510.03	(150.0, 600.0)	(360.67, 527.44)

Note(s): average dose: MT-6548: average daily dose (mg).
Note(s): There were no subjects who used Epoetin.
Note(s): Epoetin means Epoetin alfa or Epoetin beta.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_4_5_1.sas

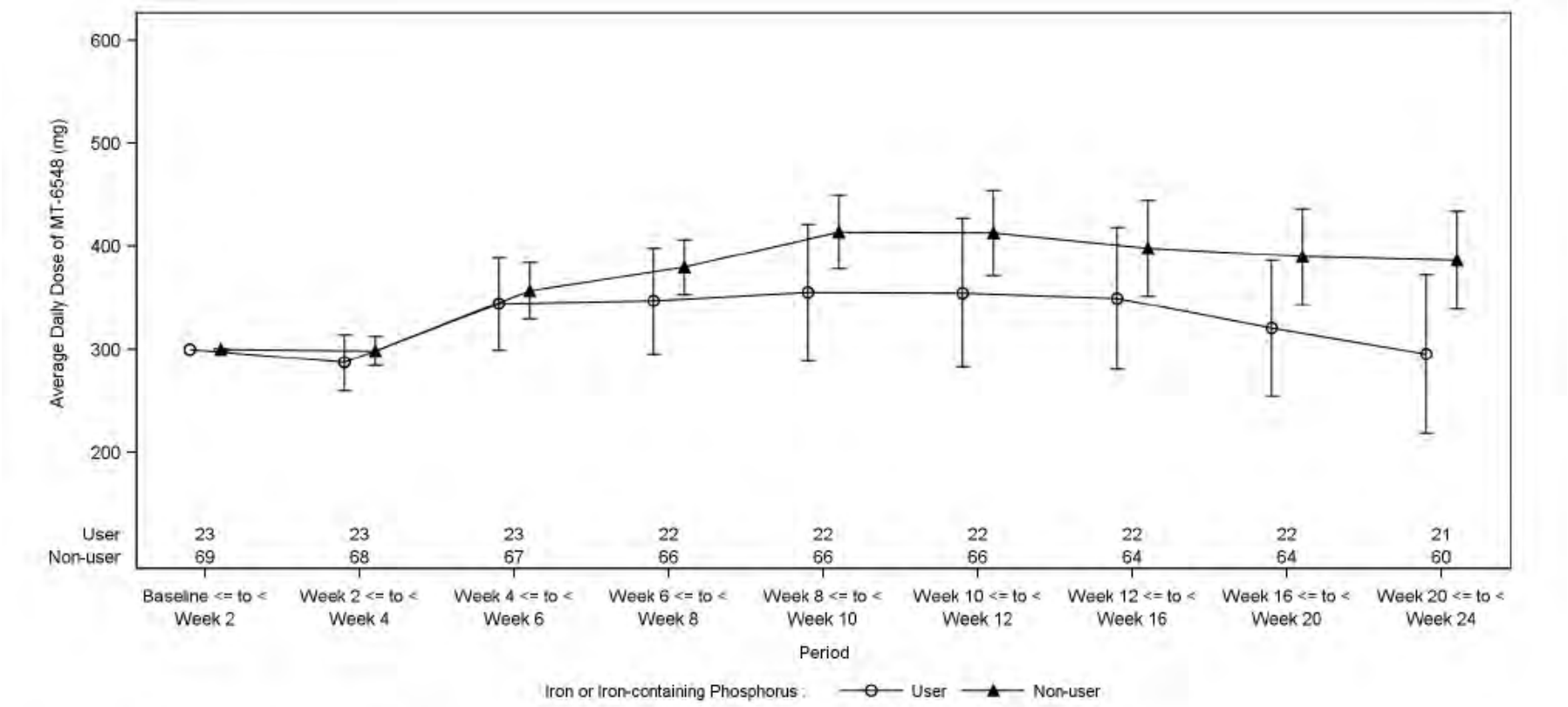
5.3.5.1—6 表 14.2.3.4.5.1 より引用

表 2.7.6.25－88　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	23	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
		Week 2 <= to < Week 4	23	286.96	62.65	300.00	(0.0, 300.0)	(259.91, 314.01)
		Week 4 <= to < Week 6	23	343.79	103.57	300.00	(150.0, 450.0)	(299.00, 388.58)
		Week 6 <= to < Week 8	22	346.75	115.47	300.00	(150.0, 589.3)	(296.56, 397.95)
		Week 8 <= to < Week 10	22	355.03	149.13	300.00	(10.7, 600.0)	(288.91, 421.15)
		Week 10 <= to < Week 12	22	354.55	162.59	300.00	(0.0, 600.0)	(282.46, 426.63)
		Week 12 <= to < Week 16	22	349.19	164.41	300.00	(150.0, 600.0)	(280.73, 417.65)
		Week 16 <= to < Week 20	22	320.70	148.48	300.00	(10.7, 600.0)	(254.86, 386.53)
		Week 20 <= to < Week 24	21	295.36	169.04	300.00	(0.0, 600.0)	(218.41, 372.30)
	Non-user	Baseline <= to < Week 2	69	299.38	5.16	300.00	(287.1, 300.0)	(298.14, 300.62)
		Week 2 <= to < Week 4	68	297.96	57.99	300.00	(0.0, 450.0)	(283.92, 311.99)
		Week 4 <= to < Week 6	67	356.61	113.57	417.96	(0.0, 589.3)	(326.91, 384.31)
		Week 6 <= to < Week 8	66	379.38	109.10	450.00	(0.0, 600.0)	(352.56, 406.20)
		Week 8 <= to < Week 10	66	413.80	146.05	450.00	(0.0, 600.0)	(377.90, 449.70)
		Week 10 <= to < Week 12	66	412.66	168.04	450.00	(0.0, 600.0)	(371.35, 453.97)
		Week 12 <= to < Week 16	64	398.02	185.47	450.00	(0.0, 600.0)	(351.69, 444.35)
		Week 16 <= to < Week 20	64	389.66	184.57	447.32	(0.0, 600.0)	(343.55, 435.76)
		Week 20 <= to < Week 24	60	386.36	183.68	393.04	(0.0, 600.0)	(338.91, 433.81)

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, Listing 16.2.3.2
Source: t_14_2_3_4_7_1_2.sas

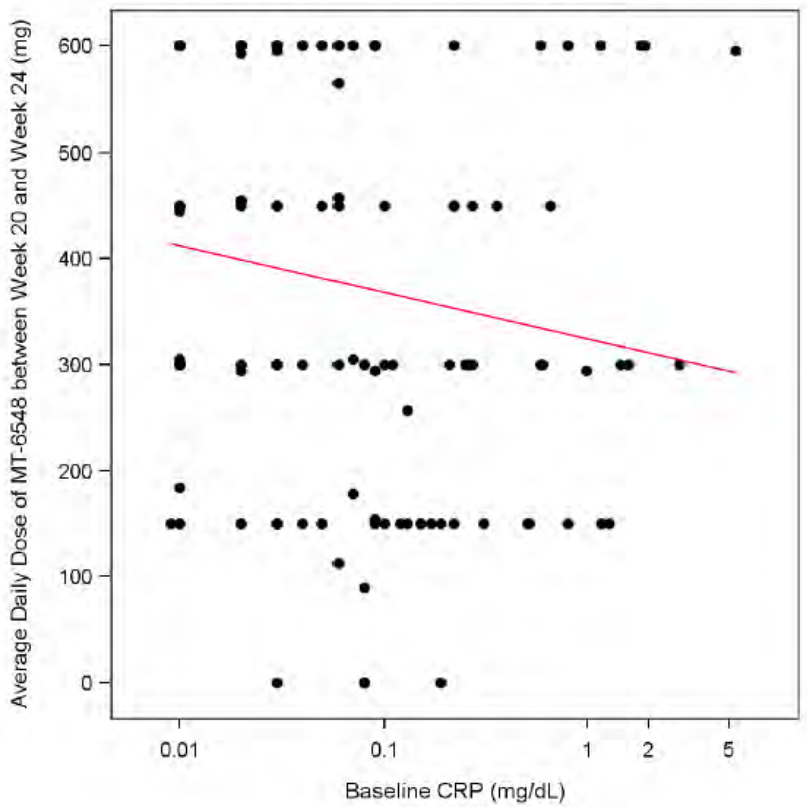
5.3.5.1—8 表 14.2.3.4.7.1.2 より引用



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 14.2.3.4.7.1.2
Source: f_14_2_4_7_1_2.sas

図 2.7.6.25－34　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—8 表 14.2.4.7.1.2 より引用



Note(s): linear regression model: Y=aX + b; Y: average daily dose between Week 20 and Week 24; X: baseline CRP.
Data Source: Listing 16.2.4.1, Listing 16.2.6.4
Source: f_14_2_4_9_1.sas

図 2.7.6.25－35　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—6 図 14.2.4.9.1 より引用

2.7.6.25.2.1.4 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 2.7.6.25－89 に示した.

安全性解析対象集団における, 治験薬投与期間の平均値±SD は MT-6548 群で 159.0±27.8 日，darbepoetin 群で 162.6±18.8 日であった.

安全性解析対象集団の治験薬の累積投与量の記述統計量を表 2.7.6.25－90 に示した.

安全性解析対象集団における，治験薬の累積投与量の平均値±SD は MT-6548 群で 60022.8±21921.0 mg，darbepoetin 群で 603.6±461.2 μg であった.

表 2.7.6.25－89　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=151)	darbepoetin (N=153)
Mean	159.0	162.6
SD	27.8	18.8
Median	168.0	168.0
Minimum, Maximum	(14, 175)	(34, 175)

Data Source: Listing 16.2.3.3
Source: t_14_1_4_4_1.sas

5.3.5.1—6 表 11.4.6—1 より引用

表 2.7.6.25－90　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=151) (mg)	darbepoetin (N=153) (ug)
Mean	60022.8	603.6
SD	21921.0	461.2
Median	59400.0	450.0
Minimum, Maximum	(3600, 94800)	(90, 3150)

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

5.3.5.1—6 表 11.4.6—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 2.7.6.25－91 に示した.

有害事象の発現割合は，MT-6548 群で 72.2%（109 名），darbepoetin 群で 73.2%（112 名）であった．副作用は MT-6548 群で 11.9%（18 名），darbepoetin 群で 4.6%（7 名）であった.

重篤な有害事象の発現割合は，MT-6548 群で 13.9%（21 名），darbepoetin 群で 14.4%（22 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 3.3%（5 名）, darbepoetin 群で 2.0%（3 名）であった.

治験薬の減量・休薬に至った有害事象の発現割合は，MT-6548 群で 4.6%（7 名），darbepoetin 群で 3.3%（5 名）であった.

死亡に至った有害事象は，MT-6548 群で認められず，darbepoetin 群で 0.7%（1 名）であった.

表 2.7.6.25－91　有害事象の要約（安全性解析対象集団）

	MT-6548 (N=151)	darbepoetin (N=153)
	n (%)	n (%)
Subjects with at least one adverse event	109 (72.2)	112 (73.2)
Subjects with at least one adverse drug reaction	18 (11.9)	7 (4.6)
Subjects with at least one serious adverse event	21 (13.9)	22 (14.4)
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	5 (3.3)	3 (2.0)
Subjects who had dose reduction or interruption of study drug due to adverse event	7 (4.6)	5 (3.3)
Deaths due to adverse event	0 (0.0)	1 (0.7)

Data Source: Listing 16.2.5.1
Source: t_14_3_1_1.sas

5.3.5.1—6 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 2.7.6.25－92 及び表 2.7.6.25－93 に示した.

有害事象の発現割合は，MT-6548 群で 72.2%（109／151 名），darbepoetin 群で 73.2%（112／153 名）であり，発現割合は両群で同程度であった．また，副作用の発現割合は，MT-6548 群で 11.9%，darbepoetin 群で 4.6%であり，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 SOC は，「感染症および寄生虫症」｛MT-6548 群：30.5%（46 名），darbepoetin 群：27.5%（42 名），以下，同順で記載｝，「胃腸障害」｛28.5%（43 名），24.2%（37 名）｝であった．これらの SOC のうち，darbepoetin 群と比較して発現割合が 10%以上高かった SOC は認められなかった．副作用のうち，MT-6548 群で発現割合が 20%以上の SOC は認められず，最も発現割合が高い副作用の SOC は，「胃腸障害」｛7.9%（12 名），0.7%（1 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」｛14.6%（22 名），12.4%（19 名）｝，「下痢」｛10.6%（16 名），3.3%（5 名）｝，「便秘」｛5.3%（8 名），3.9%（6 名）｝及び「挫傷」｛5.3%（8 名），1.3%（2 名）｝であった．これらの有害事象のうち，MT-6548 群の発現割合が darbepoetin 群と比較して 3%以上高かった有害事象は，「下痢」及び「挫傷」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ず，MT-6548 群で発現割合が最も高かった副作用は「下痢」｛4.0%（6 名），0%｝，次いで「悪心」｛2.6%（4 名），0%｝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，発現割合に両群で差が認められた主な副作用は「下痢」であった.

発現割合の高かった SOC「感染症および寄生虫症」及び SOC「胃腸障害」，発現割合が 10%以上であった有害事象「上咽頭炎」，darbepoetin 群と比較して発現割合の高かった有害事象「挫傷」，MT-6548 群で発現割合が高かった副作用「悪心」，発現割合が 10%以上で darbepoetin 群と比較しても発現割合が高く，かつ副作用としての発現割合が高かった「下痢」に関して，下記に詳細を示した.

SOC「感染症および寄生虫症」は，darbepoetin 群と同程度の発現割合であり，主な有害事象は「上咽頭炎」であった．「上咽頭炎」についても，両群で発現割合が同程度であり，MT-6548 群で認められた「上咽頭炎」は，いずれも軽度，治験薬との因果関係は合理的な可能性なしと判断された．SOC「胃腸障害」は，主な有害事象が「下痢」，「便秘」及び「嘔吐」であり，このうち MT-6548 群で最も発現割合が高かった「下痢」は，darbepoetin 群と比較して MT-6548 群で有害事象及び副作用の発現割合が高かった．MT-6548 群で認められた「下痢」の 16 名のうち，1 名の転帰は治療期間 I 期中には未回復で治療期間 II 期に移行し，それ以外の 15 名の転帰は治療期間 I 期中に軽快又は回復した．また，2 名が中等度と判断され，それ以外の 14 名は軽度と判断された．「挫傷」は，MT-6548 群で 8 名に認められ，1 名は中等度，7 名は軽度，いずれ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，転帰は軽快又は回復した．「悪心」は有害事象としての発現割合が MT-6548 群（2.6%），darbepoetin 群（2.0%）と同程度であった．「悪心」は，MT-6548 群で 4 名に認められ，いずれも軽度，治験薬との因果関係は合理的な

可能性ありと判断され，1 名は治療期間 I 期中の転帰は未回復で治療期間 II 期に移行し，3 名の転帰は回復であった.

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Subjects with at least one adverse event		109(72.2)	112(73.2)
Infections and infestations	感染症および寄生虫症	46(30.5)	42(27.5)
Nasopharyngitis	上咽頭炎	22(14.6)	19(12.4)
Cystitis	膀胱炎	3(2.0)	5(3.3)
Urinary tract infection	尿路感染	3(2.0)	4(2.6)
Pneumonia	肺炎	3(2.0)	3(2.0)
Conjunctivitis	結膜炎	3(2.0)	2(1.3)
Cellulitis	蜂巣炎	3(2.0)	0(0.0)
Gastroenteritis	胃腸炎	3(2.0)	0(0.0)
Influenza	インフルエンザ	2(1.3)	0(0.0)
Renal cyst infection	腎嚢胞感染	2(1.3)	0(0.0)
Herpes zoster	帯状疱疹	1(0.7)	2(1.3)
Otitis media	中耳炎	1(0.7)	2(1.3)
Periodontitis	歯周炎	1(0.7)	2(1.3)
Bronchitis	気管支炎	1(0.7)	1(0.7)
Upper respiratory tract infection	上気道感染	1(0.7)	1(0.7)
Body tinea	体部白癬	1(0.7)	0(0.0)
Osteomyelitis	骨髄炎	1(0.7)	0(0.0)
Pneumonia chlamydial	クラミジア性肺炎	1(0.7)	0(0.0)
Pyelonephritis	腎盂腎炎	1(0.7)	0(0.0)
Sinusitis	副鼻腔炎	1(0.7)	0(0.0)
Dermatophytosis of nail	爪の皮膚糸状菌症	0(0.0)	3(2.0)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Diverticulitis	憩室炎	0(0.0)	1(0.7)
Hordeolum	麦粒腫	0(0.0)	1(0.7)
Laryngitis	喉頭炎	0(0.0)	1(0.7)
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）	1(0.7)	3(2.0)
Oral papilloma	口腔乳頭腫	1(0.7)	0(0.0)
Gastric cancer	胃癌	0(0.0)	1(0.7)
Seborrhoeic keratosis	脂漏性角化症	0(0.0)	1(0.7)
Skin papilloma	皮膚乳頭腫	0(0.0)	1(0.7)
Kidney angiomyolipoma	腎血管筋脂肪腫	0(0.0)	1(0.7)
Blood and lymphatic system disorders	血液およびリンパ系障害	2(1.3)	6(3.9)
Iron deficiency anaemia	鉄欠乏性貧血	2(1.3)	5(3.3)
Immune thrombocytopenic purpura	免疫性血小板減少性紫斑病	0(0.0)	1(0.7)
Immune system disorders	免疫系障害	2(1.3)	0(0.0)
Allergy to arthropod sting	節足動物刺傷アレルギー	1(0.7)	0(0.0)
Allergy to arthropod bite	節足動物咬傷アレルギー	1(0.7)	0(0.0)
Endocrine disorders	内分泌障害	0(0.0)	1(0.7)
Hypoparathyroidism secondary	続発性副甲状腺機能低下症	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Metabolism and nutrition disorders	代謝および栄養障害	14(9.3)	19(12.4)
Decreased appetite	食欲減退	3(2.0)	1(0.7)
Dehydration	脱水	2(1.3)	3(2.0)
Hyperuricaemia	高尿酸血症	2(1.3)	1(0.7)
Metabolic acidosis	代謝性アシドーシス	1(0.7)	4(2.6)
Diabetes mellitus	糖尿病	1(0.7)	2(1.3)
Hyponatraemia	低ナトリウム血症	1(0.7)	2(1.3)
Hyperphosphataemia	高リン酸塩血症	1(0.7)	1(0.7)
Hypoglycaemia	低血糖	1(0.7)	1(0.7)
Hypoproteinaemia	低蛋白血症	1(0.7)	0(0.0)
Hyperlipidaemia	高脂血症	1(0.7)	0(0.0)
Hyperamylasaemia	高アミラーゼ血症	1(0.7)	0(0.0)
Type 2 diabetes mellitus	２型糖尿病	1(0.7)	0(0.0)
Hyperkalaemia	高カリウム血症	0(0.0)	5(3.3)
Psychiatric disorders	精神障害	4(2.6)	1(0.7)
Insomnia	不眠症	3(2.0)	0(0.0)
Anxiety	不安	1(0.7)	0(0.0)
Tic	チック	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Nervous system disorders	神経系障害	6(4.0)	8(5.2)
Headache	頭痛	3(2.0)	3(2.0)
Hypoaesthesia	感覚鈍麻	1(0.7)	0(0.0)
Hypoglycaemic coma	低血糖昏睡	1(0.7)	0(0.0)
Somnolence	傾眠	1(0.7)	0(0.0)
Dementia Alzheimer's type	アルツハイマー型認知症	0(0.0)	1(0.7)
Dizziness	浮動性めまい	0(0.0)	1(0.7)
Dizziness postural	体位性めまい	0(0.0)	1(0.7)
Intracranial aneurysm	頭蓋内動脈瘤	0(0.0)	1(0.7)
Sciatica	坐骨神経痛	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Eye disorders	眼障害	12(7.9)	14(9.2)
Cataract	白内障	3(2.0)	1(0.7)
Retinal haemorrhage	網膜出血	2(1.3)	3(2.0)
Blepharitis	眼瞼炎	2(1.3)	2(1.3)
Conjunctival haemorrhage	結膜出血	1(0.7)	1(0.7)
Dry eye	眼乾燥	1(0.7)	0(0.0)
Eczema eyelids	眼瞼湿疹	1(0.7)	0(0.0)
Macular oedema	黄斑浮腫	1(0.7)	0(0.0)
Retinal exudates	網膜滲出物	1(0.7)	0(0.0)
Retinal vein occlusion	網膜静脈閉塞	1(0.7)	0(0.0)
Age-related macular degeneration	加齢黄斑変性	1(0.7)	0(0.0)
Diabetic retinopathy	糖尿病網膜症	0(0.0)	3(2.0)
Eye pruritus	眼そう痒症	0(0.0)	2(1.3)
Asthenopia	眼精疲労	0(0.0)	1(0.7)
Conjunctivitis allergic	アレルギー性結膜炎	0(0.0)	1(0.7)
Eye swelling	眼部腫脹	0(0.0)	1(0.7)
Conjunctival hyperaemia	結膜充血	0(0.0)	1(0.7)
Retinal aneurysm	網膜血管瘤	0(0.0)	1(0.7)
Ear and labyrinth disorders	耳および迷路障害	2(1.3)	2(1.3)
Vertigo	回転性めまい	1(0.7)	2(1.3)
Vertigo positional	頭位性回転性めまい	1(0.7)	0(0.0)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Cardiac disorders	心臓障害	8(5.3)	3(2.0)
Cardiac failure chronic	慢性心不全	3(2.0)	0(0.0)
Cardiac failure congestive	うっ血性心不全	2(1.3)	0(0.0)
Atrial fibrillation	心房細動	1(0.7)	0(0.0)
Bradycardia	徐脈	1(0.7)	0(0.0)
Palpitations	動悸	1(0.7)	0(0.0)
Acute myocardial infarction	急性心筋梗塞	0(0.0)	1(0.7)
Cardiac failure acute	急性心不全	0(0.0)	1(0.7)
Cardiac hypertrophy	心肥大	0(0.0)	1(0.7)
Vascular disorders	血管障害	3(2.0)	8(5.2)
Hypertension	高血圧	1(0.7)	4(2.6)
Hypotension	低血圧	1(0.7)	0(0.0)
Vascular rupture	血管破裂	1(0.7)	0(0.0)
Internal haemorrhage	内出血	0(0.0)	2(1.3)
Arteriosclerosis	動脈硬化症	0(0.0)	1(0.7)
Orthostatic hypotension	起立性低血圧	0(0.0)	1(0.7)
Hot flush	ほてり	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	4(2.6)	5(3.3)
Pleural effusion	胸水	1(0.7)	2(1.3)
Cough	咳嗽	1(0.7)	1(0.7)
Pulmonary congestion	肺うっ血	1(0.7)	0(0.0)
Rhinitis allergic	アレルギー性鼻炎	1(0.7)	0(0.0)
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	0(0.0)	1(0.7)
Oropharyngeal discomfort	口腔咽頭不快感	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Gastrointestinal disorders	胃腸障害	43(28.5)	37(24.2)
Diarrhoea	下痢	16(10.6)	5(3.3)
Constipation	便秘	8(5.3)	6(3.9)
Vomiting	嘔吐	7(4.6)	1(0.7)
Nausea	悪心	4(2.6)	3(2.0)
Abdominal pain upper	上腹部痛	3(2.0)	2(1.3)
Abdominal discomfort	腹部不快感	2(1.3)	3(2.0)
Dental caries	齲歯	2(1.3)	3(2.0)
Stomatitis	口内炎	2(1.3)	2(1.3)
Gastrooesophageal reflux disease	胃食道逆流性疾患	2(1.3)	1(0.7)
Faeces soft	軟便	1(0.7)	1(0.7)
Abdominal distension	腹部膨満	1(0.7)	0(0.0)
Abdominal pain	腹痛	1(0.7)	0(0.0)
Diverticulum intestinal	腸憩室	1(0.7)	0(0.0)
Gastritis	胃炎	1(0.7)	0(0.0)
Gastrointestinal disorder	胃腸障害	1(0.7)	0(0.0)
Gastrointestinal polyp haemorrhage	胃腸ポリープ出血	1(0.7)	0(0.0)
Large intestine polyp	大腸ポリープ	0(0.0)	2(1.3)
Aphthous ulcer	アフタ性潰瘍	0(0.0)	1(0.7)
Chronic gastritis	慢性胃炎	0(0.0)	1(0.7)
Colitis ischaemic	虚血性大腸炎	0(0.0)	1(0.7)
Faeces discoloured	変色便	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Gastric ulcer haemorrhage	出血性胃潰瘍	0(0.0)	1(0.7)
Gingival swelling	歯肉腫脹	0(0.0)	1(0.7)
Inguinal hernia	鼠径ヘルニア	0(0.0)	1(0.7)
Periodontal disease	歯周病	0(0.0)	1(0.7)
Pancreatic mass	膵腫瘤	0(0.0)	1(0.7)
Anal haemorrhage	肛門出血	0(0.0)	1(0.7)
Hepatobiliary disorders	肝胆道系障害	4(2.6)	3(2.0)
Hepatic function abnormal	肝機能異常	1(0.7)	1(0.7)
Cholecystitis	胆嚢炎	1(0.7)	0(0.0)
Cholelithiasis	胆石症	1(0.7)	0(0.0)
Hepatic cirrhosis	肝硬変	1(0.7)	0(0.0)
Bile duct stone	胆管結石	0(0.0)	1(0.7)
Hepatic steatosis	脂肪肝	0(0.0)	1(0.7)
Liver disorder	肝障害	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	16(10.6)	15(9.8)
Eczema	湿疹	2(1.3)	3(2.0)
Haemorrhage subcutaneous	皮下出血	2(1.3)	3(2.0)
Dermatitis contact	接触皮膚炎	2(1.3)	2(1.3)
Pruritus	そう痒症	2(1.3)	1(0.7)
Rash	発疹	2(1.3)	1(0.7)
Urticaria	蕁麻疹	2(1.3)	1(0.7)
Decubitus ulcer	褥瘡性潰瘍	1(0.7)	0(0.0)
Drug eruption	薬疹	1(0.7)	0(0.0)
Eczema asteatotic	皮脂欠乏性湿疹	1(0.7)	0(0.0)
Prurigo	痒疹	1(0.7)	0(0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	1(0.7)	0(0.0)
Skin erosion	皮膚びらん	1(0.7)	0(0.0)
Skin ulcer	皮膚潰瘍	1(0.7)	0(0.0)
Dermatitis	皮膚炎	0(0.0)	1(0.7)
Miliaria	汗疹	0(0.0)	1(0.7)
Stasis dermatitis	うっ滞性皮膚炎	0(0.0)	1(0.7)
Xeroderma	乾皮症	0(0.0)	1(0.7)
Hand dermatitis	手皮膚炎	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	13(8.6)	20(13.1)
Arthralgia	関節痛	2(1.3)	2(1.3)
Back pain	背部痛	2(1.3)	2(1.3)
Muscle spasms	筋痙縮	2(1.3)	2(1.3)
Pain in extremity	四肢痛	2(1.3)	2(1.3)
Spinal osteoarthritis	変形性脊椎症	2(1.3)	0(0.0)
Arthritis	関節炎	1(0.7)	2(1.3)
Musculoskeletal pain	筋骨格痛	1(0.7)	2(1.3)
Bursitis	滑液包炎	1(0.7)	0(0.0)
Myalgia	筋肉痛	1(0.7)	0(0.0)
Osteoporosis	骨粗鬆症	1(0.7)	0(0.0)
Synovial cyst	滑液嚢腫	1(0.7)	0(0.0)
Trigger finger	弾発指	1(0.7)	0(0.0)
Neck pain	頚部痛	0(0.0)	2(1.3)
Lumbar spinal stenosis	腰部脊柱管狭窄症	0(0.0)	1(0.7)
Osteoarthritis	変形性関節症	0(0.0)	1(0.7)
Tendonitis	腱炎	0(0.0)	1(0.7)
Intervertebral disc protrusion	椎間板突出	0(0.0)	1(0.7)
Musculoskeletal stiffness	筋骨格硬直	0(0.0)	1(0.7)
Spondylolisthesis	脊椎すべり症	0(0.0)	1(0.7)
Tendon pain	腱痛	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Renal and urinary disorders	腎および尿路障害	16(10.6)	15(9.8)
Chronic kidney disease	慢性腎臓病	5(3.3)	6(3.9)
Renal impairment	腎機能障害	4(2.6)	3(2.0)
End stage renal disease	末期腎疾患	2(1.3)	1(0.7)
Renal failure	腎不全	2(1.3)	0(0.0)
Haematuria	血尿	1(0.7)	0(0.0)
Hypertonic bladder	緊張性膀胱	1(0.7)	0(0.0)
Oliguria	乏尿	1(0.7)	0(0.0)
Azotaemia	高窒素血症	0(0.0)	1(0.7)
Dysuria	排尿困難	0(0.0)	1(0.7)
Neurogenic bladder	神経因性膀胱	0(0.0)	1(0.7)
Nocturia	夜間頻尿	0(0.0)	1(0.7)
Ureterolithiasis	尿管結石症	0(0.0)	1(0.7)
Reproductive system and breast disorders	生殖系および乳房障害	2(1.3)	0(0.0)
Benign prostatic hyperplasia	良性前立腺肥大症	1(0.7)	0(0.0)
Nipple pain	乳頭痛	1(0.7)	0(0.0)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	16(10.6)	6(3.9)
Oedema peripheral	末梢性浮腫	7(4.6)	3(2.0)
Malaise	倦怠感	5(3.3)	1(0.7)
Pyrexia	発熱	5(3.3)	0(0.0)
Oedema due to renal disease	腎疾患による浮腫	2(1.3)	0(0.0)
Chest pain	胸痛	1(0.7)	0(0.0)
Face oedema	顔面浮腫	1(0.7)	0(0.0)
Thirst	口渇	1(0.7)	0(0.0)
Injection site haematoma	注射部位血腫	0(0.0)	1(0.7)
Injection site pain	注射部位疼痛	0(0.0)	1(0.7)
Oedema	浮腫	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Investigations	臨床検査	10(6.6)	11(7.2)
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	2(1.3)	3(2.0)
Blood pressure increased	血圧上昇	2(1.3)	1(0.7)
Blood creatinine increased	血中クレアチニン増加	1(0.7)	2(1.3)
Blood triglycerides increased	血中トリグリセリド増加	1(0.7)	1(0.7)
Blood potassium decreased	血中カリウム減少	1(0.7)	0(0.0)
Blood uric acid increased	血中尿酸増加	1(0.7)	0(0.0)
C-reactive protein increased	C－反応性蛋白増加	1(0.7)	0(0.0)
Haemoglobin decreased	ヘモグロビン減少	1(0.7)	0(0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1(0.7)	0(0.0)
Blood iron decreased	血中鉄減少	0(0.0)	1(0.7)
Blood pressure decreased	血圧低下	0(0.0)	1(0.7)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0(0.0)	1(0.7)
Intraocular pressure increased	眼圧上昇	0(0.0)	1(0.7)
Platelet count increased	血小板数増加	0(0.0)	1(0.7)

表 2.7.6.25－92　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=151) n (%)	darbepoetin(N=153) n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	17(11.3)	14(9.2)
Contusion	挫傷	8(5.3)	2(1.3)
Skin abrasion	皮膚擦過傷	2(1.3)	2(1.3)
Spinal compression fracture	脊椎圧迫骨折	2(1.3)	1(0.7)
Head injury	頭部損傷	1(0.7)	0(0.0)
Rib fracture	肋骨骨折	1(0.7)	0(0.0)
Seroma	漿液腫	1(0.7)	0(0.0)
Tendon rupture	腱断裂	1(0.7)	0(0.0)
Thermal burn	熱傷	1(0.7)	0(0.0)
Shunt stenosis	シャント狭窄	1(0.7)	0(0.0)
Nail injury	爪損傷	1(0.7)	0(0.0)
Eye contusion	眼挫傷	1(0.7)	0(0.0)
Heat illness	熱中症	0(0.0)	3(2.0)
Arthropod bite	節足動物咬傷	0(0.0)	2(1.3)
Chillblains	凍瘡	0(0.0)	1(0.7)
Humerus fracture	上腕骨骨折	0(0.0)	1(0.7)
Injury	損傷	0(0.0)	1(0.7)
Radius fracture	橈骨骨折	0(0.0)	1(0.7)
Shunt occlusion	シャント閉塞	0(0.0)	1(0.7)
Wrist fracture	手首関節骨折	0(0.0)	1(0.7)
Wound	創傷	0(0.0)	1(0.7)

Note(s): MedDRA Version 20.1 and MedDRA/J Version 20.1.
Data Source: Listing 16.2.5.1
Source: t_14_3_1_2.sas

5.3.5.1—6 表 12.2.3—1 より引用

表 2.7.6.25－93　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=151) n (%)	darbepoetin(N=153) n (%)
Subjects with at least one adverse drug reaction		18(11.9)	7(4.6)
Nervous system disorders	神経系障害	1(0.7)	1(0.7)
Somnolence	傾眠	1(0.7)	0(0.0)
Dizziness	浮動性めまい	0(0.0)	1(0.7)
Eye disorders	眼障害	1(0.7)	0(0.0)
Retinal haemorrhage	網膜出血	1(0.7)	0(0.0)
Ear and labyrinth disorders	耳および迷路障害	1(0.7)	0(0.0)
Vertigo	回転性めまい	1(0.7)	0(0.0)
Cardiac disorders	心臓障害	1(0.7)	0(0.0)
Palpitations	動悸	1(0.7)	0(0.0)
Vascular disorders	血管障害	0(0.0)	2(1.3)
Hypertension	高血圧	0(0.0)	2(1.3)
Hot flush	ほてり	0(0.0)	1(0.7)
Gastrointestinal disorders	胃腸障害	12(7.9)	1(0.7)
Diarrhoea	下痢	6(4.0)	0(0.0)
Nausea	悪心	4(2.6)	0(0.0)
Abdominal discomfort	腹部不快感	2(1.3)	1(0.7)
Faeces soft	軟便	1(0.7)	0(0.0)
Hepatobiliary disorders	肝胆道系障害	1(0.7)	0(0.0)
Hepatic function abnormal	肝機能異常	1(0.7)	0(0.0)

表 2.7.6.25－93　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=151) n (%)	darbepoetin(N=153) n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	3(2.0)	1(0.7)
Drug eruption	薬疹	1(0.7)	0(0.0)
Eczema	湿疹	1(0.7)	0(0.0)
Pruritus	そう痒症	1(0.7)	0(0.0)
Haemorrhage subcutaneous	皮下出血	0(0.0)	1(0.7)
Reproductive system and breast disorders	生殖系および乳房障害	1(0.7)	0(0.0)
Nipple pain	乳頭痛	1(0.7)	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(0.7)	1(0.7)
Malaise	倦怠感	1(0.7)	0(0.0)
Injection site pain	注射部位疼痛	0(0.0)	1(0.7)
Investigations	臨床検査	0(0.0)	1(0.7)
Blood creatinine increased	血中クレアチニン増加	0(0.0)	1(0.7)

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—6 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 2.6%（4 名）であり，内訳は,「慢性腎臓病」が 2 名,「蜂巣炎」,「骨髄炎」及び「末期腎疾患」が各 1 名であった．なお,「蜂巣炎」及び「骨髄炎」は，同一被験者で認められた．darbepoetin 群では 3.9%（6 名）であり，内訳は「肺炎」,「低ナトリウム血症」,「急性心筋梗塞」,「急性心不全」,「腰部脊柱管狭窄症」,「慢性腎臓病」及び「末期腎疾患」が各 1 名であった．なお,「急性心不全」及び「慢性腎臓病」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 16.6%（25 名），darbepoetin 群で 15.0%（23 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 53.0%（80／151 名），85 日後以降が 50.0%（72／144 名）であり，darbepoetin 群では 84 日後までが 49.7%（76／153 名），85 日後以降が 55.0%（82／149 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 2.4%（11 件），0.5%（16 件），1.3%（129 件），1.5%（81 件）及び 1.2%（63 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 1.4%（17 件），1.0%（181 件），1.2%（48 件），1.9%（21 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 2 名のうち，1 名（被験者識別コード J107101，900 mg を 1 日間服用）は，過量に服用している期間中に有害事象は認められず，別の 1 名（被験者識別コード J103901，750 mg を 12 日間服用）の被験者では，過量に服用している期間中に「胃食道逆流性疾患」及び「胃炎」が認められた．両事象は，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，治療期間 I 期中には未回復であり治療期間 II 期に移行した．

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 47.7%（72／151 名），40.0%（58／145 名），26.5%（30／113 名）及び 24.2%（16／66 名）であり，darbepoetin 群ではそれぞれ 62.7%（96／153 名），38.9%（28／72 名），33.3%（8／24 名）及び 60.0%（6／10 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 週間及び休薬後 4 週間で 14.3%（3／21 名）及び 9.5%（2／21 名）であり，darbepoetin 群では 26.3%（10／38 名）及び 28.9%（11／38 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

darbepoetin 群で，1 名に「急性心筋梗塞」による死亡が認められた．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た．本事象は，治験薬投与 58 日目に事象の発現が認められ，被験者は 60 日目に死亡した．治験責任医師は，治験薬との因果関係について，「エリスロポエチン製剤において Hb 高値の場合，血液粘稠度が上昇することによる心筋梗塞の報告があるが，被験者の Hb 値の経過より，治験薬投与に伴う Hb 値の上昇は見られてないこと，被験者は糖尿病と高血圧を合併しており，心筋梗塞のリスクは高かったことから，治験薬との因果関係はないと考える．」と報告した．

2) 重篤な有害事象及び副作用

重篤な有害事象を表 2.7.6.25－94 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，「慢性腎臓病」｛MT-6548 群：2.0%（3 名），darbepoetin 群：2.0%（3 名），以下同順で記載｝，「腎機能障害」｛2.0%（3 名），0.7%（1 名）｝，「肺炎」｛1.3%（2 名），2.0%（3 名）｝，「白内障」｛1.3%（2 名），0%｝，「うっ血性心不全」｛1.3%（2 名），0%｝，「末期腎疾患」｛1.3%（2 名），0.7%（1 名）｝，「腎不全」｛1.3%（2 名），0%｝及び「脊椎圧迫骨折」｛1.3%（2 名），0%｝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 2.7.6.25－94　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=151) n (%)	darbepoetin(N=153) n (%)
Subjects with at least one serious adverse event		21(13.9)	22(14.4)
Infections and infestations	感染症および寄生虫症	5(3.3)	5(3.3)
Pneumonia	肺炎	2(1.3)	3(2.0)
Cellulitis	蜂巣炎	1(0.7)	0(0.0)
Osteomyelitis	骨髄炎	1(0.7)	0(0.0)
Pneumonia chlamydial	クラミジア性肺炎	1(0.7)	0(0.0)
Renal cyst infection	腎嚢胞感染	1(0.7)	0(0.0)
Cystitis	膀胱炎	0(0.0)	1(0.7)
Diverticulitis	憩室炎	0(0.0)	1(0.7)
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）	0(0.0)	1(0.7)
Gastric cancer	胃癌	0(0.0)	1(0.7)
Metabolism and nutrition disorders	代謝および栄養障害	1(0.7)	4(2.6)
Hyponatraemia	低ナトリウム血症	1(0.7)	1(0.7)
Dehydration	脱水	0(0.0)	2(1.3)
Metabolic acidosis	代謝性アシドーシス	0(0.0)	1(0.7)
Nervous system disorders	神経系障害	1(0.7)	0(0.0)
Hypoglycaemic coma	低血糖昏睡	1(0.7)	0(0.0)
Eye disorders	眼障害	2(1.3)	0(0.0)
Cataract	白内障	2(1.3)	0(0.0)

表 2.7.6.25－94　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=151) n (%)	darbepoetin(N=153) n (%)
Cardiac disorders	心臓障害	2(1.3)	2(1.3)
Cardiac failure congestive	うっ血性心不全	2(1.3)	0(0.0)
Acute myocardial infarction	急性心筋梗塞	0(0.0)	1(0.7)
Cardiac failure acute	急性心不全	0(0.0)	1(0.7)
Vascular disorders	血管障害	1(0.7)	0(0.0)
Vascular rupture	血管破裂	1(0.7)	0(0.0)
Gastrointestinal disorders	胃腸障害	1(0.7)	2(1.3)
Abdominal pain	腹痛	1(0.7)	0(0.0)
Gastric ulcer haemorrhage	出血性胃潰瘍	0(0.0)	1(0.7)
Inguinal hernia	鼠径ヘルニア	0(0.0)	1(0.7)
Hepatobiliary disorders	肝胆道系障害	2(1.3)	0(0.0)
Cholecystitis	胆嚢炎	1(0.7)	0(0.0)
Cholelithiasis	胆石症	1(0.7)	0(0.0)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0(0.0)	1(0.7)
Lumbar spinal stenosis	腰部脊柱管狭窄症	0(0.0)	1(0.7)
Renal and urinary disorders	腎および尿路障害	10(6.6)	5(3.3)
Chronic kidney disease	慢性腎臓病	3(2.0)	3(2.0)
Renal impairment	腎機能障害	3(2.0)	1(0.7)
End stage renal disease	末期腎疾患	2(1.3)	1(0.7)
Renal failure	腎不全	2(1.3)	0(0.0)

表 2.7.6.25－94　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=151) n (%)	darbepoetin(N=153) n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	2(1.3)	1(0.7)
Oedema peripheral	末梢性浮腫	1(0.7)	1(0.7)
Chest pain	胸痛	1(0.7)	0(0.0)
Investigations	臨床検査	0(0.0)	1(0.7)
Blood creatinine increased	血中クレアチニン増加	0(0.0)	1(0.7)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	3(2.0)	3(2.0)
Spinal compression fracture	脊椎圧迫骨折	2(1.3)	0(0.0)
Seroma	漿液腫	1(0.7)	0(0.0)
Radius fracture	橈骨骨折	0(0.0)	1(0.7)
Shunt occlusion	シャント閉塞	0(0.0)	1(0.7)
Wrist fracture	手首関節骨折	0(0.0)	1(0.7)

Note(s): MedDRA Version 20.1 and MedDRA/J Version 20.1.
Data Source: Listing 16.2.5.2
Source: t_14_3_1_4.sas

5.3.5.1—6 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，「網膜出血」，「慢性心不全」，「腹部不快感」，「下痢」，「胃腸ポリープ出血」，「慢性腎臓病」，「倦怠感」及び「ヘモグロビン減少」が各 1 名であり，そのうち「腹部不快感」及び「倦怠感」，「胃腸ポリープ出血」及び「ヘモグロビン減少」，「慢性心不全」及び「慢性腎臓病」は，それぞれ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，「アルツハイマー型認知症」，「慢性腎臓病」及び「高窒素血症」が各 1 名であった．

MT-6548 群で認められた「網膜出血」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．「慢性心不全」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．「腹部不快感」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，転帰は軽快であった．「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，転帰は回復であった．「胃腸ポリープ出血」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，転帰は未回復であった．「慢性腎臓病」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，転帰は軽快であった．「倦怠感」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，転帰は未回復であった．

darbepoetin 群で認められた「アルツハイマー型認知症」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，転帰は未回復であった．「慢性腎臓病」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，転帰は軽快であった．「高窒素血症」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，転帰は不明であった．

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 1 名，減量 2 名），「慢性心不全」，「胆石症」及び「発熱」が各 1 名（休薬），「良性前立腺肥大症」が 1 名（減量）であった．darbepoetin 群で休薬又は減量に至った有害事象は，「高血圧」が 2 名（休薬），「肺炎」，「胃癌」及び「腹部不快感」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以下に示した．「下痢」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，治療期間 I 期中に回復した．「胆石症」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，転帰は軽快であった．「慢性心不全」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，治療期間 I 期中に回復した．「発熱」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，治療期間 I 期中に回復した．

darbepoetin 群で休薬に至った有害事象の詳細を以下に示した．「高血圧」のうち，被験者識別コード J100401 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

理的な可能性ありと判断され，治療期間 I 期中には未回復であり治療期間 II 期に移行した．被験者識別コード J102104 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ありと判断され，治療期間 I 期中には未回復であり治療期間 II 期に移行した．「肺炎」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，治療期間 I 期中には未回復であり治療期間 II 期に移行した．「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，治療期間 I 期中には未回復であり治療期間 II 期に移行した．なお，本事象は，初期の胃癌との診断を受け，腹腔鏡手術で胃癌切除後，治験責任医師より治験薬投与が再開可能と判断されて治験薬投与が再開された．「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，治療期間 I 期中に回復した．

MT-6548 群で減量に至った有害事象の詳細を以下に示した．「下痢」のうち，被験者識別コード J100601 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ありと判断され，治療期間 I 期中には未回復であり治療期間 II 期に移行した．被験者識別コード J100909 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，治療期間 I 期中に回復した．「良性前立腺肥大症」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，治療期間 I 期中には未回復であり治療期間 II 期に移行した．

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

血清クレアチニンは，MT-6548 群で 20 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，3.114±1.802 mg/dL 及び 0.315±0.731 mg/dL であり，その後も同程度で推移した．darbepoetin 群でも同様に 20 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，2.866±1.938 mg/dL 及び 0.283±0.692 mg/dL であり，その後も同程度で推移した．

中性脂肪は，MT-6548 群では，16 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，173.1±97.3 mg/dL 及び 30.6±71.4 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「血中クレアチンホスホキナーゼ増加」が 2 名，「血中クレアチニン増加」，「血中トリグリセリド増加」，「血中カリウム減少」，「血中尿酸増加」，「C－反応性蛋白増加」，「ヘモグロビン減少」及び「血中アルカリホスファターゼ増加」が各 1 名であり，darbepoetin 群では「血中クレアチンホスホキナーゼ増加」が 3 名，「血中クレアチニン増加」が 2

名，「血中トリグリセリド増加」，「血中鉄減少」，「γ-グルタミルトランスフェラーゼ増加」及び「血小板数増加」が各 1 名であった．

また，臨床検査値の血管内皮増殖因子（以下，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 3 名，darbepoetin 群で 0 名であった．MT-6548 群で本基準に該当した 3 名のうち，2 名で 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．残りの 1 名には，SOC「眼障害」に該当する有害事象として「加齢黄斑変性」が認められた．本被験者は合併症として「加齢黄斑変性」を有しており，VEGF は，ベースラインで 61.2 pg/mL，12 週後で 152 pg/mL，24 週後で 249 pg/mL であった．本事象は，治験薬投与 147 日目に発現し，軽度，非重篤，治験薬との合理的な因果関係なしと判断され，治療期間 I 期中には未回復であり治療期間 II 期に移行した．

3)　Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合

全集団における，治療期間 I 期中に Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合の記述統計量を表 2.7.6.25－95 に示した．

全集団における，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 21.9%（33 名），darbepoetin 群で 39.2%（60 名）であった．また，治療期間 I 期中に Hb 値が 14.0 g/dL 以上になった被験者の割合は，MT-6548 群で 2.0%（3 名），darbepoetin 群で 4.6%（7 名）であった．

Conversion 集団及び Correction 集団で治療期間 I 期中に Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合の記述統計量を表 2.7.6.25－96 及び表 2.7.6.25－97 に示した．

表 2.7.6.25－95　Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合（安全性解析対象集団）

		MT-6548(N=151)			darbepoetin(N=153)		
Criteria	Period	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb >=13.0 g/dL	Baseline	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)
	Baseline < to <= Week 2	135	1 (0.7)	(0.02, 4.06)	136	0 (0.0)	(0.00, 2.68)
	Week 2 < to <= Week 4	138	1 (0.7)	(0.02, 3.97)	139	0 (0.0)	(0.00, 2.62)
	Week 4 < to <= Week 6	140	1 (0.7)	(0.02, 3.92)	143	2 (1.4)	(0.17, 4.96)
	Week 6 < to <= Week 8	137	3 (2.2)	(0.45, 6.27)	140	9 (6.4)	(2.98, 11.85)
	Week 8 < to <= Week 10	129	4 (3.1)	(0.85, 7.75)	136	12 (8.8)	(4.64, 14.91)
	Week 10 < to <= Week 12	138	8 (5.8)	(2.54, 11.10)	139	23 (16.5)	(10.79, 23.79)
	Week 12 < to <= Week 16	131	10 (7.6)	(3.72, 13.59)	135	20 (14.8)	(9.29, 21.95)
	Week 16 < to <= Week 20	126	13 (10.3)	(5.61, 17.00)	139	21 (15.1)	(9.60, 22.16)
	Week 20 < to <= Week 24	136	12 (8.8)	(4.64, 14.91)	144	19 (13.2)	(8.13, 19.84)
	Baseline < to <= Week 24	151	33 (21.9)	(15.55, 29.30)	153	60 (39.2)	(31.43, 47.43)
Hb >=14.0 g/dL	Baseline	151	0 (0.0)	(0.00, 2.41)	153	0 (0.0)	(0.00, 2.38)
	Baseline < to <= Week 2	135	0 (0.0)	(0.00, 2.70)	136	0 (0.0)	(0.00, 2.68)
	Week 2 < to <= Week 4	138	0 (0.0)	(0.00, 2.64)	139	0 (0.0)	(0.00, 2.62)
	Week 4 < to <= Week 6	140	0 (0.0)	(0.00, 2.60)	143	0 (0.0)	(0.00, 2.55)
	Week 6 < to <= Week 8	137	0 (0.0)	(0.00, 2.66)	140	0 (0.0)	(0.00, 2.60)
	Week 8 < to <= Week 10	129	0 (0.0)	(0.00, 2.82)	136	0 (0.0)	(0.00, 2.68)
	Week 10 < to <= Week 12	138	0 (0.0)	(0.00, 2.64)	139	1 (0.7)	(0.02, 3.94)
	Week 12 < to <= Week 16	131	0 (0.0)	(0.00, 2.78)	135	5 (3.7)	(1.21, 8.43)
	Week 16 < to <= Week 20	126	2 (1.6)	(0.19, 5.62)	139	2 (1.4)	(0.17, 5.10)
	Week 20 < to <= Week 24	136	1 (0.7)	(0.02, 4.03)	144	0 (0.0)	(0.00, 2.53)
	Baseline < to <= Week 24	151	3 (2.0)	(0.41, 5.70)	153	7 (4.6)	(1.86, 9.20)

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_1.sas

5.3.5.1—6 表 12.4.3—1 より引用

表 2.7.6.25－96　Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合（安全性解析対象集団）（Conversion 集団）

		MT-6548(N=80)			darbepoetin(N=82)		
Criteria	Period	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb >=13.0 g/dL	Baseline	80	0 (0.0)	(0.00, 4.51)	82	0 (0.0)	(0.00, 4.40)
	Baseline < to <= Week 2	72	1 (1.4)	(0.04, 7.50)	77	0 (0.0)	(0.00, 4.68)
	Week 2 < to <= Week 4	76	0 (0.0)	(0.00, 4.74)	76	0 (0.0)	(0.00, 4.74)
	Week 4 < to <= Week 6	76	1 (1.3)	(0.03, 7.11)	77	0 (0.0)	(0.00, 4.68)
	Week 6 < to <= Week 8	76	1 (1.3)	(0.03, 7.11)	76	1 (1.3)	(0.03, 7.11)
	Week 8 < to <= Week 10	68	2 (2.9)	(0.36, 10.22)	77	1 (1.3)	(0.03, 7.02)
	Week 10 < to <= Week 12	74	4 (5.4)	(1.49, 13.27)	76	3 (3.9)	(0.82, 11.11)
	Week 12 < to <= Week 16	68	3 (4.4)	(0.92, 12.36)	76	7 (9.2)	(3.78, 18.06)
	Week 16 < to <= Week 20	66	4 (6.1)	(1.68, 14.80)	74	7 (9.5)	(3.89, 18.52)
	Week 20 < to <= Week 24	69	3 (4.3)	(0.91, 12.18)	79	7 (8.9)	(3.64, 17.41)
	Baseline < to <= Week 24	80	11 (13.8)	(7.07, 23.27)	82	19 (23.2)	(14.56, 33.80)
Hb >=14.0 g/dL	Baseline	80	0 (0.0)	(0.00, 4.51)	82	0 (0.0)	(0.00, 4.40)
	Baseline < to <= Week 2	72	0 (0.0)	(0.00, 4.99)	77	0 (0.0)	(0.00, 4.68)
	Week 2 < to <= Week 4	76	0 (0.0)	(0.00, 4.74)	76	0 (0.0)	(0.00, 4.74)
	Week 4 < to <= Week 6	76	0 (0.0)	(0.00, 4.74)	77	0 (0.0)	(0.00, 4.68)
	Week 6 < to <= Week 8	76	0 (0.0)	(0.00, 4.74)	76	0 (0.0)	(0.00, 4.74)
	Week 8 < to <= Week 10	68	0 (0.0)	(0.00, 5.28)	77	0 (0.0)	(0.00, 4.68)
	Week 10 < to <= Week 12	74	0 (0.0)	(0.00, 4.86)	76	0 (0.0)	(0.00, 4.74)
	Week 12 < to <= Week 16	68	0 (0.0)	(0.00, 5.28)	76	2 (2.6)	(0.32, 9.18)
	Week 16 < to <= Week 20	66	0 (0.0)	(0.00, 5.44)	74	0 (0.0)	(0.00, 4.86)
	Week 20 < to <= Week 24	69	0 (0.0)	(0.00, 5.21)	79	0 (0.0)	(0.00, 4.56)
	Baseline < to <= Week 24	80	0 (0.0)	(0.00, 4.51)	82	2 (2.4)	(0.30, 8.53)

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_3.sas

5.3.5.1—6 表 14.3.8.3 より引用

表 2.7.6.25－97　Hb 値が 13.0 g/dL 以上又は 14.0 g/dL 以上になった被験者の割合（安全性解析対象集団）（Correction 集団）

		MT-6548(N=71)			darbepoetin(N=71)		
Criteria	Period	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb >=13.0 g/dL	Baseline	71	0 (0.0)	(0.00, 5.06)	71	0 (0.0)	(0.00, 5.06)
	Baseline < to <= Week 2	63	0 (0.0)	(0.00, 5.69)	59	0 (0.0)	(0.00, 6.06)
	Week 2 < to <= Week 4	62	1 (1.6)	(0.04, 8.66)	63	0 (0.0)	(0.00, 5.69)
	Week 4 < to <= Week 6	64	0 (0.0)	(0.00, 5.60)	66	2 (3.0)	(0.37, 10.52)
	Week 6 < to <= Week 8	61	2 (3.3)	(0.40, 11.35)	64	8 (12.5)	(5.55, 23.15)
	Week 8 < to <= Week 10	61	2 (3.3)	(0.40, 11.35)	59	11 (18.6)	(9.69, 30.91)
	Week 10 < to <= Week 12	64	4 (6.3)	(1.73, 15.24)	63	20 (31.7)	(20.58, 44.69)
	Week 12 < to <= Week 16	63	7 (11.1)	(4.59, 21.56)	59	13 (22.0)	(12.29, 34.73)
	Week 16 < to <= Week 20	60	9 (15.0)	(7.10, 26.57)	65	14 (21.5)	(12.31, 33.49)
	Week 20 < to <= Week 24	67	9 (13.4)	(6.33, 23.97)	65	12 (18.5)	(9.92, 30.03)
	Baseline < to <= Week 24	71	22 (31.0)	(20.54, 43.08)	71	41 (57.7)	(45.44, 69.39)
Hb >=14.0 g/dL	Baseline	71	0 (0.0)	(0.00, 5.06)	71	0 (0.0)	(0.00, 5.06)
	Baseline < to <= Week 2	63	0 (0.0)	(0.00, 5.69)	59	0 (0.0)	(0.00, 6.06)
	Week 2 < to <= Week 4	62	0 (0.0)	(0.00, 5.78)	63	0 (0.0)	(0.00, 5.69)
	Week 4 < to <= Week 6	64	0 (0.0)	(0.00, 5.60)	66	0 (0.0)	(0.00, 5.44)
	Week 6 < to <= Week 8	61	0 (0.0)	(0.00, 5.87)	64	0 (0.0)	(0.00, 5.60)
	Week 8 < to <= Week 10	61	0 (0.0)	(0.00, 5.87)	59	0 (0.0)	(0.00, 6.06)
	Week 10 < to <= Week 12	64	0 (0.0)	(0.00, 5.60)	63	1 (1.6)	(0.04, 8.53)
	Week 12 < to <= Week 16	63	0 (0.0)	(0.00, 5.69)	59	3 (5.1)	(1.06, 14.15)
	Week 16 < to <= Week 20	60	2 (3.3)	(0.41, 11.53)	65	2 (3.1)	(0.37, 10.68)
	Week 20 < to <= Week 24	67	1 (1.5)	(0.04, 8.04)	65	0 (0.0)	(0.00, 5.52)
	Baseline < to <= Week 24	71	3 (4.2)	(0.88, 11.86)	71	5 (7.0)	(2.33, 15.67)

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—6 表 14.3.8.2 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

全集団における，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 2.7.6.25－98 に示した．

全集団における，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 13.9%（21 名），darbepoetin 群で 5.2%（8 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 2.6%（4 名），darbepoetin 群で 2.6%（4 名）であった．

Correction 集団で治療期間 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 2.7.6.25－99 に示した．

表 2.7.6.25－98　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）

		MT-6548(N=151)			darbepoetin(N=153)		
Criteria	Period	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb <9.0 g/dL	Baseline	151	8 (5.3)	(2.31, 10.17)	153	7 (4.6)	(1.86, 9.20)
	Baseline < to <= Week 2	135	7 (5.2)	(2.11, 10.39)	136	5 (3.7)	(1.20, 8.37)
	Week 2 < to <= Week 4	138	13 (9.4)	(5.11, 15.57)	139	4 (2.9)	(0.79, 7.20)
	Week 4 < to <= Week 6	140	10 (7.1)	(3.48, 12.74)	143	2 (1.4)	(0.17, 4.96)
	Week 6 < to <= Week 8	137	7 (5.1)	(2.08, 10.24)	140	2 (1.4)	(0.17, 5.07)
	Week 8 < to <= Week 10	129	0 (0.0)	(0.00, 2.82)	136	2 (1.5)	(0.18, 5.21)
	Week 10 < to <= Week 12	138	1 (0.7)	(0.02, 3.97)	139	0 (0.0)	(0.00, 2.62)
	Week 12 < to <= Week 16	131	1 (0.8)	(0.02, 4.18)	135	0 (0.0)	(0.00, 2.70)
	Week 16 < to <= Week 20	126	6 (4.8)	(1.77, 10.08)	139	0 (0.0)	(0.00, 2.62)
	Week 20 < to <= Week 24	136	4 (2.9)	(0.81, 7.36)	144	0 (0.0)	(0.00, 2.53)
	Baseline < to <= Week 24	151	21 (13.9)	(8.82, 20.47)	153	8 (5.2)	(2.28, 10.04)
Hb <8.0 g/dL	Baseline	151	1 (0.7)	(0.02, 3.63)	153	0 (0.0)	(0.00, 2.38)
	Baseline < to <= Week 2	135	1 (0.7)	(0.02, 4.06)	136	0 (0.0)	(0.00, 2.68)
	Week 2 < to <= Week 4	138	0 (0.0)	(0.00, 2.64)	139	2 (1.4)	(0.17, 5.10)
	Week 4 < to <= Week 6	140	1 (0.7)	(0.02, 3.92)	143	1 (0.7)	(0.02, 3.83)
	Week 6 < to <= Week 8	137	1 (0.7)	(0.02, 4.00)	140	1 (0.7)	(0.02, 3.92)
	Week 8 < to <= Week 10	129	0 (0.0)	(0.00, 2.82)	136	1 (0.7)	(0.02, 4.03)
	Week 10 < to <= Week 12	138	0 (0.0)	(0.00, 2.64)	139	0 (0.0)	(0.00, 2.62)
	Week 12 < to <= Week 16	131	0 (0.0)	(0.00, 2.78)	135	0 (0.0)	(0.00, 2.70)
	Week 16 < to <= Week 20	126	0 (0.0)	(0.00, 2.89)	139	0 (0.0)	(0.00, 2.62)
	Week 20 < to <= Week 24	136	1 (0.7)	(0.02, 4.03)	144	0 (0.0)	(0.00, 2.53)
	Baseline < to <= Week 24	151	4 (2.6)	(0.73, 6.64)	153	4 (2.6)	(0.72, 6.56)

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_6.sas

5.3.5.1—6 表 12.4.4—1 より引用

表 2.7.6.25－99　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）（Correction 集団）

		MT-6548(N=71)			darbepoetin(N=71)		
Criteria	Period	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Hb <9.0 g/dL	Baseline	71	7 (9.9)	(4.06, 19.26)	71	6 (8.5)	(3.16, 17.49)
	Baseline < to <= Week 2	63	2 (3.2)	(0.39, 11.00)	59	3 (5.1)	(1.06, 14.15)
	Week 2 < to <= Week 4	62	5 (8.1)	(2.67, 17.83)	63	2 (3.2)	(0.39, 11.00)
	Week 4 < to <= Week 6	64	3 (4.7)	(0.98, 13.09)	66	1 (1.5)	(0.04, 8.16)
	Week 6 < to <= Week 8	61	2 (3.3)	(0.40, 11.35)	64	2 (3.1)	(0.38, 10.84)
	Week 8 < to <= Week 10	61	0 (0.0)	(0.00, 5.87)	59	2 (3.4)	(0.41, 11.71)
	Week 10 < to <= Week 12	64	1 (1.6)	(0.04, 8.40)	63	0 (0.0)	(0.00, 5.69)
	Week 12 < to <= Week 16	63	1 (1.6)	(0.04, 8.53)	59	0 (0.0)	(0.00, 6.06)
	Week 16 < to <= Week 20	60	2 (3.3)	(0.41, 11.53)	65	0 (0.0)	(0.00, 5.52)
	Week 20 < to <= Week 24	67	2 (3.0)	(0.36, 10.37)	65	0 (0.0)	(0.00, 5.52)
	Baseline < to <= Week 24	71	9 (12.7)	(5.96, 22.70)	71	5 (7.0)	(2.33, 15.67)
Hb <8.0 g/dL	Baseline	71	1 (1.4)	(0.04, 7.60)	71	0 (0.0)	(0.00, 5.06)
	Baseline < to <= Week 2	63	1 (1.6)	(0.04, 8.53)	59	0 (0.0)	(0.00, 6.06)
	Week 2 < to <= Week 4	62	0 (0.0)	(0.00, 5.78)	63	1 (1.6)	(0.04, 8.53)
	Week 4 < to <= Week 6	64	1 (1.6)	(0.04, 8.40)	66	1 (1.5)	(0.04, 8.16)
	Week 6 < to <= Week 8	61	0 (0.0)	(0.00, 5.87)	64	1 (1.6)	(0.04, 8.40)
	Week 8 < to <= Week 10	61	0 (0.0)	(0.00, 5.87)	59	1 (1.7)	(0.04, 9.09)
	Week 10 < to <= Week 12	64	0 (0.0)	(0.00, 5.60)	63	0 (0.0)	(0.00, 5.69)
	Week 12 < to <= Week 16	63	0 (0.0)	(0.00, 5.69)	59	0 (0.0)	(0.00, 6.06)
	Week 16 < to <= Week 20	60	0 (0.0)	(0.00, 5.96)	65	0 (0.0)	(0.00, 5.52)
	Week 20 < to <= Week 24	67	0 (0.0)	(0.00, 5.36)	65	0 (0.0)	(0.00, 5.52)
	Baseline < to <= Week 24	71	2 (2.8)	(0.34, 9.81)	71	3 (4.2)	(0.88, 11.86)

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_7.sas

5.3.5.1—6 表 14.3.8.7 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

全集団における，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 2.7.6.25－100 に示した．また，Correction 集団の，投与初期に 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 2.7.6.25－101 に示した

全集団における，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は，MT-6548 群で 2.7%（4 名），darbepoetin 群で 1.3%（2 名）であった．

また，Correction 集団における，Hb 値の上昇速度（0～4 週）が 0.5 g/dL/week 超になった被験者の割合は，MT-6548 群で 5.8%（4 名），darbepoetin 群で 1.4%（1 名）であり，回帰直線の傾きから求めた Hb 値の上昇速度（0～6 週）が 0.5 g/dL/week 超になった被験者は，MT-6548 群で認められず，darbepoetin 群での被験者の割合は 1.4%（1 名）であった．

Conversion 集団及び Correction 集団で治療期間 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 2.7.6.25－102 及び表 2.7.6.25－103 に示した．

表 2.7.6.25－100　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）

		MT-6548(N=151)			darbepoetin(N=153)		
Criteria	Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Increase of >0.5 g/dL/week in Hb	Week 4	149	4 (2.7)	(0.74, 6.73)	153	1 (0.7)	(0.02, 3.59)
	Week 8	145	0 (0.0)	(0.00, 2.51)	151	1 (0.7)	(0.02, 3.63)
	Week 12	145	0 (0.0)	(0.00, 2.51)	148	0 (0.0)	(0.00, 2.46)
	Week 16	143	0 (0.0)	(0.00, 2.55)	148	0 (0.0)	(0.00, 2.46)
	Week 20	140	0 (0.0)	(0.00, 2.60)	144	0 (0.0)	(0.00, 2.53)
	Week 24	132	0 (0.0)	(0.00, 2.76)	140	0 (0.0)	(0.00, 2.60)
	Baseline < to <= Week 24	149	4 (2.7)	(0.74, 6.73)	153	2 (1.3)	(0.16, 4.64)

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—6 表 12.4.5—1 より引用

表 2.7.6.25－101　投与初期に Hb 値の上昇速度が 0.5 g/dL/week 超になった被験者の割合（安全性解析対象集団）

	MT-6548(N=71)			darbepoetin(N=71)		
Parameter(unit)	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Rate of increase in Hb calculated from baseline and Week 4 (g/dL/week)	69	4 (5.8)	(1.60, 14.18)	71	1 (1.4)	(0.04, 7.60)
Rate of increase in Hb calculated from baseline to Week 6 (regression) (g/dL/week)	69	0 (0.0)	(0.00, 5.21)	70	1 (1.4)	(0.04, 7.70)

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 16.2.4.2
Source: t_14_3_9_6.sas

5.3.5.1—6 表 12.4.5—2 より引用

表 2.7.6.25－102　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）（Conversion 集団）

		MT-6548(N=80)			darbepoetin(N=82)		
Criteria	Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Increase of >0.5 g/dL/week in Hb	Week 4	80	0 (0.0)	(0.00, 4.51)	82	0 (0.0)	(0.00, 4.40)
	Week 8	77	0 (0.0)	(0.00, 4.68)	81	0 (0.0)	(0.00, 4.45)
	Week 12	77	0 (0.0)	(0.00, 4.68)	80	0 (0.0)	(0.00, 4.51)
	Week 16	76	0 (0.0)	(0.00, 4.74)	80	0 (0.0)	(0.00, 4.51)
	Week 20	73	0 (0.0)	(0.00, 4.93)	79	0 (0.0)	(0.00, 4.56)
	Week 24	66	0 (0.0)	(0.00, 5.44)	75	0 (0.0)	(0.00, 4.80)
	Baseline < to <= Week 24	80	0 (0.0)	(0.00, 4.51)	82	0 (0.0)	(0.00, 4.40)

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_3.sas

5.3.5.1—6 表 14.3.9.3 より引用

表 2.7.6.25－103　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）（Correction 集団）

		MT-6548(N=71)			darbepoetin(N=71)		
Criteria	Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion
Increase of >0.5 g/dL/week in Hb	Week 4	69	4 (5.8)	(1.60, 14.18)	71	1 (1.4)	(0.04, 7.60)
	Week 8	68	0 (0.0)	(0.00, 5.28)	70	1 (1.4)	(0.04, 7.70)
	Week 12	68	0 (0.0)	(0.00, 5.28)	68	0 (0.0)	(0.00, 5.28)
	Week 16	67	0 (0.0)	(0.00, 5.36)	68	0 (0.0)	(0.00, 5.28)
	Week 20	67	0 (0.0)	(0.00, 5.36)	65	0 (0.0)	(0.00, 5.52)
	Week 24	66	0 (0.0)	(0.00, 5.44)	65	0 (0.0)	(0.00, 5.52)
	Baseline < to <= Week 24	69	4 (5.8)	(1.60, 14.18)	71	2 (2.8)	(0.34, 9.81)

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_2.sas

5.3.5.1—6 表 14.3.9.2 より引用

6)　減量・休薬前後の Hb 値

全集団における，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 2.7.6.25－104 に示した.

全集団における，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 12.61±1.05 g/dL 及び 11.79±1.44 g/dL，その前後間の Hb 値の変化量の平均値±SD は -0.60±1.00 g/dL，darbepoetin 群でそれぞれ 12.88±0.76 g/dL 及び 12.56±0.89 g/dL，その前後間の Hb 値の変化量の平均値±SD は -0.28±0.84 g/dL であった.

表 2.7.6.25－104　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	28	12.61	1.05	12.80	(9.2, 14.6)	(12.21, 13.02)
		darbepoetin	125	12.88	0.76	13.00	(10.2, 15.2)	(12.75, 13.02)
	4 weeks after interruption or dose reduction	MT-6548	27	11.79	1.44	11.90	(8.1, 14.6)	(11.22, 12.36)
		darbepoetin	115	12.56	0.89	12.60	(9.5, 15.2)	(12.40, 12.73)
	Difference of Hb	MT-6548	27	-0.60	1.00	-0.70	(-4.4, 1.2)	(-1.00, -0.21)
		darbepoetin	115	-0.28	0.84	-0.20	(-3.0, 2.3)	(-0.43, -0.12)
Interval (days)		MT-6548	27	28.04	7.31	29.00	(7.0, 42.0)	(25.15, 30.93)
		darbepoetin	115	30.09	6.49	29.00	(14.0, 44.0)	(28.89, 31.29)

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—6 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 群及び darbepoetin 群のいずれでも認められなかった.

2) 体重

体重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 -0.44±2.04 kg 及び -0.02±1.86 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 0.0±15.9 mmHg 及び 2.0±15.6 mmHg であった．拡張期血圧のベースラインからの 24 週後の変化量の平均値±SD は, MT-6548 群及び darbepoetin 群で -0.1±10.9 mmHg 及び 1.5±10.1 mmHg であった．脈拍のベースラインからの 24 週後の変化量の平均値±SD は，MT-6548 群及び darbepoetin 群で -0.2±8.6 beats/min 及び 0.1±8.9 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 0%（0／137 名）及び 2.2%（3／137 名），darbepoetin 群で 0.7%（1／145 名）及び 2.1%（3／145 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「加齢黄斑変性」,「黄斑浮腫」及び「網膜静脈閉塞」が各 1 名であり，darbepoetin 群では「糖尿病網膜症」,「網膜出血」及び「網膜血管瘤」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「白内障」が 3 名,「眼瞼炎」及び「網膜出血」が各 2 名,「結膜出血」,「眼乾燥」,「眼瞼湿疹」,「黄斑浮腫」,「網膜滲出物」,「網膜静脈閉塞」及び「加齢黄斑変性」が各 1 名，darbepoetin 群で「網膜出血」及び「糖尿病網膜症」が各 3 名,「眼瞼炎」及び「眼そう痒症」が各 2 名,「白内障」,「結膜出血」,「眼精疲労」,「アレルギー性結膜炎」,「網膜血管瘤」,「眼部腫脹」及び「結膜充血」が各 1 名で認められた．このうち，MT-6548 群 1 名の「網膜出血」を除いて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. 治験薬との因果関係は合理的な可能性ありと判断された「網膜出血」は, 軽度であり, 処置として治験中止が判断され, その後，転帰は回復した．なお，本被験者の VEGF はベースラインで 16.1 pg/mL，12 週後で 18.9 pg/mL で推移し，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の割合は, MT-6548 群で 0.7%（1／139 名）及び 2.2%（3／139 名）, darbepoetin 群で 0%（0／144 名）及び 0.7%（1／144 名）であった.

当該被験者で, 20 週～24 週後の胸部 X 線検査実施日に発現した有害事象は MT-6548 群で「胸水」,「うっ血性心不全」及び「慢性心不全」が各 1 名であり, darbepoetin 群で「心肥大」が 1 名であった. MT-6548 群で認められた「胸水」は, 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.「うっ血性心不全」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, 転帰は治療期間 I 期中には未回復であり治療期間 II 期に移行した.「慢性心不全」は, 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 群で認められた「心肥大」は, 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, 転帰は治療期間 I 期中には未回復であり治療期間 II 期に移行した.

6) 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.

2.7.6.25.2.2 結論

(1) 有効性

全集団における MMRM を用いた 20 週及び 24 週後の平均 Hb 値の LSMean 及びその 95%CI は, MT-6548 群で 11.66 g/dL 及び 11.49～11.84 g/dL, darbepoetin 群で 11.93 g/dL 及び 11.76～12.10 g/dL であり, いずれの群においても 20 週及び 24 週後の平均 Hb 値の 95%CI は, 目標範囲内（11.0 g/dL 以上 13.0 g/dL 未満）であった.

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, -0.26 g/dL 及び -0.50～ -0.02 g/dL であり, 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, Conversion 集団の Hb 値の平均値は, ESA 製剤からの切り替え後に急な変動を認めることなく推移した. その後 Hb 値の平均値は上昇し, 8 週後に目標範囲内に到達後, 24 週後まで目標範囲内を維持した. MMRM を用いた 24 週後の Hb 値の LSMean 及びその 95%CI は 11.38 g/dL 及び 11.17～11.58 g/dL であり, 目標範囲内であった. Conversion 集団の Hb 値の平均値が切り替え後に上昇した理由は, Conversion（Hb<11.0）集団で認められた切り替え後の Hb 値の平均値の上昇を反映したものと考えられる. 一方で, Conversion（Hb≥11.0）集団の Hb 値の平均値は, 切り替え後に急な変動を認めることなく, 24 週間にわたり目標範囲内で推移した. また, Conversion 集団の 24 週後に Hb 値

が目標範囲内であった被験者の割合は，MT-6548 群で 66.7%であり，ベースラインから増加した．

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

MT-6548 群に関して，Correction 集団の Hb 値の平均値はベースライン以降上昇し，8 週後に目標範囲内に到達後，24 週後まで目標範囲内を維持した．MMRM を用いた 24 週後の Hb 値の LSMean 及びその 95%CI は 11.93 g/dL 及び 11.71～12.15 g/dL であり，目標範囲内であった．

24 週後に Hb 値が目標範囲内の被験者の割合は MT-6548 群で 69.7%であり，ベースラインから増加した．

以上より，MT-6548 の Correction 集団での改善維持効果が確認された．

全集団の 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 24 週後に MT-6548 群で darbepoetin 群と比較して統計学的に有意に[redacted]し[redacted]，MCH 及び MCV は 24 週後に 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．

全集団の EPO の 2 週～24 週後の最大値は 216.0 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 SOC は，「感染症および寄生虫症」，「胃腸障害」であった．SOC「感染症および寄生虫症」は，darbepoetin 群と同程度の発現割合であり，主な有害事象は「上咽頭炎」であった．また，darbepoetin 群と比較して発現割合が 10%以上高かった SOC は認められなかった．副作用のうち，MT-6548 群で発現割合が 20%以上の SOC は認められず，最も発現割合が高い副作用の SOC は，「胃腸障害」であった．SOC「胃腸障害」は，主な有害事象は「下痢」，「便秘」及び「嘔吐」であり，このうち MT-6548 群で最も発現割合が高かった「下痢」は，darbepoetin 群と比較して MT-6548 群で有害事象及び副作用の発現割合が高かった．

MT-6548 群で発現割合が 5%以上の有害事象は，「上咽頭炎」，「下痢」，「便秘」及び「挫傷」であった．これらの有害事象のうち，MT-6548 群の発現割合が darbepoetin 群と比較して 3%以上高かった有害事象は，「下痢」，「挫傷」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ず，MT-6548 群で最も発現割合が高い副作用は「下痢」，次いで「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，発現割合に両群で差が認められた主な副作用は「下痢」であった．

MT-6548 群で darbepoetin 群と比較して有害事象及び副作用の発現割合が高かった「下痢」の計 16 名について，いずれも非重篤であり，治験薬との因果関係が合理的な可能性ありと判断された被験者数は 6 名であった．1 名の転帰は治療期間 I 期中には未回復で治療期間 II 期に移行し，それ以外の 15 名の転帰は治療期間 I 期中に軽快又は回復した．また，2 名が中等度と判断され，それ以外の 14 名は軽度と判断された．「下痢」が原因で中止に至った被験者が 1 名認められ，本事象は治験薬の投与継続中に処置なく回復したが，当該被験者はその後本事象により中止となった．また，「下痢」が原因で休薬又は減量に至った被験者数は 3 名であった．「下痢」の発現時期は，84 日後までと 85 日後以降の発現割合に大きな差は認められなかった．本治験で認められた「下痢」は，その多くが軽度で治療期間 I 期中に回復していること，更に，治験薬の中止に至る被験者は 1 名と少なく，当該被験者の「下痢」は治験薬投与中に回復していることから，安全性への大きな懸念にはならないと考えられた．MT-6548 群で darbepoetin 群と比較して有害事象の発現割合が高かった「挫傷」は，MT-6548 群で 8 名に認められ，1 名は中等度，7 名は軽度，いずれ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，転帰は軽快又は回復した．「悪心」の有害事象発現割合は両群で同程度であった．「悪心」は，MT-6548 群で 4 名に認められ，いずれも軽度，治験薬との因果関係は合理的な可能性ありと判断され，1 名は治療期間 I 期中の転帰は未回復であり，治療期間 II 期に移行し，3 名の転帰は回復であった．

死亡に至った有害事象は，darbepoetin 群で「急性心筋梗塞」が 1 名で認められた．本事象は高度，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た．

重篤な有害事象の発現割合は，MT-6548 群と darbepoetin 群で同程度であった．また，重篤な副作用は，MT-6548 群及び darbepoetin 群で認められなかった．2 名以上に認められた重篤な有害事象は，MT-6548 群で「慢性腎臓病」，「腎機能障害」，「肺炎」，「白内障」，「うっ血性心不全」，「末期腎疾患」，「腎不全」，及び「脊椎圧迫骨折」，darbepoetin 群で「慢性腎臓病」，「肺炎」及び「脱水」であった．重篤な有害事象は，両群とも原疾患である慢性腎臓病に関連する事象が認められ，それ以外に特定の事象が発現する傾向は認められなかった．

中止に至った有害事象の発現割合は，MT-6548 群と darbepoetin 群で同程度であった．中止に至った有害事象の内訳は，MT-6548 群で「網膜出血」，「腹部不快感」，「倦怠感」，「下痢」，「胃腸ポリープ出血」，「ヘモグロビン減少」，「慢性心不全」及び「慢性腎臓病」が各 1 名であり，そのうち「腹部不快感」及び「倦怠感」，「胃腸ポリープ出血」及び「ヘモグロビン減少」，「慢性心不全」及び「慢性腎臓病」は，それぞれ同一被験者で認められた．また，darbepoetin 群で「アルツハイマー型認知症」，「高窒素血症」及び「慢性腎臓病」が各 1 名であった．

休薬又は減量に至った有害事象の発現割合は，MT-6548 群と darbepoetin 群で同程度であった．MT-6548 群で休薬に至った有害事象は，「下痢」，「胆石症」，「慢性心不全」，「発熱」が各 1 名で，減量に至った有害事象は，「下痢」が 2 名，「良性前立腺肥大症」が 1 名

であった．darbepoetin 群で休薬に至った有害事象は，「高血圧」が 2 名，「肺炎」，「胃癌」，「腹部不快感」が各 1 名であり，減量に至った有害事象は認められなかった．

治療期間 I 期中において，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．また，発現直前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．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．

治験期間 I 期中に変動があった臨床検査値は，血清クレアチニン及び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．

治療期間 I 期中に安静時標準 12 誘導心電図，体重及びバイタルサインにおいて，特に臨床的に問題となる異常は認めなかった．

眼底検査では，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が，MT-6548 群及び darbepoetin 群で認められ，そ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「加齢黄斑変性」，「黄斑浮腫」及び「網膜静脈閉塞」が各 1 名であり，darbepoetin 群では「糖尿病網膜症」，「網膜出血」，「網膜血管瘤」が各 1 名であった．なお，眼底検査の判定が上記の変動に該当しない被験者において，SOC「眼障害」の有害事象で治験薬との因果関係が合理的な可能性ありと判断された事象として，MT-6548 群で「網膜出血」が 1 名認められた．本事象は，軽度であり，処置として治験中止が判断され，その後，転帰は回復した．なお，本被験者の VEGF に大きな変動はなかった．

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 3 名，darbepoetin 群で 0 名であった．当該被験者において，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ず，SOC「眼障害」に該当する有害事象の発現は 1 名に「加齢黄斑変性」が認められた．本被験者は合併症として「加齢黄斑変性」を有しており，VEGF は，ベースラインで 61.2 pg/mL，12 週後で 152 pg/mL，24 週後で 249 pg/mL であった．本事象は，治験薬投与 147 日目に発現し，軽度，非重篤，治験薬との合理的な因果関係なしと判断され，治療期間 I 期中には未回復であり治療期間 II 期に移行した．

胸部 X 線に関して，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，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．

本治験で設定した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，減量又は休薬することにより，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，MT-6548 錠の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

保存期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．また，MT-6548 は Conversion 集団，Correction 集団のいずれにおいても，良好な Hb 値のコントロールが可能であり，MT-6548 の保存期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 群で「下痢」の有害事象及び副作用の発現割合が高かったが，その多くが軽度で治療期間 I 期中に回復していること，更に，治験薬の中止に至る被験者は 1 名と少なく，当該被験者の「下痢」は治験薬投与中に回復していることから，安全性への大きな懸念にはならないと考えられた．また，その他の安全性評価においても，本治験で 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 は保存期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．

2.7.6.25.3　最終固定データ

2.7.6.25.3.1　結果の要約

2.7.6.25.3.1.1　被験者の内訳

被験者の内訳を図 2.7.6.25－36 に示した.

同意登録被験者数は 432 名であり，そのうち 128 名が治療期間移行前に脱落し，304 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 151 名, darbepoetin 群 153 名であった.

治療期間に移行した被験者のうち，Correction 集団は 142 名（MT-6548 群 71 名，darbepoetin 群 71 名），Conversion 集団は 162 名（MT-6548 群 80 名，darbepoetin 群 82 名）であった．治療期間 I 期を完了した被験者は，271 名（MT-6548 群 130 名，darbepoetin 群 141 名）であり，その内訳は Correction 集団で 131 名（MT-6548 群 66 名，darbepoetin 群 65 名），Conversion 集団で 140 名（MT-6548 群 64 名，darbepoetin 群 76 名）であった．治療期間 II 期を完了した被験者は，234 名（MT-6548 群 111 名，darbepoetin 群 123 名）であり，その内訳は Correction 集団で 116 名（MT-6548 群 57 名，darbepoetin 群 59 名），Conversion 集団で 118 名（MT-6548 群 54 名，darbepoetin 群 64 名）であった．治験期間中に中止した被験者は，70 名｛MT-6548 群 40 名（治療期間 I 期 21 名，治療期間 II 期 19 名），darbepoetin 群 30 名（治療期間 I 期 12 名，治療期間 II 期 18 名)｝であり，その内訳は Correction 集団で 26 名（MT-6548 群 14 名，darbepoetin 群 12 名），Conversion 集団で 44 名（MT-6548 群 26 名，darbepoetin 群 18 名）であった.

治療期間に移行した Conversion 集団のうち，Conversion（Hb≥11.0）集団は 75 名（MT-6548 群 37 名, darbepoetin 群 38 名）, Conversion（Hb<11.0）集団は 87 名（MT-6548 群 43 名, darbepoetin 群 44 名）であった．治験期間中に中止した被験者は，Conversion（Hb≥11.0）集団は 13 名｛MT-6548 群 7 名（治療期間 I 期 4 名，治療期間 II 期 3 名），darbepoetin 群 6 名（治療期間 I 期 1 名，治療期間 II 期 5 名)｝，Conversion（Hb<11.0）集団は 31 名｛MT-6548 群 19 名（治療期間 I 期 12 名，治療期間 II 期 7 名），darbepoetin 群 12 名（治療期間 I 期 5 名，治療期間 II 期 7 名)｝であった.

治療期間中に中止した被験者の割合及び理由を表 2.7.6.25－105，休薬に至った理由を表 2.7.6.25－106 に示した.

治療期間中に中止した被験者の割合は, MT-6548 群 26.5%（40／151 名）, darbepoetin 群 19.6%（30／153 名）であった．中止理由は，「持続的な血液透析又は腹膜透析の開始又は腎移植の実施」が MT-6548 群 13 名，darbepoetin 群 15 名，「被験者からの申し入れ」が MT-6548 群 11 名，darbepoetin 群 3 名，「有害事象」が MT-6548 群 10 名，darbepoetin 群 5 名，「過粘稠度症候群又は Hb 値のコントロール困難」が MT-6548 群 2 名，darbepoetin 群 3 名，「その他，治験責任（分担）医師の判断」が MT-6548 群 2 名，darbepoetin 群 2 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 名及び「肝機能値の異常」が MT-6548 群 0 名，darbepoetin 群 1 名であった．「過粘稠度症候群又は Hb 値のコントロール困難」により中止した MT-6548 群の 2 名の中止時の Hb 値は，8.9 g/dL 及び 7.8 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．また，「その他，治験責任（分担）医師の判断」により中止した MT-6548 群の 2 名の中止理由の詳細は，「The patient became the condition with the initiation of HD」及び「The patient became the condition with the initiation of PD」と報告された．

治療期間中の休薬は，MT-6548 群 42 回，darbepoetin 群 86 回であり，休薬理由は，「用量調節アルゴリズムに準じた休薬」が MT-6548 群 22 回，darbepoetin 群 52 回，「有害事象」が MT-6548 群 14 回，darbepoetin 群 5 回，「Hb 値の推移」が MT-6548 群 4 回，darbepoetin 群 29 回及び「その他」が MT-6548 群 2 回，darbepoetin 群 4 回であった．

有効性の解析は，FAS を対象として行った．安全性の解析は，安全性解析対象集団を対象として行った．

各解析対象集団に含まれる被験者の内訳を表 2.7.6.25－107 に示した．

治療期間に移行した 304 名（MT-6548 群 151 名，darbepoetin 群 153 名）すべてを FAS 及び安全性解析対象集団とした．

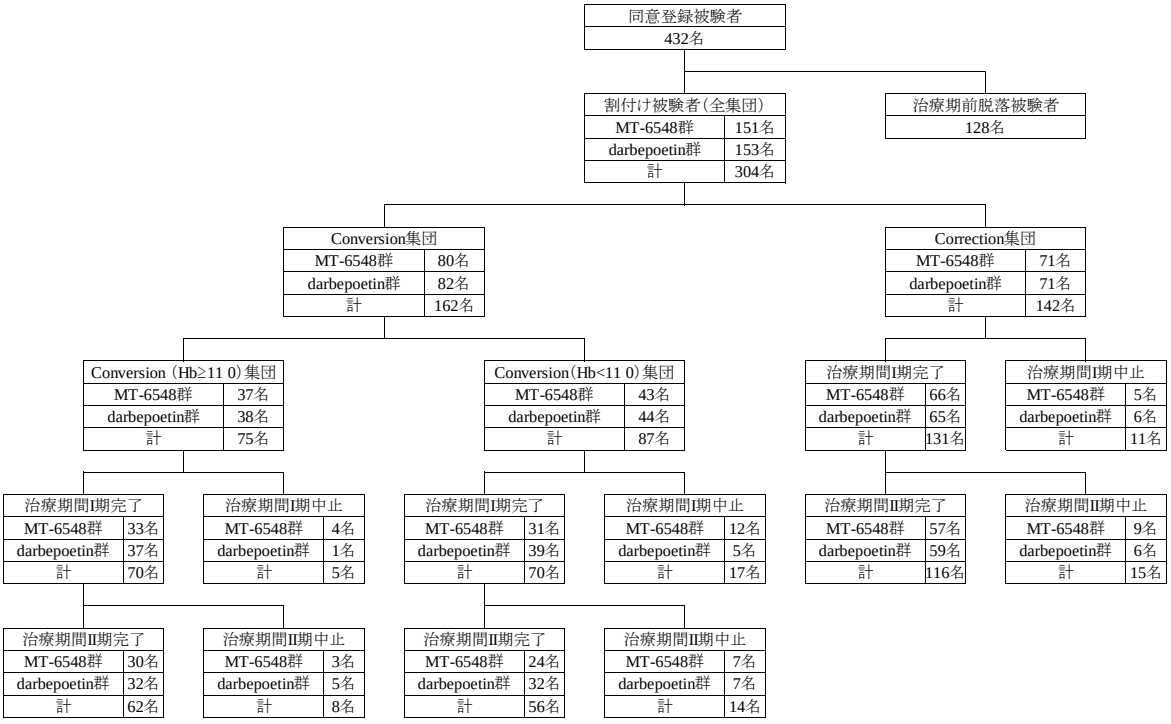


図 2.7.6.25－36　被験者の内訳

5.3.5.1—8 図 10.1—1 より引用

表 2.7.6.25－105　治療期間中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=151)	darbepoetin (N=153)
Subject discontinued during treatment period	n (%)	40 (26.5)	30 (19.6)
Primary reason for discontinuation			
Subject withdrawal of consent	n (%)	11 (7.3)	3 (2.0)
Inappropriate for participating in the study	n (%)	0 (0.0)	0 (0.0)
Adverse Events	n (%)	10 (6.6)	5 (3.3)
Hepatic function abnormalities	n (%)	0 (0.0)	1 (0.7)
Conducting rescue therapy before completing the scheduled examinations at Week 24	n (%)	2 (1.3)	1 (0.7)
Hyperviscosity syndrome, difficult to control of Hb within target range	n (%)	2 (1.3)	3 (2.0)
Initiation of chronic hemodialysis or peritoneal dialysis or a renal transplant	n (%)	13 (8.6)	15 (9.8)
Proven to be pregnant	n (%)	0 (0.0)	0 (0.0)
Other, Investigator discretion	n (%)	2 (1.3)	2 (1.3)

Data Source: Listing 16.2.1.4
Source: t_14_1_2_1.sas

5.3.5.1—8 表 10.1—1 より引用

表 2.7.6.25－106　休薬に至った理由（治療期間移行例）

	Statistic	MT-6548 (N=151)	darbepoetin (N=153)
Number of study drug interruption during treatment period	N*	42	86
Based on dose adjustment algorithm	n (%)	22 (52.4)	52 (60.5)
Not based on dose adjustment algorithm	n (%)	20 (47.6)	36 (41.9)
Adverse events	n (%)	14 (33.3)	5 (5.8)
Hepatic function abnormalities	n (%)	0 (0.0)	0 (0.0)
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 (%)	4 (9.5)	29 (33.7)
Other	n (%)	2 (4.8)	4 (4.7)

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—8 表 10.1—2 より引用

表 2.7.6.25－107　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-6548	darbepoetin
Subjects enrolled in Treatment Period	N	151	153
Subjects completed	n (%)	111 (73.5)	123 (80.4)
Subjects withdrawn	n (%)	40 (26.5)	30 (19.6)
Subjects received rescue therapy	n (%)	8 (5.3)	3 (2.0)
Subject Group:			
Correction Group	n (%)	71 (47.0)	71 (46.4)
Subjects completed	n (%)	57 (37.7)	59 (38.6)
Subjects withdrawn	n (%)	14 (9.3)	12 (7.8)
Subjects received rescue therapy	n (%)	1 (0.7)	2 (1.3)
Conversion Group	n (%)	80 (53.0)	82 (53.6)
Subjects completed	n (%)	54 (35.8)	64 (41.8)
Subjects withdrawn	n (%)	26 (17.2)	18 (11.8)
Subjects received rescue therapy	n (%)	7 (4.6)	1 (0.7)
Conversion (Hb >=11.0 g/dL) Group	n (%)	37 (24.5)	38 (24.8)
Subjects completed	n (%)	30 (19.9)	32 (20.9)
Subjects withdrawn	n (%)	7 (4.6)	6 (3.9)
Subjects received rescue therapy	n (%)	1 (0.7)	1 (0.7)
Conversion (Hb <11.0 g/dL) Group	n (%)	43 (28.5)	44 (28.8)
Subjects completed	n (%)	24 (15.9)	32 (20.9)
Subjects withdrawn	n (%)	19 (12.6)	12 (7.8)
Subjects received rescue therapy	n (%)	6 (4.0)	0 (0.0)
Subjects in FAS	n (%)	151 (100.0)	153 (100.0)
Subject Group: Correction Group	n (%)	71 (47.0)	71 (46.4)
Conversion Group	n (%)	80 (53.0)	82 (53.6)
Conversion (Hb >=11.0 g/dL) Group	n (%)	37 (24.5)	38 (24.8)
Conversion (Hb <11.0 g/dL) Group	n (%)	43 (28.5)	44 (28.8)
Subjects excluded from FAS	n (%)	0 (0.0)	0 (0.0)
Subject Group: Correction Group	n (%)	0 (0.0)	0 (0.0)
Conversion Group	n (%)	0 (0.0)	0 (0.0)
Conversion (Hb >=11.0 g/dL) Group	n (%)	0 (0.0)	0 (0.0)
Conversion (Hb <11.0 g/dL) Group	n (%)	0 (0.0)	0 (0.0)
Subjects in Safety Analysis Set	n (%)	151 (100.0)	153 (100.0)
Subject Group: Correction Group	n (%)	71 (47.0)	71 (46.4)
Conversion Group	n (%)	80 (53.0)	82 (53.6)
Conversion (Hb >=11.0 g/dL) Group	n (%)	37 (24.5)	38 (24.8)
Conversion (Hb <11.0 g/dL) Group	n (%)	43 (28.5)	44 (28.8)
Subjects excluded from Safety Analysis Set	n (%)	0 (0.0)	0 (0.0)
Subject Group: Correction Group	n (%)	0 (0.0)	0 (0.0)
Conversion Group	n (%)	0 (0.0)	0 (0.0)
Conversion (Hb >=11.0 g/dL) Group	n (%)	0 (0.0)	0 (0.0)
Conversion (Hb <11.0 g/dL) Group	n (%)	0 (0.0)	0 (0.0)

Data Source: Listing 16.2.1.1, Listing 16.2.2.1, Listing 16.2.2.6, Listing 16.2.2.7, Listing 16.2.2.8
Source: t_14_1_1_1.sas

5.3.5.1—8 表 11.1—1 より引用

2.7.6.25.3.1.2 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「2.7.6.25.2.1.2 被験者背景」と同一であった.

2.7.6.25.3.1.3　有効性

(1)　服用遵守割合及び平均投与量

FAS の全集団の治療期間における MT-6548 錠及びダルベポエチンアルファ注の服用／投与遵守割合を表 2.7.6.25－108 に示した.

全集団において，MT-6548 群の服用遵守割合の平均値±SD は 98.34±4.29%，darbepoetin 群の投与遵守割合の平均値±SD は 99.21±2.06%であった.

表 2.7.6.25－108　治験薬の服用／投与遵守割合（FAS）

	Statistic	MT-6548 (N=151)	darbepoetin (N=153)
Compliance (%)	Mean	98.34	99.21
	SD	4.29	2.06
	Median	99.73	100.00
	Minimum, Maximum	(68.3, 100.0)	(82.4, 100.0)
Category			
<80%	n (%)	2 (1.3)	0 (0.0)
>=80%	n (%)	149 (98.7)	153 (100.0)

Data Source: Listing 16.2.3.3
Source: t_14_1_4_1_1.sas

5.3.5.1—8 表 11.3—1 より引用

(2)　貧血治療効果

1)　48 週及び 52 週後の平均 Hb 値

全集団の MMRM を用いた 48 週及び 52 週後の平均 Hb 値を表 2.7.6.25－109 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 11.54 g/dL 及び 11.38～11.69 g/dL, darbepoetin 群で 11.63 g/dL 及び 11.48～11.77 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（11.0 g/dL 以上 13.0 g/dL 未満）であった.

表 2.7.6.25－109　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	151	10.44 (0.91)	11.54	0.08	(11.38, 11.69)
darbepoetin	Week 48 and Week 52	153	10.52 (0.88)	11.63	0.08	(11.48, 11.77)
Difference MT-6548 - darbepoetin	Week 48 and Week 52			-0.09	0.11	(-0.30, 0.13)

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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—8 表 11.4.1—1 より引用

2)　Hb 値の推移

MMRM を用いた Hb 値を表 2.7.6.25－110，Hb 値の記述統計量を表 2.7.6.25－111 に示した.

表 2.7.6.25－110　各評価時点の Hb 値（MMRM，FAS）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	151	10.44 (0.91)	10.66	0.07	(10.52, 10.80)	
	Week 4	149	10.44 (0.92)	10.75	0.07	(10.61, 10.89)	
	Week 6	148	10.45 (0.92)	10.90	0.07	(10.76, 11.04)	
	Week 8	145	10.45 (0.92)	11.16	0.07	(11.02, 11.31)	
	Week 10	145	10.46 (0.92)	11.36	0.07	(11.22, 11.51)	
	Week 12	145	10.45 (0.91)	11.54	0.07	(11.40, 11.68)	
	Week 16	143	10.46 (0.91)	11.59	0.07	(11.44, 11.73)	
	Week 20	139	10.46 (0.92)	11.66	0.07	(11.51, 11.80)	
	Week 24	132	10.48 (0.90)	11.67	0.08	(11.52, 11.82)	
	Week 28	125	10.48 (0.89)	11.66	0.08	(11.51, 11.81)	
	Week 32	120	10.50 (0.91)	11.66	0.08	(11.51, 11.82)	
	Week 36	115	10.49 (0.91)	11.66	0.08	(11.51, 11.82)	
	Week 40	114	10.50 (0.91)	11.52	0.08	(11.36, 11.68)	
	Week 44	114	10.51 (0.92)	11.41	0.08	(11.26, 11.57)	
	Week 48	110	10.51 (0.93)	11.59	0.08	(11.43, 11.75)	
	Week 52	109	10.51 (0.94)	11.51	0.08	(11.35, 11.67)	
darbepoetin	Week 2	153	10.52 (0.88)	10.74	0.07	(10.60, 10.88)	
	Week 4	152	10.53 (0.86)	10.91	0.07	(10.77, 11.05)	
	Week 6	152	10.53 (0.88)	11.24	0.07	(11.10, 11.38)	
	Week 8	151	10.52 (0.87)	11.44	0.07	(11.30, 11.58)	
	Week 10	150	10.53 (0.88)	11.72	0.07	(11.58, 11.86)	
	Week 12	148	10.53 (0.89)	11.89	0.07	(11.75, 12.04)	
	Week 16	148	10.54 (0.89)	12.02	0.07	(11.88, 12.16)	
	Week 20	144	10.55 (0.90)	11.92	0.07	(11.78, 12.06)	
	Week 24	140	10.54 (0.91)	11.93	0.07	(11.79, 12.07)	
	Week 28	137	10.54 (0.92)	11.88	0.07	(11.73, 12.02)	
	Week 32	132	10.54 (0.90)	11.76	0.08	(11.62, 11.91)	
	Week 36	129	10.55 (0.90)	11.95	0.08	(11.80, 12.10)	
	Week 40	127	10.56 (0.90)	11.74	0.08	(11.59, 11.89)	
	Week 44	124	10.58 (0.88)	11.63	0.08	(11.48, 11.78)	
	Week 48	124	10.58 (0.88)	11.68	0.08	(11.53, 11.83)	
	Week 52	122	10.59 (0.85)	11.58	0.08	(11.43, 11.74)	

表 2.7.6.25－110　各評価時点の Hb 値（MMRM，FAS）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin	Week 2			-0.08	0.10	(-0.28, 0.12)	0.418
	Week 4			-0.16	0.10	(-0.36, 0.04)	0.117
	Week 6			-0.34	0.10	(-0.54, -0.14)	<0.001
	Week 8			-0.28	0.10	(-0.48, -0.08)	0.006
	Week 10			-0.35	0.10	(-0.55, -0.15)	<0.001
	Week 12			-0.35	0.10	(-0.55, -0.15)	<0.001
	Week 16			-0.43	0.10	(-0.63, -0.23)	<0.001
	Week 20			-0.26	0.10	(-0.47, -0.06)	0.012
	Week 24			-0.26	0.11	(-0.47, -0.06)	0.013
	Week 28			-0.22	0.11	(-0.43, -0.01)	0.042
	Week 32			-0.10	0.11	(-0.31, 0.11)	0.357
	Week 36			-0.28	0.11	(-0.50, -0.07)	0.009
	Week 40			-0.22	0.11	(-0.43, 0.00)	0.050
	Week 44			-0.22	0.11	(-0.44, 0.00)	0.049
	Week 48			-0.09	0.11	(-0.31, 0.13)	0.433
	Week 52			-0.07	0.11	(-0.29, 0.15)	0.533

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_2_2_1.sas

5.3.5.1—8 表 14.2.2.2.1 より引用

表 2.7.6.25－111　各評価時点の Hb 値の記述統計量（FAS）

Treatment Group	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
MT-6548	Baseline	151	10.44	0.91	10.40	(7.5, 12.5)	(10.29, 10.59)							
	Week 2	151	10.64	0.98	10.70	(7.9, 13.9)	(10.48, 10.80)	151	0.20	0.61	0.20	(-1.1, 1.7)	(0.10, 0.30)	<0.001
	Week 4	149	10.71	1.07	10.90	(6.0, 13.1)	(10.54, 10.89)	149	0.27	0.84	0.30	(-2.1, 2.8)	(0.14, 0.41)	<0.001
	Week 6	148	10.87	1.08	10.90	(6.9, 13.5)	(10.69, 11.04)	148	0.42	1.03	0.40	(-3.4, 2.9)	(0.25, 0.58)	<0.001
	Week 8	145	11.13	1.04	11.20	(8.4, 13.7)	(10.96, 11.30)	145	0.68	1.03	0.70	(-2.4, 3.2)	(0.51, 0.85)	<0.001
	Week 10	145	11.33	0.99	11.40	(8.3, 13.6)	(11.17, 11.49)	145	0.87	1.12	0.80	(-2.4, 4.1)	(0.69, 1.06)	<0.001
	Week 12	145	11.50	1.02	11.60	(8.3, 13.7)	(11.34, 11.67)	145	1.06	1.24	1.10	(-2.2, 4.9)	(0.85, 1.26)	<0.001
	Week 16	143	11.56	1.07	11.60	(8.4, 14.1)	(11.39, 11.74)	143	1.10	1.32	1.10	(-2.6, 4.6)	(0.88, 1.32)	<0.001
	Week 20	139	11.66	1.10	11.70	(8.3, 14.6)	(11.47, 11.84)	139	1.19	1.34	1.20	(-3.2, 4.8)	(0.97, 1.42)	<0.001
	Week 24	132	11.68	1.10	11.80	(7.4, 14.1)	(11.49, 11.87)	132	1.21	1.32	1.20	(-2.6, 4.3)	(0.98, 1.43)	<0.001
	Week 28	125	11.72	0.91	11.80	(8.3, 14.4)	(11.56, 11.88)	125	1.24	1.18	1.10	(-1.5, 5.3)	(1.03, 1.45)	<0.001
	Week 32	120	11.74	0.94	11.85	(8.2, 13.9)	(11.57, 11.91)	120	1.24	1.28	1.15	(-1.8, 5.4)	(1.01, 1.48)	<0.001
	Week 36	119	11.74	0.90	11.80	(7.8, 13.9)	(11.58, 11.91)	119	1.25	1.21	1.20	(-2.0, 5.2)	(1.04, 1.47)	<0.001
	Week 40	114	11.61	0.83	11.60	(9.6, 14.2)	(11.46, 11.76)	114	1.11	1.16	1.05	(-2.2, 4.4)	(0.89, 1.33)	<0.001
	Week 44	114	11.50	0.82	11.60	(8.7, 13.4)	(11.35, 11.66)	114	0.99	1.17	1.10	(-2.0, 4.2)	(0.77, 1.21)	<0.001
	Week 48	110	11.68	0.84	11.70	(8.5, 13.6)	(11.52, 11.84)	110	1.17	1.14	1.10	(-1.4, 4.3)	(0.95, 1.39)	<0.001
	Week 52	109	11.62	0.81	11.70	(8.7, 13.5)	(11.47, 11.77)	109	1.11	1.16	1.10	(-1.3, 4.7)	(0.89, 1.33)	<0.001
	Week 52 (LOCF)	151	11.29	1.13	11.60	(7.4, 13.5)	(11.11, 11.47)	151	0.85	1.36	0.90	(-3.2, 4.7)	(0.63, 1.07)	<0.001

表 2.7.6.25－111　各評価時点の Hb 値の記述統計量（FAS）（続き）

Treatment Group	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
darbepoetin	Baseline	153	10.52	0.88	10.60	(8.0, 12.7)	(10.38, 10.66)							
	Week 2	153	10.75	0.85	10.80	(8.0, 12.6)	(10.62, 10.89)	153	0.23	0.54	0.30	(-1.3, 1.4)	(0.14, 0.32)	<0.001
	Week 4	152	10.90	0.90	11.10	(7.2, 12.6)	(10.76, 11.05)	152	0.38	0.76	0.30	(-2.1, 1.9)	(0.25, 0.50)	<0.001
	Week 6	152	11.23	0.95	11.30	(7.6, 13.4)	(11.08, 11.38)	152	0.70	0.96	0.70	(-1.4, 3.5)	(0.55, 0.85)	<0.001
	Week 8	151	11.42	1.04	11.60	(7.0, 13.9)	(11.26, 11.59)	151	0.91	1.19	0.90	(-2.7, 4.3)	(0.72, 1.10)	<0.001
	Week 10	150	11.70	0.96	11.75	(8.2, 13.9)	(11.54, 11.85)	150	1.16	1.23	1.10	(-2.1, 4.8)	(0.97, 1.36)	<0.001
	Week 12	148	11.88	0.98	11.80	(9.0, 15.2)	(11.72, 12.04)	148	1.35	1.34	1.40	(-1.6, 5.1)	(1.13, 1.56)	<0.001
	Week 16	148	12.00	0.97	12.00	(9.5, 14.2)	(11.84, 12.16)	148	1.46	1.42	1.50	(-1.3, 5.1)	(1.23, 1.69)	<0.001
	Week 20	144	11.92	0.87	12.00	(9.0, 13.9)	(11.77, 12.06)	144	1.37	1.35	1.20	(-2.0, 5.9)	(1.15, 1.59)	<0.001
	Week 24	140	11.94	0.83	11.90	(9.8, 13.9)	(11.80, 12.08)	140	1.40	1.21	1.20	(-1.1, 5.2)	(1.19, 1.60)	<0.001
	Week 28	137	11.89	0.86	11.90	(9.6, 14.3)	(11.74, 12.03)	137	1.35	1.20	1.30	(-1.2, 4.6)	(1.15, 1.55)	<0.001
	Week 32	132	11.79	0.74	11.80	(9.6, 13.7)	(11.66, 11.92)	132	1.25	1.11	1.15	(-1.3, 4.5)	(1.06, 1.44)	<0.001
	Week 36	129	11.99	0.88	11.90	(9.4, 14.7)	(11.84, 12.15)	129	1.44	1.24	1.40	(-1.4, 4.8)	(1.23, 1.66)	<0.001
	Week 40	127	11.78	0.71	11.80	(9.9, 14.0)	(11.66, 11.91)	127	1.23	1.09	1.30	(-1.6, 3.8)	(1.03, 1.42)	<0.001
	Week 44	124	11.68	0.68	11.70	(9.9, 13.2)	(11.56, 11.80)	124	1.10	1.10	1.10	(-2.1, 4.1)	(0.90, 1.29)	<0.001
	Week 48	124	11.73	0.79	11.70	(9.7, 15.0)	(11.59, 11.87)	124	1.15	1.16	1.15	(-1.6, 5.1)	(0.94, 1.35)	<0.001
	Week 52	122	11.64	0.68	11.60	(9.9, 13.8)	(11.52, 11.76)	122	1.05	1.14	1.00	(-1.7, 4.0)	(0.85, 1.26)	<0.001
	Week 52 (LOCF)	153	11.50	0.96	11.50	(7.0, 14.6)	(11.34, 11.65)	153	0.97	1.28	1.00	(-2.8, 4.5)	(0.77, 1.18)	<0.001

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—8 表 14.2.2.1.1 より引用

(3)　貧血治療効果（切替え維持効果）

貧血治療効果（切替え維持効果）は，特に明記しない限り Conversion 集団を対象に記載した．

1)　Hb 値の推移

Hb 値の平均値の推移を図 2.7.6.25－37，Hb 値の記述統計量を表 2.7.6.25－112，MMRM を用いた Hb 値を表 2.7.6.25－113 に示した．

MT-6548 群の Hb 値の平均値は上昇し，8 週後に目標範囲内に到達後，52 週後まで目標範囲内を維持した．darbepoetin 群の Hb 値の平均値は上昇し，6 週後に目標範囲内に到達後，52 週後まで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 11.40 g/dL 及び 11.18～11.63 g/dL，darbepoetin 群で 11.52 g/dL 及び 11.31～11.73 g/dL であった．

Conversion（Hb≥11.0）集団における，Hb 値の平均値の推移を図 2.7.6.25－38，Hb 値の記述統計量を表 2.7.6.25－114，MMRM を用いた Hb 値を表 2.7.6.25－115 に示した．

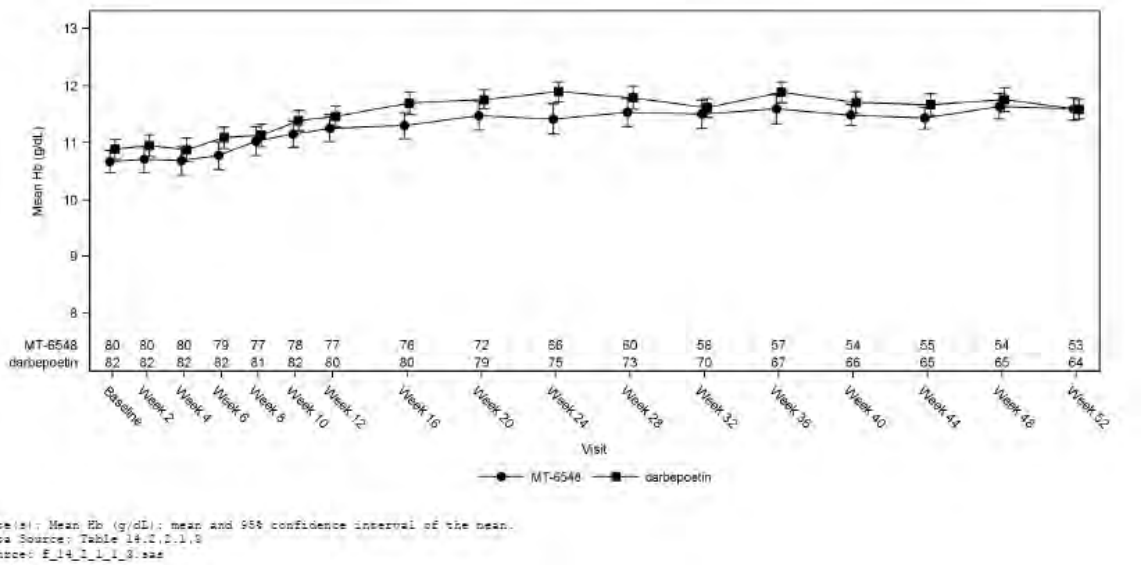
Conversion（Hb≥11.0）集団では，MT-6548 群及び darbepoetin 群の Hb 値の平均値は，急な変動なく推移し，52 週後まで目標範囲内を維持した．

MMRM を用いた 52 週後の Hb 値の LSMean 及びその 95%CI は，MT-6548 群で 11.56 g/dL 及び 11.30～11.82 g/dL，darbepoetin 群で 11.29 g/dL 及び 11.03～11.54 g/dL であった．

Conversion（Hb<11.0）集団における，Hb 値の平均値の推移を図 2.7.6.25－39，Hb 値の記述統計量を表 2.7.6.25－116，MMRM を用いた Hb 値を表 2.7.6.25－117 に示した．

Conversion（Hb<11.0）集団では，MT-6548 群の Hb 値の平均値は上昇し，12 週後に目標範囲内に到達後，52 週後まで目標範囲内を維持した．darbepoetin 群の Hb 値の平均値は上昇し，10 週後に目標範囲内に到達後，52 週後まで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 11.32 g/dL 及び 10.97～11.68 g/dL，darbepoetin 群で 11.78 g/dL 及び 11.47～12.09 g/dL であった．



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.1.3
Source: F_14_2_1_1_3.sas

図 2.7.6.25－37　Hb 値の推移（FAS）（Conversion 集団）

5.3.5.1—8 図 11.4.1—1 より引用

表 2.7.6.25－112　各評価時点の Hb 値の記述統計量（FAS）（Conversion 集団）

		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	80	10.68	0.85	10.65	(8.9, 12.5)	(10.48, 10.87)							
	Week 2	80	10.71	1.03	10.80	(8.4, 13.8)	(10.46, 10.94)	80	0.03	0.57	0.10	(-1.1, 1.7)	(-0.09, 0.16)	0.595
	Week 4	80	10.69	1.10	10.90	(8.0, 12.8)	(10.44, 10.93)	80	0.01	0.77	0.05	(-1.7, 1.6)	(-0.16, 0.19)	0.874
	Week 6	79	10.78	1.08	10.80	(8.2, 13.5)	(10.54, 11.02)	79	0.09	0.90	0.00	(-1.6, 2.4)	(-0.12, 0.29)	0.396
	Week 8	77	11.03	1.11	11.20	(8.4, 13.7)	(10.78, 11.29)	77	0.33	1.03	0.40	(-2.4, 2.6)	(0.10, 0.57)	0.006
	Week 10	78	11.15	1.00	11.30	(9.2, 13.6)	(10.93, 11.38)	78	0.45	1.06	0.50	(-2.4, 3.0)	(0.21, 0.69)	<0.001
	Week 12	77	11.26	1.05	11.40	(9.0, 13.4)	(11.02, 11.49)	77	0.57	1.15	0.70	(-2.2, 3.2)	(0.31, 0.83)	<0.001
	Week 16	76	11.31	1.02	11.40	(8.6, 13.4)	(11.07, 11.54)	76	0.60	1.26	0.70	(-2.6, 3.1)	(0.31, 0.89)	<0.001
	Week 20	72	11.47	1.07	11.60	(8.3, 13.6)	(11.22, 11.72)	72	0.75	1.29	0.70	(-3.2, 3.4)	(0.45, 1.05)	<0.001
	Week 24	66	11.42	1.08	11.60	(7.4, 13.2)	(11.15, 11.68)	66	0.68	1.23	0.70	(-2.6, 3.2)	(0.38, 0.99)	<0.001
	Week 28	60	11.53	0.96	11.70	(8.3, 14.4)	(11.28, 11.78)	60	0.79	1.06	0.70	(-1.5, 2.8)	(0.51, 1.06)	<0.001
	Week 32	58	11.50	0.94	11.70	(8.2, 13.2)	(11.25, 11.75)	58	0.73	1.10	0.70	(-1.8, 3.2)	(0.44, 1.02)	<0.001
	Week 36	57	11.59	0.95	11.70	(7.8, 13.9)	(11.34, 11.84)	57	0.83	1.13	0.80	(-2.0, 3.9)	(0.53, 1.13)	<0.001
	Week 40	54	11.49	0.69	11.40	(10.2, 13.4)	(11.30, 11.68)	54	0.71	0.99	0.85	(-2.2, 2.4)	(0.44, 0.98)	<0.001
	Week 44	55	11.43	0.69	11.50	(10.0, 13.4)	(11.25, 11.62)	55	0.64	1.09	0.80	(-2.0, 2.8)	(0.35, 0.94)	<0.001
	Week 48	54	11.64	0.83	11.55	(9.8, 13.3)	(11.41, 11.86)	54	0.85	1.04	0.85	(-1.4, 2.9)	(0.56, 1.13)	<0.001
	Week 52	53	11.59	0.71	11.70	(10.2, 12.9)	(11.40, 11.79)	53	0.80	1.06	0.60	(-1.3, 3.3)	(0.50, 1.09)	<0.001
	Week 52 (LOCF)	80	11.11	1.19	11.25	(7.4, 12.9)	(10.84, 11.37)	80	0.43	1.32	0.50	(-3.2, 3.3)	(0.14, 0.73)	0.004

表 2.7.6.25－112　各評価時点の Hb 値の記述統計量（FAS）（Conversion 集団）（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	82	10.89	0.81	11.00	(8.6, 12.7)	(10.71, 11.07)							
	Week 2	82	10.95	0.87	10.90	(8.0, 12.6)	(10.76, 11.15)	82	0.06	0.52	0.05	(-1.3, 1.2)	(-0.05, 0.18)	-
	Week 4	82	10.88	0.93	10.95	(7.2, 12.6)	(10.68, 11.08)	82	-0.01	0.64	0.05	(-2.1, 1.9)	(-0.15, 0.13)	-
	Week 6	82	11.09	0.85	11.10	(8.6, 13.0)	(10.91, 11.28)	82	0.20	0.77	0.15	(-1.4, 2.0)	(0.03, 0.37)	-
	Week 8	81	11.13	0.87	11.10	(9.1, 12.9)	(10.94, 11.32)	81	0.26	0.87	0.10	(-1.6, 2.5)	(0.07, 0.45)	-
	Week 10	82	11.89	0.81	11.80	(9.8, 13.1)	(11.21, 11.57)	82	0.60	0.97	0.50	(-2.1, 2.8)	(0.28, 0.71)	-
	Week 12	80	11.47	0.80	11.40	(9.0, 13.5)	(11.29, 11.64)	80	0.58	1.00	0.35	(-1.6, 3.1)	(0.35, 0.80)	-
	Week 16	80	11.69	0.86	11.60	(9.8, 14.2)	(11.50, 11.89)	80	0.79	1.20	0.55	(-1.3, 3.9)	(0.52, 1.05)	-
	Week 20	79	11.76	0.74	11.80	(10.3, 13.7)	(11.59, 11.92)	79	0.86	1.10	0.70	(-1.3, 3.7)	(0.61, 1.10)	-
	Week 24	75	11.89	0.76	11.90	(9.8, 13.5)	(11.72, 12.07)	75	0.97	1.08	0.80	(-1.0, 3.4)	(0.73, 1.22)	-
	Week 28	73	11.79	0.87	11.80	(9.6, 14.0)	(11.59, 11.99)	73	0.87	1.17	0.70	(-1.2, 4.6)	(0.59, 1.14)	-
	Week 32	70	11.61	0.70	11.60	(10.1, 13.6)	(11.45, 11.78)	70	0.70	0.94	0.60	(-1.3, 3.1)	(0.48, 0.92)	-
	Week 36	67	11.88	0.76	11.90	(10.0, 14.1)	(11.70, 12.07)	67	0.94	1.18	0.60	(-1.4, 4.8)	(0.65, 1.23)	-
	Week 40	66	11.70	0.78	11.70	(9.9, 14.0)	(11.51, 11.90)	66	0.76	1.15	0.60	(-1.6, 3.6)	(0.48, 1.04)	-
	Week 44	65	11.67	0.76	11.70	(9.9, 13.2)	(11.48, 11.85)	65	0.69	1.18	0.80	(-2.1, 3.5)	(0.38, 0.97)	-
	Week 48	65	11.76	0.85	11.60	(10.1, 15.0)	(11.55, 11.97)	65	0.77	1.26	0.70	(-1.6, 5.1)	(0.46, 1.08)	-
	Week 52	64	11.58	0.68	11.60	(10.1, 13.8)	(11.42, 11.75)	64	0.61	1.15	0.45	(-1.7, 3.9)	(0.33, 0.90)	-
	Week 52 (LOCF)	82	11.45	0.84	11.50	(9.1, 13.8)	(11.27, 11.64)	82	0.56	1.21	0.45	(-2.8, 3.9)	(0.30, 0.83)	-

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_3.sas

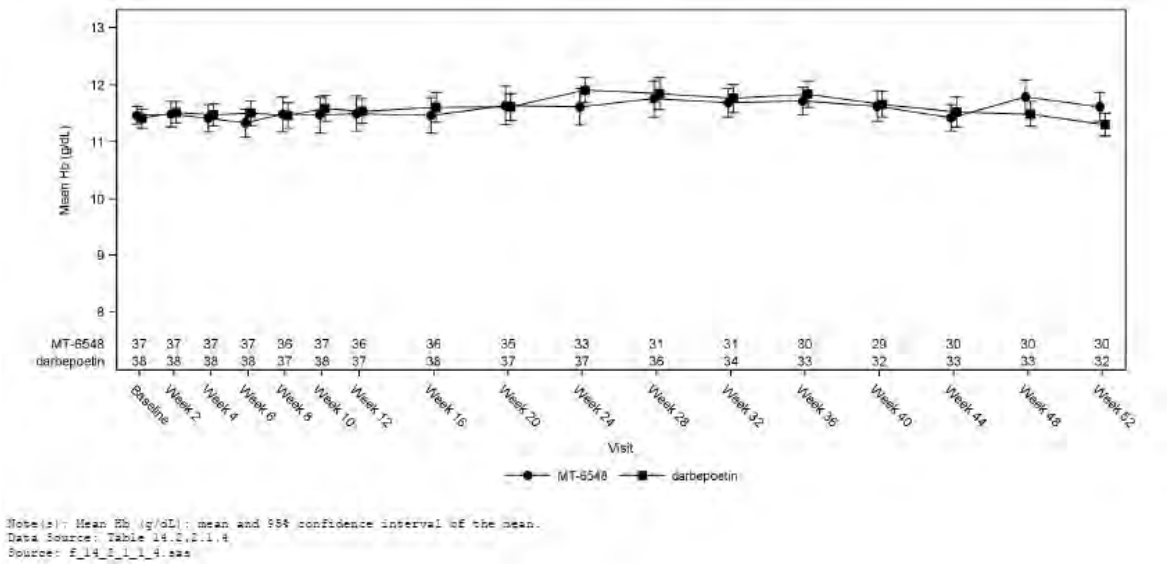
5.3.5.1—8 表 14.2.2.1.3 より引用

表 2.7.6.25－113　各評価時点の Hb 値（MMRM，FAS）（Conversion 集団）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	80	10.68 (0.89)	10.76	0.10	(10.57, 10.95)
	Week 4	80	10.68 (0.89)	10.74	0.10	(10.55, 10.93)
	Week 6	79	10.69 (0.88)	10.82	0.10	(10.62, 11.01)
	Week 8	77	10.70 (0.88)	11.07	0.10	(10.87, 11.26)
	Week 10	78	10.71 (0.88)	11.16	0.10	(10.99, 11.38)
	Week 12	77	10.69 (0.88)	11.29	0.10	(11.09, 11.48)
	Week 16	76	10.71 (0.87)	11.31	0.10	(11.12, 11.51)
	Week 20	72	10.72 (0.88)	11.46	0.10	(11.26, 11.66)
	Week 24	66	10.73 (0.88)	11.38	0.11	(11.17, 11.59)
	Week 28	60	10.75 (0.87)	11.42	0.11	(11.20, 11.63)
	Week 32	58	10.77 (0.88)	11.37	0.11	(11.16, 11.59)
	Week 36	57	10.76 (0.89)	11.46	0.11	(11.24, 11.68)
	Week 40	54	10.78 (0.89)	11.31	0.11	(11.08, 11.53)
	Week 44	55	10.79 (0.88)	11.26	0.11	(11.03, 11.47)
	Week 48	54	10.79 (0.89)	11.45	0.11	(11.23, 11.68)
	Week 52	53	10.79 (0.90)	11.40	0.11	(11.18, 11.63)
darbepoetin	Week 2	82	10.89 (0.81)	10.93	0.10	(10.74, 11.12)
	Week 4	82	10.89 (0.81)	10.86	0.10	(10.67, 11.05)
	Week 6	82	10.89 (0.81)	11.07	0.10	(10.88, 11.26)
	Week 8	81	10.87 (0.79)	11.11	0.10	(10.92, 11.30)
	Week 10	82	10.89 (0.81)	11.37	0.10	(11.18, 11.56)
	Week 12	80	10.89 (0.81)	11.44	0.10	(11.25, 11.63)
	Week 16	80	10.91 (0.81)	11.66	0.10	(11.47, 11.86)
	Week 20	79	10.90 (0.81)	11.73	0.10	(11.53, 11.92)
	Week 24	75	10.92 (0.83)	11.85	0.10	(11.66, 12.05)
	Week 28	73	10.92 (0.84)	11.76	0.10	(11.56, 11.96)
	Week 32	70	10.91 (0.85)	11.57	0.10	(11.37, 11.77)
	Week 36	67	10.94 (0.84)	11.83	0.10	(11.62, 12.03)
	Week 40	66	10.94 (0.86)	11.64	0.10	(11.44, 11.85)
	Week 44	65	10.99 (0.79)	11.60	0.11	(11.40, 11.81)
	Week 48	65	10.99 (0.79)	11.69	0.11	(11.49, 11.90)
	Week 52	64	10.97 (0.78)	11.52	0.11	(11.31, 11.73)

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_3.sas

5.3.5.1—8 表 14.2.2.2.3 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.1.4
Source: f_14_2_1_1_4.sas

図 2.7.6.25－38　Hb 値の推移（FAS）（Conversion（Hb≥11.0）集団）

5.3.5.1—8 図 11.4.1—2 より引用

表 2.7.6.25－114　各評価時点の Hb 値の記述統計量（FAS）（Conversion（Hb≥11.0）集団）

		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	37	11.47	0.47	11.50	(10.2, 12.5)	(11.31, 11.62)							
	Week 2	37	11.48	0.66	11.40	(10.4, 13.8)	(11.26, 11.70)	37	0.02	0.58	-0.10	(-0.9, 1.7)	(-0.18, 0.21)	0.867
	Week 4	37	11.41	0.73	11.40	(9.9, 12.8)	(11.17, 11.66)	37	-0.05	0.75	0.10	(-1.7, 1.2)	(-0.30, 0.19)	0.662
	Week 6	37	11.33	0.74	11.40	(10.1, 13.5)	(11.08, 11.58)	37	-0.14	0.76	-0.10	(-1.8, 1.4)	(-0.39, 0.11)	0.274
	Week 8	36	11.48	0.91	11.50	(9.2, 13.7)	(11.18, 11.79)	36	0.01	0.96	0.15	(-2.4, 1.6)	(-0.32, 0.33)	0.973
	Week 10	37	11.47	0.94	11.50	(9.7, 13.6)	(11.16, 11.78)	37	0.00	0.99	0.20	(-2.4, 1.9)	(-0.33, 0.33)	0.987
	Week 12	36	11.50	0.91	11.45	(9.9, 13.4)	(11.19, 11.80)	36	0.04	1.00	0.00	(-2.2, 2.2)	(-0.30, 0.38)	0.805
	Week 16	36	11.46	0.92	11.50	(9.5, 13.4)	(11.15, 11.77)	36	0.01	1.11	0.10	(-2.6, 2.4)	(-0.37, 0.38)	0.964
	Week 20	35	11.64	0.98	11.60	(8.9, 13.6)	(11.30, 11.98)	35	0.18	1.12	0.40	(-3.2, 2.4)	(-0.21, 0.57)	0.350
	Week 24	33	11.62	0.91	11.70	(9.3, 13.2)	(11.29, 11.94)	33	0.17	0.96	0.30	(-2.6, 1.7)	(-0.17, 0.51)	0.310
	Week 28	31	11.75	0.87	11.70	(10.0, 14.4)	(11.43, 12.07)	31	0.34	0.81	0.50	(-1.5, 2.3)	(0.04, 0.63)	0.028
	Week 32	31	11.68	0.68	11.70	(9.8, 12.9)	(11.43, 11.93)	31	0.27	0.78	0.30	(-1.8, 1.6)	(-0.02, 0.55)	0.065
	Week 36	30	11.72	0.65	11.80	(9.9, 13.1)	(11.47, 11.96)	30	0.29	0.81	0.45	(-1.7, 1.6)	(-0.01, 0.59)	0.060
	Week 40	29	11.63	0.70	11.50	(10.3, 13.4)	(11.36, 11.89)	29	0.20	0.94	0.20	(-2.2, 2.4)	(-0.16, 0.56)	0.255
	Week 44	30	11.43	0.62	11.60	(10.2, 12.5)	(11.20, 11.66)	30	0.00	0.86	-0.05	(-2.0, 1.4)	(-0.32, 0.32)	0.983
	Week 48	30	11.78	0.81	11.85	(10.1, 13.3)	(11.48, 12.08)	30	0.36	0.87	0.40	(-1.4, 2.6)	(0.03, 0.69)	0.032
	Week 52	30	11.61	0.68	11.70	(10.3, 12.7)	(11.36, 11.87)	30	0.19	0.76	0.25	(-1.3, 1.7)	(-0.09, 0.47)	0.182
	Week 52 (LOCF)	37	11.41	0.87	11.60	(8.9, 12.7)	(11.12, 11.70)	37	-0.06	1.03	0.00	(-3.2, 1.7)	(-0.40, 0.29)	0.739

表 2.7.6.25－114　各評価時点の Hb 値の記述統計量（FAS）（Conversion（Hb≥11.0）集団）（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	38	11.41	0.50	11.40	(10.3, 12.7)	(11.25, 11.58)							
	Week 2	38	11.52	0.57	11.50	(10.3, 12.6)	(11.33, 11.70)	38	0.11	0.43	0.05	(-1.0, 1.0)	(-0.04, 0.25)	-
	Week 4	38	11.48	0.57	11.50	(10.0, 12.6)	(11.29, 11.66)	38	0.06	0.68	0.10	(-0.9, 1.9)	(-0.13, 0.25)	-
	Week 6	38	11.50	0.66	11.60	(9.4, 13.0)	(11.29, 11.72)	38	0.09	0.70	0.05	(-1.4, 2.0)	(-0.14, 0.32)	-
	Week 8	37	11.47	0.66	11.50	(10.2, 12.7)	(11.25, 11.69)	37	0.08	0.71	0.00	(-1.6, 2.4)	(-0.16, 0.32)	-
	Week 10	38	11.59	0.69	11.70	(10.3, 12.9)	(11.36, 11.82)	38	0.18	0.80	0.25	(-2.1, 2.4)	(-0.09, 0.44)	-
	Week 12	37	11.54	0.68	11.60	(10.4, 12.9)	(11.32, 11.75)	37	0.13	0.73	0.10	(-1.6, 2.0)	(-0.12, 0.37)	-
	Week 16	38	11.61	0.79	11.60	(10.2, 13.9)	(11.35, 11.86)	38	0.19	0.89	0.00	(-1.1, 2.7)	(-0.10, 0.48)	-
	Week 20	37	11.61	0.70	11.60	(10.3, 13.2)	(11.38, 11.84)	37	0.19	0.66	0.30	(-0.9, 1.3)	(-0.03, 0.41)	-
	Week 24	37	11.91	0.67	11.90	(10.8, 13.5)	(11.69, 12.13)	37	0.48	0.71	0.50	(-1.0, 2.6)	(0.24, 0.71)	-
	Week 28	36	11.85	0.83	11.80	(10.2, 14.0)	(11.57, 12.13)	36	0.41	0.89	0.35	(-1.2, 3.1)	(0.11, 0.72)	-
	Week 32	34	11.76	0.69	11.80	(10.1, 13.6)	(11.52, 12.00)	34	0.32	0.83	0.40	(-1.3, 2.1)	(0.03, 0.61)	-
	Week 36	33	11.84	0.66	11.90	(10.0, 13.7)	(11.60, 12.07)	33	0.40	0.86	0.40	(-1.4, 2.4)	(0.09, 0.70)	-
	Week 40	32	11.66	0.62	11.70	(10.3, 13.5)	(11.44, 11.88)	32	0.21	0.86	0.15	(-1.6, 2.3)	(-0.10, 0.52)	-
	Week 44	33	11.53	0.73	11.60	(9.9, 13.2)	(11.27, 11.79)	33	0.09	0.93	0.10	(-2.1, 1.7)	(-0.24, 0.42)	-
	Week 48	33	11.49	0.60	11.50	(10.1, 12.9)	(11.28, 11.70)	33	0.05	0.79	0.20	(-1.6, 1.4)	(-0.23, 0.33)	-
	Week 52	32	11.30	0.55	11.30	(10.1, 12.6)	(11.10, 11.50)	32	-0.11	0.67	-0.05	(-1.7, 1.1)	(-0.35, 0.13)	-
	Week 52 (LOCF)	38	11.27	0.60	11.30	(10.1, 12.6)	(11.08, 11.47)	38	-0.14	0.70	-0.10	(-1.7, 1.1)	(-0.37, 0.09)	-

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_4.sas

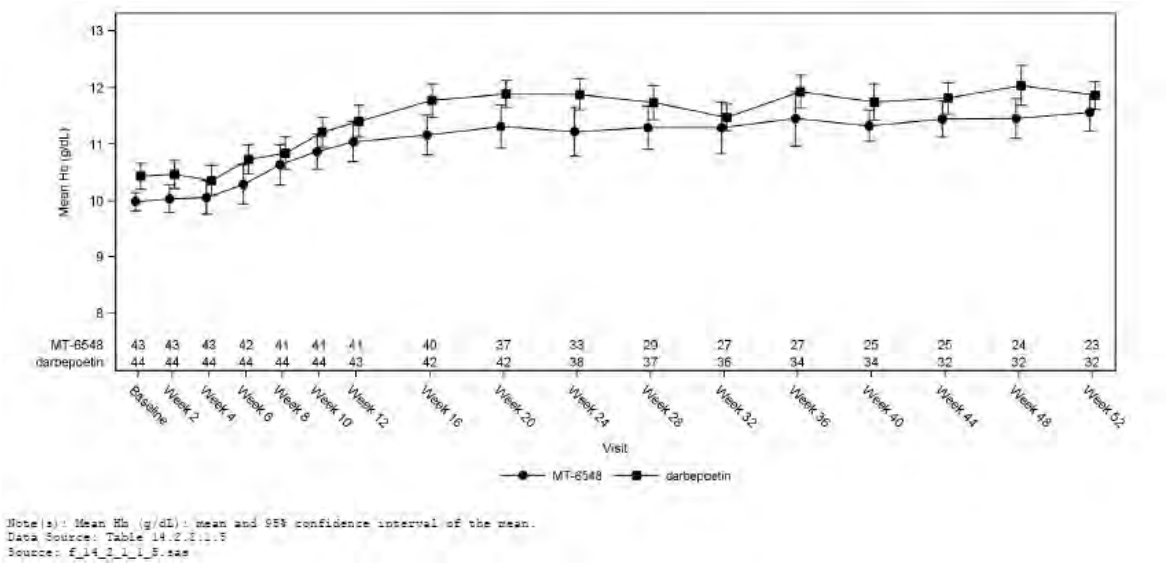
5.3.5.1—8 表 14.2.2.1.4 より引用

表 2.7.6.25－115　各評価時点の Hb 値（MMRM，FAS）（Conversion（Hb≥11.0）集団）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI
MT-6548	Week 2	37	11.47 (0.47)	11.48	0.12	(11.24, 11.72)
	Week 4	37	11.47 (0.47)	11.41	0.12	(11.17, 11.65)
	Week 6	37	11.47 (0.47)	11.82	0.12	(11.08, 11.56)
	Week 8	36	11.48 (0.47)	11.48	0.12	(11.23, 11.72)
	Week 10	37	11.47 (0.47)	11.46	0.12	(11.22, 11.70)
	Week 12	36	11.46 (0.47)	11.48	0.12	(11.24, 11.72)
	Week 16	36	11.46 (0.47)	11.45	0.12	(11.21, 11.69)
	Week 20	35	11.46 (0.48)	11.61	0.12	(11.37, 11.85)
	Week 24	33	11.44 (0.48)	11.56	0.13	(11.31, 11.81)
	Week 28	31	11.42 (0.47)	11.69	0.13	(11.44, 11.95)
	Week 32	31	11.42 (0.47)	11.62	0.13	(11.37, 11.86)
	Week 36	30	11.43 (0.47)	11.65	0.13	(11.39, 11.91)
	Week 40	29	11.42 (0.48)	11.57	0.13	(11.31, 11.83)
	Week 44	30	11.42 (0.47)	11.37	0.13	(11.11, 11.63)
	Week 48	30	11.42 (0.47)	11.73	0.13	(11.47, 11.99)
	Week 52	30	11.42 (0.47)	11.56	0.13	(11.30, 11.82)
darbepoetin	Week 2	39	11.41 (0.50)	11.52	0.12	(11.29, 11.76)
	Week 4	38	11.41 (0.50)	11.48	0.12	(11.25, 11.72)
	Week 6	38	11.41 (0.50)	11.51	0.12	(11.27, 11.74)
	Week 8	37	11.39 (0.48)	11.47	0.12	(11.24, 11.71)
	Week 10	38	11.41 (0.50)	11.59	0.12	(11.36, 11.83)
	Week 12	37	11.41 (0.51)	11.55	0.12	(11.31, 11.78)
	Week 16	39	11.41 (0.50)	11.61	0.12	(11.37, 11.84)
	Week 20	37	11.42 (0.51)	11.60	0.12	(11.37, 11.84)
	Week 24	37	11.43 (0.50)	11.89	0.12	(11.65, 12.13)
	Week 28	36	11.43 (0.51)	11.84	0.12	(11.60, 12.08)
	Week 32	34	11.44 (0.52)	11.73	0.13	(11.49, 11.98)
	Week 36	33	11.44 (0.53)	11.82	0.13	(11.57, 12.07)
	Week 40	32	11.45 (0.54)	11.63	0.13	(11.37, 11.88)
	Week 44	33	11.44 (0.53)	11.51	0.13	(11.26, 11.76)
	Week 48	33	11.44 (0.53)	11.47	0.13	(11.22, 11.72)
	Week 52	32	11.41 (0.51)	11.29	0.13	(11.03, 11.54)

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_4.sas

5.3.5.1—8 表 14.2.2.2.4 より引用



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.1.5
Source: f_14_3_1_1_5.sas

図 2.7.6.25－39　Hb 値の推移（FAS）（Conversion（Hb<11.0）集団）

5.3.5.1—8 図 11.4.1—3 より引用

表 2.7.6.25－116　各評価時点の Hb 値の記述統計量（FAS）（Conversion（Hb<11.0）集団）

		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	43	9.99	0.52	10.00	(8.9, 11.1)	(9.83, 10.15)							
	Week 2	43	10.04	0.80	10.10	(8.4, 11.5)	(9.80, 10.29)	43	0.05	0.55	0.10	(-1.1, 1.3)	(-0.12, 0.22)	0.567
	Week 4	43	10.07	0.98	10.30	(8.0, 11.4)	(9.76, 10.37)	43	0.07	0.80	0.00	(-1.3, 1.6)	(-0.17, 0.32)	0.558
	Week 6	42	10.29	1.10	10.50	(8.2, 12.2)	(9.95, 10.64)	42	0.28	0.98	0.25	(-1.8, 2.4)	(-0.02, 0.59)	0.067
	Week 8	41	10.64	1.13	10.60	(8.4, 12.7)	(10.28, 11.00)	41	0.62	1.02	0.60	(-1.6, 2.6)	(0.30, 0.94)	<0.001
	Week 10	41	10.87	0.99	10.80	(9.2, 13.0)	(10.56, 11.18)	41	0.85	0.96	0.70	(-1.2, 3.0)	(0.55, 1.15)	<0.001
	Week 12	41	11.05	1.13	11.40	(9.0, 13.1)	(10.69, 11.40)	41	1.03	1.08	1.00	(-0.9, 3.2)	(0.69, 1.37)	<0.001
	Week 16	40	11.16	1.09	11.30	(8.6, 13.0)	(10.81, 11.51)	40	1.13	1.14	1.10	(-1.2, 3.1)	(0.77, 1.50)	<0.001
	Week 20	37	11.31	1.15	11.60	(8.3, 13.0)	(10.93, 11.70)	37	1.29	1.20	1.40	(-1.7, 3.4)	(0.89, 1.69)	<0.001
	Week 24	33	11.22	1.22	11.30	(7.4, 13.0)	(10.79, 11.65)	33	1.20	1.27	1.40	(-2.6, 3.2)	(0.75, 1.65)	<0.001
	Week 28	29	11.30	1.01	11.60	(8.3, 12.8)	(10.91, 11.68)	29	1.27	1.10	1.20	(-1.5, 2.8)	(0.85, 1.68)	<0.001
	Week 32	27	11.29	1.15	11.50	(8.2, 13.2)	(10.84, 11.75)	27	1.27	1.19	1.30	(-1.6, 3.2)	(0.80, 1.74)	<0.001
	Week 36	27	11.45	1.20	11.60	(7.8, 13.9)	(10.98, 11.93)	27	1.44	1.14	1.60	(-2.0, 3.9)	(0.99, 1.89)	<0.001
	Week 40	25	11.33	0.66	11.40	(10.2, 12.6)	(11.05, 11.60)	25	1.30	0.68	1.20	(0.1, 2.4)	(1.01, 1.58)	<0.001
	Week 44	25	11.44	0.78	11.40	(10.0, 13.4)	(11.12, 11.77)	25	1.41	0.82	1.60	(-0.8, 2.8)	(1.07, 1.75)	<0.001
	Week 48	24	11.45	0.83	11.35	(9.8, 13.1)	(11.10, 11.80)	24	1.45	0.91	1.60	(-0.4, 2.9)	(1.07, 1.84)	<0.001
	Week 52	23	11.56	0.76	11.70	(10.2, 12.9)	(11.23, 11.89)	23	1.59	0.87	1.80	(0.0, 3.3)	(1.21, 1.96)	<0.001
	Week 52 (LOCF)	43	10.85	1.37	11.20	(7.4, 12.9)	(10.43, 11.27)	43	0.86	1.41	1.10	(-2.6, 3.3)	(0.42, 1.29)	<0.001

表 2.7.6.25－116　各評価時点の Hb 値の記述統計量（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	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
darbepoetin	Baseline	44	10.44	0.74	10.40	(8.5, 12.2)	(10.21, 10.66)							
	Week 2	44	10.47	0.80	10.50	(8.0, 12.4)	(10.23, 10.71)	44	0.03	0.59	0.05	(-1.3, 1.2)	(-0.15, 0.21)	0.743
	Week 4	44	10.36	0.87	10.40	(7.2, 11.9)	(10.10, 10.63)	44	-0.08	0.69	0.00	(-2.1, 1.3)	(-0.29, 0.14)	0.478
	Week 6	44	10.74	0.83	10.80	(8.6, 12.0)	(10.48, 10.99)	44	0.30	0.83	0.20	(-1.4, 1.6)	(0.05, 0.55)	0.021
	Week 8	44	10.85	0.93	10.70	(9.1, 12.9)	(10.56, 11.13)	44	0.41	0.97	0.25	(-1.6, 2.5)	(0.11, 0.70)	0.008
	Week 10	44	11.21	0.87	11.10	(9.8, 13.1)	(10.95, 11.48)	44	0.78	1.03	0.80	(-1.3, 2.8)	(0.46, 1.09)	<0.001
	Week 12	43	11.41	0.91	11.30	(9.0, 13.5)	(11.13, 11.69)	43	0.96	1.05	0.90	(-0.8, 3.1)	(0.64, 1.28)	<0.001
	Week 16	42	11.77	0.96	11.70	(9.8, 14.2)	(11.47, 12.07)	42	1.32	1.20	1.35	(-1.3, 3.9)	(0.95, 1.69)	<0.001
	Week 20	42	11.89	0.75	11.80	(10.3, 13.7)	(11.66, 12.13)	42	1.44	1.08	1.30	(-1.3, 3.7)	(1.10, 1.78)	<0.001
	Week 24	38	11.88	0.83	11.80	(9.8, 13.5)	(11.60, 12.15)	38	1.46	1.16	1.45	(-0.7, 3.4)	(1.07, 1.84)	<0.001
	Week 28	37	11.74	0.91	11.80	(9.6, 13.9)	(11.43, 12.04)	37	1.31	1.25	1.50	(-1.1, 4.6)	(0.89, 1.73)	<0.001
	Week 32	36	11.48	0.68	11.50	(10.1, 13.3)	(11.24, 11.71)	36	1.06	0.91	0.90	(-0.7, 3.1)	(0.75, 1.36)	<0.001
	Week 36	34	11.93	0.86	12.00	(10.6, 14.1)	(11.63, 12.22)	34	1.46	1.23	1.40	(-0.7, 4.8)	(1.03, 1.89)	<0.001
	Week 40	34	11.74	0.92	11.95	(9.9, 14.0)	(11.42, 12.06)	34	1.28	1.15	1.20	(-0.5, 3.6)	(0.88, 1.68)	<0.001
	Week 44	32	11.81	0.77	11.75	(10.1, 13.1)	(11.54, 12.09)	32	1.26	1.12	1.30	(-1.2, 3.5)	(0.88, 1.68)	<0.001
	Week 48	32	12.04	0.97	12.10	(10.6, 15.0)	(11.69, 12.39)	32	1.51	1.23	1.30	(-0.9, 5.1)	(1.06, 1.95)	<0.001
	Week 52	32	11.87	0.68	11.80	(10.7, 13.8)	(11.62, 12.11)	32	1.33	1.06	1.10	(-0.4, 3.9)	(0.95, 1.72)	<0.001
	Week 52 (LOCF)	44	11.61	0.98	11.70	(8.1, 13.8)	(11.31, 11.91)	44	1.17	1.24	1.10	(-2.8, 3.9)	(0.80, 1.55)	<0.001

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_5.sas

5.3.5.1—8 表 14.2.2.1.5 より引用

表 2.7.6.25－117　各評価時点の Hb 値（MMRM，FAS）（Conversion（Hb<11.0）集団）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	43	9.99 (0.52)	10.13	0.15	(9.84, 10.41)	
	Week 4	43	9.99 (0.52)	10.15	0.15	(9.87, 10.44)	
	Week 6	42	10.01 (0.52)	10.36	0.15	(10.07, 10.65)	
	Week 8	41	10.02 (0.52)	10.70	0.15	(10.41, 10.99)	
	Week 10	41	10.02 (0.52)	10.93	0.15	(10.64, 11.22)	
	Week 12	41	10.02 (0.52)	11.11	0.15	(10.82, 11.40)	
	Week 16	40	10.03 (0.52)	11.19	0.15	(10.90, 11.49)	
	Week 20	37	10.02 (0.53)	11.33	0.15	(11.03, 11.63)	
	Week 24	38	10.02 (0.56)	11.24	0.16	(10.93, 11.55)	
	Week 28	29	10.03 (0.59)	11.18	0.17	(10.85, 11.51)	
	Week 32	27	10.02 (0.60)	11.17	0.17	(10.83, 11.50)	
	Week 36	27	10.01 (0.60)	11.32	0.17	(10.98, 11.65)	
	Week 40	25	10.03 (0.62)	11.08	0.17	(10.74, 11.43)	
	Week 44	25	10.03 (0.62)	11.20	0.17	(10.86, 11.54)	
	Week 48	24	10.00 (0.61)	11.22	0.18	(10.87, 11.57)	
	Week 52	23	9.97 (0.61)	11.32	0.18	(10.97, 11.68)	
darbepoetin	Week 2	44	10.44 (0.74)	10.40	0.14	(10.12, 10.68)	
	Week 4	44	10.44 (0.74)	10.30	0.14	(10.02, 10.58)	
	Week 6	44	10.44 (0.74)	10.67	0.14	(10.39, 10.95)	
	Week 8	44	10.44 (0.74)	10.78	0.14	(10.50, 11.06)	
	Week 10	44	10.44 (0.74)	11.15	0.14	(10.87, 11.43)	
	Week 12	43	10.45 (0.75)	11.33	0.14	(11.05, 11.61)	
	Week 16	42	10.45 (0.76)	11.71	0.14	(11.42, 11.99)	
	Week 20	42	10.45 (0.76)	11.83	0.14	(11.54, 12.11)	
	Week 24	38	10.42 (0.79)	11.83	0.15	(11.54, 12.12)	
	Week 28	37	10.43 (0.80)	11.71	0.15	(11.41, 12.00)	
	Week 32	36	10.42 (0.81)	11.42	0.15	(11.13, 11.72)	
	Week 36	34	10.46 (0.81)	11.85	0.16	(11.55, 12.16)	
	Week 40	34	10.46 (0.81)	11.67	0.16	(11.36, 11.97)	
	Week 44	32	10.53 (0.76)	11.73	0.16	(11.42, 12.04)	
	Week 48	32	10.53 (0.76)	11.96	0.16	(11.64, 12.27)	
	Week 52	32	10.53 (0.76)	11.78	0.16	(11.47, 12.09)	

表 2.7.6.25－117　各評価時点の Hb 値（MMRM，FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference	Week 2			-0.29	0.21	(-0.68, 0.13)	0.182
MT-6548 - darbepoetin							
	Week 4			-0.15	0.21	(-0.55, 0.26)	0.474
	Week 6			-0.31	0.21	(-0.72, 0.10)	0.135
	Week 8			-0.08	0.21	(-0.49, 0.33)	0.688
	Week 10			-0.22	0.21	(-0.63, 0.19)	0.285
	Week 12			-0.23	0.21	(-0.64, 0.18)	0.277
	Week 16			-0.52	0.21	(-0.93, -0.10)	0.014
	Week 20			-0.50	0.21	(-0.91, -0.08)	0.020
	Week 24			-0.59	0.22	(-1.02, -0.16)	0.008
	Week 28			-0.53	0.23	(-0.97, -0.08)	0.021
	Week 32			-0.26	0.23	(-0.71, 0.20)	0.269
	Week 36			-0.53	0.23	(-0.99, -0.08)	0.022
	Week 40			-0.58	0.24	(-1.05, -0.12)	0.014
	Week 44			-0.53	0.24	(-1.00, -0.06)	0.027
	Week 48			-0.73	0.24	(-1.21, -0.26)	0.002
	Week 52			-0.46	0.24	(-0.93, 0.02)	0.059

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): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_2_5.sas

5.3.5.1—8 表 14.2.2.2.5 より引用

2)　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 2.7.6.25－40，darbepoetin 群を図 2.7.6.25－41 に示した. Hb 値が目標範囲内の被験者割合を表 2.7.6.25－118 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 45.0%であり，24 週後は 66.7%，52 週後は 79.2%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 52.4%であり，24 週後は 82.7%，52 週後は 76.6%であった.

Conversion（Hb≥11.0）集団の Hb 値が目標範囲内の被験者の割合について，MT-6548 群を図 2.7.6.25－42，darbepoetin 群を図 2.7.6.25－43 に示した．Hb 値が目標範囲内の被験者割合を表 2.7.6.25－119 に示した.

Conversion（Hb<11.0）集団の Hb 値が目標範囲内の被験者の割合について，MT-6548 群を図 2.7.6.25－44，darbepoetin 群を図 2.7.6.25－45 に示した．Hb 値が目標範囲内の被験者割合を表 2.7.6.25－120 に示した.

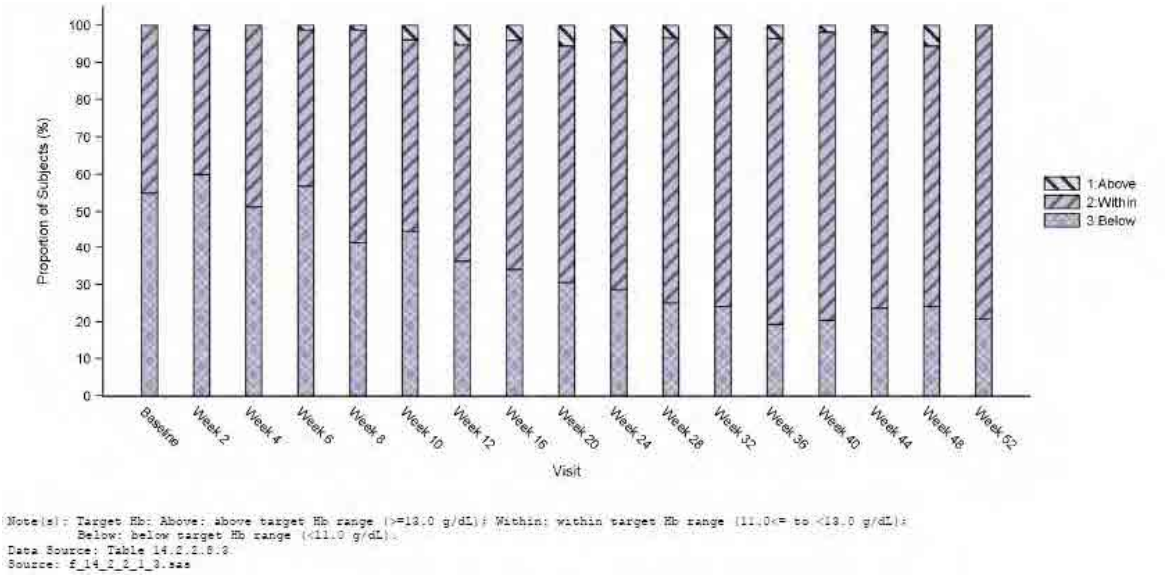


図 2.7.6.25－40　MT-6548 群の Hb 値が目標範囲内の被験者割合（FAS）（Conversion 集団）

5.3.5.1—8 図 11.4.1—4 より引用

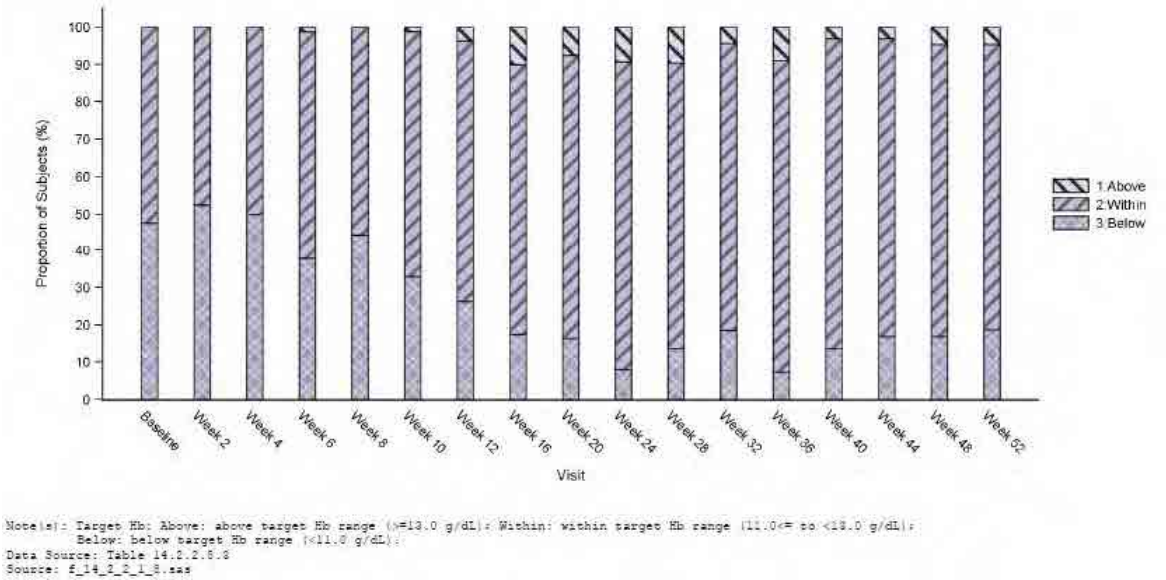


図 2.7.6.25－41　darbepoetin 群の Hb 値が目標範囲内の被験者割合（FAS）（Conversion 集団）

5.3.5.1—8 図 11.4.1—5 より引用

表 2.7.6.25－118　Hb 値が目標範囲内の被験者割合（FAS）（Conversion 集団）

		MT-6548(N=80)				darbepoetin(N=82)			
Visit	Target Hb Range	N[a]	n (%)	95% CI of proportion	p value from B	N[a]	n (%)	95% CI of proportion	p value from B
Baseline		80				82			
	Above		0 (0.0)	(0.00, 4.51)			0 (0.0)	(0.00, 4.40)	
	Within		36 (45.0)	(33.85, 56.53)			43 (52.4)	(41.11, 63.59)	
	Below		44 (55.0)	(43.47, 66.15)			39 (47.6)	(36.41, 58.89)	
Week 2		80				82			
	Above		1 (1.3)	(0.03, 6.77)			0 (0.0)	(0.00, 4.40)	
	Within		31 (38.8)	(28.06, 50.30)	0.132		39 (47.6)	(36.41, 58.89)	-
	Below		48 (60.0)	(48.44, 70.80)			43 (52.4)	(41.11, 63.59)	
Week 4		80				82			
	Above		0 (0.0)	(0.00, 4.51)			0 (0.0)	(0.00, 4.40)	
	Within		39 (48.8)	(37.41, 60.19)	0.491		41 (50.0)	(38.75, 61.25)	-
	Below		41 (51.3)	(39.81, 62.89)			41 (50.0)	(38.75, 61.25)	
Week 6		79				82			
	Above		1 (1.3)	(0.03, 6.85)			1 (1.2)	(0.03, 6.61)	
	Within		33 (41.8)	(30.77, 53.41)	0.849		50 (61.0)	(49.57, 71.56)	-
	Below		45 (57.0)	(45.83, 68.06)			31 (37.8)	(27.32, 49.19)	
Week 8		77				81			
	Above		1 (1.3)	(0.03, 7.02)			0 (0.0)	(0.00, 4.45)	
	Within		44 (57.1)	(45.35, 68.37)	0.095		45 (55.6)	(44.09, 66.60)	-
	Below		32 (41.6)	(30.43, 53.36)			36 (44.4)	(33.40, 55.91)	
Week 10		78				82			
	Above		3 (3.8)	(0.80, 10.83)			1 (1.2)	(0.03, 6.61)	
	Within		40 (51.3)	(39.69, 62.77)	0.493		54 (65.9)	(54.66, 75.97)	-
	Below		35 (44.9)	(33.59, 56.56)			27 (32.9)	(22.94, 44.19)	

表 2.7.6.25－118　Hb 値が目標範囲内の被験者割合（FAS）（Conversion 集団）（続き）

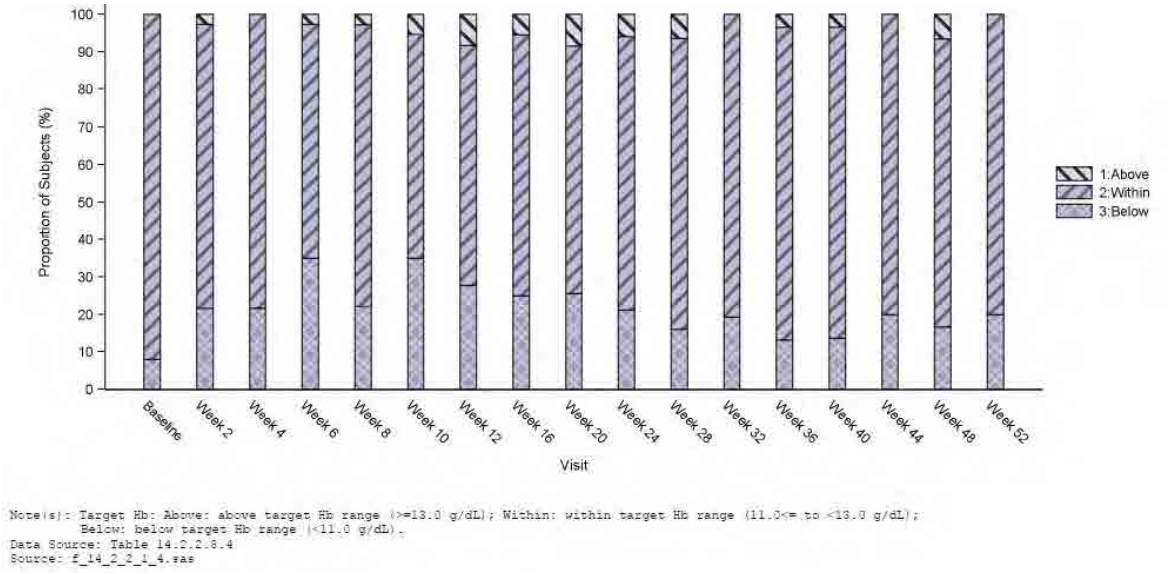
		MT-6548(N=80)				darbepoetin(N=82)			
Visit	Target Hb Range	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B
Week 12		77				80			
	Above		4 (5.2)	(1.43, 12.77)			3 (3.8)	(0.78, 10.57)	
	Within		45 (58.4)	(46.64, 69.57)	0.086		56 (70.0)	(58.72, 79.74)	-
	Below		28 (36.4)	(25.70, 48.12)			21 (26.3)	(17.04, 37.29)	
Week 16		76				80			
	Above		3 (3.9)	(0.82, 11.11)			8 (10.0)	(4.42, 18.76)	
	Within		47 (61.8)	(49.98, 72.75)	0.046		58 (72.5)	(61.38, 81.90)	-
	Below		26 (34.2)	(23.71, 46.99)			14 (17.5)	(9.91, 27.62)	
Week 20		72				79			
	Above		4 (5.6)	(1.53, 13.62)			6 (7.6)	(2.84, 15.80)	
	Within		46 (63.9)	(51.71, 74.85)	0.040		60 (75.9)	(65.02, 84.96)	-
	Below		22 (30.6)	(20.24, 42.53)			13 (16.5)	(9.06, 26.49)	
Week 24		66				75			
	Above		3 (4.5)	(0.95, 12.71)			7 (9.3)	(3.84, 18.29)	
	Within		44 (66.7)	(53.99, 77.80)	0.028		62 (82.7)	(72.15, 90.43)	-
	Below		19 (28.8)	(18.30, 41.25)			6 (8.0)	(2.99, 16.60)	
Week 28		60				73			
	Above		2 (3.3)	(0.41, 11.53)			7 (9.6)	(3.94, 18.76)	
	Within		43 (71.7)	(58.86, 82.55)	0.012		56 (76.7)	(65.35, 85.81)	-
	Below		15 (25.0)	(14.72, 37.86)			10 (13.7)	(6.77, 23.75)	
Week 32		58				70			
	Above		2 (3.4)	(0.42, 11.91)			3 (4.3)	(0.89, 12.02)	
	Within		42 (72.4)	(59.10, 83.34)	0.014		54 (77.1)	(65.55, 86.33)	-
	Below		14 (24.1)	(13.87, 37.17)			13 (18.6)	(10.29, 29.66)	

表 2.7.6.25－118　Hb 値が目標範囲内の被験者割合（FAS）（Conversion 集団）（続き）

		MT-6548(N=80)				darbepoetin(N=82)			
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		67				67			
	Above		2 (3.5)	(0.43, 12.11)			6 (9.0)	(3.36, 18.48)	
	Within		44 (77.2)	(64.16, 87.26)	0.002		56 (83.6)	(72.62, 91.51)	-
	Below		11 (19.3)	(10.05, 31.91)			5 (7.5)	(2.47, 16.86)	
Week 40		64				66			
	Above		1 (1.9)	(0.05, 9.89)			2 (3.0)	(0.37, 10.52)	
	Within		42 (77.8)	(64.40, 87.96)	0.004		55 (83.3)	(72.13, 91.38)	-
	Below		11 (20.4)	(10.63, 33.53)			9 (13.6)	(6.48, 24.31)	
Week 44		65				65			
	Above		1 (1.8)	(0.05, 9.72)			2 (3.1)	(0.37, 10.68)	
	Within		41 (74.5)	(61.00, 85.33)	0.014		52 (80.0)	(68.23, 88.90)	-
	Below		13 (23.6)	(13.23, 37.02)			11 (16.9)	(8.76, 28.27)	
Week 48		64				65			
	Above		3 (5.6)	(1.16, 15.39)			3 (4.6)	(0.96, 12.90)	
	Within		38 (70.4)	(56.39, 82.02)	0.061		51 (78.5)	(66.51, 87.69)	-
	Below		13 (24.1)	(13.49, 37.64)			11 (16.9)	(8.76, 28.27)	
Week 52		53				64			
	Above		0 (0.0)	(0.00, 6.72)			3 (4.7)	(0.98, 13.09)	
	Within		42 (79.2)	(65.89, 89.16)	0.007		49 (76.6)	(64.31, 86.25)	-
	Below		11 (20.8)	(10.84, 34.11)			12 (18.8)	(10.08, 30.46)	

Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 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_8_3.sas

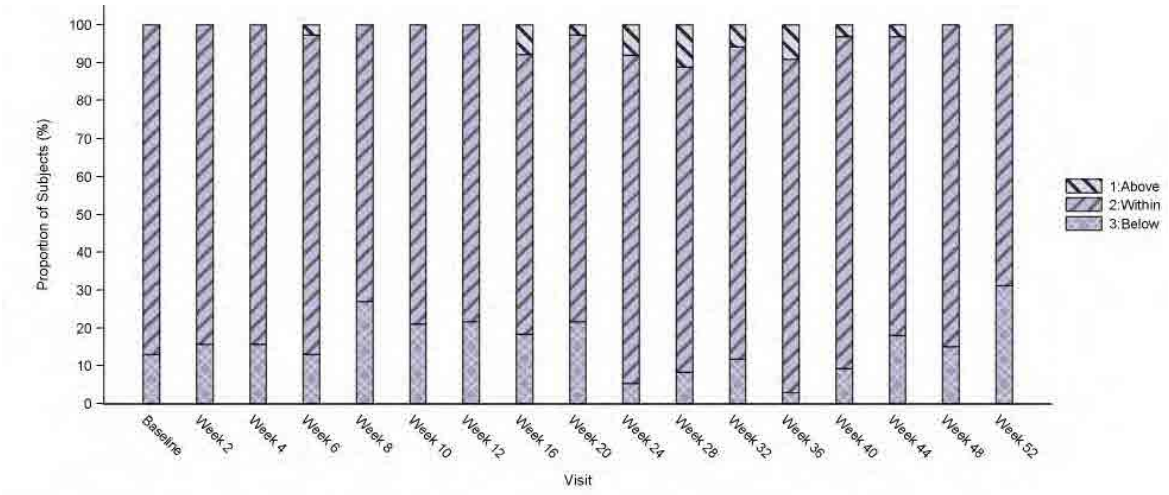
5.3.5.1—8 表 14.2.2.8.3 より引用



Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 g/dL).
Data Source: Table 14.2.2.8.4
Source: f_14_2_2_1_4.sas

図 2.7.6.25－42　MT-6548 群の Hb 値が目標範囲内の被験者割合（FAS）
（Conversion（Hb≥11.0）集団）

5.3.5.1—8 図 14.2.2.1.4 より引用



Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 g/dL).
Data Source: Table 14.2.2.8.4
Source: f_14_2_2_1_9.sas

図 2.7.6.25－43　darbepoetin 群の Hb 値が目標範囲内の被験者割合（FAS）
（Conversion（Hb≥11.0）集団）

5.3.5.1—8 図 14.2.2.1.9 より引用

表 2.7.6.25－119　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb≥11.0）集団）

		MT-6548(N=37)				darbepoetin(N=38)			
Visit	Target Hb Range	N[1]	n (%)	95% CI of proportion	p value from B	N[1]	n (%)	95% CI of proportion	p value from B
Baseline		37				38			
	Above		0 (0.0)	(0.00, 9.49)			0 (0.0)	(0.00, 9.25)	
	Within		34 (91.9)	(78.09, 98.30)			33 (86.8)	(71.91, 95.59)	
	Below		3 (8.1)	(1.70, 21.91)			5 (13.2)	(4.41, 28.09)	
Week 2		37				38			
	Above		1 (2.7)	(0.07, 14.16)			0 (0.0)	(0.00, 9.25)	
	Within		28 (75.7)	(59.80, 88.23)	0.034		32 (84.2)	(69.75, 93.96)	－
	Below		8 (21.6)	(9.83, 38.21)			6 (15.8)	(6.02, 31.25)	
Week 4		37				38			
	Above		0 (0.0)	(0.00, 9.49)			0 (0.0)	(0.00, 9.25)	
	Within		29 (78.4)	(61.79, 90.17)	0.096		32 (84.2)	(69.75, 93.96)	－
	Below		8 (21.6)	(9.83, 38.21)			6 (15.8)	(6.02, 31.25)	
Week 6		37				38			
	Above		1 (2.7)	(0.07, 14.16)			1 (2.6)	(0.07, 13.81)	
	Within		23 (62.2)	(44.76, 77.54)	0.005		32 (84.2)	(69.75, 93.96)	－
	Below		13 (35.1)	(20.21, 52.54)			5 (13.2)	(4.41, 28.09)	
Week 8		36				37			
	Above		1 (2.8)	(0.07, 14.53)			0 (0.0)	(0.00, 9.49)	
	Within		27 (75.0)	(57.80, 87.88)	0.093		27 (73.0)	(55.66, 86.21)	－
	Below		8 (22.2)	(10.12, 39.15)			10 (27.0)	(13.79, 44.12)	
Week 10		37				38			
	Above		2 (5.4)	(0.66, 18.19)			0 (0.0)	(0.00, 9.25)	
	Within		22 (59.5)	(42.10, 75.25)	0.003		30 (78.9)	(62.68, 90.45)	－
	Below		13 (35.1)	(20.21, 52.54)			8 (21.1)	(9.55, 37.32)	

表 2.7.6.25－119　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb≥11.0）集団）（続き）

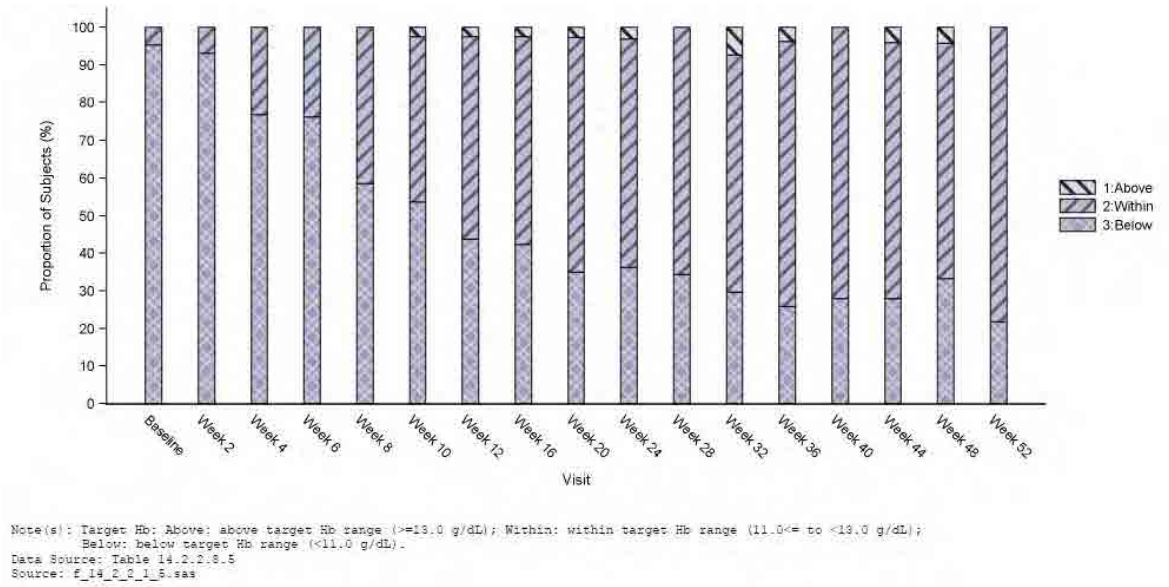
		MT-6548(N=37)				darbepoetin(N=38)			
Visit	Target Hb Range	N*	n (%)	95% CI of proportion	p value from B	N*	n (%)	95% CI of proportion	p value from B
Week 12		36				37			
	Above		3 (8.3)	(1.75, 22.47)			0 (0.0)	(0.00, 9.49)	
	Within		23 (63.9)	(46.22, 79.18)	0.004		29 (78.4)	(61.79, 90.17)	-
	Below		10 (27.8)	(14.20, 45.19)			8 (21.6)	(9.83, 38.21)	
Week 16		36				38			
	Above		2 (5.6)	(0.68, 18.66)			3 (7.9)	(1.66, 21.38)	
	Within		25 (69.4)	(51.89, 83.68)	0.033		28 (73.7)	(56.90, 86.60)	-
	Below		9 (25.0)	(12.12, 42.20)			7 (18.4)	(7.74, 34.33)	
Week 20		35				37			
	Above		3 (8.6)	(1.80, 23.06)			1 (2.7)	(0.07, 14.16)	
	Within		23 (65.7)	(47.79, 80.87)	0.007		28 (75.7)	(58.80, 88.23)	-
	Below		9 (25.7)	(12.49, 43.26)			8 (21.6)	(9.83, 38.21)	
Week 24		33				37			
	Above		2 (6.1)	(0.74, 20.23)			3 (8.1)	(1.70, 21.91)	
	Within		24 (72.7)	(54.48, 86.70)	0.058		32 (86.5)	(71.23, 95.46)	-
	Below		7 (21.2)	(8.98, 38.91)			2 (5.4)	(0.66, 18.19)	
Week 28		31				36			
	Above		2 (6.5)	(0.79, 21.42)			4 (11.1)	(3.11, 26.06)	
	Within		24 (77.4)	(58.90, 90.41)	0.157		29 (80.6)	(63.98, 91.81)	-
	Below		5 (16.1)	(5.45, 33.73)			3 (8.3)	(1.75, 22.47)	
Week 32		31				34			
	Above		0 (0.0)	(0.00, 11.22)			2 (5.9)	(0.72, 19.68)	
	Within		25 (80.6)	(62.53, 92.55)	0.257		28 (82.4)	(65.47, 93.24)	-
	Below		6 (19.4)	(7.45, 37.47)			4 (11.8)	(3.30, 27.45)	

表 2.7.6.25－119　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb≥11.0）集団）（続き）

Visit	Target Hb Range	MT-6548(N=37) N*	n (%)	95% CI of proportion	p value from B	darbepoetin(N=38) N*	n (%)	95% CI of proportion	p value from B
Week 36		30				33			
	Above		1 (3.3)	(0.08, 17.22)			3 (9.1)	(1.92, 24.33)	
	Within		25 (83.3)	(65.28, 94.36)	0.414		29 (87.9)	(71.80, 96.60)	-
	Below		4 (13.3)	(3.76, 30.72)			1 (3.0)	(0.08, 15.76)	
Week 40		29				32			
	Above		1 (3.4)	(0.09, 17.76)			1 (3.1)	(0.08, 16.22)	
	Within		24 (82.8)	(64.28, 94.15)	0.480		28 (87.5)	(71.01, 96.49)	-
	Below		4 (13.8)	(3.88, 31.66)			3 (9.4)	(1.98, 25.02)	
Week 44		30				33			
	Above		0 (0.0)	(0.00, 11.57)			1 (3.0)	(0.08, 16.76)	
	Within		24 (80.0)	(61.43, 92.29)	0.317		26 (78.8)	(61.09, 91.02)	-
	Below		6 (20.0)	(7.71, 38.57)			6 (18.2)	(6.98, 35.46)	
Week 48		30				33			
	Above		2 (6.7)	(0.82, 22.07)			0 (0.0)	(0.00, 10.58)	
	Within		23 (76.7)	(57.72, 90.07)	0.206		28 (84.8)	(68.10, 94.93)	-
	Below		5 (16.7)	(5.64, 34.72)			5 (15.2)	(5.11, 31.90)	
Week 52		30				32			
	Above		0 (0.0)	(0.00, 11.57)			0 (0.0)	(0.00, 10.89)	
	Within		24 (80.0)	(61.43, 92.29)	0.257		22 (68.8)	(49.99, 83.86)	-
	Below		6 (20.0)	(7.71, 38.57)			10 (31.3)	(16.12, 50.01)	

Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL); Below: below target Hb range (<11.0 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_8_4.sas

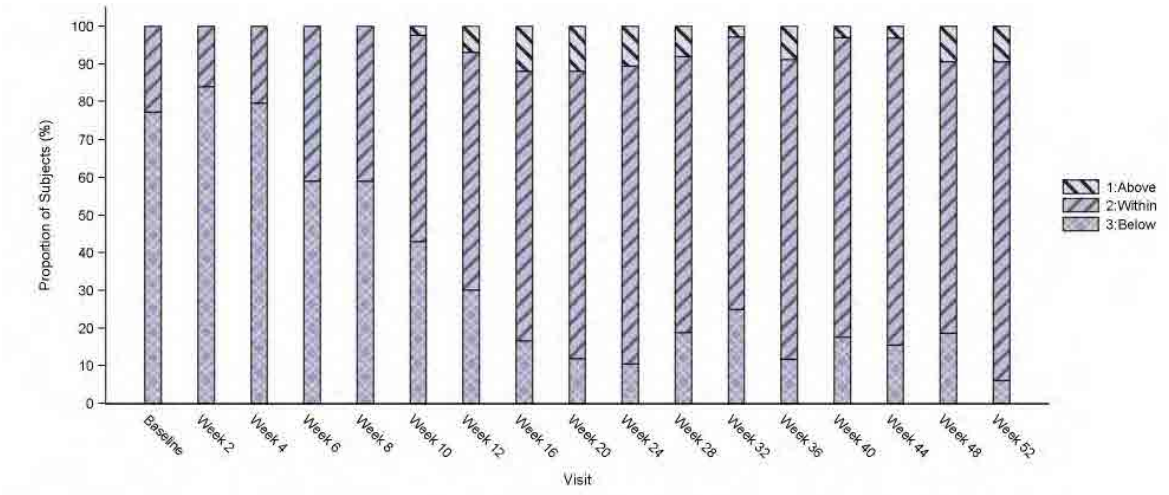
5.3.5.1—8 表 14.2.2.8.4 より引用



Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 g/dL).
Data Source: Table 14.2.2.8.5
Source: f_14_2_2_1_5.sas

図 2.7.6.25－44　MT-6548 群の Hb 値が目標範囲内の被験者割合（FAS）
（Conversion（Hb<11.0）集団）

5.3.5.1—8 図 14.2.2.1.5 より引用



Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 g/dL).
Data Source: Table 14.2.2.8.5
Source: f_14_2_2_1_10.sas

図 2.7.6.25－45　darbepoetin 群の Hb 値が目標範囲内の被験者割合（FAS）
（Conversion（Hb<11.0）集団）

5.3.5.1—8 図 14.2.2.1.10 より引用

表 2.7.6.25－120　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb<11.0）集団）

Visit	Target Hb Range	MT-6548 (N=43) N*	MT-6548 (N=43) n (%)	MT-6548 (N=43) 95% CI of proportion	MT-6548 (N=43) p value from B	darbepoetin (N=44) N*	darbepoetin (N=44) n (%)	darbepoetin (N=44) 95% CI of proportion	darbepoetin (N=44) p value from B	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Baseline		43				44						
	Above		0 (0.0)	(0.00, 8.22)			0 (0.0)	(0.00, 8.04)		-	-	-
	Within		2 (4.7)	(0.57, 15.81)			10 (22.7)	(11.47, 37.84)		-18.1	(-38.2, 2.6)	0.026
	Below		41 (95.3)	(84.19, 99.43)			34 (77.3)	(62.16, 88.53)		18.1	(-2.6, 38.2)	0.026
Week 2		43				44						
	Above		0 (0.0)	(0.00, 8.22)			0 (0.0)	(0.00, 8.04)		-	-	-
	Within		3 (7.0)	(1.46, 19.06)	0.564		7 (15.9)	(6.64, 30.07)	0.317	-8.9	(-29.6, 11.8)	0.314
	Below		40 (93.0)	(80.94, 98.54)			37 (84.1)	(69.93, 93.36)		8.9	(-11.8, 29.6)	0.314
Week 4		43				44						
	Above		0 (0.0)	(0.00, 8.22)			0 (0.0)	(0.00, 8.04)		-	-	-
	Within		10 (23.3)	(11.76, 38.63)	0.011		9 (20.5)	(9.80, 35.30)	0.763	2.8	(-18.5, 23.0)	0.800
	Below		33 (76.7)	(61.37, 88.24)			35 (79.5)	(64.70, 90.20)		-2.8	(-23.0, 18.5)	0.800
Week 6		42				44						
	Above		0 (0.0)	(0.00, 8.41)			0 (0.0)	(0.00, 8.04)		-	-	-
	Within		10 (23.8)	(12.05, 39.45)	0.011		18 (40.9)	(26.34, 56.75)	0.033	-17.1	(-37.5, 3.8)	0.110
	Below		32 (76.2)	(60.55, 87.95)			26 (59.1)	(43.25, 73.66)		17.1	(-3.8, 37.5)	0.110
Week 8		41				44						
	Above		0 (0.0)	(0.00, 8.60)			0 (0.0)	(0.00, 8.04)		-	-	-
	Within		17 (41.5)	(26.32, 57.89)	<0.001		18 (40.9)	(26.34, 56.75)	0.046	0.6	(-20.9, 21.8)	1.000
	Below		24 (58.5)	(42.11, 73.68)			26 (59.1)	(43.25, 73.66)		-0.6	(-21.8, 20.9)	1.000
Week 10		41				44						
	Above		1 (2.4)	(0.06, 12.86)			1 (2.3)	(0.06, 12.02)		0.2	(-21.1, 21.2)	1.000
	Within		18 (43.9)	(28.47, 60.25)	<0.001		24 (54.5)	(38.85, 69.61)	0.002	-10.6	(-31.6, 11.0)	0.388
	Below		22 (53.7)	(37.42, 69.34)			19 (43.2)	(28.35, 58.97)		10.5	(-11.3, 31.4)	0.389

表 2.7.6.25－120　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb<11.0）集団）（続き）

Visit	Target Hb Range	MT-6548(N=43) N*	MT-6548(N=43) n (%)	MT-6548(N=43) 95% CI of proportion	MT-6548(N=43) p value from B	darbepoetin(N=44) N*	darbepoetin(N=44) n (%)	darbepoetin(N=44) 95% CI of proportion	darbepoetin(N=44) p value from B	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Week 12		41				43						
	Above		1 (2.4)	(0.06, 12.86)			3 (7.0)	(1.46, 19.06)		-4.5	(-25.7, 17.3)	0.616
	Within		22 (53.7)	(37.42, 69.34)	<0.001		27 (62.8)	(46.73, 77.02)	<0.001	-9.1	(-30.0, 12.9)	0.507
	Below		18 (43.9)	(28.47, 60.25)			13 (30.2)	(17.18, 46.13)		13.7	(-8.3, 33.9)	0.259
Week 16		40				42						
	Above		1 (2.5)	(0.06, 13.16)			5 (11.9)	(3.98, 25.63)		-9.4	(-30.5, 12.9)	0.202
	Within		22 (55.0)	(38.49, 70.74)	<0.001		30 (71.4)	(55.42, 84.28)	<0.001	-16.4	(-36.7, 5.8)	0.169
	Below		17 (42.5)	(27.04, 59.11)			7 (16.7)	(6.97, 31.36)		25.9	(4.0, 45.5)	0.015
Week 20		37				42						
	Above		1 (2.7)	(0.07, 14.16)			5 (11.9)	(3.98, 25.63)		-9.2	(-30.8, 12.8)	0.206
	Within		23 (62.2)	(44.76, 77.54)	<0.001		32 (76.2)	(60.55, 87.95)	<0.001	-14.0	(-35.3, 8.1)	0.223
	Below		13 (35.1)	(20.21, 52.54)			5 (11.9)	(3.98, 25.63)		23.2	(1.0, 43.6)	0.017
Week 24		33				38						
	Above		1 (3.0)	(0.08, 15.76)			4 (10.5)	(2.94, 24.80)		-7.5	(-30.2, 15.9)	0.363
	Within		20 (60.6)	(42.14, 77.09)	<0.001		30 (78.9)	(62.68, 90.45)	<0.001	-18.3	(-40.3, 5.1)	0.120
	Below		12 (36.4)	(20.40, 54.88)			4 (10.5)	(2.94, 24.80)		25.8	(2.4, 47.0)	0.012
Week 28		29				37						
	Above		0 (0.0)	(0.00, 11.94)			3 (8.1)	(1.70, 21.91)		-8.1	(-31.6, 16.0)	0.250
	Within		19 (65.5)	(45.67, 82.06)	<0.001		27 (73.0)	(55.88, 86.21)	<0.001	-7.5	(-31.0, 16.7)	0.554
	Below		10 (34.5)	(17.94, 54.33)			7 (18.9)	(7.96, 35.16)		15.6	(-8.6, 38.6)	0.169
Week 32		27				36						
	Above		2 (7.4)	(0.91, 24.29)			1 (2.8)	(0.07, 14.53)		4.6	(-20.5, 29.4)	0.572
	Within		17 (63.0)	(42.37, 80.60)	<0.001		26 (72.2)	(54.81, 85.80)	<0.001	-9.3	(-33.7, 16.0)	0.585
	Below		8 (29.6)	(13.75, 50.18)			9 (25.0)	(12.12, 42.20)		4.6	(-20.5, 29.4)	0.777

表 2.7.6.25－120　Hb 値が目標範囲内の被験者割合（FAS）（Conversion（Hb<11.0）集団）（続き）

Visit	Target Hb Range	MT-6548 (N=43) N*	MT-6548 (N=43) n (%)	MT-6548 (N=43) 95% CI of proportion	MT-6548 (N=43) p value from B	darbepoetin (N=44) N*	darbepoetin (N=44) n (%)	darbepoetin (N=44) 95% CI of proportion	darbepoetin (N=44) p value from B	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Week 36		27				34						
	Above		1 (3.7)	(0.09, 18.97)			3 (8.8)	(1.86, 23.68)		-5.1	(-29.7, 19.9)	0.623
	Within		19 (70.4)	(49.82, 86.25)	<0.001		27 (79.4)	(62.10, 91.30)	<0.001	-9.0	(-33.2, 16.3)	0.551
	Below		7 (25.9)	(11.11, 46.28)			4 (11.8)	(3.30, 27.45)		14.2	(-11.2, 38.0)	0.190
Week 40		25				34						
	Above		0 (0.0)	(0.00, 13.72)			1 (2.9)	(0.07, 15.33)		-2.9	(-28.3, 22.8)	1.000
	Within		18 (72.0)	(50.61, 87.93)	<0.001		27 (79.4)	(62.10, 91.30)	<0.001	-7.4	(-32.3, 18.2)	0.549
	Below		7 (28.0)	(12.07, 49.39)			6 (17.6)	(6.76, 34.53)		10.4	(-15.3, 35.1)	0.362
Week 44		25				32						
	Above		1 (4.0)	(0.10, 20.35)			1 (3.1)	(0.09, 16.22)		0.9	(-24.9, 26.4)	1.000
	Within		17 (68.0)	(46.50, 85.05)	<0.001		26 (81.3)	(63.56, 92.79)	<0.001	-13.3	(-38.2, 12.7)	0.354
	Below		7 (28.0)	(12.07, 49.39)			5 (15.6)	(5.28, 32.79)		12.4	(-13.5, 37.5)	0.332
Week 48		24				32						
	Above		1 (4.2)	(0.11, 21.12)			3 (9.4)	(1.98, 25.02)		-5.2	(-31.4, 21.5)	0.627
	Within		15 (62.5)	(40.59, 81.20)	<0.001		23 (71.9)	(53.25, 86.25)	<0.001	-9.4	(-35.3, 17.5)	0.566
	Below		8 (33.3)	(15.63, 55.32)			6 (18.8)	(7.21, 36.44)		14.6	(-12.4, 40.0)	0.232
Week 52		23				32						
	Above		0 (0.0)	(0.00, 14.82)			3 (9.4)	(1.98, 25.02)		-9.4	(-35.1, 17.4)	0.257
	Within		18 (78.3)	(56.30, 92.54)	<0.001		27 (84.4)	(67.21, 94.72)	<0.001	-6.1	(-32.2, 20.4)	0.726
	Below		5 (21.7)	(7.46, 43.70)			2 (6.3)	(0.77, 20.81)		15.5	(-11.3, 40.8)	0.116

Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 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): 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 to comparer proportion of subjects in target range (Within) and proportion of subjects out of target range (Above + Below).
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_5.sas

5.3.5.1—8 表 14.2.2.8.5 より引用

3)　治験薬の投与量

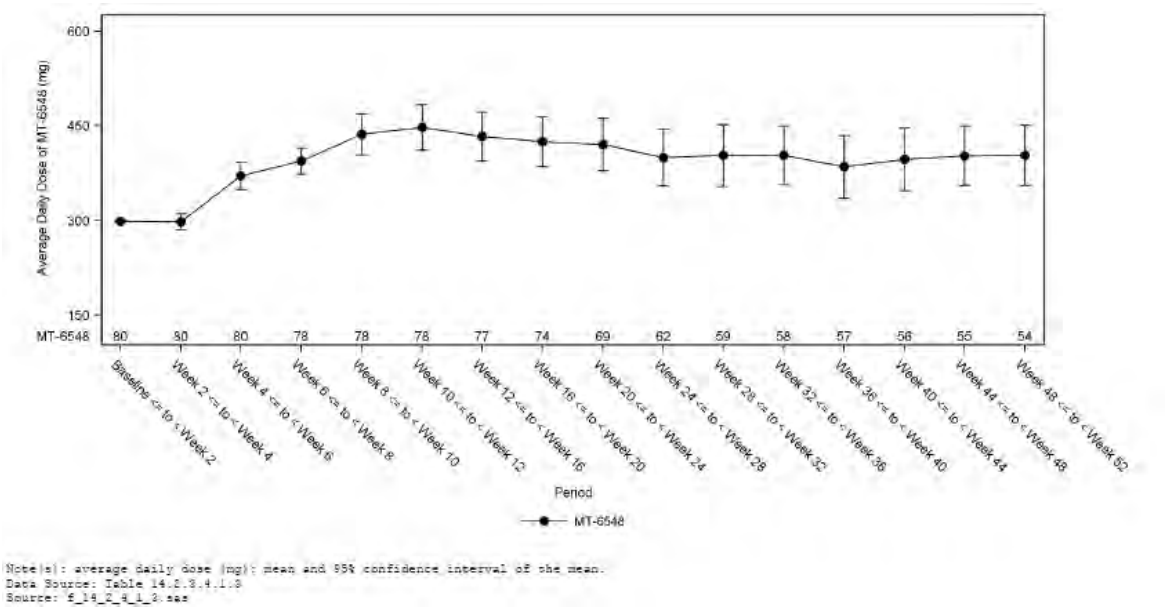
規定来院間の治験薬の平均投与量の推移について，MT-6548 群を図 2.7.6.25－46，その記述統計量を表 2.7.6.25－121 に示した．また，規定来院日における MT-6548 錠の 1 日投与量の分布を図 2.7.6.25－47，治験薬の投与量の分布を表 2.7.6.25－122 に示した．

MT-6548 は，300 mg/日で投与を開始し，1 日平均投与量の平均値及びその 95%CI は，20 週～24 週後で 420.52 mg/日及び 378.92～462.11 mg/日，48 週～52 週後で 403.67 mg/日及び 355.84～451.50 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 週後で 14.23 μg/週及び 12.08～16.38 μg/週，20 週～24 週後で 30.92 μg/週及び 24.03～37.81 μg/週，48 週～52 週後で 23.15 μg/週及び 18.29～28.00 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 4.2%，12.7%，28.2%，16.9%及び 38.0%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 1.9%，16.7%，25.9%，20.4%及び 35.2%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 1.3%，65.8%，25.3%，3.8%，1.3%及び 2.5%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 4.6%，73.8%，16.9%，4.6%，0%及び 0%であった．

Conversion（Hb≥11.0）集団の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 2.7.6.25－48，その記述統計量を表 2.7.6.25－123 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 2.7.6.25－49，治験薬の投与量の分布を表 2.7.6.25－124 に示した．

Conversion（Hb<11.0）集団の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 2.7.6.25－50，その記述統計量を表 2.7.6.25－125 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 2.7.6.25－51，治験薬の投与量の分布を表 2.7.6.25－126 に示した．



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.3.4.1.3
Source: f_14_2_4_1_3.sas

図 2.7.6.25－46　MT-6548 の 1 日平均投与量の推移（FAS）（Conversion 集団）

5.3.5.1—8 図 11.4.1—6 より引用

表 2.7.6.25－121　治験薬の平均投与量の記述統計量（FAS）（Conversion 集団）

Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Baseline <= to < Week 2	80	299.46	4.79	300.00	(257.1, 300.0)	(298.40, 300.53)
	Week 2 <= to < Week 4	80	297.99	56.10	300.00	(0.0, 450.0)	(285.51, 310.48)
	Week 4 <= to < Week 6	80	371.12	97.85	439.29	(0.0, 589.3)	(349.34, 392.89)
	Week 6 <= to < Week 8	78	394.78	92.72	450.00	(150.0, 600.0)	(373.86, 415.68)
	Week 8 <= to < Week 10	78	436.81	143.37	450.00	(10.7, 600.0)	(404.49, 469.14)
	Week 10 <= to < Week 12	78	447.53	158.70	450.00	(0.0, 600.0)	(411.75, 483.31)
	Week 12 <= to < Week 16	77	433.16	170.27	450.00	(85.7, 664.3)	(394.52, 471.81)
	Week 16 <= to < Week 20	74	424.89	170.50	450.00	(10.7, 600.0)	(385.36, 464.39)
	Week 20 <= to < Week 24	69	420.62	173.14	450.00	(0.0, 600.0)	(378.92, 462.11)
	Week 24 <= to < Week 28	62	400.06	177.80	450.00	(0.0, 600.0)	(354.90, 445.21)
	Week 28 <= to < Week 32	59	403.33	188.85	450.00	(0.0, 600.0)	(354.11, 452.55)
	Week 32 <= to < Week 36	58	403.73	178.79	450.00	(37.5, 600.0)	(356.71, 450.74)
	Week 36 <= to < Week 40	57	385.34	188.40	428.57	(0.0, 600.0)	(335.36, 435.33)
	Week 40 <= to < Week 44	56	397.10	186.16	447.32	(10.7, 600.0)	(347.24, 446.95)
	Week 44 <= to < Week 48	55	403.05	174.03	450.00	(16.1, 600.0)	(356.01, 450.10)
	Week 48 <= to < Week 52	54	403.67	175.23	450.00	(17.3, 600.0)	(355.94, 451.50)
darbepoetin	Baseline <= to < Week 2	82	14.23	9.60	7.50	(5.0, 45.0)	(12.08, 16.38)
	Week 2 <= to < Week 4	82	16.72	10.98	15.00	(0.0, 45.0)	(14.31, 19.13)
	Week 4 <= to < Week 6	82	22.48	14.77	15.00	(5.0, 60.0)	(19.23, 25.72)
	Week 6 <= to < Week 8	82	26.88	20.90	15.00	(5.0, 90.0)	(21.29, 30.47)
	Week 8 <= to < Week 10	82	28.51	21.61	22.50	(4.0, 90.0)	(23.76, 33.25)
	Week 10 <= to < Week 12	82	25.74	24.36	22.50	(3.8, 117.5)	(24.38, 35.10)
	Week 12 <= to < Week 16	80	30.78	28.86	22.50	(3.8, 175.7)	(24.35, 37.20)
	Week 16 <= to < Week 20	80	31.77	33.32	22.50	(0.0, 180.0)	(24.36, 39.19)
	Week 20 <= to < Week 24	80	30.92	30.96	22.50	(0.0, 180.0)	(24.03, 37.81)
	Week 24 <= to < Week 28	75	27.36	28.04	15.80	(0.0, 180.0)	(20.90, 33.81)
	Week 28 <= to < Week 32	73	26.49	29.08	15.84	(0.0, 180.0)	(19.71, 33.28)
	Week 32 <= to < Week 36	69	26.66	27.59	21.16	(0.0, 180.0)	(20.03, 33.29)
	Week 36 <= to < Week 40	67	24.67	25.27	15.00	(0.0, 180.0)	(18.51, 30.83)
	Week 40 <= to < Week 44	67	24.60	26.20	15.00	(0.0, 180.0)	(18.21, 31.00)
	Week 44 <= to < Week 48	66	25.04	22.26	15.00	(3.8, 136.1)	(19.62, 30.56)
	Week 48 <= to < Week 52	65	23.15	19.59	15.00	(0.0, 90.0)	(18.29, 28.00)

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_4_1_3.sas

5.3.5.1—8 表 14.2.3.4.1.3 より引用

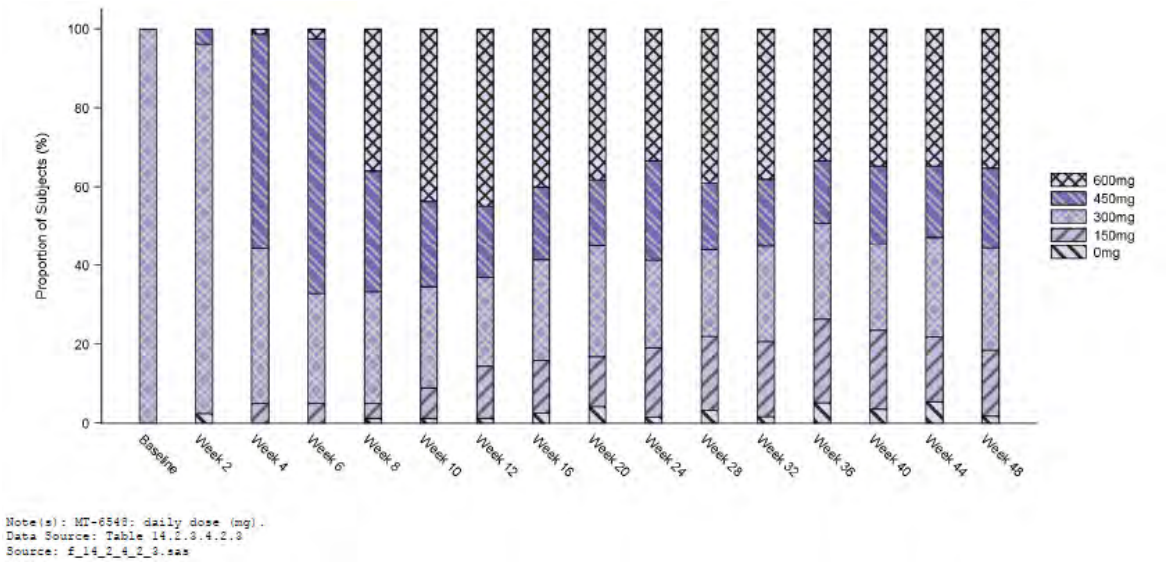


図 2.7.6.25－47　MT-6548 錠の 1 日投与量の分布（FAS）（Conversion 集団）

5.3.5.1—8 図 11.4.1—7 より引用

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
MT-6548	Baseline		80		
		0mg		0 (0.0)	(0.00, 4.51)
		150mg		0 (0.0)	(0.00, 4.51)
		300mg		80 (100.0)	(95.49, 100.00)
		450mg		0 (0.0)	(0.00, 4.51)
		600mg		0 (0.0)	(0.00, 4.51)
	Week 2		80		
		0mg		2 (2.5)	(0.30, 8.74)
		150mg		0 (0.0)	(0.00, 4.51)
		300mg		75 (93.8)	(86.01, 97.94)
		450mg		3 (3.8)	(0.78, 10.57)
		600mg		0 (0.0)	(0.00, 4.51)
	Week 4		79		
		0mg		0 (0.0)	(0.00, 4.56)
		150mg		4 (5.1)	(1.40, 12.46)
		300mg		31 (39.2)	(28.44, 50.67)
		450mg		43 (54.4)	(42.83, 65.69)
		600mg		1 (1.3)	(0.03, 6.85)
	Week 6		79		
		0mg		0 (0.0)	(0.00, 4.56)
		150mg		4 (5.1)	(1.40, 12.46)
		300mg		22 (27.8)	(18.35, 39.07)
		450mg		51 (64.6)	(52.99, 75.00)
		600mg		2 (2.5)	(0.31, 8.85)
	Week 8		78		
		0mg		1 (1.3)	(0.03, 6.94)
		150mg		3 (3.8)	(0.80, 10.83)
		300mg		22 (28.2)	(18.59, 39.53)
		450mg		24 (30.8)	(20.81, 42.24)
		600mg		28 (35.9)	(25.34, 47.56)
	Week 10		78		
		0mg		1 (1.3)	(0.03, 6.94)
		150mg		6 (7.7)	(2.88, 15.99)
		300mg		20 (25.6)	(16.42, 36.79)
		450mg		17 (21.8)	(13.24, 32.59)
		600mg		34 (43.6)	(32.39, 55.30)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 12		76		
		0mg		1 (1.3)	(0.03, 7.11)
		150mg		10 (13.2)	(6.49, 22.87)
		300mg		17 (22.4)	(13.60, 33.38)
		450mg		14 (18.4)	(10.45, 28.97)
		600mg		34 (44.7)	(33.81, 56.59)
	Week 16		75		
		0mg		2 (2.7)	(0.32, 9.30)
		150mg		10 (13.3)	(6.58, 23.16)
		300mg		19 (25.3)	(15.99, 36.70)
		450mg		14 (18.7)	(10.60, 29.33)
		600mg		30 (40.0)	(28.85, 51.96)
	Week 20		71		
		0mg		3 (4.2)	(0.88, 11.86)
		150mg		9 (12.7)	(5.96, 22.70)
		300mg		20 (28.2)	(18.13, 40.10)
		450mg		12 (16.9)	(9.05, 27.66)
		600mg		27 (38.0)	(26.76, 50.33)
	Week 24		63		
		0mg		1 (1.6)	(0.04, 8.53)
		150mg		11 (17.5)	(9.06, 29.10)
		300mg		14 (22.2)	(12.72, 34.46)
		450mg		16 (25.4)	(15.27, 37.94)
		600mg		21 (33.3)	(21.95, 46.34)
	Week 28		59		
		0mg		2 (3.4)	(0.41, 11.71)
		150mg		11 (18.6)	(9.69, 30.91)
		300mg		13 (22.0)	(12.29, 34.73)
		450mg		10 (16.9)	(8.44, 28.97)
		600mg		23 (39.0)	(26.55, 52.56)
	Week 32		58		
		0mg		1 (1.7)	(0.04, 9.24)
		150mg		11 (19.0)	(9.87, 31.41)
		300mg		14 (24.1)	(13.87, 37.17)
		450mg		10 (17.2)	(8.69, 29.43)
		600mg		22 (37.9)	(25.51, 51.63)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 36		57		
		0mg		3 (5.3)	(1.10, 14.62)
		150mg		12 (21.1)	(11.38, 33.69)
		300mg		14 (24.6)	(14.13, 37.76)
		450mg		9 (15.8)	(7.48, 27.87)
		600mg		19 (33.3)	(21.40, 47.06)
	Week 40		55		
		0mg		2 (3.6)	(0.44, 12.53)
		150mg		11 (20.0)	(10.43, 32.97)
		300mg		12 (21.8)	(11.81, 35.01)
		450mg		11 (20.0)	(10.43, 32.97)
		600mg		19 (34.5)	(22.24, 48.58)
	Week 44		55		
		0mg		3 (5.5)	(1.14, 15.12)
		150mg		9 (16.4)	(7.77, 29.60)
		300mg		14 (25.5)	(14.67, 39.00)
		450mg		10 (18.2)	(9.09, 30.90)
		600mg		19 (34.5)	(22.24, 48.58)
	Week 48		54		
		0mg		1 (1.9)	(0.05, 9.89)
		150mg		9 (16.7)	(7.92, 29.29)
		300mg		14 (25.9)	(14.96, 39.65)
		450mg		11 (20.4)	(10.63, 33.53)
		600mg		19 (35.2)	(22.68, 49.38)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
darbepoetin	Baseline		82		
		0ug		0 (0.0)	(0.00, 4.40)
		0ug < to <= 30ug		81 (98.8)	(93.39, 99.97)
		30ug < to <= 60ug		1 (1.2)	(0.03, 6.61)
		60ug < to <= 90ug		0 (0.0)	(0.00, 4.40)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.40)
		> 120ug		0 (0.0)	(0.00, 4.40)
	Week 2		82		
		0ug		1 (1.2)	(0.03, 6.61)
		0ug < to <= 30ug		76 (92.7)	(84.75, 97.27)
		30ug < to <= 60ug		5 (6.1)	(2.01, 13.66)
		60ug < to <= 90ug		0 (0.0)	(0.00, 4.40)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.40)
		> 120ug		0 (0.0)	(0.00, 4.40)
	Week 4		82		
		0ug		0 (0.0)	(0.00, 4.40)
		0ug < to <= 30ug		71 (86.6)	(77.26, 93.11)
		30ug < to <= 60ug		11 (13.4)	(6.89, 22.74)
		60ug < to <= 90ug		0 (0.0)	(0.00, 4.40)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.40)
		> 120ug		0 (0.0)	(0.00, 4.40)
	Week 6		82		
		0ug		0 (0.0)	(0.00, 4.40)
		0ug < to <= 30ug		64 (78.0)	(67.54, 86.44)
		30ug < to <= 60ug		13 (15.9)	(8.72, 25.58)
		60ug < to <= 90ug		5 (6.1)	(2.01, 13.66)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.40)
		> 120ug		0 (0.0)	(0.00, 4.40)
	Week 8		82		
		0ug		0 (0.0)	(0.00, 4.40)
		0ug < to <= 30ug		63 (76.8)	(66.20, 85.44)
		30ug < to <= 60ug		14 (17.1)	(9.66, 26.98)
		60ug < to <= 90ug		5 (6.1)	(2.01, 13.66)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.40)
		> 120ug		0 (0.0)	(0.00, 4.40)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 10		81		
		0ug		0 (0.0)	(0.00, 4.45)
		0ug < to <= 30ug		62 (76.5)	(65.82, 85.25)
		30ug < to <= 60ug		12 (14.8)	(7.90, 24.45)
		60ug < to <= 90ug		6 (7.4)	(2.77, 15.49)
		90ug < to <= 120ug		1 (1.2)	(0.03, 6.69)
		> 120ug		0 (0.0)	(0.00, 4.45)
	Week 12		80		
		0ug		1 (1.3)	(0.03, 6.77)
		0ug < to <= 30ug		59 (73.8)	(62.71, 82.96)
		30ug < to <= 60ug		12 (15.0)	(8.00, 24.74)
		60ug < to <= 90ug		7 (8.8)	(3.59, 17.20)
		90ug < to <= 120ug		0 (0.0)	(0.00, 4.51)
		> 120ug		1 (1.3)	(0.03, 6.77)
	Week 16		80		
		0ug		5 (6.3)	(2.06, 14.99)
		0ug < to <= 30ug		51 (63.8)	(52.24, 74.21)
		30ug < to <= 60ug		17 (21.3)	(12.99, 31.83)
		60ug < to <= 90ug		4 (5.0)	(1.38, 12.31)
		90ug < to <= 120ug		1 (1.3)	(0.03, 6.77)
		> 120ug		2 (2.5)	(0.30, 8.74)
	Week 20		79		
		0ug		1 (1.3)	(0.03, 6.86)
		0ug < to <= 30ug		52 (65.8)	(54.29, 76.13)
		30ug < to <= 60ug		20 (25.3)	(16.20, 36.36)
		60ug < to <= 90ug		3 (3.8)	(0.79, 10.70)
		90ug < to <= 120ug		1 (1.3)	(0.03, 6.86)
		> 120ug		2 (2.5)	(0.31, 9.85)
	Week 24		76		
		0ug		4 (5.3)	(1.45, 12.93)
		0ug < to <= 30ug		53 (69.7)	(58.13, 79.75)
		30ug < to <= 60ug		16 (21.1)	(12.54, 31.92)
		60ug < to <= 90ug		1 (1.3)	(0.03, 7.11)
		90ug < to <= 120ug		1 (1.3)	(0.03, 7.11)
		> 120ug		1 (1.3)	(0.03, 7.11)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

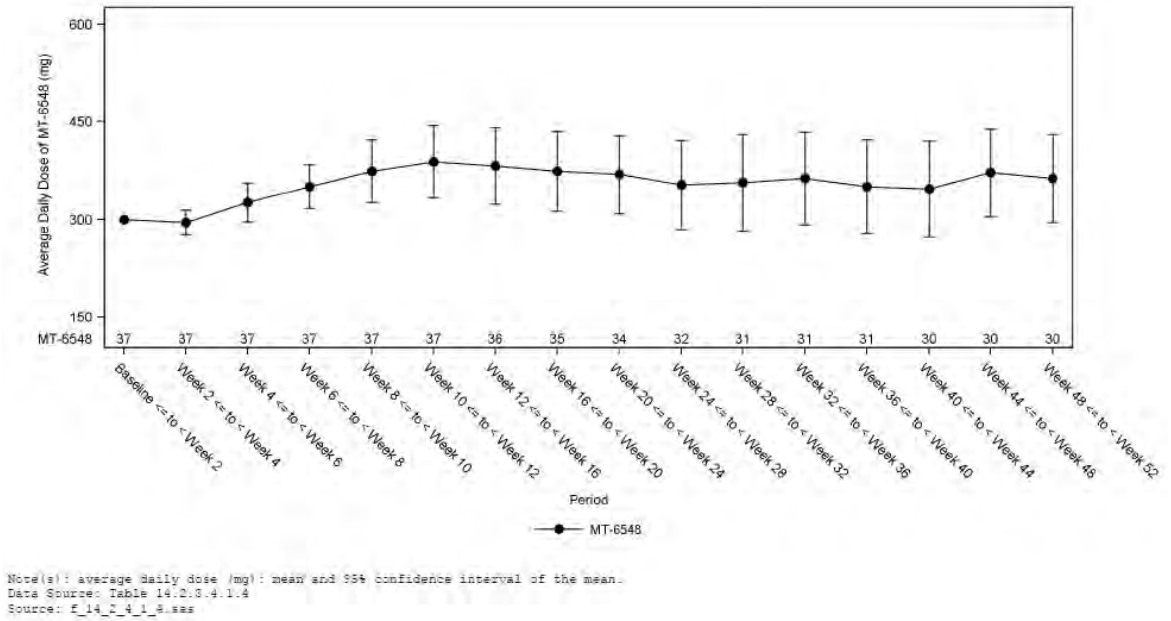
Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 28		71		
		0ug		2 (2.8)	(0.34, 9.81)
		0ug < to <= 30ug		53 (74.6)	(62.92, 84.23)
		30ug < to <= 60ug		12 (16.9)	(9.05, 27.66)
		60ug < to <= 90ug		2 (2.8)	(0.34, 9.81)
		90ug < to <= 120ug		1 (1.4)	(0.04, 7.60)
		> 120ug		1 (1.4)	(0.04, 7.60)
	Week 32		70		
		0ug		2 (2.9)	(0.35, 9.94)
		0ug < to <= 30ug		50 (71.4)	(59.38, 81.60)
		30ug < to <= 60ug		13 (18.6)	(10.28, 29.66)
		60ug < to <= 90ug		2 (2.9)	(0.35, 9.94)
		90ug < to <= 120ug		2 (2.9)	(0.35, 9.94)
		> 120ug		1 (1.4)	(0.04, 7.70)
	Week 36		67		
		0ug		3 (4.5)	(0.93, 12.53)
		0ug < to <= 30ug		48 (71.6)	(59.31, 81.99)
		30ug < to <= 60ug		14 (20.9)	(11.92, 32.57)
		60ug < to <= 90ug		1 (1.5)	(0.04, 8.04)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.36)
		> 120ug		1 (1.5)	(0.04, 8.04)
	Week 40		67		
		0ug		2 (3.0)	(0.36, 10.37)
		0ug < to <= 30ug		50 (74.6)	(62.51, 84.47)
		30ug < to <= 60ug		13 (19.4)	(10.76, 30.89)
		60ug < to <= 90ug		1 (1.5)	(0.04, 8.04)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.36)
		> 120ug		1 (1.5)	(0.04, 8.04)
	Week 44		65		
		0ug		0 (0.0)	(0.00, 5.52)
		0ug < to <= 30ug		49 (75.4)	(63.13, 85.23)
		30ug < to <= 60ug		13 (20.0)	(11.10, 31.77)
		60ug < to <= 90ug		2 (3.1)	(0.37, 10.68)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.52)
		> 120ug		1 (1.5)	(0.04, 8.28)

表 2.7.6.25－122　治験薬の投与量の分布（FAS）（Conversion 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 48		65		
		0ug		3 (4.6)	(0.96, 12.90)
		0ug < to <= 30ug		48 (73.8)	(61.46, 83.97)
		30ug < to <= 60ug		11 (16.9)	(8.76, 28.27)
		60ug < to <= 90ug		3 (4.6)	(0.96, 12.90)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.52)
		> 120ug		0 (0.0)	(0.00, 5.52)

Note(s): Dose: MT-6548: daily dose (mg); darbepoetin: weekly dose (ug).
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.8.1, Listing 16.2.8.2
Source: t_14_2_8_4_2_8.sas

5.3.5.1—8 表 14.2.3.4.2.3 より引用



Note(s): average daily dose (mg): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.8.4.1.4
Source: f_14_2_4_1_8.sas

図 2.7.6.25－48　MT-6548 の 1 日平均投与量の推移（FAS）
（Conversion（Hb≥11.0）集団）

5.3.5.1—8 図 14.2.4.1.4 より引用

表 2.7.6.25－123　治験薬の平均投与量の記述統計量（FAS）（Conversion（Hb≥11.0）集団）

Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Baseline <= to < Week 2	37	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
	Week 2 <= to < Week 4	37	296.37	57.45	300.00	(0.0, 450.0)	(276.21, 314.52)
	Week 4 <= to < Week 6	37	326.35	89.20	300.00	(150.0, 450.0)	(296.61, 356.09)
	Week 6 <= to < Week 8	37	350.68	99.51	300.00	(150.0, 450.0)	(317.50, 383.85)
	Week 8 <= to < Week 10	37	374.13	144.04	300.00	(10.7, 600.0)	(326.10, 422.16)
	Week 10 <= to < Week 12	37	388.32	165.99	300.00	(0.0, 600.0)	(332.98, 443.67)
	Week 12 <= to < Week 16	36	381.70	173.01	300.00	(150.0, 600.0)	(323.16, 440.23)
	Week 16 <= to < Week 20	35	374.08	178.65	300.00	(10.7, 600.0)	(312.71, 435.45)
	Week 20 <= to < Week 24	34	368.90	171.53	302.68	(0.0, 600.0)	(309.05, 428.75)
	Week 24 <= to < Week 28	32	353.07	189.00	300.00	(0.0, 600.0)	(284.93, 421.21)
	Week 28 <= to < Week 32	31	356.34	202.85	300.00	(0.0, 600.0)	(282.04, 430.63)
	Week 32 <= to < Week 36	31	363.42	193.99	300.00	(37.5, 600.0)	(292.27, 434.58)
	Week 36 <= to < Week 40	31	350.46	197.03	300.00	(0.0, 600.0)	(278.19, 422.73)
	Week 40 <= to < Week 44	30	346.96	197.84	300.00	(10.7, 600.0)	(273.09, 420.84)
	Week 44 <= to < Week 48	30	371.79	179.93	300.00	(16.1, 600.0)	(304.60, 438.97)
	Week 48 <= to < Week 52	30	362.85	180.41	300.00	(17.3, 600.0)	(295.48, 430.21)
darbepoetin	Baseline <= to < Week 2	36	14.04	9.08	7.80	(6.4, 30.0)	(11.05, 17.02)
	Week 2 <= to < Week 4	38	14.61	9.05	15.00	(0.0, 30.0)	(11.63, 17.58)
	Week 4 <= to < Week 6	38	16.20	10.23	15.00	(7.5, 45.0)	(12.83, 19.56)
	Week 6 <= to < Week 8	38	17.23	11.30	15.00	(7.5, 47.1)	(13.51, 20.94)
	Week 8 <= to < Week 10	38	19.26	13.73	15.00	(7.5, 60.0)	(14.74, 23.77)
	Week 10 <= to < Week 12	38	20.33	16.81	15.00	(7.5, 90.0)	(14.80, 25.85)
	Week 12 <= to < Week 16	38	22.04	19.42	15.00	(3.8, 90.0)	(15.66, 28.43)
	Week 16 <= to < Week 20	36	22.80	21.82	15.00	(0.0, 116.8)	(15.62, 29.97)
	Week 20 <= to < Week 24	38	25.81	29.44	15.00	(3.8, 173.6)	(16.14, 35.49)
	Week 24 <= to < Week 28	36	22.21	18.33	15.00	(3.8, 79.3)	(16.01, 28.41)
	Week 28 <= to < Week 32	35	19.02	14.81	15.00	(0.0, 45.0)	(13.93, 24.10)
	Week 32 <= to < Week 36	34	18.93	14.17	15.00	(0.0, 45.0)	(13.99, 23.86)
	Week 36 <= to < Week 40	33	17.97	14.58	15.00	(0.0, 45.0)	(12.80, 23.14)
	Week 40 <= to < Week 44	33	18.42	14.44	15.00	(3.8, 45.0)	(13.30, 23.54)
	Week 44 <= to < Week 48	33	18.83	14.68	15.00	(3.8, 52.5)	(13.63, 24.04)
	Week 48 <= to < Week 52	33	20.03	18.37	15.00	(3.8, 90.0)	(13.51, 26.54)

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_4_1_4.sas

5.3.5.1—8 表 14.2.3.4.1.4 より引用

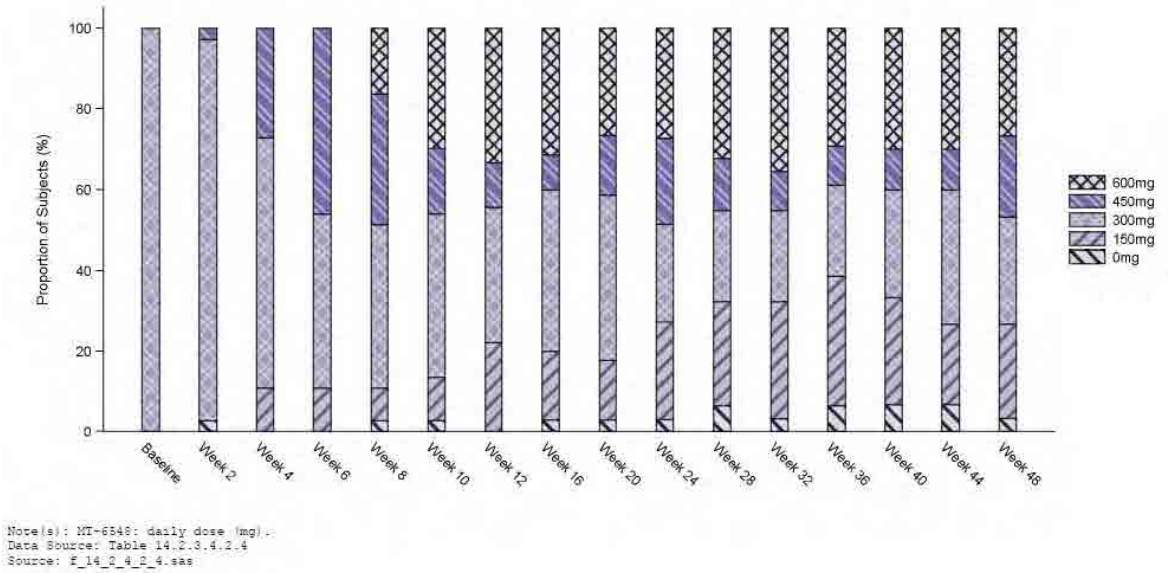


図 2.7.6.25－49　MT-6548 錠の 1 日投与量の分布（FAS）

（Conversion（Hb≥11.0）集団）

5.3.5.1—8 図 14.2.4.2.4 より引用

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
MT-6548	Baseline		37		
		0mg		0 (0.0)	(0.00, 9.49)
		150mg		0 (0.0)	(0.00, 9.49)
		300mg		37 (100.0)	(90.51, 100.00)
		450mg		0 (0.0)	(0.00, 9.49)
		600mg		0 (0.0)	(0.00, 9.49)
	Week 2		37		
		0mg		1 (2.7)	(0.07, 14.16)
		150mg		0 (0.0)	(0.00, 9.49)
		300mg		35 (94.6)	(81.81, 99.34)
		450mg		1 (2.7)	(0.07, 14.16)
		600mg		0 (0.0)	(0.00, 9.49)
	Week 4		37		
		0mg		0 (0.0)	(0.00, 9.49)
		150mg		4 (10.8)	(3.03, 25.42)
		300mg		23 (62.2)	(44.76, 77.54)
		450mg		10 (27.0)	(13.79, 44.12)
		600mg		0 (0.0)	(0.00, 9.49)
	Week 6		37		
		0mg		0 (0.0)	(0.00, 9.49)
		150mg		4 (10.8)	(3.03, 25.42)
		300mg		16 (43.2)	(27.10, 60.91)
		450mg		17 (45.9)	(29.49, 63.08)
		600mg		0 (0.0)	(0.00, 9.49)
	Week 8		37		
		0mg		1 (2.7)	(0.07, 14.16)
		150mg		3 (8.1)	(1.70, 21.91)
		300mg		15 (40.5)	(24.75, 57.90)
		450mg		12 (32.4)	(18.01, 49.79)
		600mg		6 (16.2)	(6.19, 32.01)
	Week 10		37		
		0mg		1 (2.7)	(0.07, 14.16)
		150mg		4 (10.8)	(3.03, 25.42)
		300mg		15 (40.5)	(24.75, 57.90)
		450mg		6 (16.2)	(6.19, 32.01)
		600mg		11 (29.7)	(15.87, 46.98)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 12		36		
		0mg		0 (0.0)	(0.00, 9.74)
		150mg		8 (22.2)	(10.12, 39.15)
		300mg		12 (33.3)	(18.56, 50.97)
		450mg		4 (11.1)	(3.11, 26.06)
		600mg		12 (33.3)	(18.56, 50.97)
	Week 16		35		
		0mg		1 (2.9)	(0.07, 14.92)
		150mg		6 (17.1)	(6.56, 33.65)
		300mg		14 (40.0)	(23.87, 57.89)
		450mg		3 (8.6)	(1.80, 23.06)
		600mg		11 (31.4)	(16.85, 49.29)
	Week 20		34		
		0mg		1 (2.9)	(0.07, 15.33)
		150mg		5 (14.7)	(4.95, 31.06)
		300mg		14 (41.2)	(24.65, 59.30)
		450mg		5 (14.7)	(4.95, 31.06)
		600mg		9 (26.5)	(12.86, 44.36)
	Week 24		33		
		0mg		1 (3.0)	(0.08, 15.76)
		150mg		8 (24.2)	(11.09, 42.26)
		300mg		8 (24.2)	(11.09, 42.26)
		450mg		7 (21.2)	(8.98, 38.91)
		600mg		9 (27.3)	(13.30, 45.52)
	Week 28		31		
		0mg		2 (6.5)	(0.79, 21.42)
		150mg		8 (25.8)	(11.86, 44.61)
		300mg		7 (22.6)	(9.59, 41.10)
		450mg		4 (12.9)	(3.63, 29.83)
		600mg		10 (32.3)	(16.68, 51.37)
	Week 32		31		
		0mg		1 (3.2)	(0.08, 16.70)
		150mg		9 (29.0)	(14.22, 48.04)
		300mg		7 (22.6)	(9.59, 41.10)
		450mg		3 (9.7)	(2.04, 25.75)
		600mg		11 (35.5)	(19.23, 54.63)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 36		31		
		0mg		2 (6.5)	(0.79, 21.42)
		150mg		10 (32.3)	(16.68, 51.37)
		300mg		7 (22.6)	(9.59, 41.10)
		450mg		3 (9.7)	(2.04, 25.75)
		600mg		9 (29.0)	(14.22, 48.04)
	Week 40		30		
		0mg		2 (6.7)	(0.82, 22.07)
		150mg		8 (26.7)	(12.28, 45.89)
		300mg		8 (26.7)	(12.28, 45.89)
		450mg		3 (10.0)	(2.11, 26.53)
		600mg		9 (30.0)	(14.73, 49.40)
	Week 44		30		
		0mg		2 (6.7)	(0.82, 22.07)
		150mg		6 (20.0)	(7.71, 38.57)
		300mg		10 (33.3)	(17.29, 52.81)
		450mg		3 (10.0)	(2.11, 26.53)
		600mg		9 (30.0)	(14.73, 49.40)
	Week 48		30		
		0mg		1 (3.3)	(0.08, 17.22)
		150mg		7 (23.3)	(9.93, 42.28)
		300mg		8 (26.7)	(12.28, 45.89)
		450mg		6 (20.0)	(7.71, 38.57)
		600mg		8 (26.7)	(12.28, 45.89)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
darbepoetin	Baseline		38		
		0ug		0 (0.0)	(0.00, 9.25)
		0ug < to <= 30ug		38 (100.0)	(90.75, 100.00)
		30ug < to <= 60ug		0 (0.0)	(0.00, 9.25)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 2		38		
		0ug		1 (2.6)	(0.07, 13.81)
		0ug < to <= 30ug		37 (97.4)	(86.19, 99.93)
		30ug < to <= 60ug		0 (0.0)	(0.00, 9.25)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 4		38		
		0ug		0 (0.0)	(0.00, 9.25)
		0ug < to <= 30ug		37 (97.4)	(86.19, 99.93)
		30ug < to <= 60ug		1 (2.6)	(0.07, 13.81)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 6		38		
		0ug		0 (0.0)	(0.00, 9.25)
		0ug < to <= 30ug		36 (94.7)	(82.25, 99.36)
		30ug < to <= 60ug		2 (5.3)	(0.64, 17.75)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 8		38		
		0ug		0 (0.0)	(0.00, 9.25)
		0ug < to <= 30ug		35 (92.1)	(78.62, 98.34)
		30ug < to <= 60ug		3 (7.9)	(1.66, 21.38)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 10		38		
		0ug		0 (0.0)	(0.00, 9.25)
		0ug < to <= 30ug		35 (92.1)	(78.62, 98.34)
		30ug < to <= 60ug		2 (5.3)	(0.64, 17.75)
		60ug < to <= 90ug		1 (2.6)	(0.07, 13.81)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 12		38		
		0ug		1 (2.6)	(0.07, 13.81)
		0ug < to <= 30ug		34 (89.5)	(75.20, 97.06)
		30ug < to <= 60ug		1 (2.6)	(0.07, 13.81)
		60ug < to <= 90ug		2 (5.3)	(0.64, 17.75)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 16		38		
		0ug		3 (7.9)	(1.66, 21.38)
		0ug < to <= 30ug		28 (73.7)	(56.90, 86.60)
		30ug < to <= 60ug		6 (15.8)	(6.02, 31.25)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		1 (2.6)	(0.07, 13.81)
		> 120ug		0 (0.0)	(0.00, 9.25)
	Week 20		38		
		0ug		1 (2.6)	(0.07, 13.81)
		0ug < to <= 30ug		27 (71.1)	(54.10, 84.58)
		30ug < to <= 60ug		9 (23.7)	(11.44, 40.24)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.25)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.25)
		> 120ug		1 (2.6)	(0.07, 13.81)
	Week 24		37		
		0ug		2 (5.4)	(0.66, 18.19)
		0ug < to <= 30ug		28 (75.7)	(58.80, 88.23)
		30ug < to <= 60ug		7 (18.9)	(7.96, 35.16)
		60ug < to <= 90ug		0 (0.0)	(0.00, 9.49)
		90ug < to <= 120ug		0 (0.0)	(0.00, 9.49)
		> 120ug		0 (0.0)	(0.00, 9.49)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 28		35		
		0ug		1 (2.9)	(0.07, 14.92)
		0ug < to <= 30ug		27 (77.1)	(59.86, 89.58)
		30ug < to <= 60ug		7 (20.0)	(8.44, 36.94)
		60ug < to <= 90ug		0 (0.0)	(0.00, 10.00)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.00)
		> 120ug		0 (0.0)	(0.00, 10.00)
	Week 32		34		
		0ug		1 (2.9)	(0.07, 15.33)
		0ug < to <= 30ug		27 (79.4)	(62.10, 91.30)
		30ug < to <= 60ug		5 (14.7)	(4.95, 31.06)
		60ug < to <= 90ug		1 (2.9)	(0.07, 15.33)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.28)
		> 120ug		0 (0.0)	(0.00, 10.28)
	Week 36		33		
		0ug		2 (6.1)	(0.74, 20.23)
		0ug < to <= 30ug		25 (75.8)	(57.74, 88.91)
		30ug < to <= 60ug		6 (18.2)	(6.98, 35.46)
		60ug < to <= 90ug		0 (0.0)	(0.00, 10.58)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.58)
		> 120ug		0 (0.0)	(0.00, 10.58)
	Week 40		33		
		0ug		0 (0.0)	(0.00, 10.58)
		0ug < to <= 30ug		27 (81.8)	(64.54, 93.02)
		30ug < to <= 60ug		6 (18.2)	(6.98, 35.46)
		60ug < to <= 90ug		0 (0.0)	(0.00, 10.58)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.58)
		> 120ug		0 (0.0)	(0.00, 10.58)
	Week 44		33		
		0ug		0 (0.0)	(0.00, 10.58)
		0ug < to <= 30ug		27 (81.8)	(64.54, 93.02)
		30ug < to <= 60ug		6 (18.2)	(6.98, 35.46)
		60ug < to <= 90ug		0 (0.0)	(0.00, 10.58)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.58)
		> 120ug		0 (0.0)	(0.00, 10.58)

表 2.7.6.25－124　治験薬の投与量の分布（FAS）（Conversion（Hb≥11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 48		33		
		0ug		1 (3.0)	(0.08, 15.76)
		0ug < to <= 30ug		27 (81.8)	(64.54, 93.02)
		30ug < to <= 60ug		4 (12.1)	(3.40, 28.20)
		60ug < to <= 90ug		1 (3.0)	(0.08, 15.76)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.68)
		> 120ug		0 (0.0)	(0.00, 10.68)

Note(s): Dose: MT-6548: daily dose (mg); darbepoetin: weekly dose (ug).
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.8.1, Listing 16.2.3.2
Source: t_14_2_8_4_2_4.sas

5.3.5.1—8 表 14.2.3.4.2.4 より引用

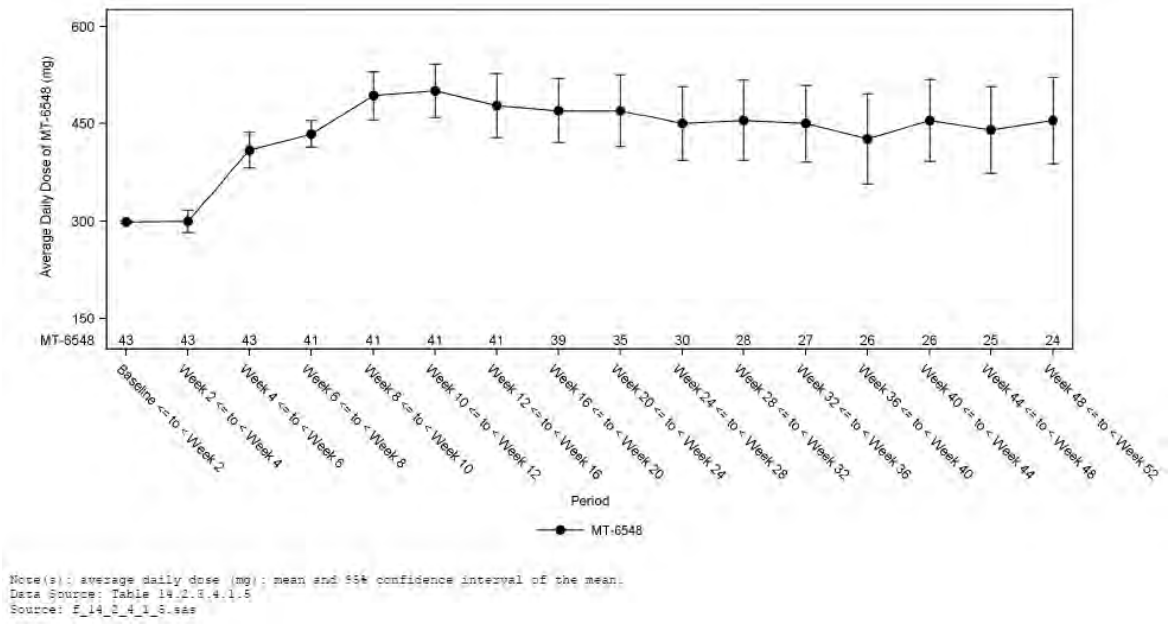


図 2.7.6.25－50　MT-6548 の 1 日平均投与量の推移（FAS）

（Conversion（Hb<11.0）集団）

5.3.5.1—8 図 14.2.4.1.5 より引用

表 2.7.6.25－125　治験薬の平均投与量の記述統計量（FAS）（Conversion（Hb<11.0）集団）

Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Baseline <= to < Week 2	43	299.00	6.54	300.00	(257.1, 300.0)	(296.99, 301.01)
	Week 2 <= to < Week 4	43	300.26	55.50	300.00	(0.0, 439.3)	(283.17, 317.33)
	Week 4 <= to < Week 6	43	409.63	89.90	439.29	(0.0, 589.3)	(382.27, 436.99)
	Week 6 <= to < Week 8	41	434.58	64.91	450.00	(300.0, 600.0)	(414.09, 455.07)
	Week 8 <= to < Week 10	41	493.38	118.24	589.29	(257.1, 600.0)	(456.06, 530.70)
	Week 10 <= to < Week 12	41	500.96	132.35	600.00	(139.3, 600.0)	(459.18, 542.73)
	Week 12 <= to < Week 16	41	476.35	156.27	600.00	(85.7, 664.3)	(429.03, 527.68)
	Week 16 <= to < Week 20	39	470.48	150.94	487.50	(144.6, 600.0)	(421.55, 519.41)
	Week 20 <= to < Week 24	35	470.66	161.70	594.64	(150.0, 600.0)	(415.12, 526.21)
	Week 24 <= to < Week 28	30	450.18	152.57	450.00	(150.0, 600.0)	(393.21, 507.15)
	Week 28 <= to < Week 32	28	456.36	160.27	450.00	(150.0, 600.0)	(393.21, 517.50)
	Week 32 <= to < Week 36	27	450.00	150.00	450.00	(150.0, 600.0)	(390.66, 509.34)
	Week 36 <= to < Week 40	26	426.92	172.11	450.00	(5.4, 600.0)	(357.41, 496.44)
	Week 40 <= to < Week 44	26	454.95	156.02	450.00	(144.6, 600.0)	(391.93, 517.96)
	Week 44 <= to < Week 48	25	440.57	162.27	450.00	(150.0, 600.0)	(373.59, 507.55)
	Week 48 <= to < Week 52	24	454.70	157.58	450.00	(150.0, 600.0)	(388.16, 521.24)
darbepoetin	Baseline <= to < Week 2	44	14.40	10.48	7.50	(5.0, 45.0)	(11.21, 17.59)
	Week 2 <= to < Week 4	44	18.55	12.21	15.00	(5.0, 45.0)	(14.84, 22.26)
	Week 4 <= to < Week 6	44	27.90	16.00	30.00	(5.0, 60.0)	(23.03, 32.76)
	Week 6 <= to < Week 8	44	33.35	24.25	30.00	(5.0, 90.0)	(26.97, 40.74)
	Week 8 <= to < Week 10	44	36.50	24.01	30.00	(4.0, 90.0)	(29.20, 43.79)
	Week 10 <= to < Week 12	44	37.87	27.04	30.00	(3.8, 117.9)	(29.64, 46.09)
	Week 12 <= to < Week 16	42	38.68	33.61	30.00	(3.8, 175.7)	(28.20, 49.15)
	Week 16 <= to < Week 20	42	39.90	39.59	30.00	(0.0, 180.0)	(27.56, 52.23)
	Week 20 <= to < Week 24	42	35.54	31.92	30.00	(0.0, 180.0)	(25.59, 45.49)
	Week 24 <= to < Week 28	39	32.11	34.26	22.50	(0.0, 180.0)	(21.00, 43.21)
	Week 28 <= to < Week 32	38	33.38	36.64	22.50	(0.0, 180.0)	(21.94, 45.42)
	Week 32 <= to < Week 36	35	34.17	34.77	22.50	(0.0, 180.0)	(22.23, 46.12)
	Week 36 <= to < Week 40	34	31.17	31.34	22.50	(3.8, 180.0)	(20.24, 42.11)
	Week 40 <= to < Week 44	34	30.61	33.09	22.50	(0.0, 180.0)	(19.06, 42.15)
	Week 44 <= to < Week 48	32	31.44	26.81	22.50	(3.8, 136.1)	(21.77, 41.11)
	Week 48 <= to < Week 52	32	26.36	20.55	22.50	(0.0, 90.0)	(18.95, 33.77)

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_4_1_5.sas

5.3.5.1—8 表 14.2.3.4.1.5 より引用

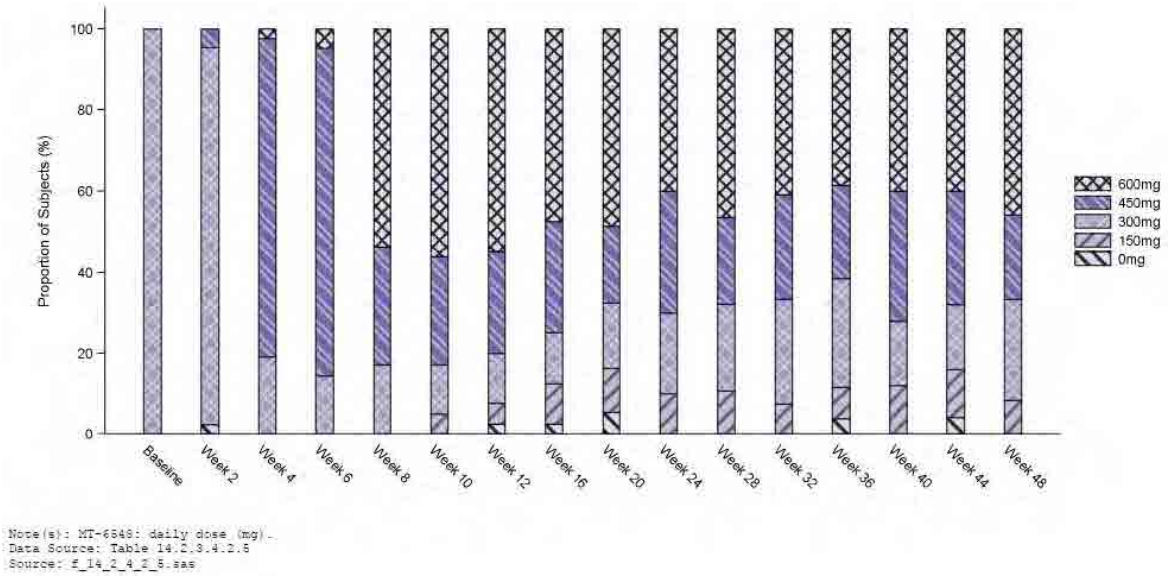


図 2.7.6.25－51　MT-6548 錠の 1 日投与量の分布（FAS）（Conversion（Hb<11.0）集団）

5.3.5.1—8 図 14.2.4.2.5 より引用

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
MT-6548	Baseline		43		
		0mg		0 (0.0)	(0.00, 8.22)
		150mg		0 (0.0)	(0.00, 8.22)
		300mg		43 (100.0)	(91.78, 100.00)
		450mg		0 (0.0)	(0.00, 8.22)
		600mg		0 (0.0)	(0.00, 8.22)
	Week 2		43		
		0mg		1 (2.3)	(0.06, 12.29)
		150mg		0 (0.0)	(0.00, 8.22)
		300mg		40 (93.0)	(80.94, 98.54)
		450mg		2 (4.7)	(0.57, 15.51)
		600mg		0 (0.0)	(0.00, 8.22)
	Week 4		42		
		0mg		0 (0.0)	(0.00, 8.41)
		150mg		0 (0.0)	(0.00, 8.41)
		300mg		8 (19.0)	(8.60, 34.12)
		450mg		33 (78.6)	(63.19, 89.70)
		600mg		1 (2.4)	(0.06, 12.57)
	Week 6		42		
		0mg		0 (0.0)	(0.00, 8.41)
		150mg		0 (0.0)	(0.00, 8.41)
		300mg		6 (14.3)	(5.43, 28.54)
		450mg		34 (81.0)	(65.88, 91.40)
		600mg		2 (4.8)	(0.58, 16.16)
	Week 8		41		
		0mg		0 (0.0)	(0.00, 8.60)
		150mg		0 (0.0)	(0.00, 8.60)
		300mg		7 (17.1)	(7.15, 32.06)
		450mg		12 (29.3)	(16.13, 45.54)
		600mg		22 (53.7)	(37.42, 69.34)
	Week 10		41		
		0mg		0 (0.0)	(0.00, 8.60)
		150mg		2 (4.9)	(0.60, 16.53)
		300mg		5 (12.2)	(4.08, 26.20)
		450mg		11 (26.8)	(14.22, 42.94)
		600mg		23 (56.1)	(39.75, 71.53)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 12		40		
		0mg		1 (2.5)	(0.06, 13.16)
		150mg		2 (5.0)	(0.61, 16.92)
		300mg		5 (12.5)	(4.19, 26.80)
		450mg		10 (25.0)	(12.69, 41.20)
		600mg		22 (55.0)	(38.49, 70.74)
	Week 16		40		
		0mg		1 (2.5)	(0.06, 13.16)
		150mg		4 (10.0)	(2.79, 23.66)
		300mg		5 (12.5)	(4.19, 26.80)
		450mg		11 (27.5)	(14.60, 43.89)
		600mg		19 (47.5)	(31.51, 63.87)
	Week 20		37		
		0mg		2 (5.4)	(0.66, 18.19)
		150mg		4 (10.8)	(3.03, 25.42)
		300mg		6 (16.2)	(6.19, 32.01)
		450mg		7 (18.9)	(7.96, 35.16)
		600mg		18 (48.6)	(31.92, 65.60)
	Week 24		30		
		0mg		0 (0.0)	(0.00, 11.57)
		150mg		3 (10.0)	(2.11, 26.53)
		300mg		6 (20.0)	(7.71, 38.57)
		450mg		9 (30.0)	(14.73, 49.40)
		600mg		12 (40.0)	(22.66, 59.40)
	Week 28		28		
		0mg		0 (0.0)	(0.00, 12.34)
		150mg		3 (10.7)	(2.27, 28.23)
		300mg		6 (21.4)	(8.30, 40.95)
		450mg		6 (21.4)	(8.30, 40.95)
		600mg		13 (46.4)	(27.51, 66.13)
	Week 32		27		
		0mg		0 (0.0)	(0.00, 12.77)
		150mg		2 (7.4)	(0.91, 24.29)
		300mg		7 (25.9)	(11.11, 46.28)
		450mg		7 (25.9)	(11.11, 46.28)
		600mg		11 (40.7)	(22.39, 61.20)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 36		26		
		0mg		1 (3.8)	(0.10, 19.64)
		150mg		2 (7.7)	(0.95, 25.13)
		300mg		7 (26.9)	(11.57, 47.79)
		450mg		6 (23.1)	(8.97, 43.65)
		600mg		10 (38.5)	(20.23, 59.43)
	Week 40		25		
		0mg		0 (0.0)	(0.00, 13.72)
		150mg		3 (12.0)	(2.55, 31.22)
		300mg		4 (16.0)	(4.54, 36.08)
		450mg		8 (32.0)	(14.95, 53.50)
		600mg		10 (40.0)	(21.13, 61.33)
	Week 44		25		
		0mg		1 (4.0)	(0.10, 20.35)
		150mg		3 (12.0)	(2.55, 31.22)
		300mg		4 (16.0)	(4.54, 36.08)
		450mg		7 (28.0)	(12.07, 49.39)
		600mg		10 (40.0)	(21.13, 61.33)
	Week 48		24		
		0mg		0 (0.0)	(0.00, 14.26)
		150mg		2 (8.3)	(1.03, 27.00)
		300mg		6 (25.0)	(9.77, 46.71)
		450mg		5 (20.8)	(7.13, 42.15)
		600mg		11 (45.8)	(25.56, 67.18)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
darbepoetin	Baseline		44		
		0ug		0 (0.0)	(0.00, 8.04)
		0ug < to <= 30ug		43 (97.7)	(87.98, 99.94)
		30ug < to <= 60ug		1 (2.3)	(0.06, 12.02)
		60ug < to <= 90ug		0 (0.0)	(0.00, 8.04)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.04)
		> 120ug		0 (0.0)	(0.00, 8.04)
	Week 2		44		
		0ug		0 (0.0)	(0.00, 8.04)
		0ug < to <= 30ug		39 (88.6)	(75.44, 96.21)
		30ug < to <= 60ug		5 (11.4)	(3.79, 24.56)
		60ug < to <= 90ug		0 (0.0)	(0.00, 8.04)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.04)
		> 120ug		0 (0.0)	(0.00, 8.04)
	Week 4		44		
		0ug		0 (0.0)	(0.00, 8.04)
		0ug < to <= 30ug		34 (77.3)	(62.16, 88.53)
		30ug < to <= 60ug		10 (22.7)	(11.47, 37.84)
		60ug < to <= 90ug		0 (0.0)	(0.00, 8.04)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.04)
		> 120ug		0 (0.0)	(0.00, 8.04)
	Week 6		44		
		0ug		0 (0.0)	(0.00, 8.04)
		0ug < to <= 30ug		28 (63.6)	(47.77, 77.69)
		30ug < to <= 60ug		11 (25.0)	(13.19, 40.34)
		60ug < to <= 90ug		5 (11.4)	(3.79, 24.56)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.04)
		> 120ug		0 (0.0)	(0.00, 8.04)
	Week 8		44		
		0ug		0 (0.0)	(0.00, 8.04)
		0ug < to <= 30ug		28 (63.6)	(47.77, 77.69)
		30ug < to <= 60ug		11 (25.0)	(13.19, 40.34)
		60ug < to <= 90ug		5 (11.4)	(3.79, 24.56)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.04)
		> 120ug		0 (0.0)	(0.00, 8.04)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 10		43		
		0ug		0 (0.0)	(0.00, 8.22)
		0ug < to <= 30ug		27 (62.8)	(46.73, 77.02)
		30ug < to <= 60ug		10 (23.3)	(11.76, 38.63)
		60ug < to <= 90ug		5 (11.6)	(3.89, 25.09)
		90ug < to <= 120ug		1 (2.3)	(0.06, 12.29)
		> 120ug		0 (0.0)	(0.00, 8.22)
	Week 12		42		
		0ug		0 (0.0)	(0.00, 8.41)
		0ug < to <= 30ug		25 (59.5)	(43.28, 74.37)
		30ug < to <= 60ug		11 (26.2)	(13.86, 42.04)
		60ug < to <= 90ug		5 (11.9)	(3.98, 25.63)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.41)
		> 120ug		1 (2.4)	(0.06, 12.57)
	Week 16		42		
		0ug		2 (4.8)	(0.58, 16.16)
		0ug < to <= 30ug		23 (54.8)	(38.67, 70.15)
		30ug < to <= 60ug		11 (26.2)	(13.86, 42.04)
		60ug < to <= 90ug		4 (9.5)	(2.66, 22.62)
		90ug < to <= 120ug		0 (0.0)	(0.00, 8.41)
		> 120ug		2 (4.8)	(0.58, 16.16)
	Week 20		41		
		0ug		0 (0.0)	(0.00, 8.60)
		0ug < to <= 30ug		25 (61.0)	(44.80, 75.80)
		30ug < to <= 60ug		11 (26.8)	(14.22, 42.94)
		60ug < to <= 90ug		3 (7.3)	(1.54, 19.92)
		90ug < to <= 120ug		1 (2.4)	(0.06, 12.86)
		> 120ug		1 (2.4)	(0.06, 12.86)
	Week 24		39		
		0ug		2 (5.1)	(0.63, 17.32)
		0ug < to <= 30ug		25 (64.1)	(47.18, 78.80)
		30ug < to <= 60ug		9 (23.1)	(11.13, 39.33)
		60ug < to <= 90ug		1 (2.6)	(0.06, 13.48)
		90ug < to <= 120ug		1 (2.6)	(0.06, 13.48)
		> 120ug		1 (2.6)	(0.06, 13.48)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 28		36		
		0ug		1 (2.8)	(0.07, 14.53)
		0ug < to <= 30ug		26 (72.2)	(54.81, 85.80)
		30ug < to <= 60ug		5 (13.9)	(4.67, 29.50)
		60ug < to <= 90ug		2 (5.6)	(0.68, 18.66)
		90ug < to <= 120ug		1 (2.8)	(0.07, 14.53)
		> 120ug		1 (2.8)	(0.07, 14.53)
	Week 32		36		
		0ug		1 (2.8)	(0.07, 14.53)
		0ug < to <= 30ug		23 (63.9)	(46.22, 79.18)
		30ug < to <= 60ug		8 (22.2)	(10.12, 39.15)
		60ug < to <= 90ug		1 (2.8)	(0.07, 14.53)
		90ug < to <= 120ug		2 (5.6)	(0.68, 18.66)
		> 120ug		1 (2.8)	(0.07, 14.53)
	Week 36		34		
		0ug		1 (2.9)	(0.07, 15.33)
		0ug < to <= 30ug		23 (67.6)	(49.47, 82.61)
		30ug < to <= 60ug		8 (23.5)	(10.75, 41.17)
		60ug < to <= 90ug		1 (2.9)	(0.07, 15.33)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.28)
		> 120ug		1 (2.9)	(0.07, 15.33)
	Week 40		34		
		0ug		2 (5.9)	(0.72, 19.68)
		0ug < to <= 30ug		23 (67.6)	(49.47, 82.61)
		30ug < to <= 60ug		7 (20.6)	(8.70, 37.90)
		60ug < to <= 90ug		1 (2.9)	(0.07, 15.33)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.28)
		> 120ug		1 (2.9)	(0.07, 15.33)
	Week 44		32		
		0ug		0 (0.0)	(0.00, 10.89)
		0ug < to <= 30ug		22 (68.8)	(49.95, 83.88)
		30ug < to <= 60ug		7 (21.9)	(9.28, 39.97)
		60ug < to <= 90ug		2 (6.3)	(0.77, 20.81)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.89)
		> 120ug		1 (3.1)	(0.08, 16.22)

表 2.7.6.25－126　治験薬の投与量の分布（FAS）（Conversion（Hb<11.0）集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 48		32		
		0ug		2 (6.3)	(0.77, 20.81)
		0ug < to <= 30ug		21 (65.6)	(46.81, 81.43)
		30ug < to <= 60ug		7 (21.9)	(9.29, 39.97)
		60ug < to <= 90ug		2 (6.3)	(0.77, 20.81)
		90ug < to <= 120ug		0 (0.0)	(0.00, 10.89)
		> 120ug		0 (0.0)	(0.00, 10.89)

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 16.2.3.1, Listing 16.2.3.2
Source: t_14_2_3_4_2_5.sas

5.3.5.1—8 表 14.2.3.4.2.5 より引用

4)　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 2.7.6.25－127 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 54.4%であり，20 週～24 週後では 20.0%，48 週～52 週後では 12.7%であった.

表 2.7.6.25－127　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）（Conversion 集団）

Parameter	Period	Category	N*	MT-6548(N=80) n (%)	95% CI of proportion
Cumulative number of dose adjustment		0		4 (5.0)	(1.38, 12.31)
		1		12 (15.0)	(8.00, 24.74)
		2		34 (42.5)	(31.51, 54.06)
		3		13 (16.3)	(8.95, 26.18)
		4		8 (10.0)	(4.42, 18.76)
		5		4 (5.0)	(1.38, 12.31)
		6		3 (3.8)	(0.78, 10.57)
		7		2 (2.5)	(0.30, 8.74)
Proportion of subjects by category of dose adjustment	Baseline <= to < Week 2		80		
		No change		80 (100.0)	(95.49, 100.00)
		Dose adjustment		0 (0.0)	(0.00, 4.51)
		Increase		0 (0.0)	(0.00, 4.51)
		Decrease		0 (0.0)	(0.00, 4.51)
		Interrupt		0 (0.0)	(0.00, 4.51)
	Week 2 <= to < Week 4		80		
		No change		70 (87.5)	(78.21, 93.84)
		Dose adjustment		10 (12.5)	(6.16, 21.79)
		Increase		7 (8.8)	(3.59, 17.20)
		Decrease		1 (1.3)	(0.03, 6.77)
		Interrupt		2 (2.5)	(0.30, 8.74)
	Week 4 <= to < Week 6		79		
		No change		36 (45.6)	(34.31, 57.17)
		Dose adjustment		43 (54.4)	(42.83, 65.69)
		Increase		41 (51.9)	(40.36, 63.29)
		Decrease		2 (2.5)	(0.31, 8.85)
		Interrupt		0 (0.0)	(0.00, 4.56)

表 2.7.6.25－127　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）（Conversion 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=80) n (%)	95% CI of proportion
	Week 6 <= to < Week 8		78		
		No change		66 (84.6)	(74.67, 91.79)
		Dose adjustment		12 (15.4)	(8.21, 25.33)
		Increase		10 (12.8)	(6.32, 22.32)
		Decrease		2 (2.6)	(0.31, 8.96)
		Interrupt		0 (0.0)	(0.00, 4.62)
	Week 8 <= to < Week 10		78		
		No change		48 (61.5)	(49.83, 72.34)
		Dose adjustment		30 (38.5)	(27.66, 50.17)
		Increase		27 (34.6)	(24.20, 46.24)
		Decrease		2 (2.6)	(0.31, 8.96)
		Interrupt		2 (2.6)	(0.31, 8.96)
	Week 10 <= to < Week 12		78		
		No change		69 (88.5)	(79.22, 94.59)
		Dose adjustment		9 (11.5)	(5.41, 20.78)
		Increase		5 (6.4)	(2.11, 14.33)
		Decrease		3 (3.8)	(0.80, 10.93)
		Interrupt		1 (1.3)	(0.03, 6.94)
	Week 12 <= to < Week 16		77		
		No change		66 (85.7)	(75.87, 92.65)
		Dose adjustment		11 (14.3)	(7.35, 24.13)
		Increase		4 (5.2)	(1.43, 12.77)
		Decrease		7 (9.1)	(3.73, 17.84)
		Interrupt		1 (1.3)	(0.03, 7.02)
	Week 16 <= to < Week 20		74		
		No change		61 (82.4)	(71.83, 90.30)
		Dose adjustment		13 (17.6)	(9.70, 28.17)
		Increase		4 (5.4)	(1.49, 13.27)
		Decrease		7 (9.5)	(3.89, 18.52)
		Interrupt		3 (4.1)	(0.84, 11.39)

表 2.7.6.25－127　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）（Conversion 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=80) n (%)	95% CI of proportion
	Week 20 <= to < Week 24		70		
		No change		56 (80.0)	(68.73, 88.61)
		Dose adjustment		14 (20.0)	(11.39, 31.27)
		Increase		7 (10.0)	(4.12, 19.52)
		Decrease		5 (7.1)	(2.36, 15.89)
		Interrupt		2 (2.9)	(0.35, 9.94)
	Week 24 <= to < Week 28		64		
		No change		55 (85.9)	(74.98, 93.36)
		Dose adjustment		9 (14.1)	(6.64, 25.02)
		Increase		3 (4.7)	(0.98, 13.09)
		Decrease		5 (7.8)	(2.59, 17.30)
		Interrupt		1 (1.6)	(0.04, 8.40)
	Week 28 <= to < Week 32		60		
		No change		53 (88.3)	(77.43, 95.18)
		Dose adjustment		7 (11.7)	(4.82, 22.57)
		Increase		4 (6.7)	(1.85, 16.20)
		Decrease		2 (3.3)	(0.41, 11.53)
		Interrupt		1 (1.7)	(0.04, 8.94)
	Week 32 <= to < Week 36		59		
		No change		53 (89.8)	(79.17, 96.18)
		Dose adjustment		6 (10.2)	(3.82, 20.83)
		Increase		3 (5.1)	(1.06, 14.15)
		Decrease		1 (1.7)	(0.04, 9.09)
		Interrupt		2 (3.4)	(0.41, 11.71)
	Week 36 <= to < Week 40		57		
		No change		47 (82.5)	(70.09, 91.25)
		Dose adjustment		10 (17.5)	(8.75, 29.91)
		Increase		3 (5.3)	(1.10, 14.62)
		Decrease		4 (7.0)	(1.95, 17.00)
		Interrupt		3 (5.3)	(1.10, 14.62)

表 2.7.6.25－127　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）（Conversion 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=80) n (%)	95% CI of proportion
	Week 40 <= to < Week 44		57		
		No change		49 (86.0)	(74.21, 93.74)
		Dose adjustment		8 (14.0)	(6.26, 25.79)
		Increase		7 (12.3)	(5.08, 23.68)
		Decrease		0 (0.0)	(0.00, 6.27)
		Interrupt		1 (1.8)	(0.04, 9.39)
	Week 44 <= to < Week 48		55		
		No change		46 (83.6)	(71.20, 92.23)
		Dose adjustment		9 (16.4)	(7.77, 28.80)
		Increase		3 (5.5)	(1.14, 15.12)
		Decrease		4 (7.3)	(2.02, 17.59)
		Interrupt		2 (3.6)	(0.44, 12.53)
	Week 48 <= to < Week 52		55		
		No change		48 (87.3)	(75.52, 94.73)
		Dose adjustment		7 (12.7)	(5.27, 24.48)
		Increase		4 (7.3)	(2.02, 17.59)
		Decrease		2 (3.6)	(0.44, 12.53)
		Interrupt		1 (1.8)	(0.05, 9.72)
	Baseline <= to < Week 52		80		
		No change		4 (5.0)	(1.38, 12.31)
		Dose adjustment		76 (95.0)	(87.69, 98.62)
		Increase		67 (83.8)	(73.82, 91.05)
		Decrease		37 (46.3)	(35.03, 57.76)
		Interrupt		15 (18.8)	(10.89, 29.03)

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 analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.3.1
Source: t_14_2_3_5_3.sas

5.3.5.1—8 表 11.4.1—2 より引用

(4)　貧血治療効果（改善維持効果）

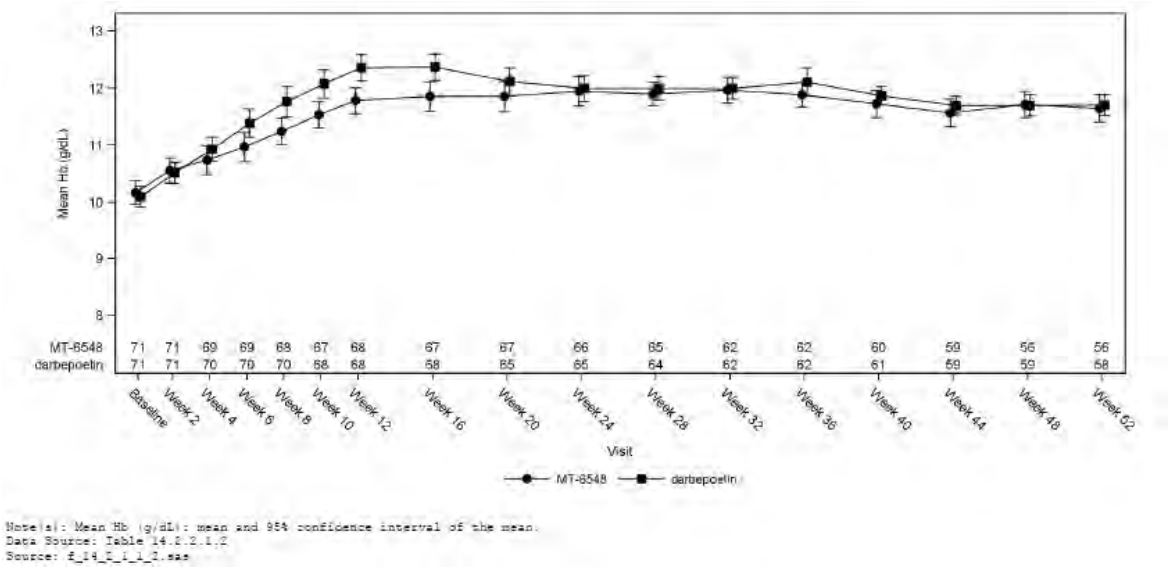
貧血治療効果（改善維持効果）は，特に明記しない限り Correction 集団を対象に記載した．

1)　Hb 値の推移

Hb 値の平均値の推移を図 2.7.6.25－52，Hb 値の記述統計量を表 2.7.6.25－128，MMRM を用いた Hb 値を表 2.7.6.25－129 に示した．

MT-6548 群の Hb 値の平均値は上昇し，8 週後に目標範囲内に到達後，52 週後まで目標範囲内を維持した．darbepoetin 群の Hb 値の平均値は上昇し，6 週後に目標範囲内に到達後，52 週後まで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 11.60 g/dL 及び 11.37～11.83 g/dL，darbepoetin 群で 11.63 g/dL 及び 11.41～11.86 g/dL であった．



Note(s): Mean Hb (g/dL): mean and 95% confidence interval of the mean.
Data Source: Table 14.2.2.1.2
Source: f_14_2_1_1_2.sas

図 2.7.6.25－52　Hb 値の推移（FAS）（Correction 集団）

5.3.5.1—8 図 11.4.1—8 より引用

表 2.7.6.25－128 各評価時点の Hb 値の記述統計量（FAS）（Correction 集団）

Treatment Group	Visit	Absolute N	Mean	SD	Median	Minimum, Maximum	95% CI	Change from Baseline N	Mean	SD	Median	Minimum, Maximum	95% CI	p value
MT-6548	Baseline	71	10.17	0.87	10.40	(7.6, 11.6)	(9.97, 10.38)							
	Week 2	71	10.56	0.92	10.60	(7.9, 12.4)	(10.35, 10.78)	71	0.39	0.61	0.40	(-1.0, 1.7)	(0.25, 0.54)	<0.001
	Week 4	69	10.74	1.03	10.90	(8.4, 13.1)	(10.49, 10.99)	69	0.57	0.82	0.50	(-2.1, 2.8)	(0.37, 0.77)	<0.001
	Week 6	69	10.97	1.08	10.90	(6.9, 12.8)	(10.71, 11.23)	69	0.80	1.04	0.70	(-3.4, 2.9)	(0.55, 1.05)	<0.001
	Week 8	68	11.25	0.96	11.30	(8.5, 13.2)	(11.01, 11.48)	68	1.08	0.89	1.05	(-1.1, 3.2)	(0.86, 1.29)	<0.001
	Week 10	67	11.53	0.95	11.60	(8.3, 13.3)	(11.30, 11.77)	67	1.37	0.97	1.30	(-1.3, 4.1)	(1.13, 1.61)	<0.001
	Week 12	68	11.78	0.92	11.90	(8.3, 13.7)	(11.56, 12.00)	68	1.61	1.10	1.55	(-1.3, 4.9)	(1.34, 1.88)	<0.001
	Week 16	67	11.85	1.05	11.90	(8.4, 14.1)	(11.60, 12.11)	67	1.67	1.15	1.60	(-0.8, 4.6)	(1.39, 1.95)	<0.001
	Week 20	67	11.85	1.10	11.90	(8.9, 14.6)	(11.59, 12.12)	67	1.67	1.23	1.40	(-1.1, 4.8)	(1.37, 1.97)	<0.001
	Week 24	66	11.95	1.06	12.10	(8.5, 14.1)	(11.69, 12.21)	66	1.73	1.20	1.75	(-1.1, 4.3)	(1.43, 2.02)	<0.001
	Week 28	65	11.90	0.83	12.10	(8.9, 13.4)	(11.70, 12.10)	65	1.67	1.13	1.60	(-0.7, 5.3)	(1.39, 1.95)	<0.001
	Week 32	62	11.96	0.88	12.00	(9.1, 13.9)	(11.74, 12.19)	62	1.72	1.26	1.50	(-0.7, 5.4)	(1.40, 2.04)	<0.001
	Week 36	62	11.88	0.84	12.10	(9.1, 13.5)	(11.67, 12.10)	62	1.64	1.15	1.50	(-0.5, 5.2)	(1.35, 1.93)	<0.001
	Week 40	60	11.72	0.92	11.70	(9.6, 14.2)	(11.48, 11.96)	60	1.47	1.19	1.30	(-1.1, 4.4)	(1.16, 1.78)	<0.001
	Week 44	59	11.67	0.93	11.70	(8.7, 13.4)	(11.32, 11.81)	59	1.32	1.15	1.30	(-1.5, 4.2)	(1.02, 1.61)	<0.001
	Week 48	56	11.72	0.86	11.80	(8.5, 13.6)	(11.49, 11.95)	56	1.48	1.16	1.40	(-1.1, 4.3)	(1.17, 1.79)	<0.001
	Week 52	56	11.65	0.89	11.75	(8.7, 13.5)	(11.41, 11.89)	56	1.41	1.17	1.30	(-0.9, 4.7)	(1.09, 1.72)	<0.001
	Week 52 (LOCF)	71	11.50	1.02	11.60	(8.1, 13.5)	(11.26, 11.74)	71	1.33	1.25	1.30	(-2.2, 4.7)	(1.03, 1.62)	<0.001

表 2.7.6.25－128　各評価時点の Hb 値の記述統計量（FAS）（Correction 集団）（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	71	10.10	0.77	10.30	(8.0, 11.5)	(9.91, 10.28)							
	Week 2	71	10.52	0.77	10.60	(8.3, 12.2)	(10.33, 10.70)	71	0.42	0.49	0.50	(-1.0, 1.4)	(0.30, 0.54)	<0.001
	Week 4	70	10.93	0.88	11.10	(7.7, 12.2)	(10.72, 11.14)	70	0.83	0.63	0.90	(-1.0, 1.9)	(0.68, 0.98)	<0.001
	Week 6	70	11.39	1.04	11.50	(7.6, 13.4)	(11.14, 11.64)	70	1.29	0.82	1.20	(-1.0, 3.5)	(1.09, 1.48)	<0.001
	Week 8	70	11.76	1.11	11.90	(7.0, 13.9)	(11.50, 12.03)	70	1.66	1.05	1.60	(-2.7, 4.3)	(1.41, 1.91)	<0.001
	Week 10	68	12.07	1.01	12.20	(8.2, 13.9)	(11.83, 12.32)	68	1.97	1.01	1.90	(-0.1, 4.8)	(1.72, 2.21)	<0.001
	Week 12	68	12.36	0.96	12.40	(10.0, 15.2)	(12.13, 12.59)	68	2.25	1.10	2.20	(-0.9, 5.1)	(1.99, 2.52)	<0.001
	Week 16	68	12.36	0.96	12.40	(9.5, 14.2)	(12.13, 12.60)	68	2.26	1.24	2.10	(-1.0, 5.1)	(1.96, 2.56)	<0.001
	Week 20	65	12.11	0.99	12.10	(9.0, 13.9)	(11.87, 12.36)	65	2.00	1.36	2.00	(-2.0, 5.9)	(1.66, 2.34)	<0.001
	Week 24	65	11.99	0.92	12.00	(9.6, 13.9)	(11.77, 12.22)	65	1.88	1.18	1.80	(-1.1, 5.2)	(1.59, 2.17)	<0.001
	Week 28	64	12.00	0.84	12.00	(9.7, 14.3)	(11.79, 12.21)	64	1.90	0.97	1.85	(-1.0, 4.2)	(1.66, 2.15)	<0.001
	Week 32	62	11.99	0.75	12.00	(9.6, 13.7)	(11.80, 12.18)	62	1.87	0.96	1.70	(0.1, 4.5)	(1.63, 2.11)	<0.001
	Week 36	62	12.11	1.00	12.10	(9.4, 14.7)	(11.86, 12.36)	62	1.99	1.06	1.90	(-0.2, 4.4)	(1.72, 2.25)	<0.001
	Week 40	61	11.87	0.62	11.90	(10.0, 13.4)	(11.71, 12.02)	61	1.73	0.77	1.60	(0.3, 3.8)	(1.53, 1.92)	<0.001
	Week 44	59	11.69	0.60	11.70	(9.9, 12.7)	(11.54, 11.85)	59	1.56	0.79	1.60	(-0.3, 4.1)	(1.36, 1.77)	<0.001
	Week 48	59	11.70	0.72	11.80	(9.7, 13.4)	(11.51, 11.89)	59	1.57	0.87	1.40	(-0.5, 3.9)	(1.34, 1.79)	<0.001
	Week 52	58	11.71	0.69	11.70	(9.9, 13.6)	(11.52, 11.89)	58	1.54	0.93	1.55	(-0.6, 4.0)	(1.30, 1.79)	<0.001
	Week 52 (LOCF)	71	11.55	1.08	11.60	(7.0, 14.6)	(11.29, 11.80)	71	1.45	1.20	1.40	(-2.7, 4.5)	(1.16, 1.73)	<0.001

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_2.sas

5.3.5.1—8 表 14.2.2.1.2 より引用

表 2.7.6.25－129　各評価時点の Hb 値（MMRM，FAS）（Correction 集団）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 2	71	10.17 (0.87)	10.56	0.11	(10.35, 10.77)	
	Week 4	69	10.17 (0.88)	10.74	0.11	(10.53, 10.95)	
	Week 6	69	10.17 (0.88)	10.97	0.11	(10.76, 11.18)	
	Week 8	68	10.17 (0.88)	11.24	0.11	(11.02, 11.45)	
	Week 10	67	10.16 (0.89)	11.52	0.11	(11.31, 11.74)	
	Week 12	68	10.17 (0.88)	11.77	0.11	(11.56, 11.98)	
	Week 16	67	10.19 (0.88)	11.84	0.11	(11.63, 12.05)	
	Week 20	67	10.19 (0.88)	11.84	0.11	(11.63, 12.06)	
	Week 24	66	10.22 (0.85)	11.94	0.11	(11.72, 12.15)	
	Week 28	65	10.23 (0.84)	11.87	0.11	(11.66, 12.09)	
	Week 32	62	10.24 (0.86)	11.93	0.11	(11.71, 12.15)	
	Week 36	62	10.24 (0.86)	11.84	0.11	(11.63, 12.06)	
	Week 40	60	10.25 (0.87)	11.70	0.11	(11.49, 11.92)	
	Week 44	59	10.25 (0.88)	11.55	0.11	(11.32, 11.77)	
	Week 48	56	10.24 (0.89)	11.70	0.12	(11.48, 11.93)	
	Week 52	56	10.24 (0.89)	11.60	0.12	(11.37, 11.83)	
darbepoetin	Week 2	71	10.10 (0.77)	10.54	0.11	(10.33, 10.75)	
	Week 4	70	10.10 (0.77)	10.95	0.11	(10.74, 11.16)	
	Week 6	70	10.10 (0.77)	11.41	0.11	(11.20, 11.62)	
	Week 8	70	10.10 (0.77)	11.78	0.11	(11.57, 11.99)	
	Week 10	68	10.10 (0.78)	12.07	0.11	(11.86, 12.28)	
	Week 12	68	10.11 (0.78)	12.36	0.11	(12.15, 12.57)	
	Week 16	68	10.11 (0.78)	12.37	0.11	(12.16, 12.58)	
	Week 20	65	10.11 (0.80)	12.10	0.11	(11.89, 12.32)	
	Week 24	65	10.11 (0.80)	11.98	0.11	(11.77, 12.20)	
	Week 28	64	10.10 (0.80)	11.98	0.11	(11.76, 12.19)	
	Week 32	62	10.12 (0.76)	11.94	0.11	(11.73, 12.16)	
	Week 36	62	10.12 (0.76)	12.06	0.11	(11.84, 12.28)	
	Week 40	61	10.14 (0.76)	11.82	0.11	(11.60, 12.04)	
	Week 44	59	10.13 (0.76)	11.65	0.11	(11.42, 11.87)	
	Week 48	59	10.13 (0.76)	11.65	0.11	(11.43, 11.87)	
	Week 52	58	10.16 (0.72)	11.63	0.11	(11.41, 11.86)	

表 2.7.6.25－129　各評価時点の Hb 値（MMRM，FAS）（Correction 集団）（続き）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
Difference MT-6548 - darbepoetin	Week 2			0.02	0.15	(-0.27, 0.31)	0.889
	Week 4			-0.21	0.15	(-0.51, 0.09)	0.165
	Week 6			-0.44	0.15	(-0.74, -0.14)	0.004
	Week 8			-0.55	0.15	(-0.84, -0.25)	<0.001
	Week 10			-0.55	0.15	(-0.85, -0.25)	<0.001
	Week 12			-0.59	0.15	(-0.88, -0.29)	<0.001
	Week 16			-0.53	0.15	(-0.83, -0.23)	<0.001
	Week 20			-0.26	0.15	(-0.56, 0.04)	0.092
	Week 24			-0.05	0.15	(-0.35, 0.26)	0.762
	Week 28			-0.10	0.16	(-0.41, 0.20)	0.505
	Week 32			-0.02	0.16	(-0.33, 0.29)	0.910
	Week 36			-0.22	0.16	(-0.53, 0.09)	0.171
	Week 40			-0.12	0.16	(-0.43, 0.20)	0.467
	Week 44			-0.10	0.16	(-0.42, 0.21)	0.530
	Week 48			0.05	0.16	(-0.27, 0.37)	0.742
	Week 52			-0.03	0.16	(-0.35, 0.29)	0.835

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): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_2_2.sas

5.3.5.1—8 表 14.2.2.2.2 より引用

2)　48 週及び 52 週後の平均 Hb 変化量

MMRM を用いた 48 週及び 52 週後の平均 Hb 値のベースラインからの変化量を表 2.7.6.25－130 に示した.

MMRM を用いた 48 週及び 52 週後の平均 Hb 値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 1.48 g/dL 及び 1.30～1.67 g/dL，darbepoetin 群で 1.52 g/dL 及び 1.34～1.70 g/dL であった.

表 2.7.6.25－130　48 週及び 52 週後の平均 Hb 値の変化量（MMRM，FAS）（Correction 集団）

Treatment Group	Visit	N	Mean at Baseline (SD)	LSMean	SE	95% CI	p value
MT-6548	Week 48 and Week 52	71	10.17 (0.87)	1.48	0.09	(1.30, 1.67)	
darbepoetin	Week 48 and Week 52	71	10.10 (0.77)	1.52	0.09	(1.34, 1.70)	
Difference MT-6548 - darbepoetin	Week 48 and Week 52			0.01	0.13	(-0.24, 0.26)	0.940

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.
Note(s): p value is analyzed by MMRM model.
Data Source: Listing 16.2.4.1
Source: t_14_2_3_1_2_1.sas

5.3.5.1―8 表 11.4.1－3 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 2.7.6.25－53，darbepoetin 群を図 2.7.6.25－54 に示した．また，Hb 値が目標範囲内の被験者割合を表 2.7.6.25－131 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 15.5%であり，24 週後は 69.7%，52 週後は 71.4%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 9.9%であり，24 週後は 72.3%，52 週後は 84.5%であった．

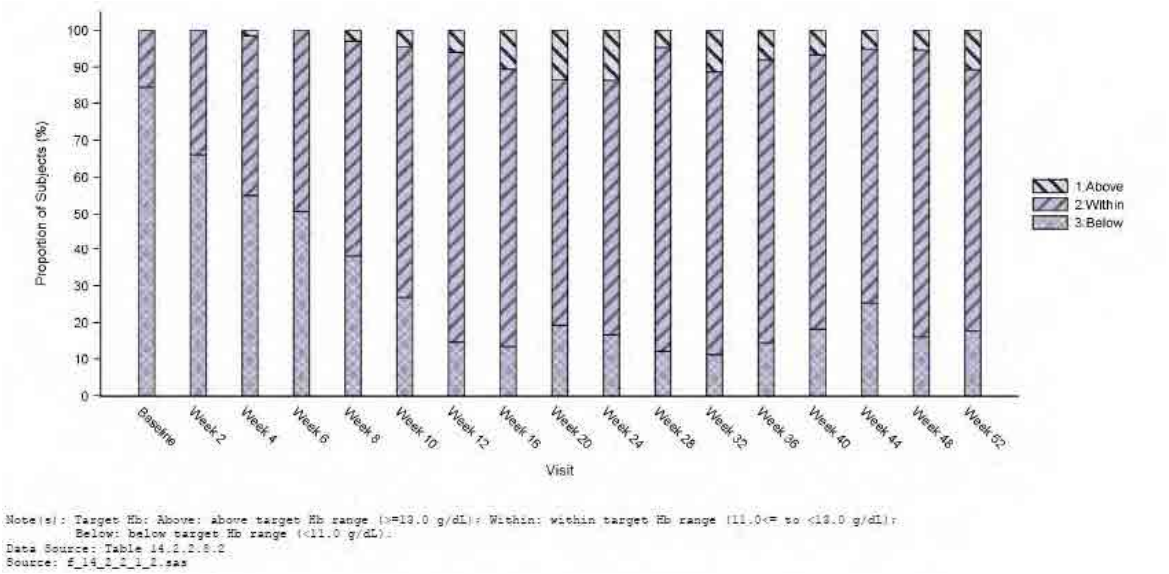


図 2.7.6.25－53　MT-6548 群の Hb 値が目標範囲内の被験者割合（FAS）（Correction 集団）

5.3.5.1—8 図 11.4.1—9 より引用

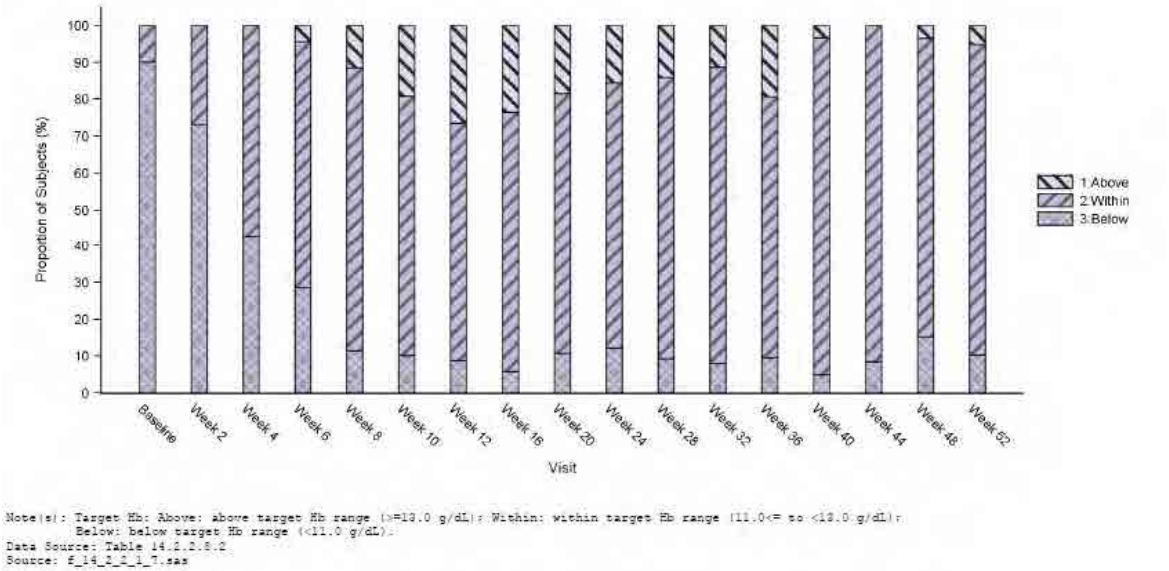


図 2.7.6.25－54　darbepoetin 群の Hb 値が目標範囲内の被験者割合（FAS）（Correction 集団）

5.3.5.1—8 図 11.4.1—10 より引用

表 2.7.6.25－131　Hb 値が目標範囲内の被験者割合（FAS）（Correction 集団）

		MT-6548(N=71)				darbepoetin(N=71)				Difference of proportion (MT-6548 - darbepoetin)		
Visit	Target Hb Range	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		71				71						
	Above		0 (0.0)	(0.00, 5.06)			0 (0.0)	(0.00, 5.06)		-	-	-
	Within		11 (15.5)	(8.00, 26.03)			7 (9.9)	(4.06, 19.26)		5.6	(-11.5, 22.5)	0.450
	Below		60 (84.5)	(73.97, 92.00)			64 (90.1)	(80.74, 95.94)		-5.6	(-22.5, 11.5)	0.450
Week 2		71				71						
	Above		0 (0.0)	(0.00, 5.06)			0 (0.0)	(0.00, 5.06)		-	-	-
	Within		24 (33.8)	(23.00, 46.01)	<0.001		19 (26.8)	(16.94, 38.59)	0.011	7.0	(-10.1, 23.9)	0.465
	Below		47 (66.2)	(53.99, 77.00)			52 (73.2)	(61.41, 83.06)		-7.0	(-23.9, 10.1)	0.465
Week 4		69				70						
	Above		1 (1.4)	(0.04, 7.81)			0 (0.0)	(0.00, 5.13)		1.4	(-15.1, 17.9)	0.496
	Within		30 (43.5)	(31.58, 55.96)	<0.001		40 (57.1)	(44.75, 68.91)	<0.001	-13.7	(-30.1, 3.4)	0.128
	Below		38 (55.1)	(42.62, 67.08)			30 (42.9)	(31.09, 55.25)		12.2	(-4.9, 28.7)	0.176
Week 6		69				70						
	Above		0 (0.0)	(0.00, 5.21)			3 (4.3)	(0.89, 12.02)		-4.3	(-20.7, 12.3)	0.245
	Within		34 (49.3)	(37.02, 61.59)	<0.001		47 (67.1)	(54.88, 77.91)	<0.001	-17.9	(-33.8, -0.7)	0.040
	Below		35 (50.7)	(38.41, 62.98)			20 (28.6)	(18.40, 40.62)		22.2	(5.0, 37.7)	0.009
Week 8		68				70						
	Above		2 (2.9)	(0.36, 10.22)			8 (11.4)	(5.07, 21.28)		-8.5	(-24.9, 8.6)	0.097
	Within		40 (58.8)	(46.23, 70.63)	<0.001		54 (77.1)	(65.55, 86.33)	<0.001	-18.3	(-34.1, -1.4)	0.028
	Below		26 (38.2)	(26.71, 50.82)			8 (11.4)	(5.07, 21.28)		26.8	(10.3, 42.3)	<0.001
Week 10		67				68						
	Above		3 (4.5)	(0.93, 12.53)			13 (19.1)	(10.59, 30.47)		-14.6	(-31.1, 2.1)	0.014
	Within		46 (68.7)	(56.16, 79.44)	<0.001		48 (70.6)	(58.29, 81.02)	<0.001	-1.9	(-18.2, 15.3)	0.853
	Below		18 (26.9)	(16.76, 39.10)			7 (10.3)	(4.24, 20.07)		16.6	(-0.6, 32.5)	0.015

表 2.7.6.25－131　Hb 値が目標範囲内の被験者割合（FAS）（Correction 集団）（続き）

Visit	Target Hb Range	MT-6548 (N=71) N*	MT-6548 (N=71) n (%)	MT-6548 (N=71) 95% CI of proportion	MT-6548 (N=71) p value from B	darbepoetin (N=71) N*	darbepoetin (N=71) n (%)	darbepoetin (N=71) 95% CI of proportion	darbepoetin (N=71) p value from B	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Week 12		68				68						
	Above		4 (5.9)	(1.63, 14.39)			18 (26.5)	(16.50, 38.57)		-20.6	(-37.2, -3.1)	0.002
	Within		54 (79.4)	(67.88, 88.26)	<0.001		44 (64.7)	(52.17, 75.92)	<0.001	14.7	(-2.8, 31.6)	0.085
	Below		10 (14.7)	(7.29, 25.39)			6 (8.8)	(3.31, 18.22)		5.9	(-11.6, 23.1)	0.426
Week 16		67				68						
	Above		7 (10.4)	(4.30, 20.35)			16 (23.5)	(14.09, 35.38)		-13.1	(-29.6, 3.5)	0.066
	Within		51 (76.1)	(64.14, 85.69)	<0.001		48 (70.6)	(58.29, 81.02)	<0.001	5.5	(-10.9, 22.5)	0.560
	Below		9 (13.4)	(6.33, 23.97)			4 (5.9)	(1.63, 14.38)		7.6	(-9.4, 23.9)	0.156
Week 20		67				65						
	Above		9 (13.4)	(6.33, 23.97)			12 (18.5)	(9.92, 30.03)		-5.0	(-22.1, 11.8)	0.482
	Within		45 (67.2)	(54.60, 78.15)	<0.001		46 (70.8)	(58.17, 81.40)	<0.001	-3.6	(-20.7, 13.3)	0.709
	Below		13 (19.4)	(10.76, 30.89)			7 (10.8)	(4.44, 20.94)		8.6	(-8.8, 25.1)	0.226
Week 24		66				65						
	Above		9 (13.6)	(6.43, 24.31)			10 (15.4)	(7.63, 26.48)		-1.7	(-18.5, 15.5)	0.809
	Within		46 (69.7)	(57.15, 80.41)	<0.001		47 (72.3)	(59.81, 82.69)	<0.001	-2.6	(-20.0, 14.0)	0.848
	Below		11 (16.7)	(8.62, 27.87)			8 (12.3)	(5.47, 22.82)		4.4	(-12.5, 21.4)	0.621
Week 28		65				64						
	Above		3 (4.6)	(0.96, 12.90)			9 (14.1)	(6.64, 25.02)		-9.4	(-26.1, 7.9)	0.076
	Within		54 (83.1)	(71.73, 91.24)	<0.001		49 (76.6)	(64.31, 86.25)	<0.001	6.5	(-11.0, 23.1)	0.387
	Below		8 (12.3)	(5.47, 22.82)			6 (9.4)	(3.52, 19.30)		2.9	(-14.1, 20.1)	0.778
Week 32		62				62						
	Above		7 (11.3)	(4.66, 21.89)			7 (11.3)	(4.66, 21.89)		0.0	(-18.2, 18.2)	1.000
	Within		48 (77.4)	(65.03, 87.07)	<0.001		50 (80.6)	(68.63, 89.58)	<0.001	-3.2	(-21.4, 15.1)	0.826
	Below		7 (11.3)	(4.66, 21.89)			5 (8.1)	(2.67, 17.83)		3.2	(-15.1, 21.4)	0.763

表 2.7.6.25－131　Hb 値が目標範囲内の被験者割合（FAS）（Correction 集団）（続き）

Visit	Target Hb Range	MT-6548 (N=71) N*	MT-6548 (N=71) n (%)	MT-6548 (N=71) 95% CI of proportion	MT-6548 (N=71) p value from B	darbepoetin (N=71) N*	darbepoetin (N=71) n (%)	darbepoetin (N=71) 95% CI of proportion	darbepoetin (N=71) p value from B	Difference of proportion (MT-6548 - darbepoetin) Difference	95% CI	p value
Week 36		62				62						
	Above		5 (8.1)	(2.67, 17.83)			12 (19.4)	(10.42, 31.37)		-11.3	(-29.1, 7.1)	0.115
	Within		48 (77.4)	(65.03, 87.07)	<0.001		44 (71.0)	(58.05, 81.80)	<0.001	6.5	(-11.9, 24.5)	0.539
	Below		9 (14.5)	(6.86, 25.78)			6 (9.7)	(3.63, 19.88)		4.8	(-13.5, 22.9)	0.583
Week 40		60				61						
	Above		4 (6.7)	(1.85, 16.20)			2 (3.3)	(0.40, 11.35)		3.4	(-14.4, 20.9)	0.439
	Within		45 (75.0)	(62.14, 85.28)	<0.001		56 (91.8)	(81.90, 97.28)	<0.001	-16.8	(-33.6, 1.3)	0.015
	Below		11 (18.3)	(9.52, 30.44)			3 (4.9)	(1.03, 13.71)		13.4	(-4.6, 30.4)	0.025
Week 44		59				59						
	Above		3 (5.1)	(1.06, 14.15)			0 (0.0)	(0.00, 6.06)		5.1	(-13.7, 23.6)	0.244
	Within		41 (69.5)	(56.13, 80.81)	<0.001		54 (91.5)	(81.32, 97.19)	<0.001	-22.0	(-39.7, -3.2)	0.005
	Below		15 (25.4)	(14.98, 38.44)			5 (8.5)	(2.81, 18.68)		16.9	(-1.9, 34.9)	0.025
Week 48		56				59						
	Above		3 (5.4)	(1.12, 14.87)			2 (3.4)	(0.41, 11.71)		2.0	(-16.5, 20.0)	0.674
	Within		44 (78.6)	(65.56, 88.41)	<0.001		48 (81.4)	(69.09, 90.31)	<0.001	-2.8	(-21.2, 15.6)	0.817
	Below		9 (16.1)	(7.62, 28.33)			9 (15.3)	(7.22, 26.99)		0.8	(-17.6, 19.1)	1.000
Week 52		56				58						
	Above		6 (10.7)	(4.03, 21.88)			3 (5.2)	(1.08, 14.38)		5.5	(-12.8, 24.1)	0.317
	Within		40 (71.4)	(57.79, 82.70)	<0.001		49 (84.5)	(72.58, 92.65)	<0.001	-13.1	(-30.9, 5.3)	0.115
	Below		10 (17.9)	(8.91, 30.40)			6 (10.3)	(3.89, 21.17)		7.5	(-10.5, 25.9)	0.289

Note(s): Target Hb: Above: above target Hb range (>=13.0 g/dL); Within: within target Hb range (11.0<= to <13.0 g/dL);
Below: below target Hb range (<11.0 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): 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 to comparer proportion of subjects in target range (Within) and proportion of subjects out of target range (Above + Below).
Note(s): p value of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_8_2.sas

5.3.5.1—8 表 14.2.2.8.2 より引用

4)　Hb 値が 1.0 g/dL 以上上昇した被験者の割合

Hb 値がベースラインより 1.0 g/dL 以上上昇した被験者の割合を表 2.7.6.25－132 に示した.

Hb 値がベースラインより 1.0 g/dL 以上上昇した被験者の割合は，MT-6548 群において 24 週後で 74.2%，52 週後で 64.3%，darbepoetin 群において 24 週後で 83.1%，52 週後で 79.3%であった.

表 2.7.6.25－132　Hb 値が 1.0 g/dL 以上上昇した被験者の割合（FAS）（Correction 集団）

	MT-6548(N=71)			darbepoetin(N=71)			Difference of proportion (MT-6548 - darbepoetin)		
Visit	N*	n (%)	95% CI of proportion	N*	n (%)	95% CI of proportion	Difference	95% CI	p value
Week 2	71	16 (22.5)	(13.46, 34.00)	71	7 (9.9)	(4.06, 19.26)	12.7	(-4.5, 29.3)	0.067
Week 4	69	20 (29.0)	(18.69, 41.16)	70	34 (48.6)	(36.44, 60.83)	-19.6	(-35.9, -3.3)	0.024
Week 6	69	28 (40.6)	(28.91, 53.08)	70	53 (75.7)	(63.99, 85.17)	-35.1	(-50.0, -18.4)	<0.001
Week 8	68	37 (54.4)	(41.88, 66.55)	70	55 (78.6)	(67.13, 87.48)	-24.2	(-39.5, -7.3)	0.004
Week 10	67	43 (64.2)	(51.53, 75.53)	68	56 (82.4)	(71.20, 90.53)	-18.2	(-33.9, -0.9)	0.020
Week 12	68	51 (75.0)	(63.02, 84.71)	68	61 (89.7)	(79.93, 95.76)	-14.7	(-31.6, 2.8)	0.041
Week 16	67	50 (74.6)	(62.51, 84.47)	68	60 (88.2)	(78.13, 94.78)	-13.6	(-29.6, 3.5)	0.048
Week 20	67	49 (73.1)	(60.90, 83.24)	65	52 (80.0)	(68.23, 88.90)	-6.9	(-23.6, 10.3)	0.414
Week 24	66	49 (74.2)	(61.99, 84.22)	65	54 (83.1)	(71.73, 91.24)	-8.8	(-25.9, 8.0)	0.287
Week 28	65	51 (78.5)	(66.51, 87.69)	64	55 (85.9)	(74.98, 93.36)	-7.5	(-24.6, 9.5)	0.358
Week 32	62	44 (71.0)	(58.05, 81.80)	62	53 (85.5)	(74.22, 93.14)	-14.5	(-32.2, 3.9)	0.081
Week 36	62	44 (71.0)	(58.05, 81.80)	62	54 (87.1)	(76.15, 94.26)	-16.1	(-33.7, 2.3)	0.046
Week 40	60	39 (65.0)	(51.60, 76.87)	61	53 (86.9)	(75.78, 94.16)	-21.9	(-38.2, -3.7)	0.006
Week 44	59	36 (61.0)	(47.44, 73.45)	59	48 (81.4)	(69.09, 90.31)	-20.3	(-38.1, -1.5)	0.025
Week 48	56	37 (66.1)	(52.19, 78.19)	59	45 (76.3)	(63.41, 86.38)	-10.2	(-28.2, 8.0)	0.303
Week 52	56	36 (64.3)	(50.36, 76.64)	58	46 (79.3)	(66.65, 88.83)	-15.0	(-32.6, 3.5)	0.096

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 of difference of proportion (MT-6548 - darbepoetin) is analyzed by Fisher's exact test.
Data Source: Listing 16.2.4.1
Source: t_14_2_3_2_1.sas

5.3.5.1—8 表 11.4.1－4 より引用

5)　Hb 値が目標範囲内に到達するまでに要したベースラインからの日数

Hb 値が目標範囲内に到達するまでに要したベースラインからの日数の記述統計量を表 2.7.6.25－133 に示した.

Hb 値が目標範囲内に到達するまでに要したベースラインからの日数の中央値は, MT-6548 群では 43.0 日，darbepoetin 群では 29.0 日であった.

表 2.7.6.25－133　Hb 値が目標範囲内に到達するまでの日数（FAS）（Correction 集団）

Treatment Group	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	60	60.5	59.5	43.0	(12, 361)	(45.2, 75.9)
darbepoetin	64	40.8	32.8	29.0	(14, 225)	(32.6, 49.0)

Note(s): Time (days).
Note(s): Subjects whose Hb is 11.0 g/dL or more at baseline were excluded from the analysis.
Data Source: Listing 16.2.4.1
Source: t_14_2_2_9_1.sas

5.3.5.1—8 表 11.4.1－5 より引用

6)　治験薬の投与量

規定来院間の治験薬の 1 日平均投与量の推移について, MT-6548 群を図 2.7.6.25－55, その記述統計量を表 2.7.6.25－134 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 2.7.6.25－56，治験薬の投与量の分布を表 2.7.6.25－135 に示した．

MT-6548 は, 300 mg/日で投与を開始し, 1 日平均投与量の平均値及びその 95%CI は, 20 週～24 週後で 336.76 mg/日及び 289.79～383.74 mg/日，48 週～52 週後で 335.65 mg/日及び 286.72～384.58 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 週後で 15.08 μg/週及び 15.01～15.14 μg/週，20 週～24 週後で 17.92 μg/週及び 13.70～22.14 μg/週，48 週～52 週後で 16.37 μg/週及び 13.09～19.65 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 4.5%，32.8%，23.9%，11.9%及び 26.9%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 1.8%，35.1%，24.6%，14.0%及び 24.6%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 7.7%，78.5%，10.8%，3.1%，0%及び 0%であった．また，ダルベポエチンアルファ注の 48 週後の 1 日投与量の分布は，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 3.4%，84.5%，12.1%，0%，0%及び 0%であった．

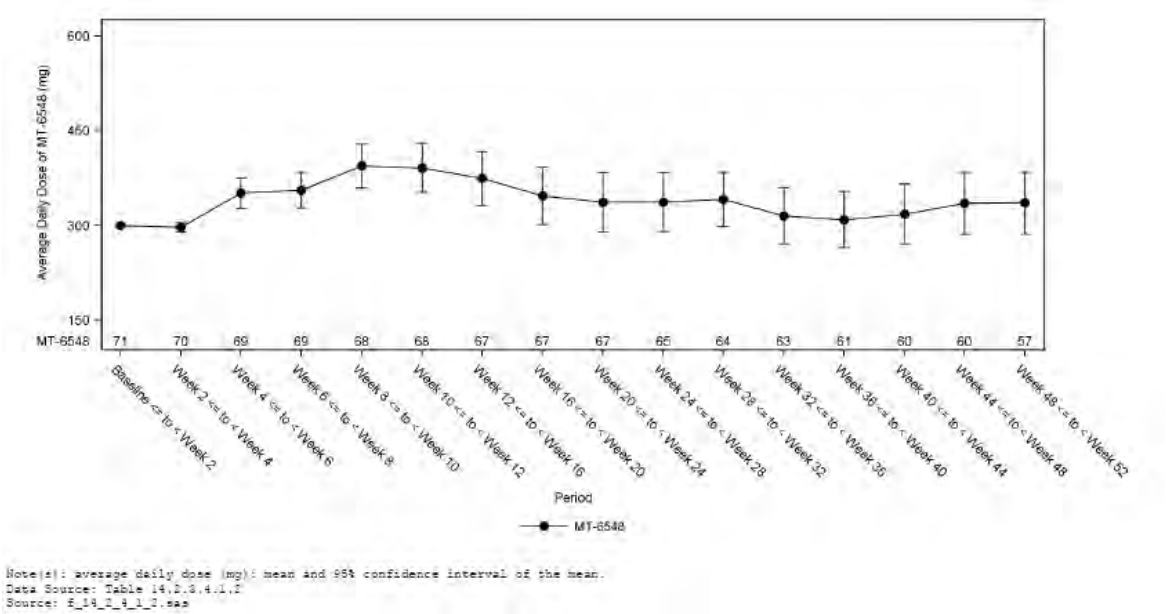


図 2.7.6.25－55　MT-6548 の 1 日平均投与量の推移（FAS）（Correction 集団）

5.3.5.1—8 図 11.4.1—11 より引用

表 2.7.6.25－134　治験薬の平均投与量の記述統計量（FAS）（Correction 集団）

Treatment Group	Period	N	Mean	SD	Median	Minimum, Maximum	95% CI
MT-6548	Baseline <= to < Week 2	71	300.00	0.00	300.00	(300.0, 300.0)	(-, -)
	Week 2 <= to < Week 4	70	297.24	31.53	300.00	(42.9, 332.1)	(289.73, 304.76)
	Week 4 <= to < Week 6	69	351.24	100.07	300.00	(21.4, 450.0)	(327.20, 375.28)
	Week 6 <= to < Week 8	69	356.21	117.55	439.29	(0.0, 589.3)	(327.97, 384.45)
	Week 8 <= to < Week 10	68	394.22	142.53	450.00	(0.0, 600.0)	(359.72, 428.72)
	Week 10 <= to < Week 12	68	391.39	163.70	450.00	(0.0, 600.0)	(351.76, 431.01)
	Week 12 <= to < Week 16	67	374.28	175.95	300.00	(0.0, 600.0)	(331.36, 417.20)
	Week 16 <= to < Week 20	67	346.93	187.07	300.00	(0.0, 600.0)	(301.81, 392.06)
	Week 20 <= to < Week 24	67	336.76	192.57	300.00	(0.0, 600.0)	(289.79, 383.74)
	Week 24 <= to < Week 28	65	337.09	187.59	300.00	(5.4, 600.0)	(290.61, 383.57)
	Week 28 <= to < Week 32	64	341.35	172.22	300.00	(144.6, 600.0)	(298.33, 384.37)
	Week 32 <= to < Week 36	63	315.56	176.69	300.00	(21.4, 600.0)	(271.06, 360.06)
	Week 36 <= to < Week 40	61	309.22	175.07	300.00	(10.7, 600.0)	(264.38, 354.06)
	Week 40 <= to < Week 44	60	318.12	182.81	300.00	(0.0, 600.0)	(270.90, 365.35)
	Week 44 <= to < Week 48	60	334.73	186.76	300.00	(0.0, 600.0)	(286.49, 382.98)
	Week 48 <= to < Week 52	57	335.65	184.41	300.00	(28.6, 600.0)	(286.72, 384.58)
darbepoetin	Baseline <= to < Week 2	71	15.08	0.28	15.00	(15.0, 16.1)	(15.01, 15.14)
	Week 2 <= to < Week 4	71	24.86	7.51	30.00	(1.1, 33.2)	(23.08, 26.64)
	Week 4 <= to < Week 6	70	29.80	13.11	30.00	(0.0, 46.1)	(26.68, 32.93)
	Week 6 <= to < Week 8	70	33.24	17.66	30.00	(5.9, 60.0)	(29.03, 37.45)
	Week 8 <= to < Week 10	70	35.11	26.85	30.00	(0.0, 90.0)	(28.70, 41.51)
	Week 10 <= to < Week 12	69	29.78	27.74	16.07	(0.0, 90.0)	(23.12, 36.45)
	Week 12 <= to < Week 16	69	25.83	30.26	15.00	(0.0, 150.0)	(18.56, 33.10)
	Week 16 <= to < Week 20	67	19.09	21.85	7.50	(0.0, 90.0)	(13.76, 24.42)
	Week 20 <= to < Week 24	65	17.92	17.04	10.98	(0.0, 77.1)	(13.70, 22.14)
	Week 24 <= to < Week 28	65	17.91	15.45	15.00	(0.0, 90.0)	(14.08, 21.74)
	Week 28 <= to < Week 32	64	16.44	13.80	15.00	(0.0, 63.8)	(12.99, 19.88)
	Week 32 <= to < Week 36	62	16.17	14.22	15.00	(0.0, 92.5)	(12.56, 19.79)
	Week 36 <= to < Week 40	62	15.08	13.60	15.00	(0.0, 60.0)	(11.62, 18.53)
	Week 40 <= to < Week 44	61	16.12	13.44	15.00	(0.5, 54.6)	(12.68, 19.56)
	Week 44 <= to < Week 48	59	16.08	12.61	15.00	(3.8, 45.0)	(12.79, 19.36)
	Week 48 <= to < Week 52	58	16.37	12.47	15.00	(3.5, 48.0)	(13.09, 19.65)

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_4_1_2.sas

5.3.5.1—8 表 14.2.3.4.1.2 より引用

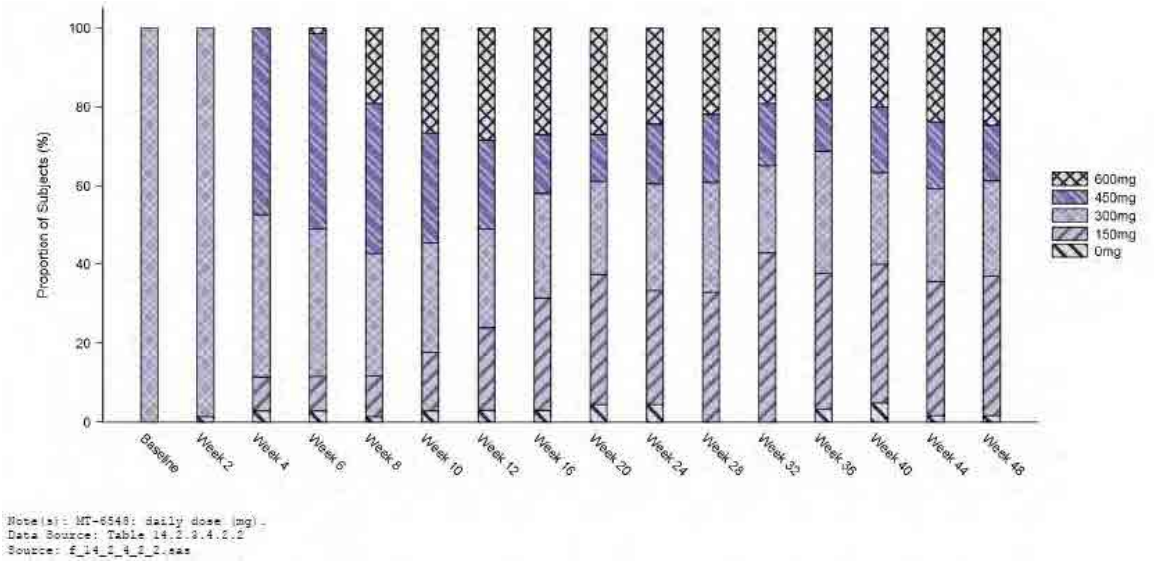


図 2.7.6.25－56　MT-6548 錠の 1 日投与量の分布（FAS）（Correction 集団）

5.3.5.1—8 図 11.4.1—12 より引用

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
MT-6548	Baseline		71		
		0mg		0 (0.0)	(0.00, 5.06)
		150mg		0 (0.0)	(0.00, 5.06)
		300mg		71 (100.0)	(94.94, 100.00)
		450mg		0 (0.0)	(0.00, 5.06)
		600mg		0 (0.0)	(0.00, 5.06)
	Week 2		70		
		0mg		1 (1.4)	(0.04, 7.70)
		150mg		0 (0.0)	(0.00, 5.13)
		300mg		69 (98.6)	(92.30, 99.96)
		450mg		0 (0.0)	(0.00, 5.13)
		600mg		0 (0.0)	(0.00, 5.13)
	Week 4		70		
		0mg		2 (2.9)	(0.35, 9.94)
		150mg		6 (8.6)	(3.21, 17.73)
		300mg		29 (41.4)	(29.77, 53.83)
		450mg		33 (47.1)	(35.09, 59.45)
		600mg		0 (0.0)	(0.00, 5.13)
	Week 6		69		
		0mg		2 (2.9)	(0.35, 10.09)
		150mg		6 (8.7)	(3.26, 17.97)
		300mg		26 (37.7)	(26.29, 50.17)
		450mg		34 (49.3)	(37.02, 61.59)
		600mg		1 (1.4)	(0.04, 7.81)
	Week 8		68		
		0mg		1 (1.5)	(0.04, 7.92)
		150mg		7 (10.3)	(4.24, 20.07)
		300mg		21 (30.9)	(20.24, 43.26)
		450mg		26 (38.2)	(26.71, 50.82)
		600mg		13 (19.1)	(10.59, 30.47)
	Week 10		68		
		0mg		2 (2.9)	(0.36, 10.22)
		150mg		10 (14.7)	(7.28, 25.39)
		300mg		19 (27.9)	(17.73, 40.15)
		450mg		19 (27.9)	(17.73, 40.15)
		600mg		18 (26.5)	(16.50, 38.97)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 12		67		
		0mg		2 (3.0)	(0.36, 10.37)
		150mg		14 (20.9)	(11.92, 32.57)
		300mg		17 (25.4)	(15.53, 37.49)
		450mg		15 (22.4)	(13.11, 34.22)
		600mg		19 (28.4)	(18.01, 40.69)
	Week 16		67		
		0mg		2 (3.0)	(0.36, 10.37)
		150mg		19 (28.4)	(18.01, 40.69)
		300mg		18 (26.9)	(16.76, 39.10)
		450mg		10 (14.9)	(7.40, 25.74)
		600mg		18 (26.9)	(16.76, 39.10)
	Week 20		67		
		0mg		3 (4.5)	(0.93, 12.63)
		150mg		22 (32.8)	(21.85, 45.40)
		300mg		16 (23.9)	(14.31, 35.86)
		450mg		8 (11.9)	(5.30, 22.18)
		600mg		18 (26.9)	(16.76, 39.10)
	Week 24		66		
		0mg		3 (4.5)	(0.95, 12.71)
		150mg		19 (28.8)	(18.30, 41.25)
		300mg		18 (27.3)	(17.03, 39.64)
		450mg		10 (15.2)	(7.51, 26.10)
		600mg		16 (24.2)	(14.54, 36.36)
	Week 28		64		
		0mg		0 (0.0)	(0.00, 5.60)
		150mg		21 (32.8)	(21.59, 45.69)
		300mg		18 (28.1)	(17.60, 40.76)
		450mg		11 (17.2)	(8.90, 28.69)
		600mg		14 (21.9)	(12.51, 33.97)
	Week 32		63		
		0mg		0 (0.0)	(0.00, 5.69)
		150mg		27 (42.9)	(30.46, 55.95)
		300mg		14 (22.2)	(12.72, 34.46)
		450mg		10 (15.9)	(7.68, 27.26)
		600mg		12 (19.0)	(10.25, 30.91)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 36		61		
		0mg		2 (3.3)	(0.40, 11.35)
		150mg		21 (34.4)	(22.73, 47.69)
		300mg		19 (31.1)	(19.90, 44.29)
		450mg		8 (13.1)	(5.84, 24.22)
		600mg		11 (18.0)	(9.36, 29.98)
	Week 40		60		
		0mg		3 (5.0)	(1.04, 13.92)
		150mg		21 (35.0)	(23.13, 48.40)
		300mg		14 (23.3)	(13.38, 36.04)
		450mg		10 (16.7)	(8.29, 28.92)
		600mg		12 (20.0)	(10.78, 32.33)
	Week 44		59		
		0mg		1 (1.7)	(0.04, 9.09)
		150mg		20 (33.9)	(22.08, 47.39)
		300mg		14 (23.7)	(13.62, 36.55)
		450mg		10 (16.9)	(8.44, 28.97)
		600mg		14 (23.7)	(13.62, 36.55)
	Week 48		57		
		0mg		1 (1.8)	(0.04, 9.39)
		150mg		20 (35.1)	(22.91, 48.67)
		300mg		14 (24.6)	(14.13, 37.76)
		450mg		8 (14.0)	(6.26, 25.79)
		600mg		14 (24.6)	(14.13, 37.76)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
darbepoetin	Baseline		71		
		0ug		0 (0.0)	(0.00, 5.06)
		0ug < to <= 30ug		71 (100.0)	(94.94, 100.00)
		30ug < to <= 60ug		0 (0.0)	(0.00, 5.06)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.06)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.06)
		> 120ug		0 (0.0)	(0.00, 5.06)
	Week 2		71		
		0ug		1 (1.4)	(0.04, 7.60)
		0ug < to <= 30ug		70 (98.6)	(92.40, 99.96)
		30ug < to <= 60ug		0 (0.0)	(0.00, 5.06)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.06)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.06)
		> 120ug		0 (0.0)	(0.00, 5.06)
	Week 4		70		
		0ug		2 (2.9)	(0.35, 9.94)
		0ug < to <= 30ug		43 (61.4)	(49.03, 72.83)
		30ug < to <= 60ug		25 (35.7)	(24.61, 48.07)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.13)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.13)
		> 120ug		0 (0.0)	(0.00, 5.13)
	Week 6		70		
		0ug		0 (0.0)	(0.00, 5.13)
		0ug < to <= 30ug		43 (61.4)	(49.03, 72.83)
		30ug < to <= 60ug		27 (38.6)	(27.17, 50.97)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.13)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.13)
		> 120ug		0 (0.0)	(0.00, 5.13)
	Week 8		70		
		0ug		3 (4.3)	(0.89, 12.02)
		0ug < to <= 30ug		42 (60.0)	(47.59, 71.53)
		30ug < to <= 60ug		15 (21.4)	(12.52, 32.87)
		60ug < to <= 90ug		10 (14.3)	(7.07, 24.71)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.13)
		> 120ug		0 (0.0)	(0.00, 5.13)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 10		69		
		0ug		7 (10.1)	(4.18, 19.79)
		0ug < to <= 30ug		45 (65.2)	(52.79, 76.29)
		30ug < to <= 60ug		8 (11.6)	(5.14, 21.57)
		60ug < to <= 90ug		9 (13.0)	(6.14, 23.32)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.21)
		> 120ug		0 (0.0)	(0.00, 5.21)
	Week 12		69		
		0ug		12 (17.4)	(9.32, 28.41)
		0ug < to <= 30ug		41 (59.4)	(46.92, 71.09)
		30ug < to <= 60ug		8 (11.6)	(5.14, 21.57)
		60ug < to <= 90ug		7 (10.1)	(4.18, 19.79)
		90ug < to <= 120ug		1 (1.4)	(0.04, 7.81)
		> 120ug		0 (0.0)	(0.00, 5.21)
	Week 16		67		
		0ug		14 (20.9)	(11.92, 32.57)
		0ug < to <= 30ug		41 (61.2)	(48.50, 72.96)
		30ug < to <= 60ug		8 (11.9)	(5.30, 22.18)
		60ug < to <= 90ug		3 (4.5)	(0.93, 12.53)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.36)
		> 120ug		1 (1.5)	(0.04, 8.04)
	Week 20		65		
		0ug		5 (7.7)	(2.54, 17.05)
		0ug < to <= 30ug		51 (78.5)	(66.51, 87.69)
		30ug < to <= 60ug		7 (10.8)	(4.44, 20.94)
		60ug < to <= 90ug		2 (3.1)	(0.37, 10.68)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.52)
		> 120ug		0 (0.0)	(0.00, 5.52)
	Week 24		64		
		0ug		4 (6.3)	(1.73, 15.24)
		0ug < to <= 30ug		54 (84.4)	(73.14, 92.24)
		30ug < to <= 60ug		5 (7.8)	(2.59, 17.30)
		60ug < to <= 90ug		1 (1.6)	(0.04, 8.40)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.60)
		> 120ug		0 (0.0)	(0.00, 5.60)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 28		63		
		0ug		3 (4.8)	(0.99, 13.29)
		0ug < to <= 30ug		52 (82.5)	(70.90, 90.95)
		30ug < to <= 60ug		8 (12.7)	(5.65, 23.50)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.69)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.69)
		> 120ug		0 (0.0)	(0.00, 5.69)
	Week 32		61		
		0ug		1 (1.6)	(0.04, 8.80)
		0ug < to <= 30ug		55 (90.2)	(79.81, 96.30)
		30ug < to <= 60ug		4 (6.6)	(1.82, 16.95)
		60ug < to <= 90ug		1 (1.6)	(0.04, 8.80)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.87)
		> 120ug		0 (0.0)	(0.00, 5.87)
	Week 36		61		
		0ug		7 (11.5)	(4.74, 22.22)
		0ug < to <= 30ug		47 (77.0)	(64.60, 86.85)
		30ug < to <= 60ug		7 (11.5)	(4.74, 22.22)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.87)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.87)
		> 120ug		0 (0.0)	(0.00, 5.87)
	Week 40		60		
		0ug		3 (5.0)	(1.04, 13.92)
		0ug < to <= 30ug		51 (85.0)	(73.48, 92.50)
		30ug < to <= 60ug		6 (10.0)	(3.76, 20.51)
		60ug < to <= 90ug		0 (0.0)	(0.00, 5.96)
		90ug < to <= 120ug		0 (0.0)	(0.00, 5.96)
		> 120ug		0 (0.0)	(0.00, 5.96)
	Week 44		59		
		0ug		1 (1.7)	(0.04, 9.09)
		0ug < to <= 30ug		51 (86.4)	(75.02, 93.96)
		30ug < to <= 60ug		7 (11.9)	(4.91, 22.93)
		60ug < to <= 90ug		0 (0.0)	(0.00, 6.06)
		90ug < to <= 120ug		0 (0.0)	(0.00, 6.06)
		> 120ug		0 (0.0)	(0.00, 6.06)

表 2.7.6.25－135　治験薬の投与量の分布（FAS）（Correction 集団）（続き）

Treatment Group	Visit	Dose	N	n (%)	95% CI of proportion
	Week 48		58		
		0ug		2 (3.4)	(0.42, 11.91)
		0ug < to <= 30ug		49 (84.5)	(72.58, 92.65)
		30ug < to <= 60ug		7 (12.1)	(4.99, 23.30)
		60ug < to <= 90ug		0 (0.0)	(0.00, 6.16)
		90ug < to <= 120ug		0 (0.0)	(0.00, 6.16)
		> 120ug		0 (0.0)	(0.00, 6.16)

Note(s): Dose: MT-6548: daily dose (mg); darbepoetin: weekly dose (ug).
Note(s): 95%CI of proportion: 95% confidence interval of proportion is analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.3.1, Listing 16.2.3.2
Source: t_I4_2_3_4_2_2.sas

5.3.5.1—8 表 14.2.3.4.2.2 より引用

7)　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 2.7.6.25－136 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 58.0%であり，20 週～24 週後では 19.4%，48 週～52 週後では 8.6%であった.

表 2.7.6.25－136　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）（Correction 集団）

Parameter	Period	Category	N*	MT-6548 (N=71) n (%)	95% CI of proportion
Cumulative number of dose adjustment		0		3 (4.2)	(0.88, 11.86)
		1		12 (16.9)	(9.05, 27.66)
		2		19 (26.8)	(16.94, 38.59)
		3		14 (19.7)	(11.22, 30.86)
		4		11 (15.5)	(8.00, 26.03)
		5		7 (9.9)	(4.06, 19.26)
		6		4 (5.6)	(1.56, 13.80)
		7		1 (1.4)	(0.04, 7.60)
Proportion of subjects by category of dose adjustment	Baseline <= to < Week 2		71		
		No change		71 (100.0)	(94.94, 100.00)
		Dose adjustment		0 (0.0)	(0.00, 5.06)
		Increase		0 (0.0)	(0.00, 5.06)
		Decrease		0 (0.0)	(0.00, 5.06)
		Interrupt		0 (0.0)	(0.00, 5.06)
	Week 2 <= to < Week 4		71		
		No change		66 (93.0)	(84.33, 97.67)
		Dose adjustment		5 (7.0)	(2.33, 15.67)
		Increase		3 (4.2)	(0.88, 11.86)
		Decrease		0 (0.0)	(0.00, 5.06)
		Interrupt		2 (2.8)	(0.34, 9.81)
	Week 4 <= to < Week 6		69		
		No change		29 (42.0)	(30.24, 54.52)
		Dose adjustment		40 (58.0)	(45.48, 69.76)
		Increase		31 (44.9)	(32.92, 57.38)
		Decrease		7 (10.1)	(4.18, 19.79)
		Interrupt		2 (2.9)	(0.35, 10.08)

表 2.7.6.25－136　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）（Correction 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=71) n (%)	95% CI of proportion
	Week 6 <= to < Week 8		68		
		No change		59 (86.8)	(76.36, 93.77)
		Dose adjustment		9 (13.2)	(6.23, 23.64)
		Increase		6 (8.8)	(3.31, 18.22)
		Decrease		3 (4.4)	(0.92, 12.36)
		Interrupt		0 (0.0)	(0.00, 5.28)
	Week 8 <= to < Week 10		68		
		No change		48 (70.6)	(58.29, 81.02)
		Dose adjustment		20 (29.4)	(18.98, 41.71)
		Increase		18 (26.5)	(16.50, 38.57)
		Decrease		2 (2.9)	(0.36, 10.22)
		Interrupt		0 (0.0)	(0.00, 5.28)
	Week 10 <= to < Week 12		68		
		No change		55 (80.9)	(69.53, 89.41)
		Dose adjustment		13 (19.1)	(10.59, 30.47)
		Increase		6 (8.8)	(3.31, 18.22)
		Decrease		6 (8.8)	(3.31, 18.22)
		Interrupt		1 (1.5)	(0.04, 7.92)
	Week 12 <= to < Week 16		67		
		No change		52 (77.6)	(65.78, 86.89)
		Dose adjustment		15 (22.4)	(13.11, 34.22)
		Increase		3 (4.5)	(0.93, 12.53)
		Decrease		10 (14.9)	(7.40, 25.74)
		Interrupt		2 (3.0)	(0.36, 10.37)
	Week 16 <= to < Week 20		67		
		No change		50 (74.6)	(62.51, 84.47)
		Dose adjustment		17 (25.4)	(15.53, 37.49)
		Increase		3 (4.5)	(0.93, 12.53)
		Decrease		12 (17.9)	(9.61, 29.20)
		Interrupt		2 (3.0)	(0.36, 10.37)

表 2.7.6.25－136　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）（Correction 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=71) n (%)	95% CI of proportion
	Week 20 <= to < Week 24		67		
		No change		54 (80.6)	(69.11, 89.24)
		Dose adjustment		13 (19.4)	(10.76, 30.89)
		Increase		7 (10.4)	(4.30, 20.35)
		Decrease		5 (7.5)	(2.47, 16.56)
		Interrupt		1 (1.5)	(0.04, 8.04)
	Week 24 <= to < Week 28		65		
		No change		56 (86.2)	(75.34, 93.47)
		Dose adjustment		9 (13.8)	(6.53, 24.66)
		Increase		1 (1.5)	(0.04, 8.28)
		Decrease		5 (7.7)	(2.54, 17.05)
		Interrupt		3 (4.6)	(0.96, 12.90)
	Week 28 <= to < Week 32		64		
		No change		53 (82.8)	(71.32, 91.10)
		Dose adjustment		11 (17.2)	(8.90, 28.68)
		Increase		5 (7.8)	(2.59, 17.30)
		Decrease		6 (9.4)	(3.52, 19.30)
		Interrupt		0 (0.0)	(0.00, 5.60)
	Week 32 <= to < Week 36		63		
		No change		50 (79.4)	(67.30, 88.53)
		Dose adjustment		13 (20.6)	(11.47, 32.70)
		Increase		1 (1.6)	(0.04, 8.53)
		Decrease		11 (17.5)	(9.05, 29.10)
		Interrupt		1 (1.6)	(0.04, 8.53)
	Week 36 <= to < Week 40		61		
		No change		51 (83.6)	(71.91, 91.85)
		Dose adjustment		10 (16.4)	(8.15, 28.09)
		Increase		4 (6.6)	(1.82, 15.95)
		Decrease		3 (4.9)	(1.03, 13.71)
		Interrupt		3 (4.9)	(1.03, 13.71)

表 2.7.6.25－136　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）（Correction 集団）（続き）

Parameter	Period	Category	N*	MT-6548(N=71) n (%)	95% CI of proportion
	Week 40 <= to < Week 44		59		
		No change		47 (79.7)	(67.17, 89.02)
		Dose adjustment		12 (20.3)	(10.98, 32.83)
		Increase		7 (11.9)	(4.91, 22.93)
		Decrease		4 (6.8)	(1.88, 16.46)
		Interrupt		1 (1.7)	(0.04, 9.09)
	Week 44 <= to < Week 48		59		
		No change		49 (83.1)	(71.03, 91.56)
		Dose adjustment		10 (16.9)	(8.44, 28.97)
		Increase		9 (15.3)	(7.22, 26.99)
		Decrease		1 (1.7)	(0.04, 9.09)
		Interrupt		0 (0.0)	(0.00, 6.06)
	Week 48 <= to < Week 52		58		
		No change		53 (91.4)	(81.02, 97.14)
		Dose adjustment		5 (8.6)	(2.86, 18.98)
		Increase		1 (1.7)	(0.04, 9.24)
		Decrease		2 (3.4)	(0.42, 11.91)
		Interrupt		2 (3.4)	(0.42, 11.91)
	Baseline <= to < Week 52		71		
		No change		3 (4.2)	(0.88, 11.86)
		Dose adjustment		68 (95.8)	(88.14, 99.12)
		Increase		55 (77.5)	(66.00, 86.54)
		Decrease		51 (71.8)	(59.90, 81.87)
		Interrupt		18 (25.4)	(15.77, 37.08)

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 analyzed by Clopper-Pearson (Exact) method.
Data Source: Listing 16.2.3.1
Source: t_14_2_3_5_2.sas

5.3.5.1—8 表 11.4.1—6 より引用

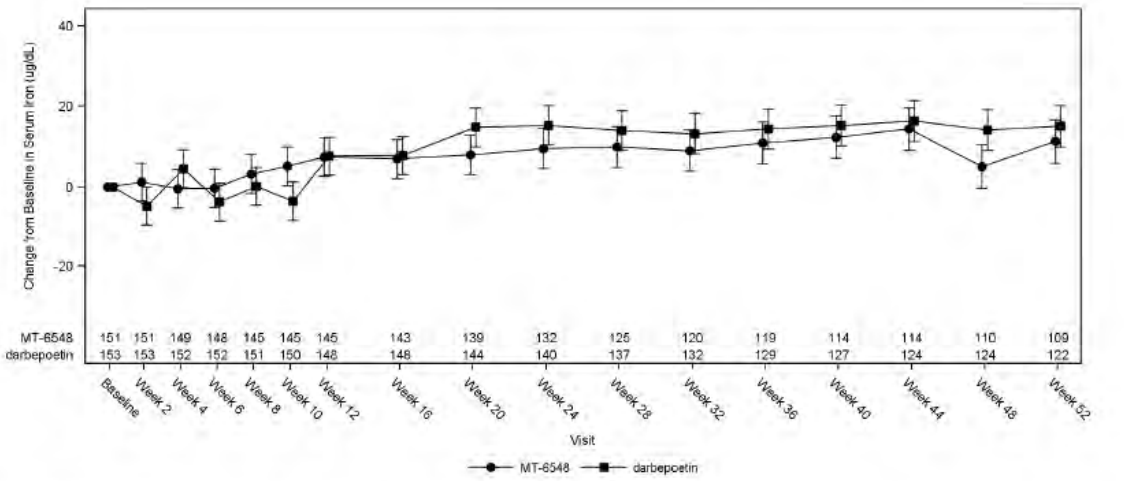
(5)　鉄関連指標（血清鉄，TIBC，TSAT 及び血清フェリチン値）及びヘプシジン

鉄関連評価項目及びヘプシジンは，全集団を対象に記載した.

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 2.7.6.25－57 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 2.7.6.25－137 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 11.3 μg/dL 及び 5.9～16.7 μg/dL，darbepoetin 群で 15.1 μg/dL 及び 10.0～20.2 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 群の差の LSMean 及びその 95%CI は，-3.8 μg/dL 及び -11.2～3.6 μg/dL 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 iron (ug/dL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.8.9.2.1
Source: f_14_2_8_1_1.sas

図 2.7.6.25－57　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—8 図 11.4.1—13 より引用

表 2.7.6.25－137 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	151	81.9 (27.5)	1.2	2.4	(-3.5, 5.9)		151	8.0	3.5	(1.2, 14.7)	
	Week 4	149	81.9 (27.7)	-0.5	2.4	(-5.2, 4.3)		149	7.2	3.5	(0.4, 14.0)	
	Week 6	148	82.0 (27.8)	-0.3	2.4	(-5.1, 4.5)		148	7.1	3.5	(0.3, 13.9)	
	Week 8	145	81.6 (27.6)	3.3	2.4	(-1.5, 8.1)		145	12.6	3.5	(5.7, 19.5)	
	Week 10	145	81.6 (27.7)	5.1	2.4	(0.3, 9.9)		145	15.1	3.5	(8.2, 22.0)	
	Week 12	145	81.7 (27.6)	7.4	2.4	(2.6, 12.2)		145	17.3	3.5	(10.4, 24.2)	
	Week 16	143	81.8 (27.8)	6.9	2.5	(2.1, 11.7)		143	21.1	3.5	(14.2, 28.1)	
	Week 20	139	82.1 (27.9)	8.0	2.5	(3.1, 12.9)		139	18.0	3.6	(11.0, 25.0)	
	Week 24	132	81.4 (26.6)	9.6	2.5	(4.6, 14.5)		132	20.7	3.6	(13.5, 27.8)	
	Week 28	125	80.9 (26.7)	10.0	2.6	(4.9, 15.1)		125	21.1	3.7	(13.8, 28.4)	
	Week 32	120	80.5 (24.8)	9.0	2.6	(3.8, 14.2)		120	22.2	3.8	(14.8, 29.6)	
	Week 36	119	80.3 (24.8)	11.0	2.6	(5.8, 16.2)		119	25.2	3.8	(17.7, 32.6)	
	Week 40	114	80.5 (24.9)	12.4	2.7	(7.1, 17.7)		114	25.5	3.9	(17.9, 33.0)	
	Week 44	114	80.4 (24.9)	14.4	2.7	(9.1, 19.7)		114	27.4	3.9	(19.8, 34.9)	
	Week 48	110	81.5 (24.5)	5.1	2.7	(-0.3, 10.4)		110	14.7	3.9	(7.0, 22.3)	
	Week 52	109	81.2 (24.4)	11.3	2.7	(5.9, 16.7)		109	22.8	3.9	(15.1, 30.5)	
darbepoetin												
	Week 2	153	79.8 (24.0)	-4.8	2.4	(-9.5, -0.1)		153	-1.3	3.4	(-8.1, 5.4)	
	Week 4	152	79.7 (24.0)	4.6	2.4	(-0.2, 9.2)		152	11.6	3.4	(4.8, 18.3)	
	Week 6	152	79.7 (24.0)	-3.7	2.4	(-8.4, 1.0)		152	0.0	3.4	(-6.8, 6.7)	
	Week 8	151	79.8 (24.0)	0.1	2.4	(-4.6, 4.8)		151	4.7	3.4	(-2.1, 11.4)	
	Week 10	150	80.0 (23.9)	-3.6	2.4	(-8.3, 1.2)		150	1.9	3.5	(-4.8, 8.7)	
	Week 12	148	79.4 (24.0)	7.6	2.4	(2.9, 12.4)		148	15.7	3.5	(8.5, 22.6)	
	Week 16	148	79.8 (24.2)	7.8	2.4	(3.0, 12.5)		148	15.6	3.5	(8.8, 22.4)	
	Week 20	144	80.0 (24.0)	14.8	2.4	(10.0, 19.6)		144	26.2	3.5	(19.3, 33.1)	
	Week 24	140	80.4 (24.3)	15.3	2.5	(10.5, 20.2)		140	28.0	3.6	(21.0, 35.0)	
	Week 28	137	80.4 (24.2)	14.0	2.5	(9.1, 18.9)		137	24.6	3.6	(17.6, 31.6)	
	Week 32	132	80.2 (23.9)	13.2	2.5	(8.2, 18.2)		132	23.5	3.6	(16.3, 30.6)	
	Week 36	129	80.0 (24.0)	14.4	2.6	(9.4, 19.4)		129	25.5	3.7	(18.4, 32.7)	
	Week 40	127	80.3 (24.1)	15.2	2.6	(10.2, 20.3)		127	25.9	3.7	(18.7, 33.2)	
	Week 44	124	80.3 (24.2)	16.4	2.6	(11.3, 21.5)		124	26.9	3.7	(19.6, 34.2)	
	Week 48	124	80.3 (24.2)	14.2	2.6	(9.1, 19.3)		124	24.9	3.7	(17.6, 32.2)	
	Week 52	122	80.6 (24.2)	15.1	2.6	(10.0, 20.2)		122	25.5	3.7	(18.2, 32.9)	

表 2.7.6.25－137　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
Difference MT-6548 - darbepoetin												
	Week 2			5.9	3.4	(-0.7, 12.6)	0.079		9.3	4.9	(-0.3, 18.8)	0.056
	Week 4			-5.0	3.4	(-11.6, 1.7)	0.143		-4.3	4.9	(-13.9, 5.2)	0.374
	Week 6			3.4	3.4	(-3.2, 10.1)	0.314		7.1	4.9	(-2.5, 16.7)	0.145
	Week 8			3.1	3.4	(-3.6, 9.8)	0.360		8.0	4.9	(-1.7, 17.6)	0.106
	Week 10			8.7	3.4	(1.9, 15.4)	0.012		13.1	4.9	(3.5, 22.8)	0.008
	Week 12			-0.2	3.4	(-6.9, 6.5)	0.956		1.6	4.9	(-8.1, 11.3)	0.746
	Week 16			-0.8	3.4	(-7.6, 5.9)	0.808		5.5	5.0	(-4.2, 15.2)	0.264
	Week 20			-6.8	3.5	(-13.7, 0.0)	0.051		-8.2	5.0	(-18.0, 1.6)	0.102
	Week 24			-5.8	3.5	(-12.7, 1.2)	0.103		-7.3	5.1	(-17.3, 2.6)	0.150
	Week 28			-4.1	3.6	(-11.1, 3.0)	0.259		-3.5	5.2	(-13.6, 6.7)	0.504
	Week 32			-4.2	3.7	(-11.4, 3.0)	0.251		-1.3	5.2	(-11.6, 9.0)	0.806
	Week 36			-3.4	3.7	(-10.6, 3.8)	0.355		-0.4	5.3	(-10.7, 10.0)	0.944
	Week 40			-2.8	3.7	(-10.1, 4.5)	0.445		-0.5	5.3	(-10.9, 10.0)	0.927
	Week 44			-2.0	3.7	(-9.3, 5.4)	0.598		0.5	5.4	(-10.1, 11.0)	0.933
	Week 48			-9.1	3.8	(-16.5, -1.7)	0.016		-10.2	5.4	(-20.8, 0.4)	0.059
	Week 52			-3.8	3.8	(-11.2, 3.6)	0.314		-2.7	5.4	(-13.3, 7.9)	0.617

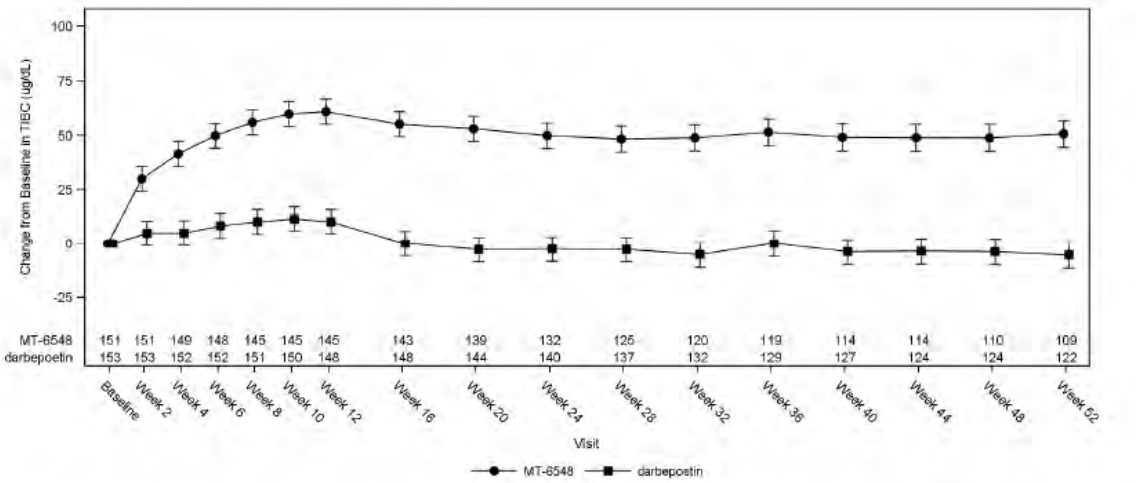
Note(s): Serum Iron (ug/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_9_2_1.sas

5.3.5.1—8 表 14.2.3.9.2.1 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 2.7.6.25－58 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 2.7.6.25－138 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 50.6 μg/dL 及び 44.3～56.8 μg/dL，darbepoetin 群で -5.4 μg/dL 及び -11.5～0.6 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 群の差の LSMean 及びその 95%CI は，56.0 μg/dL 及び 47.3～64.7 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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.9.2.6
Source: f_14_2_5_2_1.sas

図 2.7.6.25－58　TIBC のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—8 図 11.4.1—14 より引用

表 2.7.6.25－138　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	151	267.4 (40.7)	30.1	2.9	(24.4, 35.8)		151	11.6	1.1	(9.5, 13.7)	
	Week 4	149	267.5 (40.9)	41.5	2.9	(35.8, 47.2)		149	16.1	1.1	(13.9, 18.2)	
	Week 6	148	267.7 (41.0)	48.8	2.9	(44.1, 55.5)		148	19.1	1.1	(17.0, 21.2)	
	Week 8	145	267.6 (41.4)	55.9	2.9	(50.2, 61.7)		145	21.5	1.1	(19.3, 23.6)	
	Week 10	145	267.4 (41.4)	59.9	2.9	(54.1, 65.7)		145	22.9	1.1	(20.7, 25.0)	
	Week 12	145	267.2 (41.2)	60.8	2.9	(55.0, 66.6)		145	23.4	1.1	(21.3, 25.6)	
	Week 16	143	267.3 (41.4)	55.2	2.9	(49.4, 60.9)		143	21.3	1.1	(19.2, 23.5)	
	Week 20	139	267.5 (41.7)	53.0	3.0	(47.2, 58.9)		139	20.2	1.1	(18.0, 22.3)	
	Week 24	132	269.0 (41.5)	49.6	3.0	(43.9, 55.7)		132	19.2	1.1	(17.1, 21.4)	
	Week 28	125	270.0 (41.6)	48.4	3.1	(42.4, 54.4)		125	18.7	1.1	(16.5, 20.9)	
	Week 32	120	269.7 (42.4)	48.9	3.1	(42.8, 55.0)		120	19.1	1.2	(16.8, 21.3)	
	Week 36	119	270.1 (42.6)	51.4	3.1	(45.3, 57.5)		119	20.0	1.2	(17.7, 22.3)	
	Week 40	114	270.3 (43.1)	49.1	3.1	(42.9, 55.3)		114	18.8	1.2	(16.5, 21.1)	
	Week 44	114	270.4 (43.0)	48.9	3.1	(42.7, 55.0)		114	18.9	1.2	(16.6, 21.2)	
	Week 48	110	271.1 (41.9)	48.9	3.2	(42.7, 55.2)		110	18.9	1.2	(16.6, 21.2)	
	Week 52	109	271.1 (42.2)	50.6	3.2	(44.3, 56.8)		109	19.4	1.2	(17.1, 21.7)	
darbepoetin												
	Week 2	153	273.3 (42.3)	5.0	2.9	(-0.6, 10.6)		153	2.0	1.1	(-0.1, 4.1)	
	Week 4	152	273.5 (42.4)	5.0	2.9	(-0.6, 10.7)		152	2.0	1.1	(-0.1, 4.1)	
	Week 6	152	273.5 (42.4)	8.4	2.9	(2.8, 14.1)		152	3.4	1.1	(1.3, 5.5)	
	Week 8	151	273.6 (42.5)	10.3	2.9	(4.6, 15.9)		151	4.1	1.1	(2.0, 6.2)	
	Week 10	150	273.2 (42.5)	11.7	2.9	(6.0, 17.4)		150	4.9	1.1	(2.8, 7.0)	
	Week 12	148	273.3 (42.8)	10.4	2.9	(4.7, 16.1)		148	4.5	1.1	(2.4, 6.6)	
	Week 16	148	273.6 (42.6)	0.1	2.9	(-5.6, 5.8)		148	0.9	1.1	(-1.2, 3.0)	
	Week 20	144	271.9 (40.6)	-2.8	2.9	(-8.6, 2.9)		144	-0.4	1.1	(-2.5, 1.8)	
	Week 24	140	273.3 (40.0)	-2.6	3.0	(-8.4, 3.2)		140	-0.1	1.1	(-2.2, 2.1)	
	Week 28	137	272.9 (40.3)	-2.8	3.0	(-8.6, 3.0)		137	-0.3	1.1	(-2.4, 1.9)	
	Week 32	132	272.4 (40.2)	-5.2	3.0	(-11.1, 0.6)		132	-1.2	1.1	(-3.4, 1.0)	
	Week 36	129	272.9 (40.5)	0.0	3.0	(-5.9, 6.0)		129	0.8	1.1	(-1.4, 3.0)	
	Week 40	127	273.6 (40.3)	-4.0	3.0	(-9.9, 2.0)		127	-0.5	1.1	(-2.7, 1.7)	
	Week 44	124	274.2 (40.5)	-3.5	3.1	(-9.5, 2.5)		124	-0.5	1.1	(-2.7, 1.7)	
	Week 48	124	274.2 (40.5)	-3.9	3.1	(-9.9, 2.1)		124	-0.7	1.1	(-2.9, 1.6)	
	Week 52	122	274.3 (40.8)	-5.4	3.1	(-11.5, 0.6)		122	-1.2	1.1	(-3.4, 1.1)	

表 2.7.6.25－138　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			25.1	4.1	(17.1, 33.1)	<0.001		9.6	1.5	(6.6, 12.5)	<0.001
	Week 4			36.4	4.1	(28.4, 44.5)	<0.001		14.0	1.5	(11.1, 17.0)	<0.001
	Week 6			41.4	4.1	(33.3, 49.4)	<0.001		15.7	1.5	(12.7, 18.7)	<0.001
	Week 8			45.7	4.1	(37.6, 53.7)	<0.001		17.3	1.5	(14.3, 20.3)	<0.001
	Week 10			48.2	4.1	(40.1, 56.3)	<0.001		18.0	1.5	(15.0, 21.0)	<0.001
	Week 12			50.4	4.1	(42.3, 58.5)	<0.001		18.9	1.5	(15.9, 21.9)	<0.001
	Week 16			55.0	4.1	(46.9, 63.2)	<0.001		20.4	1.5	(17.4, 23.4)	<0.001
	Week 20			55.9	4.2	(47.7, 64.1)	<0.001		20.5	1.5	(17.5, 23.6)	<0.001
	Week 24			52.4	4.2	(44.1, 60.6)	<0.001		19.3	1.6	(16.3, 22.4)	<0.001
	Week 28			51.2	4.3	(42.8, 59.6)	<0.001		18.9	1.6	(15.8, 22.1)	<0.001
	Week 32			54.2	4.3	(45.7, 62.6)	<0.001		20.3	1.6	(17.1, 23.4)	<0.001
	Week 36			51.4	4.3	(42.9, 59.9)	<0.001		19.1	1.6	(16.0, 22.3)	<0.001
	Week 40			53.1	4.4	(44.5, 61.6)	<0.001		19.4	1.6	(16.2, 22.5)	<0.001
	Week 44			52.4	4.4	(43.8, 61.0)	<0.001		19.4	1.6	(16.2, 22.6)	<0.001
	Week 48			52.9	4.4	(44.2, 61.5)	<0.001		19.5	1.6	(16.3, 22.7)	<0.001
	Week 52			56.0	4.4	(47.3, 64.7)	<0.001		20.6	1.6	(17.3, 23.8)	<0.001

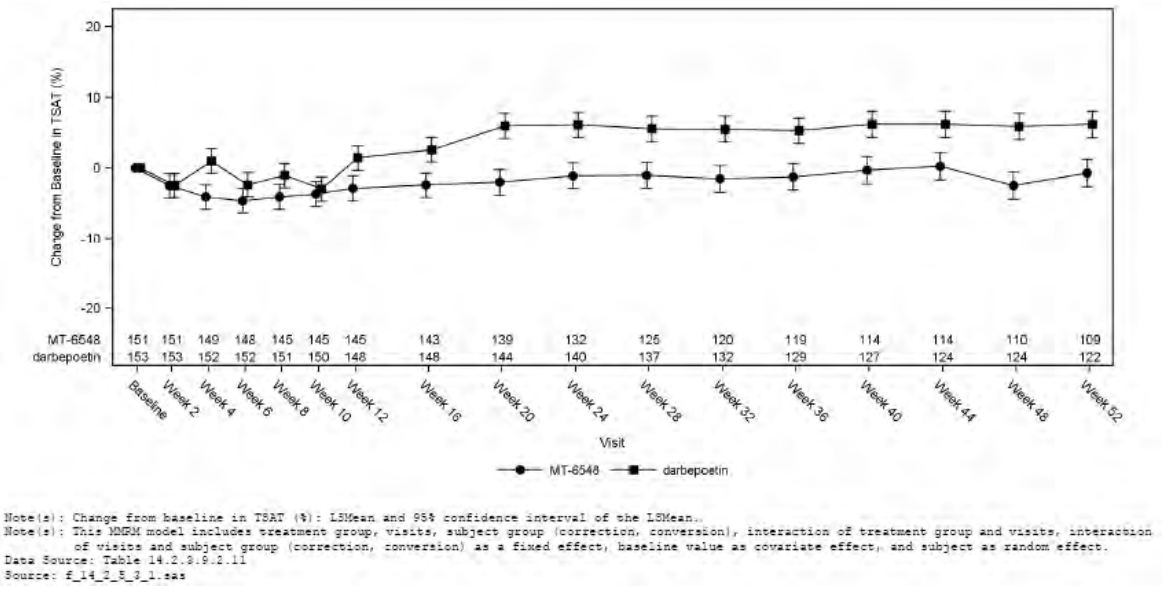
Note(s): TIBC (ug/dL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed 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_9_2_6.sas

5.3.5.1—8 表 14.2.3.9.2.6 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 2.7.6.25－59 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 2.7.6.25－139 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 -0.7%及び -2.7%～1.3%，darbepoetin 群で 6.2%及び 4.3%～8.0%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 群の差の LSMean 及びその 95%CI は，-6.9%及び -9.6%～ -4.2%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 TSAT (%): LSMean and 95% confidence interval of the LSMean..
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.3.9.2.11
Source: f_14_2_5_3_1.sas

図 2.7.6.25－59　TSAT のベースラインからの変化量の推移（MMRM，FAS）

5.3.5.1—8 図 11.4.1—15 より引用

表 2.7.6.25－139 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	151	31.1 (10.9)	-2.5	0.9	(-4.2, -0.8)		151	-2.9	3.4	(-9.5, 3.8)	
	Week 4	149	31.1 (10.9)	-4.1	0.9	(-5.8, -2.4)		149	-6.5	3.4	(-13.2, 0.1)	
	Week 6	148	31.1 (11.0)	-4.6	0.9	(-6.4, -2.9)		148	-8.9	3.4	(-15.6, -2.2)	
	Week 8	145	31.0 (10.9)	-4.1	0.9	(-5.8, -2.3)		145	-6.2	3.4	(-12.9, 0.6)	
	Week 10	145	31.1 (11.0)	-3.7	0.9	(-5.5, -1.9)		145	-4.4	3.4	(-11.2, 2.3)	
	Week 12	145	31.1 (11.0)	-2.9	0.9	(-4.6, -1.1)		145	-2.8	3.4	(-9.6, 3.9)	
	Week 16	143	31.1 (11.0)	-2.4	0.9	(-4.2, -0.7)		143	2.1	3.4	(-4.7, 8.8)	
	Week 20	139	31.2 (11.1)	-2.0	0.9	(-3.8, -0.2)		139	1.1	3.5	(-5.7, 7.9)	
	Week 24	132	30.8 (10.6)	-1.1	0.9	(-2.9, 0.7)		132	4.0	3.5	(-3.0, 11.0)	
	Week 28	125	30.4 (10.5)	-1.1	0.9	(-2.9, 0.8)		125	4.4	3.6	(-2.7, 11.5)	
	Week 32	120	30.3 (10.0)	-1.5	1.0	(-3.4, 0.4)		120	5.0	3.7	(-2.2, 12.3)	
	Week 36	119	30.2 (10.0)	-1.3	1.0	(-3.2, 0.6)		119	5.9	3.7	(-1.4, 13.1)	
	Week 40	114	30.3 (10.1)	-0.3	1.0	(-2.3, 1.6)		114	7.6	3.8	(0.2, 15.0)	
	Week 44	114	30.3 (10.1)	0.3	1.0	(-1.6, 2.2)		114	9.7	3.8	(2.3, 17.1)	
	Week 48	110	30.6 (10.0)	-2.5	1.0	(-4.4, -0.5)		110	-1.2	3.8	(-8.6, 6.3)	
	Week 52	109	30.5 (9.9)	-0.7	1.0	(-2.7, 1.3)		109	5.1	3.8	(-2.4, 12.6)	
darbepoetin												
	Week 2	153	29.8 (9.5)	-2.5	0.9	(-4.2, -0.8)		153	-3.4	3.3	(-10.0, 3.2)	
	Week 4	152	29.7 (9.4)	1.0	0.9	(-0.7, 2.7)		152	9.0	3.4	(2.4, 15.6)	
	Week 6	152	29.7 (9.4)	-2.4	0.9	(-4.1, -0.7)		152	-3.5	3.4	(-10.1, 3.1)	
	Week 8	151	29.7 (9.5)	-1.1	0.9	(-2.8, 0.7)		151	0.9	3.4	(-5.7, 7.5)	
	Week 10	150	29.8 (9.4)	-3.0	0.9	(-4.7, -1.2)		150	-3.0	3.4	(-9.6, 3.6)	
	Week 12	148	29.6 (9.5)	1.4	0.9	(-0.3, 3.2)		148	11.4	3.4	(4.7, 18.0)	
	Week 16	148	29.7 (9.5)	2.6	0.9	(0.9, 4.4)		148	14.9	3.4	(8.2, 21.5)	
	Week 20	144	29.9 (9.4)	5.9	0.9	(4.2, 7.7)		144	28.6	3.4	(21.9, 35.4)	
	Week 24	140	29.9 (9.5)	6.1	0.9	(4.3, 7.9)		140	30.8	3.5	(24.0, 37.6)	
	Week 28	137	29.9 (9.5)	5.5	0.9	(3.7, 7.3)		137	26.8	3.5	(20.0, 33.7)	
	Week 32	132	29.9 (9.5)	5.5	0.9	(3.7, 7.3)		132	27.7	3.5	(20.8, 34.7)	
	Week 36	129	29.8 (9.5)	5.3	0.9	(3.4, 7.1)		129	26.7	3.6	(19.7, 33.7)	
	Week 40	127	29.8 (9.6)	6.2	0.9	(4.4, 8.1)		127	28.3	3.6	(21.9, 36.0)	
	Week 44	124	29.8 (9.6)	6.2	0.9	(4.3, 8.0)		124	29.1	3.6	(22.0, 36.2)	
	Week 48	124	29.8 (9.6)	5.9	0.9	(4.0, 7.7)		124	28.2	3.6	(21.1, 35.3)	
	Week 52	122	29.9 (9.6)	6.2	1.0	(4.3, 8.0)		122	29.6	3.6	(22.4, 36.7)	

表 2.7.6.25－139　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			0.0	1.2	(-2.5, 2.4)	0.979		0.6	4.7	(-8.8, 9.9)	0.906
	Week 4			-5.1	1.2	(-7.6, -2.7)	<0.001		-15.5	4.8	(-24.9, -6.2)	0.001
	Week 6			-2.2	1.2	(-4.7, 0.2)	0.074		-5.4	4.8	(-14.7, 4.0)	0.262
	Week 8			-3.0	1.3	(-5.5, -0.5)	0.017		-7.1	4.8	(-16.5, 2.3)	0.140
	Week 10			-0.7	1.3	(-3.2, 1.7)	0.556		-1.4	4.8	(-10.9, 8.0)	0.763
	Week 12			-4.3	1.3	(-6.8, -1.8)	<0.001		-14.2	4.8	(-23.6, -4.7)	0.003
	Week 16			-5.1	1.3	(-7.5, -2.6)	<0.001		-12.8	4.8	(-22.3, -3.3)	0.008
	Week 20			-8.0	1.3	(-10.5, -5.5)	<0.001		-27.5	4.9	(-37.1, -18.0)	<0.001
	Week 24			-7.2	1.3	(-9.7, -4.6)	<0.001		-26.8	5.0	(-36.5, -17.1)	<0.001
	Week 28			-6.6	1.3	(-9.1, -4.0)	<0.001		-22.5	5.0	(-32.3, -12.6)	<0.001
	Week 32			-7.0	1.3	(-9.6, -4.4)	<0.001		-22.7	5.1	(-32.7, -12.7)	<0.001
	Week 36			-6.5	1.3	(-9.2, -3.9)	<0.001		-20.9	5.1	(-30.9, -10.8)	<0.001
	Week 40			-6.6	1.4	(-9.2, -3.9)	<0.001		-21.3	5.2	(-31.5, -11.1)	<0.001
	Week 44			-5.9	1.4	(-8.6, -3.2)	<0.001		-19.4	5.2	(-29.7, -9.2)	<0.001
	Week 48			-8.3	1.4	(-11.0, -5.6)	<0.001		-29.4	5.3	(-39.7, -19.1)	<0.001
	Week 52			-6.9	1.4	(-9.6, -4.2)	<0.001		-24.5	5.3	(-34.8, -14.1)	<0.001

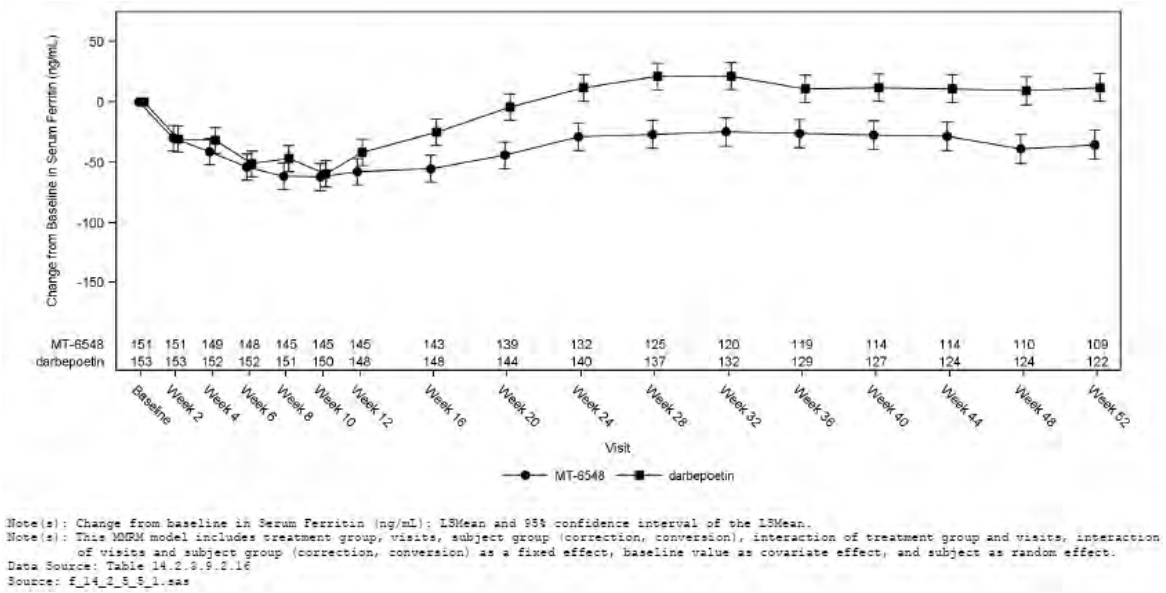
Note(s): TSAT (%).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed 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_9_2_11.sas

5.3.5.1—8 表 14.2.3.9.2.11 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 2.7.6.25－60 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 2.7.6.25－140 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 -35.12 ng/mL 及び -47.11～ -23.13 ng/mL，darbepoetin 群で 12.02 ng/mL 及び 0.52～23.52 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 群の差の LSMean 及びその 95%CI は，-47.14 ng/mL 及び -63.76～ -30.53 ng/mL 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 Ferritin (ng/mL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.8.9.2.16
Source: f_14_2_5_5_1.sas

図 2.7.6.25－60　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—8 図 11.4.1—16 より引用

表 2.7.6.25－140 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	151	151.24 (119.82)	-29.82	5.48	(-40.67, -19.08)		151	-19.82	7.67	(-34.87, -4.77)	
	Week 4	149	151.29 (120.59)	-41.11	5.51	(-51.93, -30.30)		149	-25.64	7.71	(-40.77, -10.51)	
	Week 6	148	149.80 (119.61)	-53.44	5.52	(-64.27, -42.60)		148	-32.15	7.73	(-47.32, -16.99)	
	Week 8	145	146.01 (107.28)	-61.22	5.56	(-72.13, -50.31)		145	-35.52	7.78	(-50.77, -20.26)	
	Week 10	145	145.45 (107.26)	-61.89	5.56	(-72.81, -50.98)		145	-35.32	7.78	(-50.58, -20.06)	
	Week 12	145	146.09 (107.25)	-57.42	5.56	(-68.33, -46.51)		145	-30.58	7.78	(-45.84, -15.32)	
	Week 16	143	144.50 (106.84)	-54.92	5.59	(-65.88, -43.96)		143	-26.55	7.81	(-41.87, -11.22)	
	Week 20	139	145.56 (108.21)	-43.84	5.64	(-54.90, -32.79)		139	-13.09	7.87	(-28.54, 2.35)	
	Week 24	132	145.31 (107.59)	-28.81	5.78	(-40.06, -17.57)		132	4.04	7.99	(-11.64, 19.73)	
	Week 28	125	147.04 (109.76)	-26.66	5.84	(-38.11, -15.20)		125	3.62	8.13	(-12.33, 19.57)	
	Week 32	120	149.65 (110.85)	-24.69	5.92	(-36.19, -12.98)		120	6.80	8.23	(-7.35, 24.95)	
	Week 36	119	148.93 (111.47)	-25.96	5.93	(-37.60, -14.31)		119	10.34	8.26	(-5.85, 26.54)	
	Week 40	114	152.29 (112.65)	-27.39	6.02	(-39.20, -15.58)		114	10.93	8.37	(-5.48, 27.35)	
	Week 44	114	151.50 (112.58)	-28.37	6.02	(-40.18, -16.56)		114	12.35	8.37	(-4.06, 28.76)	
	Week 48	110	151.38 (113.63)	-38.64	6.09	(-50.60, -26.69)		110	5.89	8.46	(-10.70, 22.48)	
	Week 52	109	153.66 (113.98)	-35.12	6.11	(-47.11, -23.13)		109	5.05	8.48	(-11.59, 21.69)	
darbepoetin												
	Week 2	153	138.12 (107.56)	-30.69	5.44	(-41.27, -19.92)		153	-23.94	7.62	(-38.89, -8.99)	
	Week 4	152	137.83 (107.85)	-31.62	5.46	(-42.33, -20.92)		152	-20.90	7.64	(-35.85, -5.91)	
	Week 6	152	137.83 (107.85)	-50.96	5.46	(-61.67, -40.26)		152	-32.36	7.64	(-47.35, -17.37)	
	Week 8	151	138.13 (108.15)	-46.56	5.47	(-57.29, -35.83)		151	-28.49	7.65	(-43.50, -13.47)	
	Week 10	150	137.20 (108.26)	-58.39	5.48	(-70.15, -48.63)		150	-35.32	7.67	(-50.38, -20.26)	
	Week 12	148	138.11 (108.57)	-41.30	5.51	(-52.11, -30.50)		148	-18.17	7.70	(-33.27, -3.06)	
	Week 16	148	138.51 (108.53)	-24.92	5.51	(-35.73, -14.12)		148	6.88	7.70	(-8.23, 21.99)	
	Week 20	144	139.38 (109.62)	-4.03	5.56	(-14.94, 6.87)		144	31.12	7.77	(15.88, 46.37)	
	Week 24	140	137.46 (104.09)	11.70	5.61	(0.70, 22.70)		140	47.75	7.83	(32.39, 63.11)	
	Week 28	137	138.53 (104.83)	21.14	5.65	(10.06, 32.21)		137	56.42	7.88	(40.96, 71.88)	
	Week 32	132	139.68 (106.29)	21.45	5.71	(10.24, 32.66)		132	61.15	7.97	(45.52, 76.78)	
	Week 36	129	139.84 (107.47)	10.79	5.76	(-0.50, 22.08)		129	51.24	8.02	(35.51, 66.97)	
	Week 40	127	139.86 (108.26)	11.85	5.79	(0.50, 23.20)		127	58.34	8.06	(42.53, 74.14)	
	Week 44	124	137.74 (106.19)	11.15	5.83	(-0.29, 22.59)		124	56.88	8.12	(40.96, 72.81)	
	Week 48	124	137.74 (106.19)	9.34	5.83	(-2.10, 20.78)		124	49.98	8.12	(34.06, 65.91)	
	Week 52	122	138.53 (106.88)	12.02	5.86	(0.52, 23.52)		122	53.86	8.16	(37.85, 69.86)	

表 2.7.6.25－140　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
Difference MT-6548 - darbepoetin												
	Week 2			0.77	7.72	(-14.37, 15.91)	0.921		4.12	10.80	(-17.07, 25.32)	0.703
	Week 4			-9.49	7.75	(-24.69, 5.71)	0.221		-4.74	10.85	(-26.02, 16.54)	0.662
	Week 6			-2.48	7.76	(-17.70, 12.74)	0.749		0.21	10.86	(-21.10, 21.51)	0.985
	Week 8			-14.66	7.79	(-29.95, 0.63)	0.060		-7.03	10.90	(-28.42, 14.36)	0.519
	Week 10			-2.50	7.80	(-17.81, 12.80)	0.748		0.00	10.91	(-21.41, 21.41)	1.000
	Week 12			-16.12	7.82	(-31.46, -0.78)	0.039		-12.41	10.93	(-33.87, 9.04)	0.257
	Week 16			-30.00	7.84	(-45.38, -14.62)	<0.001		-33.43	10.96	(-54.93, -11.92)	0.002
	Week 20			-39.81	7.91	(-55.33, -24.29)	<0.001		-44.22	11.05	(-65.91, -22.53)	<0.001
	Week 24			-40.51	8.02	(-56.24, -24.79)	<0.001		-43.71	11.19	(-65.66, -21.75)	<0.001
	Week 28			-47.79	8.12	(-63.73, -31.86)	<0.001		-52.61	11.33	(-75.03, -30.59)	<0.001
	Week 32			-46.04	8.23	(-62.18, -29.90)	<0.001		-52.35	11.46	(-74.83, -29.87)	<0.001
	Week 36			-36.74	8.27	(-52.96, -20.52)	<0.001		-40.90	11.51	(-63.48, -18.31)	<0.001
	Week 40			-39.24	8.35	(-55.62, -22.85)	<0.001		-47.40	11.62	(-70.20, -24.61)	<0.001
	Week 44			-39.53	8.38	(-55.97, -23.08)	<0.001		-44.53	11.66	(-67.40, -21.66)	<0.001
	Week 48			-47.98	8.43	(-64.52, -31.44)	<0.001		-44.09	11.72	(-67.09, -21.09)	<0.001
	Week 52			-47.14	8.47	(-63.76, -30.53)	<0.001		-48.80	11.77	(-71.89, -25.71)	<0.001

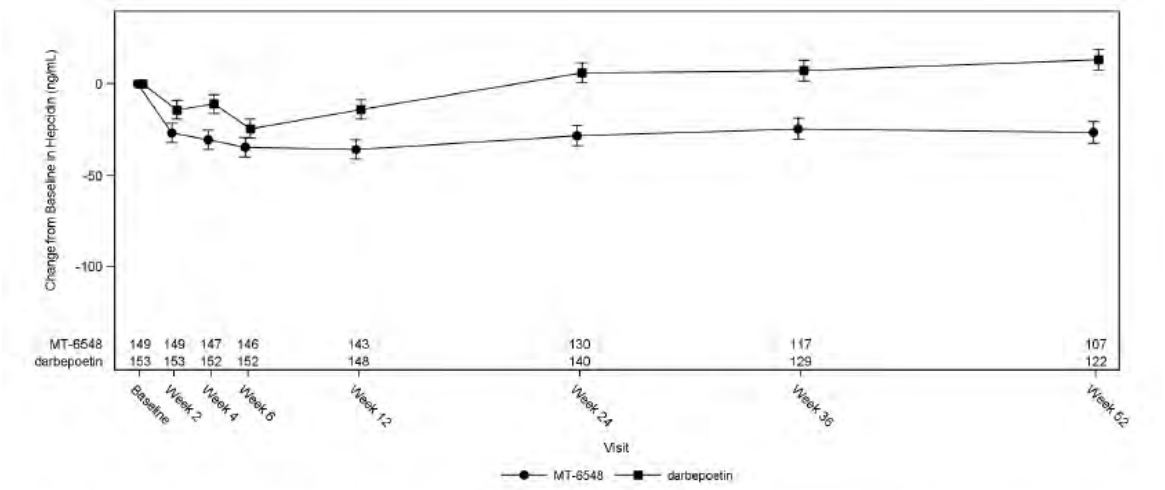
Note(s): Serum Ferritin (ng/mL).
Note(s): N: number of subjects in each treatment group by visit.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_9_2_16.sas

5.3.5.1—8 表 14.2.3.9.2.16 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 2.7.6.25－61 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 2.7.6.25－141 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 -26.211 ng/mL 及び -32.155～ -20.267 ng/mL，darbepoetin 群で 13.166 ng/mL 及び 7.537～18.794 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 群の差の LSMean 及びその 95%CI は，-39.376 ng/mL 及び -47.563～ -31.190 ng/mL 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 Hepcidin (ng/mL): LSMean and 95% confidence interval of the LSMean.
Note(s): This MMRM model includes treatment group, visits, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) as a fixed effect, baseline value as covariate effect, and subject as random effect.
Data Source: Table 14.2.8.9.2.21
Source: f_14_2_5_9_1.sas

図 2.7.6.25－61　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—8 図 11.4.1—17 より引用

表 2.7.6.25－141　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	149	62.625 (46.451)	-26.692	2.664	(-31.920, -21.463)		149	-28.082	82.101	(-189.162, 132.999)	
	Week 4	147	62.882 (46.684)	-30.381	2.682	(-35.643, -25.118)		147	-39.422	82.635	(-201.550, 122.706)	
	Week 6	146	61.358 (43.020)	-34.466	2.688	(-39.741, -29.192)		146	-38.726	82.837	(-201.250, 123.798)	
	Week 12	143	61.655 (43.416)	-35.743	2.710	(-41.060, -30.425)		143	-36.207	83.511	(-200.049, 127.636)	
	Week 24	130	60.061 (43.678)	-28.091	2.809	(-33.601, -22.580)		130	14.644	86.562	(-155.174, 184.462)	
	Week 36	117	59.901 (43.109)	-24.375	2.926	(-30.116, -18.634)		117	10.591	90.201	(-166.354, 187.536)	
	Week 52	107	61.622 (44.141)	-26.211	3.030	(-32.155, -20.267)		107	7.067	93.411	(-176.167, 190.301)	
darbepoetin												
	Week 2	153	56.946 (47.479)	-14.055	2.630	(-19.216, -8.894)		153	11.114	81.042	(-147.889, 170.118)	
	Week 4	152	56.890 (47.631)	-10.888	2.638	(-16.066, -5.711)		152	2.814	81.299	(-156.694, 162.321)	
	Week 6	152	56.890 (47.631)	-24.389	2.638	(-29.566, -19.211)		152	-17.257	81.299	(-176.763, 142.250)	
	Week 12	148	56.674 (47.775)	-13.833	2.666	(-19.064, -8.603)		148	98.673	82.140	(-62.481, 259.827)	
	Week 24	140	57.736 (48.021)	6.144	2.723	(0.802, 11.487)		140	255.787	83.911	(91.165, 420.409)	
	Week 36	129	58.396 (49.477)	7.343	2.808	(1.835, 12.851)		129	233.141	86.531	(63.388, 402.894)	
	Week 52	122	58.734 (50.740)	13.166	2.869	(7.537, 18.794)		122	480.557	88.427	(307.090, 654.024)	

表 2.7.6.25－141　ヘプシジン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			-12.637	3.740	(-19.977, -5.297)	<0.001		-39.196	115.258	(-265.331, 186.939)	0.734
	Week 4			-19.492	3.787	(-26.868, -12.119)	<0.001		-42.236	115.778	(-269.390, 184.918)	0.715
	Week 6			-10.078	3.762	(-17.459, -2.696)	0.008		-21.469	115.918	(-248.898, 205.959)	0.853
	Week 12			-21.910	3.797	(-29.359, -14.460)	<0.001		-134.879	116.996	(-364.418, 94.659)	0.249
	Week 24			-34.235	3.911	(-41.908, -26.562)	<0.001		-241.143	120.521	(-477.685, -4.701)	0.046
	Week 36			-31.718	4.056	(-39.675, -23.762)	<0.001		-222.550	125.008	(-467.779, 22.679)	0.075
	Week 52			-39.376	4.173	(-47.563, -31.190)	<0.001		-473.490	128.633	(-725.822, -221.158)	<0.001

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, subject group (correction, conversion), interaction of treatment group and visits, interaction of visits and subject group (correction, conversion) 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_9_2_21.sas

5.3.5.1—8 表 14.2.3.9.2.21 より引用

(6)　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 2.7.6.25－142 に示した．鉄剤の投与量は，全集団を対象に記載した．

経口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 434.85 mg/月及び 24.83～844.88 mg/月，darbepoetin 群で 483.77 mg/月及び 109.43～858.11 mg/月であった．経口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，-48.92 mg/月及び -600.10～502.27 mg/月であり，統計学的に有意な差は認められなかった．

表 2.7.6.25－142 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 (mg)	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	79	1005.98	1320.96	0.00	(0.0, 6087.5)	(710.10, 1301.86)								
		Baseline <= to < Week 2	79	913.13	1260.46	0.00	(0.0, 3195.9)	(630.80, 1195.45)	79	-92.86	1005.98 (1320.96)	721.13	0.00	(-3043.8, 3043.8)	(-254.38, 68.67)	0.256
		Week 2 <= to < Week 4	79	848.31	1191.24	0.00	(0.0, 3195.9)	(591.49, 1115.14)	79	-157.67	1005.98 (1320.96)	901.20	0.00	(-3043.8, 3043.8)	(-359.53, 44.19)	0.124
		Week 4 <= to < Week 6	79	957.71	1199.76	0.00	(0.0, 3195.9)	(688.98, 1226.44)	79	-48.27	1005.98 (1320.96)	992.79	0.00	(-3043.8, 3043.8)	(-270.65, 174.10)	0.667
		Week 6 <= to < Week 8	79	1251.83	1360.49	1521.88	(0.0, 6087.5)	(947.10, 1556.57)	79	245.85	1005.98 (1320.96)	1390.74	0.00	(-3043.8, 6087.5)	(-65.66, 557.36)	0.120
		Week 8 <= to < Week 10	78	1381.53	1335.51	1521.88	(0.0, 4565.6)	(1080.42, 1682.65)	78	362.65	1005.98 (1320.96)	1403.27	0.00	(-3043.8, 3195.9)	(46.26, 679.04)	0.025
		Week 10 <= to < Week 12	78	1413.03	1314.82	1521.88	(0.0, 4565.6)	(1116.58, 1709.48)	78	394.15	1005.98 (1320.96)	1364.72	0.00	(-3043.8, 3195.9)	(86.45, 701.85)	0.013
		Week 12 <= to < Week 16	78	1490.17	1274.01	1521.88	(0.0, 4565.6)	(1202.93, 1777.41)	78	471.29	1005.98 (1320.96)	1390.94	0.00	(-3043.8, 3195.9)	(157.68, 784.90)	0.004
		Week 16 <= to < Week 20	76	1502.28	1318.86	1521.88	(0.0, 4565.6)	(1200.91, 1803.65)	76	456.59	1005.98 (1320.96)	1440.98	0.00	(-3043.8, 3735.5)	(127.31, 785.86)	0.007
		Week 20 <= to < Week 24	74	1694.55	1481.56	1521.88	(0.0, 6087.5)	(1351.31, 2037.80)	74	698.07	1005.98 (1320.96)	1650.24	0.00	(-3043.8, 5989.7)	(315.74, 1080.40)	<0.001
		Week 24 <= to < Week 28	72	1633.98	1402.37	1521.88	(0.0, 6087.5)	(1304.44, 1963.52)	72	630.94	1005.98 (1320.96)	1521.83	0.00	(-3043.8, 3735.5)	(273.33, 988.56)	<0.001
		Week 28 <= to < Week 32	69	1538.89	1419.87	1521.88	(0.0, 6087.5)	(1197.80, 1879.98)	69	548.17	1005.98 (1320.96)	1594.75	0.00	(-3043.8, 3735.5)	(165.08, 931.27)	0.006
		Week 32 <= to < Week 36	67	1506.46	1422.20	1521.88	(0.0, 6087.5)	(1159.56, 1853.36)	67	486.17	1005.98 (1320.96)	1552.96	0.00	(-3043.8, 3735.5)	(107.38, 864.97)	0.013
		Week 36 <= to < Week 40	66	1559.51	1441.20	1521.88	(0.0, 6087.5)	(1205.22, 1913.80)	66	523.76	1005.98 (1320.96)	1552.06	0.00	(-3043.8, 3735.5)	(142.22, 905.31)	0.008
		Week 40 <= to < Week 44	65	1470.70	1466.46	1521.88	(0.0, 6087.5)	(1107.33, 1834.07)	65	419.02	1005.98 (1320.96)	1584.29	0.00	(-3043.8, 3735.5)	(26.45, 811.59)	0.037
		Week 44 <= to < Week 48	64	1454.10	1477.54	1521.88	(0.0, 6087.5)	(1085.03, 1823.18)	64	385.99	1005.98 (1320.96)	1595.93	0.00	(-3043.8, 3735.5)	(-12.66, 784.64)	0.057
		Week 48 <= to < Week 52	63	1519.92	1478.68	1521.88	(0.0, 6087.5)	(1147.52, 1892.32)	63	434.85	1005.98 (1320.96)	1628.07	0.00	(-3043.8, 3735.5)	(24.83, 844.88)	0.038

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Baseline <= to < Week 52	79	1416.94	1118.45	1244.27	(0.0, 5283.5)	(1166.42, 1667.46)	79	410.96	1005.98 (1320.96)	1213.39	321.94	(-3043.8, 3019.3)	(139.17, 682.74)	0.004

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
	darbepoetin	Screening period	75	907.96	1292.97	0.00	(0.0, 3195.9)	(610.47, 1205.44)								
		Baseline <= to < Week 2	75	914.28	1302.46	0.00	(0.0, 3195.9)	(614.62, 1213.95)	75	6.33	907.96 (1292.97)	494.28	0.00	(-2397.0, 2826.3)	(-107.39, 120.05)	0.912
		Week 2 <= to < Week 4	75	1033.14	1326.21	0.00	(0.0, 3195.9)	(728.00, 1338.27)	75	125.18	907.96 (1292.97)	680.14	0.00	(-2397.0, 3043.8)	(-31.31, 281.67)	0.115
		Week 4 <= to < Week 6	74	1294.48	1370.82	1358.82	(0.0, 3195.9)	(976.88, 1612.07)	74	415.38	907.96 (1292.97)	1065.48	0.00	(-2397.0, 3195.9)	(168.53, 662.23)	0.001
		Week 6 <= to < Week 8	74	1335.90	1444.28	1521.88	(0.0, 5935.3)	(1001.29, 1670.51)	74	456.81	907.96 (1292.97)	1302.19	0.00	(-3195.9, 5935.3)	(155.11, 758.50)	0.004
		Week 8 <= to < Week 10	74	1464.36	1499.21	1521.88	(0.0, 6087.5)	(1117.02, 1811.70)	74	585.27	907.96 (1292.97)	1330.08	0.00	(-3195.9, 6087.5)	(277.12, 893.42)	<0.001
		Week 10 <= to < Week 12	74	1674.36	1523.85	1521.88	(0.0, 6087.5)	(1321.31, 2027.40)	74	795.26	907.96 (1292.97)	1510.39	0.00	(-3195.9, 6087.5)	(445.33, 1145.19)	<0.001
		Week 12 <= to < Week 16	73	1825.65	1500.45	1521.88	(0.0, 6087.5)	(1475.57, 2175.74)	73	976.21	907.96 (1292.97)	1587.57	54.35	(-3195.9, 6087.5)	(605.80, 1346.62)	<0.001
		Week 16 <= to < Week 20	71	1902.34	1480.21	1521.88	(0.0, 6087.5)	(1551.98, 2252.70)	71	1028.97	907.96 (1292.97)	1606.99	101.46	(-3195.9, 6087.5)	(648.61, 1409.34)	<0.001
		Week 20 <= to < Week 24	70	1653.25	1447.81	1521.88	(0.0, 6087.5)	(1308.03, 1998.47)	70	767.41	907.96 (1292.97)	1512.60	0.00	(-3195.9, 6087.5)	(406.74, 1128.07)	<0.001
		Week 24 <= to < Week 28	69	1460.43	1386.95	1521.88	(0.0, 6087.5)	(1127.25, 1793.61)	69	561.75	907.96 (1292.97)	1450.51	0.00	(-3195.9, 3261.2)	(213.30, 910.20)	0.002
		Week 28 <= to < Week 32	68	1437.63	1409.32	1521.88	(0.0, 6087.5)	(1096.50, 1778.76)	68	547.34	907.96 (1292.97)	1448.65	0.00	(-3195.9, 3195.9)	(196.69, 897.99)	0.003
		Week 32 <= to < Week 36	65	1411.83	1405.49	1521.88	(0.0, 6087.5)	(1063.57, 1760.09)	65	550.69	907.96 (1292.97)	1475.78	0.00	(-3195.9, 3195.9)	(185.01, 916.37)	0.004
		Week 36 <= to < Week 40	64	1378.35	1399.50	1521.88	(0.0, 6087.5)	(1028.77, 1727.93)	64	527.53	907.96 (1292.97)	1450.77	0.00	(-3195.9, 3195.9)	(165.14, 889.92)	0.005
		Week 40 <= to < Week 44	63	1351.57	1396.74	1521.88	(0.0, 6087.5)	(999.80, 1703.34)	63	535.56	907.96 (1292.97)	1437.01	0.00	(-3195.9, 3195.9)	(173.66, 897.47)	0.004
		Week 44 <= to < Week 48	61	1389.02	1396.87	1521.88	(0.0, 6087.5)	(1031.27, 1746.78)	61	546.26	907.96 (1292.97)	1452.73	0.00	(-3195.9, 3195.9)	(174.20, 918.32)	0.005
		Week 48 <= to < Week 52	60	1340.58	1399.63	1521.88	(0.0, 6087.5)	(979.02, 1702.14)	60	483.77	907.96 (1292.97)	1449.09	0.00	(-3195.9, 3195.9)	(109.43, 858.11)	0.012

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Baseline <= to < Week 52	75	1490.68	1135.99	1254.29	(0.0, 5619.2)	(1229.31, 1752.05)	75	582.72	907.96 (1292.97)	1081.26	383.90	(-2827.2, 3035.4)	(333.95, 831.50)	<0.001

表 2.7.6.25－142　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 (mg)	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	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)								
		Baseline <= to < Week 2	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 2 <= to < Week 4	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 4 <= to < Week 6	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 6 <= to < Week 8	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 8 <= to < Week 10	6	14.49	35.50	0.00	(0.0, 87.0)	(-22.76, 51.75)	6	14.49	0.00 (0.00)	35.50	0.00	(0.0, 87.0)	(-22.76, 51.75)	0.363
		Week 10 <= to < Week 12	6	28.99	44.91	0.00	(0.0, 87.0)	(-18.14, 76.12)	6	28.99	0.00 (0.00)	44.91	0.00	(0.0, 87.0)	(-18.14, 76.12)	0.175
		Week 12 <= to < Week 16	6	21.74	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	6	21.74	0.00 (0.00)	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	0.203
		Week 16 <= to < Week 20	6	21.74	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	6	21.74	0.00 (0.00)	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	0.203
		Week 20 <= to < Week 24	6	36.24	42.75	21.74	(0.0, 87.0)	(-8.63, 81.10)	6	36.24	0.00 (0.00)	42.75	21.74	(0.0, 87.0)	(-8.63, 81.10)	0.093
		Week 24 <= to < Week 28	6	36.24	42.75	21.74	(0.0, 87.0)	(-8.63, 81.10)	6	36.24	0.00 (0.00)	42.75	21.74	(0.0, 87.0)	(-8.63, 81.10)	0.093
		Week 28 <= to < Week 32	6	21.74	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	6	21.74	0.00 (0.00)	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	0.203
		Week 32 <= to < Week 36	6	28.99	52.66	0.00	(0.0, 130.4)	(-26.27, 84.25)	6	28.99	0.00 (0.00)	52.66	0.00	(0.0, 130.4)	(-26.27, 84.25)	0.235
		Week 36 <= to < Week 40	6	14.49	35.50	0.00	(0.0, 87.0)	(-22.76, 51.75)	6	14.49	0.00 (0.00)	35.50	0.00	(0.0, 87.0)	(-22.76, 51.75)	0.363
		Week 40 <= to < Week 44	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 44 <= to < Week 48	6	21.74	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	6	21.74	0.00 (0.00)	36.38	0.00	(0.0, 87.0)	(-16.44, 59.92)	0.203
		Week 48 <= to < Week 52	6	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	6	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Baseline <= to < Week 52	6	17.31	8.29	18.48	(6.7, 30.1)	(8.61, 26.01)	6	17.31	0.00 (0.00)	8.29	18.48	(6.7, 30.1)	(8.61, 26.01)	0.004

表 2.7.6.25－142　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 (mg)	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	11	0.00	0.00	0.00	(0.0, 0.0)	(-, -)								
		Baseline <= to < Week 2	11	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	11	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 2 <= to < Week 4	11	15.81	52.44	0.00	(0.0, 173.9)	(-19.42, 51.04)	11	15.81	0.00 (0.00)	52.44	0.00	(0.0, 173.9)	(-19.42, 51.04)	0.341
		Week 4 <= to < Week 6	11	71.15	101.55	0.00	(0.0, 260.9)	(2.93, 139.38)	11	71.15	0.00 (0.00)	101.55	0.00	(0.0, 260.9)	(2.93, 139.38)	0.042
		Week 6 <= to < Week 8	11	23.72	78.66	0.00	(0.0, 260.9)	(-29.13, 76.56)	11	23.72	0.00 (0.00)	78.66	0.00	(0.0, 260.9)	(-29.13, 76.56)	0.341
		Week 8 <= to < Week 10	11	102.78	101.55	173.93	(0.0, 260.9)	(34.55, 171.00)	11	102.78	0.00 (0.00)	101.55	173.93	(0.0, 260.9)	(34.55, 171.00)	0.007
		Week 10 <= to < Week 12	11	23.72	78.66	0.00	(0.0, 260.9)	(-29.13, 76.56)	11	23.72	0.00 (0.00)	78.66	0.00	(0.0, 260.9)	(-29.13, 76.56)	0.341
		Week 12 <= to < Week 16	11	71.15	48.70	86.96	(0.0, 130.4)	(38.43, 103.87)	11	71.15	0.00 (0.00)	48.70	86.96	(0.0, 130.4)	(38.43, 103.87)	<0.001
		Week 16 <= to < Week 20	11	49.26	86.57	0.00	(0.0, 281.0)	(-8.90, 107.42)	11	49.26	0.00 (0.00)	86.57	0.00	(0.0, 281.0)	(-8.90, 107.42)	0.088
		Week 20 <= to < Week 24	10	13.04	41.25	0.00	(0.0, 130.4)	(-16.46, 42.55)	10	13.04	0.00 (0.00)	41.25	0.00	(0.0, 130.4)	(-16.46, 42.55)	0.343
		Week 24 <= to < Week 28	10	8.70	27.50	0.00	(0.0, 87.0)	(-10.98, 28.37)	10	8.70	0.00 (0.00)	27.50	0.00	(0.0, 87.0)	(-10.98, 28.37)	0.343
		Week 28 <= to < Week 32	10	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	10	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 32 <= to < Week 36	10	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	10	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 36 <= to < Week 40	10	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	10	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 40 <= to < Week 44	10	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	10	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 44 <= to < Week 48	10	0.00	0.00	0.00	(0.0, 0.0)	(-, -)	10	0.00	0.00 (0.00)	0.00	0.00	(0.0, 0.0)	(-, -)	-
		Week 48 <= to < Week 52	10	17.39	55.00	0.00	(0.0, 173.9)	(-21.95, 56.74)	10	17.39	0.00 (0.00)	55.00	0.00	(0.0, 173.9)	(-21.95, 56.74)	0.343

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Baseline <= to < Week 52	11	30.54	48.60	20.07	(6.6, 175.3)	(-2.11, 63.19)	11	30.54	0.00 (0.00)	48.60	20.07	(6.6, 175.3)	(-2.11, 63.19)	0.064

表 2.7.6.25－142　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 (mg)	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	85	934.97	1299.03	0.00	(0.0, 6087.5)	(654.78, 1215.17)								
		Baseline <= to < Week 2	85	848.67	1237.19	0.00	(0.0, 3195.9)	(581.81, 1115.52)	85	-86.30	934.97 (1299.03)	695.31	0.00	(-3043.8, 3043.8)	(-236.28, 63.67)	0.256
		Week 2 <= to < Week 4	85	788.43	1168.53	0.00	(0.0, 3195.9)	(536.39, 1040.48)	85	-146.54	934.97 (1299.03)	869.37	0.00	(-3043.8, 3043.8)	(-334.06, 40.98)	0.124
		Week 4 <= to < Week 6	85	890.11	1182.16	0.00	(0.0, 3195.9)	(635.12, 1145.09)	85	-44.87	934.97 (1299.03)	956.75	0.00	(-3043.8, 3043.8)	(-251.23, 161.50)	0.667
		Week 6 <= to < Week 8	85	1163.47	1350.10	456.56	(0.0, 6087.5)	(872.26, 1454.68)	85	228.49	934.97 (1299.03)	1341.65	0.00	(-3043.8, 6087.5)	(-60.89, 517.88)	0.120
		Week 8 <= to < Week 10	84	1283.89	1334.23	1521.88	(0.0, 4565.6)	(994.34, 1573.43)	84	337.79	934.97 (1299.03)	1354.64	0.00	(-3043.8, 3195.9)	(43.81, 631.76)	0.025
		Week 10 <= to < Week 12	84	1314.17	1316.24	1521.88	(0.0, 4565.6)	(1028.53, 1599.81)	84	368.07	934.97 (1299.03)	1317.92	0.00	(-3043.8, 3195.9)	(82.06, 654.07)	0.012
		Week 12 <= to < Week 16	84	1385.28	1284.75	1521.88	(0.0, 4565.6)	(1106.47, 1664.09)	84	439.18	934.97 (1299.03)	1344.80	0.00	(-3043.8, 3195.9)	(147.34, 731.02)	0.004
		Week 16 <= to < Week 20	82	1393.95	1327.07	1521.88	(0.0, 4565.6)	(1102.36, 1685.54)	82	424.77	934.97 (1299.03)	1391.28	0.00	(-3043.8, 3735.5)	(119.07, 730.47)	0.007
		Week 20 <= to < Week 24	80	1570.18	1490.51	1521.88	(0.0, 6087.5)	(1238.48, 1901.88)	80	648.43	934.97 (1299.03)	1596.04	0.00	(-3043.8, 5989.7)	(293.25, 1003.61)	<0.001
		Week 24 <= to < Week 28	78	1511.07	1413.20	1521.88	(0.0, 6087.5)	(1192.45, 1829.70)	78	585.20	934.97 (1299.03)	1470.06	0.00	(-3043.8, 3735.5)	(253.75, 916.64)	<0.001
		Week 28 <= to < Week 32	75	1417.52	1422.80	1521.88	(0.0, 6087.5)	(1090.16, 1744.87)	75	506.06	934.97 (1299.03)	1535.50	0.00	(-3043.8, 3735.5)	(152.77, 859.35)	0.006
		Week 32 <= to < Week 36	73	1385.03	1421.71	1521.88	(0.0, 6087.5)	(1053.32, 1716.73)	73	448.60	934.97 (1299.03)	1492.28	0.00	(-3043.8, 3735.5)	(100.42, 796.77)	0.012
		Week 36 <= to < Week 40	72	1430.76	1444.49	1521.88	(0.0, 6087.5)	(1091.32, 1770.20)	72	481.32	934.97 (1299.03)	1491.81	0.00	(-3043.8, 3735.5)	(130.77, 831.88)	0.008
		Week 40 <= to < Week 44	71	1346.42	1461.47	1521.88	(0.0, 6087.5)	(1000.49, 1692.34)	71	383.61	934.97 (1299.03)	1519.41	0.00	(-3043.8, 3735.5)	(23.97, 743.25)	0.037
		Week 44 <= to < Week 48	70	1331.33	1468.50	1521.88	(0.0, 6087.5)	(981.18, 1681.48)	70	354.77	934.97 (1299.03)	1528.45	0.00	(-3043.8, 3735.5)	(-9.68, 719.21)	0.056
		Week 48 <= to < Week 52	69	1387.75	1476.37	1521.88	(0.0, 6087.5)	(1033.09, 1742.42)	69	397.04	934.97 (1299.03)	1559.48	0.00	(-3043.8, 3735.5)	(22.41, 771.67)	0.038

表 2.7.6.25－142　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 (mg)	SD	Median	Minimum, Maximum	95% CI	N	Mean	Mean in Screening period (SD)	SD	Median	Minimum, Maximum	95% CI	p value
		Baseline <= to < Week 52	85	1318.14	1136.50	1170.67	(0.0, 5283.5)	(1073.01, 1563.28)	85	383.17	934.97 (1299.03)	1173.65	281.22	(-3043.8, 3019.3)	(130.02, 636.32)	0.003

表 2.7.6.25－142　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 (mg)	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	86	791.82	1244.38	0.00	(0.0, 3195.9)	(525.03, 1058.62)								
		Baseline <= to < Week 2	86	797.34	1253.48	0.00	(0.0, 3195.9)	(528.59, 1066.09)	86	5.52	791.82 (1244.38)	461.19	0.00	(-2397.0, 2826.3)	(-93.36, 104.40)	0.912
		Week 2 <= to < Week 4	86	903.01	1283.88	0.00	(0.0, 3195.9)	(627.75, 1178.28)	86	111.19	791.82 (1244.38)	635.92	0.00	(-2397.0, 3043.8)	(-25.15, 247.53)	0.109
		Week 4 <= to < Week 6	85	1136.16	1343.47	173.93	(0.0, 3195.9)	(846.38, 1425.94)	85	370.83	791.82 (1244.38)	1000.66	0.00	(-2397.0, 3195.9)	(155.00, 586.67)	<0.001
		Week 6 <= to < Week 8	85	1166.09	1417.68	0.00	(0.0, 5935.3)	(860.30, 1471.87)	85	400.76	791.82 (1244.38)	1223.02	0.00	(-3195.9, 5935.3)	(136.96, 664.56)	0.003
		Week 8 <= to < Week 10	85	1288.16	1471.70	913.13	(0.0, 6087.5)	(970.72, 1605.60)	85	522.83	791.82 (1244.38)	1251.08	0.00	(-3195.9, 6097.5)	(252.96, 792.68)	<0.001
		Week 10 <= to < Week 12	85	1460.74	1626.23	1521.88	(0.0, 6087.5)	(1131.54, 1789.94)	85	695.42	791.82 (1244.38)	1432.18	0.00	(-3195.9, 6087.5)	(386.50, 1004.33)	<0.001
		Week 12 <= to < Week 16	84	1596.90	1619.15	1521.88	(0.0, 6087.5)	(1266.22, 1925.57)	84	857.69	791.82 (1244.38)	1510.29	86.96	(-3195.9, 6087.5)	(529.94, 1185.45)	<0.001
		Week 16 <= to < Week 20	82	1653.76	1615.98	1521.88	(0.0, 6087.5)	(1320.66, 1986.86)	82	897.55	791.82 (1244.38)	1531.51	26.24	(-3195.9, 6087.5)	(561.04, 1234.06)	<0.001
		Week 20 <= to < Week 24	80	1440.23	1459.11	1521.88	(0.0, 6087.5)	(1123.62, 1772.94)	80	673.11	791.82 (1244.38)	1435.81	0.00	(-3195.9, 6087.5)	(353.59, 992.64)	<0.001
		Week 24 <= to < Week 28	79	1276.67	1383.15	1521.88	(0.0, 6087.5)	(966.86, 1586.48)	79	491.74	791.82 (1244.38)	1366.95	0.00	(-3195.9, 3261.2)	(185.56, 797.92)	0.002
		Week 28 <= to < Week 32	78	1253.32	1400.80	1141.41	(0.0, 6087.5)	(937.48, 1569.15)	78	477.17	791.82 (1244.38)	1363.81	0.00	(-3195.9, 3195.9)	(169.67, 784.66)	0.003
		Week 32 <= to < Week 36	75	1223.59	1393.52	760.94	(0.0, 6087.5)	(902.97, 1544.21)	75	477.26	791.82 (1244.38)	1385.32	0.00	(-3195.9, 3195.9)	(159.53, 796.00)	0.004
		Week 36 <= to < Week 40	74	1192.09	1383.97	722.89	(0.0, 6087.5)	(871.45, 1512.73)	74	456.24	791.82 (1244.38)	1359.92	0.00	(-3195.9, 3195.9)	(141.18, 771.31)	0.005
		Week 40 <= to < Week 44	73	1166.42	1378.00	760.94	(0.0, 6087.5)	(844.91, 1487.94)	73	462.20	791.82 (1244.38)	1346.32	0.00	(-3195.9, 3195.9)	(148.08, 776.31)	0.004
		Week 44 <= to < Week 48	71	1193.39	1381.78	760.94	(0.0, 6087.5)	(866.32, 1520.45)	71	469.32	791.82 (1244.38)	1358.51	0.00	(-3195.9, 3195.9)	(147.77, 790.88)	0.005
		Week 48 <= to < Week 52	70	1151.55	1375.84	467.43	(0.0, 6087.5)	(823.49, 1479.61)	70	417.14	791.82 (1244.38)	1350.16	0.00	(-3195.9, 3195.9)	(95.21, 739.08)	0.012

表 2.7.6.25－142　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 (mg)	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
		Baseline <= to < Week 52	86	1303.92	1168.06	1185.11	(0.0, 5619.2)	(1053.48, 1554.35)	86	512.09	791.82 (1244.38)	1025.92	253.19	(-2827.2, 3035.4)	(292.14, 732.05)	<0.001

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_6_1.sas

5.3.5.1—8 表 11.4.1—7 より引用

(7)　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 2.7.6.25－143 に示した．鉄剤の投与を受けた被験者の割合は，全集団を対象に記載した．

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及び 48 週～52 週後でいずれも 0%であり，darbepoetin 群においてスクリーニング期間 0%に対し，48 週～52 週後では 0.8%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 23.8%に対し，48 週～52 週後では 33.6%であり，darbepoetin 群においてスクリーニング期間 18.3%に対し，48 週～52 週後では 29.0%であった．

表 2.7.6.25－143 鉄剤の投与を受けた被験者の割合（FAS）

		MT-6548(N=151)				darbepoetin(N=153)				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	151	36(23.8)	(17.29, 31.45)		153	28(18.3)	(12.52, 25.35)		5.5	(-5.7, 16.7)	0.262
	Baseline <= to < Week 2	151	31(20.5)	(14.40, 27.86)	0.059	153	27(17.6)	(11.96, 24.63)	0.655	2.9	(-8.3, 14.1)	0.561
	Week 2 <= to < Week 4	150	31(20.7)	(14.49, 28.03)	0.132	153	31(20.3)	(14.20, 27.51)	0.180	0.4	(-10.9, 11.8)	1.000
	Week 4 <= to < Week 6	149	37(24.8)	(18.13, 32.57)	0.796	153	39(25.5)	(18.80, 33.16)	0.001	-0.7	(-12.0, 10.7)	1.000
	Week 6 <= to < Week 8	147	44(29.9)	(22.66, 38.03)	0.074	152	39(25.7)	(18.93, 33.36)	0.003	4.3	(-7.2, 15.6)	0.440
	Week 8 <= to < Week 10	146	46(31.5)	(24.08, 39.71)	0.033	152	44(28.9)	(21.89, 36.85)	<0.001	2.6	(-8.9, 13.9)	0.705
	Week 10 <= to < Week 12	146	49(33.6)	(25.97, 41.84)	0.007	151	50(33.1)	(25.68, 41.23)	<0.001	0.4	(-10.9, 11.9)	1.000
	Week 12 <= to < Week 16	144	54(37.5)	(29.58, 45.95)	<0.001	149	57(38.3)	(30.42, 46.57)	<0.001	-0.8	(-12.2, 10.8)	0.905
	Week 16 <= to < Week 20	141	52(36.9)	(28.92, 45.41)	0.002	147	55(37.4)	(29.58, 45.77)	<0.001	-0.5	(-12.1, 11.1)	1.000
	Week 20 <= to < Week 24	136	53(39.0)	(30.73, 47.70)	<0.001	145	51(35.2)	(27.43, 43.53)	<0.001	3.8	(-7.9, 15.5)	0.538
	Week 24 <= to < Week 28	129	51(39.5)	(31.04, 48.52)	<0.001	140	46(32.9)	(25.16, 41.30)	<0.001	6.7	(-5.3, 18.5)	0.309
	Week 28 <= to < Week 32	124	45(36.3)	(27.85, 45.40)	0.006	137	42(30.7)	(23.07, 39.10)	0.001	5.6	(-6.5, 17.7)	0.359
	Week 32 <= to < Week 36	122	44(36.1)	(27.57, 45.25)	0.009	132	39(29.5)	(21.93, 38.11)	0.002	6.5	(-5.8, 18.7)	0.286
	Week 36 <= to < Week 40	119	43(36.1)	(27.53, 45.45)	0.014	130	39(30.0)	(22.28, 38.66)	0.001	6.1	(-6.3, 18.4)	0.345
	Week 40 <= to < Week 44	117	39(33.3)	(24.89, 42.64)	0.102	129	37(28.7)	(21.07, 37.30)	0.001	4.7	(-7.9, 17.0)	0.490
	Week 44 <= to < Week 48	115	40(34.8)	(26.14, 44.23)	0.072	125	37(29.6)	(21.77, 38.42)	0.001	5.2	(-7.5, 17.8)	0.409
	Week 48 <= to < Week 52	113	38(33.6)	(25.01, 43.12)	0.144	124	36(29.0)	(21.23, 37.86)	0.002	4.6	(-8.2, 17.2)	0.484
	Baseline <= to < Week 52	151	78(51.7)	(43.39, 59.85)	<0.001	153	74(48.4)	(40.22, 56.58)	<0.001	3.3	(-8.1, 14.7)	0.646

表 2.7.6.25－143　鉄剤の投与を受けた被験者の割合（FAS）（続き）

		MT-6548(N=151)				darbepoetin(N=153)				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
Intravenous	Screening period	151	0(0.0)	(0.00, 2.41)		153	0(0.0)	(0.00, 2.38)		-	-	-
	Baseline <= to < Week 2	151	0(0.0)	(0.00, 2.41)	-	153	0(0.0)	(0.00, 2.38)	-	-	-	-
	Week 2 <= to < Week 4	150	0(0.0)	(0.00, 2.43)	-	153	1(0.7)	(0.02, 3.59)	0.317	-0.7	(-11.9, 10.6)	1.000
	Week 4 <= to < Week 6	149	0(0.0)	(0.00, 2.45)	-	153	4(2.6)	(0.72, 6.56)	0.046	-2.6	(-13.9, 8.8)	0.123
	Week 6 <= to < Week 8	147	0(0.0)	(0.00, 2.48)	-	152	1(0.7)	(0.02, 3.61)	0.317	-0.7	(-12.0, 10.7)	1.000
	Week 8 <= to < Week 10	146	1(0.7)	(0.02, 3.76)	0.317	152	6(3.9)	(1.46, 8.39)	0.014	-3.3	(-14.6, 8.2)	0.121
	Week 10 <= to < Week 12	146	2(1.4)	(0.17, 4.86)	0.157	151	1(0.7)	(0.02, 3.63)	0.317	0.7	(-10.7, 12.1)	0.617
	Week 12 <= to < Week 16	144	2(1.4)	(0.17, 4.93)	0.157	149	8(5.4)	(2.35, 10.31)	0.005	-4.0	(-15.5, 7.5)	0.104
	Week 16 <= to < Week 20	141	2(1.4)	(0.17, 5.03)	0.157	147	4(2.7)	(0.75, 6.82)	0.046	-1.3	(-12.9, 10.3)	0.685
	Week 20 <= to < Week 24	136	3(2.2)	(0.46, 6.31)	0.083	145	1(0.7)	(0.02, 3.78)	0.317	1.5	(-10.2, 13.2)	0.357
	Week 24 <= to < Week 28	129	3(2.3)	(0.48, 6.65)	0.083	140	1(0.7)	(0.02, 3.92)	0.317	1.6	(-10.3, 13.5)	0.353
	Week 28 <= to < Week 32	124	2(1.6)	(0.20, 5.70)	0.157	137	0(0.0)	(0.00, 2.66)	-	1.6	(-10.5, 13.7)	0.225
	Week 32 <= to < Week 36	122	2(1.6)	(0.20, 5.80)	0.157	132	0(0.0)	(0.00, 2.76)	-	1.6	(-10.7, 13.9)	0.230
	Week 36 <= to < Week 40	119	1(0.8)	(0.02, 4.59)	0.317	130	0(0.0)	(0.00, 2.80)	-	0.8	(-11.6, 13.2)	0.478
	Week 40 <= to < Week 44	117	0(0.0)	(0.00, 3.10)	-	129	0(0.0)	(0.00, 2.82)	-	-	-	-
	Week 44 <= to < Week 48	115	2(1.7)	(0.21, 6.14)	0.157	125	0(0.0)	(0.00, 2.91)	-	1.7	(-10.9, 14.4)	0.229
	Week 48 <= to < Week 52	113	0(0.0)	(0.00, 3.21)	-	124	1(0.8)	(0.02, 4.41)	0.317	-0.8	(-13.5, 11.9)	1.000
	Baseline <= to < Week 52	151	6(4.0)	(1.47, 8.45)	0.014	153	11(7.2)	(3.64, 12.50)	<0.001	-3.2	(-14.4, 8.2)	0.318