4) 被験者番号 54179060GVH3001-[redacted]

■ REASON FOR NARRATIVE SELECTION

Treatment-emergent serious adverse events (SAEs)

■ Death

No Death reported

■ Treatment-emergent serious adverse events (SAEs)

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
肺炎	PNEUMONIA	20[redacted] 20[redacted]	305 11	Y 3	POSSIBLE DOSE NOT CHANGED	Y RECOVERED/RESOLVED	5

Note: Adverse Events are coded using MedDRA 22.1

■ Adverse events (AEs) leading to ibrutinib discontinuation

No Adverse events (AEs) leading to ibrutinib discontinuation reported

■ Other malignancies

No Other malignancies reported

■ Major hemorrhage

No Major hemorrhage reported

■ Demographics, Baseline Characteristics

- Country: JPN
- Race: Asian
- Age: 5[redacted]
- Sex: Female
- Baseline height (cm):[redacted]
- Baseline weight (kg)[redacted]
- Baseline karnofsky/Lansky performance status score: 90
- Overall severity of cGVHD: Severe
- cGVHD disease state: STEROID REFRACTORY DISEASE
- Month from initial diagnosis date: 21.6
- Number of prior cGVHD treatment regimens: 1
- First study drug intake: 20[redacted] (Study Day 1)
- Last study drug intake: 20[redacted] (Study Day 421)

■ Disposition Information

□ End of treatment: Subject Ongoing on Treatment

□ End of trial: Subject Ongoing on Study

■ Other Adverse Events

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
筋痙縮	CRAMPS IN THE CALVES	20[redacted] 20	1 112	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	1
サイトメガロウイルス感染	CYTOMEGALOVIRUS INFECTION	20 20	113 43	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	2
咳嗽	DRY COUGH	20 20	141 15	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	3
上気道感染	UPPER RESPIRATORY TRACT INFECTION	20 20	260 45	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	8
副鼻腔炎	SINUSITIS	20 20	276 17	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	7
白内障	LEFT EYE CATARACT	20 -	312 -	N 2	NOT RELATED DOSE NOT CHANGED	N NOT RECOVERED/NOT RESOLVED	4
白内障	RIGHT EYE CATARACT	20 -	312 -	N 2	NOT RELATED DOSE NOT CHANGED	N NOT RECOVERED/NOT RESOLVED	6
上気道感染	UPPER RESPIRATORY TRACT INFECTION	20 20	323 99	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	9

Note: Adverse Events are coded using MedDRA 22.1

■ Medical History

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Metabolism and nutrition disorders	Hyperlipidaemia	HYPERLIPIDAEMIA	ONGOING	2
Vascular disorders	Hypertension	HYPERTENSION	ONGOING	2

Note: Medical History are coded using MedDRA 22.1

■ Transplant History

Transplantation Date	Dictionary-Derived Term	Transplant Type	HLA matching and donor relation to recipient	Sex matching between donor and recipient	Stem Cell Source
20[redacted]	Acute myeloid leukaemia	Myeloablative	Matched related	Unmatched	Bone Marrow

■ Disease History

Date of Initial Diagnosis	Initial Diagnosis
20[redacted]	CGVHD

■ Study Medication

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 1 DAY 1	20[redacted]	20[redacted]	1	1	420.0	-	-	-
WEEK 1 DAY 2	20	20	2	7	420.0	-	-	-
WEEK 2	20	20	8	28	420.0	-	-	-
WEEK 5	20	20	29	58	420.0	-	-	-
WEEK 9	20	20	59	86	420.0	-	-	-
WEEK 13	20	20	87	112	420.0	-	-	-
WEEK 17	20	20	113	140	420.0	-	-	-
WEEK 21	20	20	141	170	420.0	-	-	-
WEEK 25	20	20	171	259	420.0	-	-	-
WEEK 37	20	20	260	311	420.0	-	-	-
WEEK 37	20	20	312	329	280.0	-	CYP3A INHIBITOR	-
WEEK 49	20	20	330	330	280.0	-	-	-
WEEK 49	20	20	331	420	420.0	-	CYP3A INHIBITOR	-
WEEK 61	20	20	421	421	420.0	-	-	-

■ Prior and Concomitant Medications

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
DIMEMORFAN PHOSPHATE (ASTOMIN [DIMEMORFAN PHOSPHATE])	20[redacted] 305	-	20[redacted] 315	ADVERSE EVENT	10 mg	TID ORAL	5
DIMEMORFAN PHOSPHATE (ASTOMIN [DIMEMORFAN PHOSPHATE])	20[redacted] 316	-	20[redacted] 325	PROPHYLAXIS	10 mg	TID ORAL	-
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 311	-	20[redacted] 315	ADVERSE EVENT	1 TABLET	TID ORAL	5
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 316	-	20[redacted] 325	PROPHYLAXIS	1 TABLET	TID ORAL	-
SULFAMETHOXAZOLE; TRIMETHOPRIM (BACTRAMIN)	- -	Y	- -	PROPHYLAXIS	1 TABLET	QD ORAL	-
BROMHEXINE HYDROCHLORIDE (BISOLVON)	20[redacted] 141	-	20[redacted] 154	ADVERSE EVENT	4 mg	TID ORAL	3
BROMHEXINE HYDROCHLORIDE (BISOLVON)	20[redacted] 260	-	20[redacted] 292	ADVERSE EVENT	4 mg	TID ORAL	7
BROMHEXINE HYDROCHLORIDE (BISOLVON)	20[redacted] 260	-	20[redacted] 292	ADVERSE EVENT	4 mg	TID ORAL	8
BROMHEXINE HYDROCHLORIDE (BISOLVON)	20[redacted] 323	-	20[redacted] 420	ADVERSE EVENT	4 mg	TID ORAL	9
ALENDRONATE SODIUM (BONALON TABLET)	- -	Y	- -	PROPHYLAXIS	35 mg	EVERY WEEK ORAL	-
CASPOFUNGIN ACETATE (CANCIDAS FOR INTRAVENOUS)	20[redacted] 305	-	20[redacted] 305	ADVERSE EVENT	70 mg	PRN INTRAVENOUS	5
CASPOFUNGIN ACETATE (CANCIDAS FOR INTRAVENOUS)	20[redacted] 306	-	20[redacted] 311	ADVERSE EVENT	50 mg	QD INTRAVENOUS	5
CLARITHROMYCIN (CLARITH TAB.)	20[redacted] 323	-	20[redacted] 325	PROPHYLAXIS	- mg	BID ORAL	-
ROSUVASTATIN CALCIUM (CRESTOR)	20[redacted] 87	-	- -	MEDICAL HISTORY	2.5 mg	QD ORAL	-

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Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
CEFCAPENE PIVOXIL HYDROCHLORIDE (FLOMOX [CEFCAPENE PIVOXIL HYDROCHLORIDE])	20[redacted] 276	-	20[redacted] 282	ADVERSE EVENT	100 mg	TID ORAL	8
CEFCAPENE PIVOXIL HYDROCHLORIDE (FLOMOX [CEFCAPENE PIVOXIL HYDROCHLORIDE])	20[redacted] 276	-	20[redacted] 282	ADVERSE EVENT	100 mg	TID ORAL	7
INFLUENZA VACCINE (FLUBIK HA)	20[redacted] 421	-	20[redacted] 421	PROPHYLAXIS	0.5 mL	ONCE SUBCUTANEOUS	-
CEFEPIME HYDROCHLORIDE (MAXIPIME FOR INJECTION)	20[redacted] 305	-	20[redacted] 310	ADVERSE EVENT	2 g	QD INTRAVENOUS	5
CEFEPIME HYDROCHLORIDE (MAXIPIME FOR INJECTION)	20[redacted] 311	-	20[redacted] 311	ADVERSE EVENT	1 g	QD INTRAVENOUS	5
DEXTROMETHORPHAN HYDROBROMIDE (MEDICON [DEXTROMETHORPHAN HYDROBROMIDE])	20[redacted] 141	-	20[redacted] 154	ADVERSE EVENT	30 mg	TID ORAL	3
DEXTROMETHORPHAN HYDROBROMIDE (MEDICON [DEXTROMETHORPHAN HYDROBROMIDE])	20[redacted] 260	-	20[redacted] 290	ADVERSE EVENT	15 mg	TID ORAL	8
DEXTROMETHORPHAN HYDROBROMIDE (MEDICON [DEXTROMETHORPHAN HYDROBROMIDE])	20[redacted] 260	-	20[redacted] 290	ADVERSE EVENT	15 mg	TID ORAL	7
MINOCYCLINE HYDROCHLORIDE (MINOMYCIN)	20[redacted] 281	-	20[redacted] 290	ADVERSE EVENT	50 mg	BID ORAL	8
MINOCYCLINE HYDROCHLORIDE (MINOMYCIN)	20[redacted] 281	-	20[redacted] 290	ADVERSE EVENT	50 mg	BID ORAL	7
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 276	-	20[redacted] 292	ADVERSE EVENT	500 mg	TID ORAL	8
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 276	-	20[redacted] 292	ADVERSE EVENT	500 mg	TID ORAL	7
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 307	-	20[redacted] 309	ADVERSE EVENT	500 mg	TID ORAL	5
ESOMEPRAZOLE MAGNESIUM (NEXIUM CAPSULES)	- -	Y	- -	CGVHD	20 mg	QD ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
OLMESARTAN MEDOXOMIL (OLMETEC OD TABLETS)	20[redacted] 171	-	20[redacted] 217	MEDICAL HISTORY	20 mg	QD ORAL	-
OXYGEN (OXYGEN)	20[redacted] 306	-	20[redacted] 306	ADVERSE EVENT	1 L	OTHER OTHER	5
OXYGEN (OXYGEN)	20[redacted] 307	-	20[redacted] 307	ADVERSE EVENT	2 L	OTHER OTHER	5
MONTELUKAST SODIUM (SINGULAIR)	20[redacted] 141	-	20[redacted] 154	ADVERSE EVENT	10 mg	QD ORAL	3
CALCIUM CHLORIDE DIHYDRATE; POTASSIUM CHLORIDE; SODIUM ACETATE TRIHYDRATE; SODIUM CHLORIDE (SOLYUGEN F INJ.)	20[redacted] 305	-	20[redacted] 305	ADVERSE EVENT	500 mL	PRN INTRAVENOUS	5
GLYCYRRHIZA SPP. ROOT; PAEONIA LACTIFLORA ROOT (TSUMURA SHAKUYAKUKANZOTO)	20[redacted] 1	-	20[redacted] 112	ADVERSE EVENT	2.5 g	BID ORAL	1
VALGANCICLOVIR HYDROCHLORIDE (VALIXA TABLETS)	20[redacted] 141	-	20[redacted] 154	ADVERSE EVENT	450 mg	QD ORAL	2
VALGANCICLOVIR HYDROCHLORIDE (VALIXA TABLETS)	20[redacted] 155	-	20[redacted] 167	ADVERSE EVENT	450 mg	QOD ORAL	2
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN IH)	20[redacted] 308	-	20[redacted] 310	ADVERSE EVENT	5 g	QD INTRAVENOUS	5
VORICONAZOLE (VFEND)	20[redacted] 312	-	20[redacted] 312	ADVERSE EVENT	100 mg	BID ORAL	5
VORICONAZOLE (VFEND)	20[redacted] 312	-	20[redacted] 315	ADVERSE EVENT	200 mg	BID ORAL	5
VORICONAZOLE (VFEND)	20[redacted] 316	-	20[redacted] 329	PROPHYLAXIS	200 mg	BID ORAL	-
LEVOCETIRIZINE DIHYDROCHLORIDE (XYZAL TABLET)	20[redacted] 141	-	20[redacted] 154	ADVERSE EVENT	5 mg	QD ORAL	3

■ Karnofsky/Lansky performance status score

Date of Finding Study Day of Finding	Visit Name	Result
20[redacted]-21	SCREENING	90
20[redacted]1	WEEK 1 DAY 1	90
20[redacted]29	WEEK 5	80
20[redacted]59	WEEK 9	90
20[redacted]87	WEEK 13	90
20[redacted]113	WEEK 17	90
20[redacted]141	WEEK 21	90
20[redacted]171	WEEK 25	90
20[redacted]260	WEEK 37	90
20[redacted]330	WEEK 49	90
20[redacted]421	WEEK 61	90

■ Laboratory Data

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted]-21	SCREENING	22	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted]1	WEEK 1 DAY 1	21	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted]8	WEEK 2	24	0	34.99	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	25	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 59	WEEK 9	30	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 87	WEEK 13	32	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 113	WEEK 17	29	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	30	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 171	WEEK 25	30	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 260	WEEK 37	23	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 330	WEEK 49	20	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 421	WEEK 61	20	0	34.99	NORMAL	0
Albumin (g/L)	20[redacted] -21	SCREENING	39	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 1	WEEK 1 DAY 1	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 8	WEEK 2	38	39	48	LOW	1
Albumin (g/L)	20[redacted] 29	WEEK 5	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 59	WEEK 9	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 87	WEEK 13	39	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 113	WEEK 17	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 141	WEEK 21	38	39	48	LOW	1

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Albumin (g/L)	20[redacted] 171	WEEK 25	39	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 260	WEEK 37	36	39	48	LOW	1
Albumin (g/L)	20[redacted] 330	WEEK 49	38	39	48	LOW	1
Albumin (g/L)	20[redacted] 421	WEEK 61	41	39	48	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] -21	SCREENING	87	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	87	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 8	WEEK 2	87	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 29	WEEK 5	72	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 59	WEEK 9	91	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 87	WEEK 13	78	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 113	WEEK 17	79	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 141	WEEK 21	86	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 171	WEEK 25	78	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 260	WEEK 37	74	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 330	WEEK 49	70	100	310	LOW	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 421	WEEK 61	70	100	310	LOW	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] -21	SCREENING	23	0	29.99	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	18	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	20	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	19	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 59	WEEK 9	25	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 87	WEEK 13	21	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 113	WEEK 17	21	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	20	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 171	WEEK 25	24	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 260	WEEK 37	22	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 330	WEEK 49	23	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 421	WEEK 61	22	0	29.99	NORMAL	0
Bilirubin (umol/L)	20[redacted] -21	SCREENING	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 1	WEEK 1 DAY 1	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 8	WEEK 2	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 29	WEEK 5	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 59	WEEK 9	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 87	WEEK 13	6.84	3.42	18.81	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Bilirubin (umol/L)	20[redacted] 113	WEEK 17	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 141	WEEK 21	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 171	WEEK 25	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 260	WEEK 37	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 330	WEEK 49	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 421	WEEK 61	10.26	3.42	18.81	NORMAL	0
Creatinine (umol/L)	20[redacted] -21	SCREENING	106.08	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 1	WEEK 1 DAY 1	116.688	44.2	70.72	HIGH	2
Creatinine (umol/L)	20[redacted] 8	WEEK 2	100.776	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 29	WEEK 5	113.152	44.2	70.72	HIGH	2
Creatinine (umol/L)	20[redacted] 59	WEEK 9	99.892	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 87	WEEK 13	101.66	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 113	WEEK 17	103.428	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 141	WEEK 21	108.732	44.2	70.72	HIGH	2
Creatinine (umol/L)	20[redacted] 171	WEEK 25	112.268	44.2	70.72	HIGH	2
Creatinine (umol/L)	20[redacted] 260	WEEK 37	104.312	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 330	WEEK 49	99.892	44.2	70.72	HIGH	1

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Creatinine (umol/L)	20[redacted] 421	WEEK 61	116.688	44.2	70.72	HIGH	2
Eosinophils (10^9/L)	20[redacted] -21	SCREENING	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 8	WEEK 2	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 29	WEEK 5	0.077	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 59	WEEK 9	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 87	WEEK 13	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 113	WEEK 17	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 141	WEEK 21	0.075	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 171	WEEK 25	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 260	WEEK 37	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 330	WEEK 49	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 421	WEEK 61	0	0.04	0.32	LOW	-
Glucose (mmol/L)	20[redacted] -21	SCREENING	6.0506	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	7.1608	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 8	WEEK 2	6.2171	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 29	WEEK 5	5.9951	3.8857	6.1061	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Glucose (mmol/L)	20[redacted] 59	WEEK 9	5.6065	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 87	WEEK 13	6.5502	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 113	WEEK 17	5.6065	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 141	WEEK 21	5.2735	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 171	WEEK 25	5.2179	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 260	WEEK 37	5.551	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 330	WEEK 49	5.6065	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 421	WEEK 61	5.329	3.8857	6.1061	NORMAL	0
HIV Antibody	20[redacted] -21	SCREENING	NEGATIVE	-	-	-	-
Hemoglobin (g/L)	20[redacted] -21	SCREENING	137	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 1	WEEK 1 DAY 1	130	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 8	WEEK 2	137	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 29	WEEK 5	133	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 59	WEEK 9	134	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 87	WEEK 13	138	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 113	WEEK 17	130	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 141	WEEK 21	136	115	155	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Hemoglobin (g/L)	20[redacted] 171	WEEK 25	134	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 260	WEEK 37	125	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 330	WEEK 49	115	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 421	WEEK 61	132	115	155	NORMAL	0
Hepatitis B Virus Core Antibody	20[redacted] -21	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antibody	20[redacted] -21	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antigen	20[redacted] -21	SCREENING	NEGATIVE	-	-	-	-
Hepatitis C Virus Antibody	20[redacted] -21	SCREENING	NEGATIVE	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] -21	SCREENING	1.58	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 87	WEEK 13	1.21	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 171	WEEK 25	1.03	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 260	WEEK 37	1.06	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 330	WEEK 49	1.33	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 421	WEEK 61	1.46	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] -21	SCREENING	7.22	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 87	WEEK 13	3.63	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 171	WEEK 25	2.92	-	-	-	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Immunoglobulin G (g/L)	20[redacted] 260	WEEK 37	2.48	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 330	WEEK 49	5.78	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 421	WEEK 61	4.72	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] -21	SCREENING	0.57	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 87	WEEK 13	0.28	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 171	WEEK 25	0.34	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 260	WEEK 37	0.21	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 330	WEEK 49	0.4	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 421	WEEK 61	0.23	-	-	-	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] -21	SCREENING	272	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	277	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 8	WEEK 2	314	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 29	WEEK 5	345	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 59	WEEK 9	408	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 87	WEEK 13	398	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 113	WEEK 17	420	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 141	WEEK 21	421	110	219	HIGH	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 171	WEEK 25	407	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 260	WEEK 37	323	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 330	WEEK 49	370	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 421	WEEK 61	261	110	219	HIGH	-
Leukocytes (10^9/L)	20[redacted] -21	SCREENING	10.4	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	9	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 8	WEEK 2	10.4	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 29	WEEK 5	15.4	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 59	WEEK 9	12.9	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 87	WEEK 13	9.8	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 113	WEEK 17	17.6	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 141	WEEK 21	15	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 171	WEEK 25	13.7	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 260	WEEK 37	16.3	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 330	WEEK 49	13	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 421	WEEK 61	14.3	4	8	HIGH	0
Lymphocytes (10^9/L)	20[redacted] -21	SCREENING	1.3	0.8	3.2	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lymphocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	2.25	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 8	WEEK 2	1.456	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 29	WEEK 5	1.001	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 59	WEEK 9	1.871	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 87	WEEK 13	1.96	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 113	WEEK 17	1.76	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 141	WEEK 21	3.675	0.8	3.2	HIGH	0
Lymphocytes (10^9/L)	20[redacted] 171	WEEK 25	1.918	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 260	WEEK 37	2.364	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 330	WEEK 49	1.755	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 421	WEEK 61	1.93	0.8	3.2	NORMAL	0
Neutrophils (10^9/L)	20[redacted] -21	SCREENING	8.892	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	6.21	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 8	WEEK 2	8.736	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 29	WEEK 5	13.629	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 59	WEEK 9	10.514	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 87	WEEK 13	6.762	1.6	6.32	HIGH	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Neutrophils (10^9/L)	20[redacted] 113	WEEK 17	15.048	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 141	WEEK 21	9.825	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 171	WEEK 25	10.96	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 260	WEEK 37	12.959	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 330	WEEK 49	10.855	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 421	WEEK 61	12.226	1.6	6.32	HIGH	0
Platelets (10^9/L)	20[redacted] -21	SCREENING	170	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	162	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 8	WEEK 2	134	140	400	LOW	1
Platelets (10^9/L)	20[redacted] 29	WEEK 5	176	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 59	WEEK 9	159	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 87	WEEK 13	163	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 113	WEEK 17	159	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 141	WEEK 21	164	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 171	WEEK 25	162	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 260	WEEK 37	177	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 330	WEEK 49	154	140	400	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Platelets (10^9/L)	20[redacted] 421	WEEK 61	172	140	400	NORMAL	0
Potassium (mmol/L)	20[redacted] -21	SCREENING	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 8	WEEK 2	3.6	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 29	WEEK 5	4.2	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 59	WEEK 9	4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 87	WEEK 13	3.7	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 113	WEEK 17	4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 141	WEEK 21	3.7	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 171	WEEK 25	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 260	WEEK 37	4.1	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 330	WEEK 49	4.1	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 421	WEEK 61	3.8	3.5	4.8	NORMAL	0
Protein (g/L)	20[redacted] -21	SCREENING	70	67	83	NORMAL	-
Protein (g/L)	20[redacted] 1	WEEK 1 DAY 1	65	67	83	LOW	-
Protein (g/L)	20[redacted] 8	WEEK 2	66	67	83	LOW	-
Protein (g/L)	20[redacted] 29	WEEK 5	64	67	83	LOW	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Protein (g/L)	20[redacted] 59	WEEK 9	63	67	83	LOW	-
Protein (g/L)	20[redacted] 87	WEEK 13	65	67	83	LOW	-
Protein (g/L)	20[redacted] 113	WEEK 17	62	67	83	LOW	-
Protein (g/L)	20[redacted] 141	WEEK 21	66	67	83	LOW	-
Protein (g/L)	20[redacted] 171	WEEK 25	64	67	83	LOW	-
Protein (g/L)	20[redacted] 260	WEEK 37	60	67	83	LOW	-
Protein (g/L)	20[redacted] 330	WEEK 49	66	67	83	LOW	-
Protein (g/L)	20[redacted] 421	WEEK 61	66	67	83	LOW	-
Sodium (mmol/L)	20[redacted] -21	SCREENING	143	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	146	136	145	HIGH	1
Sodium (mmol/L)	20[redacted] 8	WEEK 2	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 29	WEEK 5	146	136	145	HIGH	1
Sodium (mmol/L)	20[redacted] 59	WEEK 9	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 87	WEEK 13	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 113	WEEK 17	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 141	WEEK 21	146	136	145	HIGH	1
Sodium (mmol/L)	20[redacted] 171	WEEK 25	142	136	145	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Sodium (mmol/L)	20[redacted] 260	WEEK 37	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 330	WEEK 49	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 421	WEEK 61	144	136	145	NORMAL	0
Urate (umol/L)	20[redacted] -21	SCREENING	303.348	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 1	WEEK 1 DAY 1	309.296	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 8	WEEK 2	273.608	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 29	WEEK 5	356.88	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 59	WEEK 9	327.14	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 87	WEEK 13	362.828	178.44	356.88	HIGH	1
Urate (umol/L)	20[redacted] 113	WEEK 17	327.14	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 141	WEEK 21	356.88	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 171	WEEK 25	344.984	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 260	WEEK 37	327.14	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 330	WEEK 49	315.244	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 421	WEEK 61	362.828	178.44	356.88	HIGH	1
Urea Nitrogen (mmol/L)	20[redacted] -21	SCREENING	7.854	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	8.568	2.856	7.14	HIGH	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urea Nitrogen (mmol/L)	20[redacted] 8	WEEK 2	6.783	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 29	WEEK 5	8.925	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 59	WEEK 9	8.568	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 87	WEEK 13	8.568	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 113	WEEK 17	8.211	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 141	WEEK 21	7.14	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 171	WEEK 25	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 260	WEEK 37	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 330	WEEK 49	8.568	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 421	WEEK 61	6.783	2.856	7.14	NORMAL	-

5) 被験者番号 54179060GVH3001-[redacted]

■ REASON FOR NARRATIVE SELECTION

Treatment-emergent serious adverse events (SAEs)

Major hemorrhage

■ Death

No Death reported

■ Treatment-emergent serious adverse events (SAEs)

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
胃腸出血	HEMORRHAGE OF DIGESTIVE TRACT	20[redacted] 20[redacted]	134 14	Y 3	PROBABLE DRUG INTERRUPTED	Y RECOVERED/RESOLVED	2
胃腸出血	HEMORRHAGE OF DIGESTIVE TRACT	20[redacted] 20[redacted]	150 32	Y 3	PROBABLE DOSE REDUCED	Y RECOVERED/RESOLVED	3

Note: Adverse Events are coded using MedDRA 22.1

■ Adverse events (AEs) leading to ibrutinib discontinuation

No Adverse events (AEs) leading to ibrutinib discontinuation reported

■ Other malignancies

No Other malignancies reported

■ Major hemorrhage

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
胃腸出血	HEMORRHAGE OF DIGESTIVE TRACT	20[redacted] 20[redacted]	134 14	Y 3	PROBABLE DRUG INTERRUPTED	Y RECOVERED/RESOLVED	2
胃腸出血	HEMORRHAGE OF DIGESTIVE TRACT	20[redacted] 20[redacted]	150 32	Y 3	PROBABLE DOSE REDUCED	Y RECOVERED/RESOLVED	3

Note: Adverse Events are coded using MedDRA 22.1

■ Demographics, Baseline Characteristics

- Country: JPN
- Race: Asian
- Age: 6[redacted]
- Sex: Female
- Baseline height (cm): [redacted]
- Baseline weight (kg): [redacted]
- Baseline karnofsky/Lansky performance status score: 90
- Overall severity of cGVHD: Moderate
- cGVHD disease state: STEROID REFRACTORY DISEASE
- Month from initial diagnosis date: 13.9
- Number of prior cGVHD treatment regimens: 1
- First study drug intake: 20[redacted] (Study Day 1)
- Last study drug intake: 20[redacted] (Study Day 363)

■ Disposition Information

□ End of treatment: Subject Ongoing on Treatment

□ End of trial: Subject Ongoing on Study

■ Other Adverse Events

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
低γグロブリン血症	HYPOGAMMAGLOBULINEMIA	20[redacted] -	69 -	N 2	VERY LIKELY DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	4
肺炎	PNEUMONIA	20[redacted] 20[redacted]	106 10	N 1	DOUBTFUL DOSE NOT CHANGED	Y RECOVERED/RESOLVED	6
上気道感染	UPPER RESPIRATORY INFECTION	20[redacted] 20[redacted]	131 8	N 2	PROBABLE DOSE NOT CHANGED	Y RECOVERED/RESOLVED	9
皮膚剥脱	SKIN PEEKING	20[redacted] 20[redacted]	290 32	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	8

Note: Adverse Events are coded using MedDRA 22.1

■ Medical History

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Immune system disorders	Acute graft versus host disease	ACUTE GRAFT VERSUS HOST DISEASE	BEFORE	-
Blood and lymphatic system disorders	Haemolytic anaemia	HAEMOLYTIC ANEMIA	ONGOING	1
Metabolism and nutrition disorders	Hyperlipidaemia	HYPERLIPIDAEMIA	ONGOING	1
Psychiatric disorders	Insomnia	INSOMNIA	ONGOING	1
Gastrointestinal disorders	Haemorrhoids	INTERNAL HEMORRHOID	ONGOING	1
Musculoskeletal and connective tissue disorders	Back pain	LUMBAGO	ONGOING	1
Blood and lymphatic system disorders	Iron deficiency anaemia	IRON DEFICIENCY ANEMIA	ONGOING	2

Note: Medical History are coded using MedDRA 22.1

■ Transplant History

Transplantation Date	Dictionary-Derived Term	Transplant Type	HLA matching and donor relation to recipient	Sex matching between donor and recipient	Stem Cell Source
20[redacted]	Acute myeloid leukaemia	Nmyeloablative	Pmatched unrelated	Unknown	Cord Blood

■ Disease History

Date of Initial Diagnosis	Initial Diagnosis
20[redacted]	CGVHD

■ Study Medication

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 1 DAY 1	20[redacted]	20[redacted]	1	1	280.0	-	CYP3A INHIBITOR	-
WEEK 1 DAY 2	20	20	2	7	280.0	-	-	-
WEEK 2	20	20	8	28	280.0	-	-	-
WEEK 5	20	20	29	54	280.0	-	-	-
WEEK 9	20	20	55	82	280.0	-	-	-
WEEK 13	20	20	83	110	280.0	-	-	-
WEEK 17	20	20	111	125	280.0	-	-	-
WEEK 17	20	20	126	141	0.0	ADVERSE EVENT	-	-
WEEK 17	20	20	126	141	0.0	ADVERSE EVENT	-	-
WEEK 21	20	20	142	142	0.0	ADVERSE EVENT	-	-
WEEK 21	20	20	143	150	280.0	-	-	-
WEEK 21	20	20	151	168	0.0	ADVERSE EVENT	-	-
WEEK 25	20	20	169	195	0.0	ADVERSE EVENT	-	-
WEEK 25	20	20	196	257	140.0	-	ADVERSE EVENT	3
WEEK 37	20	20	258	334	140.0	-	-	-
WEEK 49	20	20	335	363	140.0	-	-	-

■ Prior and Concomitant Medications

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
WHITE SOFT PARAFFIN (ABSORPIVE CREAM[WHITE PETROLATUM])	20[redacted] 216	-	20[redacted] 362	PROPHYLAXIS	1 FINGERTIP UNIT	PRN TRANSDERMAL	-
ACICLOVIR (ACICLOVIR TABLETS)	20[redacted] -1038	Y	- -	PROPHYLAXIS	100 mg	QD ORAL	-
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 127	-	20[redacted] 138	ADVERSE EVENT	30 mg	TID ORAL	2
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 127	-	20[redacted] 138	ADVERSE EVENT	30 mg	TID ORAL	1
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 134	-	20[redacted] 134	ADVERSE EVENT	50 mg	QD INTRAVENOUS	2
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 135	-	20[redacted] 141	ADVERSE EVENT	50 mg	BID INTRAVENOUS	2
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 153	-	20[redacted] 166	ADVERSE EVENT	30 mg	TID ORAL	3
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 164	-	20[redacted] 169	ADVERSE EVENT	50 mg	BID INTRAVENOUS	3
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 209	-	- -	ADVERSE EVENT	30 mg	TID ORAL	7
CARBAZOCHROME SODIUM SULFONATE (ADONA [CARBAZOCHROME SODIUM SULFONATE])	20[redacted] 209	-	- -	ADVERSE EVENT	30 mg	TID ORAL	5
SODIUM ALGINATE (ALLOID G ORAL SOLUTION 5%)	20[redacted] 160	-	20[redacted] 166	PROPHYLAXIS	20 mL	TID ORAL	-
ZOPICLONE (AMOBAN)	20[redacted] 216	-	20[redacted] 225	MEDICAL HISTORY	7.5 mg	QD ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
AMOXICILLIN TRIHYDRATE (AMOXICILLIN HYDRATE)	20[redacted] 106	-	20[redacted] 111	ADVERSE EVENT	25 mg	TID ORAL	6
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] -16	-	20[redacted] 1	PROPHYLAXIS	1 TABLET	TID ORAL	-
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 106	-	20[redacted] 116	ADVERSE EVENT	1 TABLET	TID ORAL	6
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 131	-	20[redacted] 138	PROPHYLAXIS	1 TABLET	TID ORAL	-
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 156	-	20[redacted] 159	PROPHYLAXIS	1 TABLET	TID ORAL	-
AMOXICILLIN TRIHYDRATE; CLAVULANATE POTASSIUM (AUGMENTIN COMBINATION TABLETS)	20[redacted] 177	-	20[redacted] 181	PROPHYLAXIS	1 TABLET	TID ORAL	-
SULFAMETHOXAZOLE; TRIMETHOPRIM (BACTRAMIN)	20[redacted] -1082	Y	- -	PROPHYLAXIS	0.5 TABLET	QD ORAL	-
BECLOMETASONE (BECLOMETASONE ENTERIC CAPSULE)	20[redacted] -9	-	20[redacted] 82	CGVHD	1 mg	TID ORAL	-
BECLOMETASONE (BECLOMETASONE ENTERIC CAPSULE)	20[redacted] 83	-	20[redacted] 110	CGVHD	1 mg	BID ORAL	-
AMINO ACIDS NOS; ELECTROLYTES NOS; GLUCOSE; THIAMINE HYDROCHLORIDE (BFLUID INJECTION)	20[redacted] 134	-	20[redacted] 143	ADVERSE EVENT	1000 mL	QD INTRAVENOUS	2
CALCIUM CARBONATE; COLECALCIFEROL; MAGNESIUM CARBONATE (DENOTAS CHEWABLE COMBINATION TABLETS)	20[redacted] 131	-	20[redacted] 168	PROPHYLAXIS	2 TABLET	QD ORAL	-
CALCIUM CARBONATE; COLECALCIFEROL; MAGNESIUM CARBONATE (DENOTAS CHEWABLE COMBINATION TABLETS)	20[redacted] 177	-	20[redacted] 264	PROPHYLAXIS	2 TABLET	QD ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
DOMPERIDONE (DOMPERIDONE)	20[redacted] 156	-	20[redacted] 158	ADVERSE EVENT	10 mg	QD ORAL	3
FERROUS SULFATE (FERO-GRADUMET)	20[redacted] -219	Y	20[redacted] 138	MEDICAL HISTORY	105 mg	QD ORAL	-
GUAIFENESIN (FESIN [GUAIFENESIN])	20[redacted] 195	-	20[redacted] 195	MEDICAL HISTORY	120 mg	ONCE INTRAVENOUS	-
GUAIFENESIN (FESIN [GUAIFENESIN])	20[redacted] 230	-	20[redacted] 230	MEDICAL HISTORY	120 mg	ONCE INTRAVENOUS	-
GUAIFENESIN (FESIN [GUAIFENESIN])	20[redacted] 300	-	20[redacted] 300	MEDICAL HISTORY	120 mg	ONCE INTRAVENOUS	-
GUAIFENESIN (FESIN [GUAIFENESIN])	20[redacted] 335	-	20[redacted] 335	MEDICAL HISTORY	120 mg	ONCE INTRAVENOUS	-
MICAFUNGIN SODIUM (FUNGUARD)	20[redacted] 135	-	20[redacted] 138	PROPHYLAXIS	50 mg	QD INTRAVENOUS	-
DIMETICONE (GASCON DROPS 2%)	20[redacted] 167	-	20[redacted] 167	OTHER	4 mL	PRN ORAL	-
GENTAMICIN SULFATE (GENTACIN)	20[redacted] 293	-	20[redacted] 303	ADVERSE EVENT	- FINGERTIP UNIT	OTHER TOPICAL	8
MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER (HIRUDOID)	20[redacted] 363	-	- -	PROPHYLAXIS	- FINGERTIP UNIT	PRN TOPICAL	-
INFLUENZA VACCINE (INFLUENZA VACCINE)	20[redacted] -	-	20[redacted] -	PROPHYLAXIS	1 OTHER	ONCE SUBCUTANEOUS	-
ITRACONAZOLE (ITRIZOLE CAPSULES)	- -	Y	20[redacted] -1	PROPHYLAXIS	100 mg	BID ORAL	-
TOCOPHERYL ACETATE (JUVELA OINTMENT [TOCOPHEROL])	20[redacted] 244	-	20[redacted] 362	PROPHYLAXIS	1 FINGERTIP UNIT	PRN TRANSDERMAL	-
BROTIZOLAM (LENDORMIN TABLETS)	20[redacted] 29	-	20[redacted] 138	MEDICAL HISTORY	0.25 mg	PRN ORAL	-
BROTIZOLAM (LENDORMIN TABLETS)	20[redacted] 307	-	- -	MEDICAL HISTORY	0.25 mg	QD ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
MAGNESIUM OXIDE (MAGMITT TAB.)	20[redacted] 170	-	20[redacted] 181	PROPHYLAXIS	330 mg	QD ORAL	-
MAGNESIUM OXIDE (MAGMITT TAB.)	20[redacted] 349	-	- -	PROPHYLAXIS	330 mg	BID ORAL	-
MAGNESIUM OXIDE (MAGMITT TABLETS)	20[redacted] 182	-	20[redacted] 348	PROPHYLAXIS	330 mg	TID ORAL	-
CLOSTRIDIUM BUTYRICUM (MIYA-BM TABLETS)	20[redacted] -112	Y	20[redacted] 257	CGVHD	40 mg	TID ORAL	-
KETOPROFEN (MOHRUS TAPE)	20[redacted] 216	-	20[redacted] 236	MEDICAL HISTORY	20 mg	PRN TRANSDERMAL	-
KETOPROFEN (MOHRUS TAPE)	20[redacted] 307	-	- -	MEDICAL HISTORY	40 mg	PRN TRANSDERMAL	-
ASCORBIC ACID; MACROGOL 4000; POTASSIUM CHLORIDE; SODIUM ASCORBATE; SODIUM CHLORIDE; SODIUM SULFATE ANHYDROUS (MOVIPREP[MACROGOL 4000])	20[redacted] 167	-	20[redacted] 167	OTHER	2 L	PRN ORAL	-
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 106	-	20[redacted] 115	ADVERSE EVENT	500 mg	TID ORAL	6
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 131	-	20[redacted] 138	PROPHYLAXIS	500 mg	TID ORAL	-
CARBOCISTEINE (MUCODYNE TABLETS)	20[redacted] 144	-	20[redacted] 174	PROPHYLAXIS	500 mg	TID ORAL	-
REBAMIPIDE (MUCOSTA TABLETS)	20[redacted] 142	-	20[redacted] 181	PROPHYLAXIS	100 mg	TID ORAL	-
REBAMIPIDE (MUCOSTA TABLETS)	20[redacted] 182	-	- -	PROPHYLAXIS	100 mg	TID ORAL	-
ZOLPIDEM TARTRATE (MYSLEE TABLETS)	20[redacted] 136	-	20[redacted] 156	MEDICAL HISTORY	5 mg	PRN ORAL	-
ZOLPIDEM TARTRATE (MYSLEE TABLETS)	20[redacted] 169	-	20[redacted] 173	MEDICAL HISTORY	5 mg	PRN ORAL	-
ZOLPIDEM TARTRATE (MYSLEE TABLETS)	20[redacted] 244	-	20[redacted] 248	MEDICAL HISTORY	10 mg	PRN ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
DOMPERIDONE (NAUZELIN OD TABLETS)	20[redacted] -118	Y	20[redacted] 163	PROPHYLAXIS	10 mg	PRN ORAL	-
ESOMEPRAZOLE MAGNESIUM (NEXIUM CAPSULES)	20[redacted] -1082	Y	20[redacted] 138	PROPHYLAXIS	20 mg	QD ORAL	-
PROCHLORPERAZINE (NOVAMIN [PROCHLORPERAZINE])	20[redacted] 156	-	20[redacted] 156	ADVERSE EVENT	5 mg	ONCE INTRAMUSCULAR	3
CHLORHEXIDINE GLUCONATE (ORONINE[CHLORHEXIDINE GLUCONATE])	20[redacted] 290	-	20[redacted] 293	ADVERSE EVENT	- FINGERTIP UNIT	OTHER TOPICAL	8
ESCHERICHIA COLI (POSTERISAN [ESCHERICHIA COLI])	20[redacted] 168	-	20[redacted] 229	MEDICAL HISTORY	- FINGERTIP UNIT	PRN TRANSDERMAL	-
DENOSUMAB (PRALIA SUBCUTANEOUS INJECTION SYRINGE)	20[redacted] 111	-	20[redacted] 111	PROPHYLAXIS	60 mg	ONCE SUBCUTANEOUS	-
DENOSUMAB (PRALIA SUBCUTANEOUS INJECTION SYRINGE)	20[redacted] 300	-	20[redacted] 300	PROPHYLAXIS	60 mg	ONCE SUBCUTANEOUS	-
METOCLOPRAMIDE HYDROCHLORIDE (PRIMPERAN INJECTION)	20[redacted] 164	-	20[redacted] 169	ADVERSE EVENT	10 mg	BID INTRAVENOUS	3
METOCLOPRAMIDE HYDROCHLORIDE (PRIMPERAN INJECTION)	20[redacted] 164	-	20[redacted] 164	ADVERSE EVENT	10 mg	QD INTRAVENOUS	3
CALCIUM CHLORIDE DIHYDRATE; POTASSIUM CHLORIDE; SODIUM ACETATE TRIHYDRATE; SODIUM CHLORIDE (SOLYUGEN F INJECTION)	20[redacted] 156	-	20[redacted] 156	ADVERSE EVENT	500 mL	QD INTRAVENOUS	3
CALCIUM CHLORIDE DIHYDRATE; POTASSIUM CHLORIDE; SODIUM ACETATE TRIHYDRATE; SODIUM CHLORIDE (SOLYUGEN F INJECTION)	20[redacted] 164	-	20[redacted] 164	ADVERSE EVENT	500 mL	TID INTRAVENOUS	3
CEFOPERAZONE SODIUM; SULBACTAM SODIUM (SULPERAZON FOR INTRAVENOUS USE)	20[redacted] 164	-	20[redacted] 164	PROPHYLAXIS	1 g	QD INTRAVENOUS	-

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Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
CEFOPERAZONE SODIUM; SULBACTAM SODIUM (SULPERAZON FOR INTRAVENOUS USE)	20[redacted] 165	-	20[redacted] 169	PROPHYLAXIS	1 g	BID INTRAVENOUS	-
VONOPRAZAN FUMARATE (TAKECAB TABLETS)	20[redacted] 143	-	20[redacted] 181	PROPHYLAXIS	20 mg	QD ORAL	-
VONOPRAZAN FUMARATE (TAKECAB TABLETS)	20[redacted] 182	-	- -	PROPHYLAXIS	20 mg	QD ORAL	-
LANSOPRAZOLE (TAKEPRON INTRAVENOUS)	20[redacted] 134	-	20[redacted] 134	ADVERSE EVENT	30 mg	ONCE INTRAVENOUS	2
LANSOPRAZOLE (TAKEPRON INTRAVENOUS)	20[redacted] 135	-	20[redacted] 142	ADVERSE EVENT	30 mg	BID INTRAVENOUS	2
LANSOPRAZOLE (TAKEPRON INTRAVENOUS)	20[redacted] 164	-	20[redacted] 169	ADVERSE EVENT	30 mg	BID INTRAVENOUS	3
TRANEXAMIC ACID (TRANSAMIN INJECTION)	20[redacted] 134	-	20[redacted] 134	ADVERSE EVENT	500 mg	QD INTRAVENOUS	2
TRANEXAMIC ACID (TRANSAMIN INJECTION)	20[redacted] 135	-	20[redacted] 141	ADVERSE EVENT	500 mg	BID INTRAVENOUS	2
TRANEXAMIC ACID (TRANSAMIN INJECTION)	20[redacted] 164	-	20[redacted] 169	ADVERSE EVENT	500 mg	BID INTRAVENOUS	3
TRANEXAMIC ACID (TRANSAMIN TABLETS)	20[redacted] 127	-	20[redacted] 138	ADVERSE EVENT	250 mg	TID ORAL	2
TRANEXAMIC ACID (TRANSAMIN TABLETS)	20[redacted] 127	-	20[redacted] 138	ADVERSE EVENT	250 mg	TID ORAL	1
UREA (UREPEARL CREAM)	20[redacted] -9	-	20[redacted] 362	PROPHYLAXIS	1 FINGERTIP UNIT	PRN TRANSDERMAL	-
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 69	-	20[redacted] 69	ADVERSE EVENT	5 g	ONCE INTRAVENOUS	4
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 106	-	20[redacted] 106	ADVERSE EVENT	5 g	ONCE INTRAVENOUS	4
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 131	-	20[redacted] 131	ADVERSE EVENT	5 g	ONCE INTRAVENOUS	4

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 135	-	20[redacted] 137	ADVERSE EVENT	5 g	QD INTRAVENOUS	4
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 164	-	20[redacted] 166	ADVERSE EVENT	5 g	QD INTRAVENOUS	4
IMMUNOGLOBULIN HUMAN NORMAL (VENILON-I)	20[redacted] 230	-	20[redacted] 230	ADVERSE EVENT	10 g	ONCE INTRAVENOUS	4
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN IH)	20[redacted] 300	-	20[redacted] 300	ADVERSE EVENT	10 g	ONCE INTRAVENOUS	4
VORICONAZOLE (VFEND TABLETS)	20[redacted] 1	-	20[redacted] 258	PROPHYLAXIS	100 mg	BID ORAL	-
VORICONAZOLE (VFEND TABLETS)	20[redacted] 259	-	- -	PROPHYLAXIS	50 mg	BID ORAL	-
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 106	-	20[redacted] 106	ADVERSE EVENT	4.5 g	ONCE INTRAVENOUS	6
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 131	-	20[redacted] 131	ADVERSE EVENT	4.5 g	ONCE INTRAVENOUS	9

■ Karnofsky/Lansky performance status score

Date of Finding Study Day of Finding	Visit Name	Result
20[redacted] -16	SCREENING	90
20[redacted] 1	WEEK 1 DAY 1	90
20[redacted] 29	WEEK 5	90
20[redacted] 55	WEEK 9	90
20[redacted] 83	WEEK 13	90

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Date of Finding Study Day of Finding	Visit Name	Result
20[redacted] 111	WEEK 17	100
20[redacted] 142	WEEK 21	90
20[redacted] 170	WEEK 25	90
20[redacted] 258	WEEK 37	90
20[redacted] 335	WEEK 49	90

■ Laboratory Data

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] -9	SCREENING	14	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	12	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	13	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	13	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 55	WEEK 9	13	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 83	WEEK 13	21	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 111	WEEK 17	15	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 142	WEEK 21	9	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 169	WEEK 25	9	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 258	WEEK 37	20	0	34.99	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 335	WEEK 49	15	0	34.99	NORMAL	0
Albumin (g/L)	20[redacted] -9	SCREENING	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 1	WEEK 1 DAY 1	38	39	48	LOW	1
Albumin (g/L)	20[redacted] 8	WEEK 2	38	39	48	LOW	1
Albumin (g/L)	20[redacted] 29	WEEK 5	38	39	48	LOW	1
Albumin (g/L)	20[redacted] 55	WEEK 9	39	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 83	WEEK 13	42	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 111	WEEK 17	31	39	48	LOW	1
Albumin (g/L)	20[redacted] 142	WEEK 21	34	39	48	LOW	1
Albumin (g/L)	20[redacted] 169	WEEK 25	34	39	48	LOW	1
Albumin (g/L)	20[redacted] 258	WEEK 37	40	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 335	WEEK 49	40	39	48	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] -9	SCREENING	269	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	248	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 8	WEEK 2	197	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 29	WEEK 5	210	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 55	WEEK 9	258	100	310	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 83	WEEK 13	198	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 111	WEEK 17	226	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 169	WEEK 25	146	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 258	WEEK 37	243	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 335	WEEK 49	181	100	310	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] -9	SCREENING	15	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	16	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	19	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	17	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 55	WEEK 9	16	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 83	WEEK 13	21	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 111	WEEK 17	16	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 142	WEEK 21	14	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 169	WEEK 25	11	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 258	WEEK 37	19	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 335	WEEK 49	20	0	29.99	NORMAL	0
Bilirubin (umol/L)	20[redacted] -9	SCREENING	6.84	3.42	18.81	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Bilirubin (umol/L)	20[redacted] 1	WEEK 1 DAY 1	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 8	WEEK 2	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 29	WEEK 5	5.13	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 55	WEEK 9	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 83	WEEK 13	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 111	WEEK 17	3.42	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 142	WEEK 21	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 169	WEEK 25	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 258	WEEK 37	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 335	WEEK 49	5.13	3.42	18.81	NORMAL	0
Creatinine (umol/L)	20[redacted] -9	SCREENING	53.04	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 1	WEEK 1 DAY 1	52.156	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 8	WEEK 2	52.156	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 29	WEEK 5	53.924	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 55	WEEK 9	51.272	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 83	WEEK 13	55.692	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 111	WEEK 17	46.852	44.2	70.72	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Creatinine (umol/L)	20[redacted] 142	WEEK 21	45.084	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 169	WEEK 25	46.852	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 258	WEEK 37	60.996	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 335	WEEK 49	52.156	44.2	70.72	NORMAL	0
Eosinophils (10^9/L)	20[redacted] -9	SCREENING	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 8	WEEK 2	0.103	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 29	WEEK 5	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 55	WEEK 9	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 83	WEEK 13	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 111	WEEK 17	0.161	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 142	WEEK 21	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 169	WEEK 25	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 258	WEEK 37	0.064	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 335	WEEK 49	0.062	0.04	0.32	NORMAL	-
Glucose (mmol/L)	20[redacted] -9	SCREENING	5.6065	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	4.9959	3.8857	6.1061	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Glucose (mmol/L)	20[redacted] 8	WEEK 2	4.2188	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 29	WEEK 5	4.8294	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 55	WEEK 9	6.4947	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 83	WEEK 13	4.9959	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 111	WEEK 17	5.4955	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 142	WEEK 21	5.4955	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 169	WEEK 25	6.4392	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 258	WEEK 37	5.4955	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 335	WEEK 49	5.8841	3.8857	6.1061	NORMAL	0
HIV Antibody	20[redacted] -9	SCREENING	NEGATIVE	-	-	-	-
Hemoglobin (g/L)	20[redacted] -9	SCREENING	121	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 1	WEEK 1 DAY 1	130	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 8	WEEK 2	124	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 29	WEEK 5	129	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 55	WEEK 9	132	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 83	WEEK 13	135	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 111	WEEK 17	125	115	155	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Hemoglobin (g/L)	20[redacted] 142	WEEK 21	102	115	155	LOW	1
Hemoglobin (g/L)	20[redacted] 169	WEEK 25	92	115	155	LOW	2
Hemoglobin (g/L)	20[redacted] 258	WEEK 37	102	115	155	LOW	1
Hemoglobin (g/L)	20[redacted] 335	WEEK 49	97	115	155	LOW	2
Hepatitis B Virus Core Antibody	20[redacted] -9	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antibody	20[redacted] -9	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antigen	20[redacted] -9	SCREENING	NEGATIVE	-	-	-	-
Hepatitis C Virus Antibody	20[redacted] -9	SCREENING	NEGATIVE	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] -16	SCREENING	1.72	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 83	WEEK 13	2.07	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 169	WEEK 25	1.52	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 258	WEEK 37	1.37	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 335	WEEK 49	1.66	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] -16	SCREENING	3.72	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 83	WEEK 13	4.59	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 169	WEEK 25	9.03	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 258	WEEK 37	4.21	-	-	-	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Immunoglobulin G (g/L)	20[redacted] 335	WEEK 49	3.77	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] -16	SCREENING	0.48	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 83	WEEK 13	0.65	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 169	WEEK 25	0.45	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 258	WEEK 37	0.28	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 335	WEEK 49	0.3	-	-	-	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] -9	SCREENING	156	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	162	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 8	WEEK 2	163	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 29	WEEK 5	166	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 55	WEEK 9	166	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 83	WEEK 13	213	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 111	WEEK 17	227	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 142	WEEK 21	160	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 169	WEEK 25	141	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 258	WEEK 37	246	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 335	WEEK 49	194	110	219	NORMAL	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Leukocytes (10^9/L)	20[redacted] -9	SCREENING	3	4	8	LOW	1
Leukocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	2.6	4	8	LOW	2
Leukocytes (10^9/L)	20[redacted] 8	WEEK 2	10.3	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 29	WEEK 5	7.9	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 55	WEEK 9	7.4	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 83	WEEK 13	10.2	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 111	WEEK 17	16.1	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 142	WEEK 21	4.2	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 169	WEEK 25	3.3	4	8	LOW	1
Leukocytes (10^9/L)	20[redacted] 258	WEEK 37	6.4	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 335	WEEK 49	6.2	4	8	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] -9	SCREENING	1.41	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	1.3	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 8	WEEK 2	1.648	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 29	WEEK 5	1.343	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 55	WEEK 9	1.036	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 83	WEEK 13	0.561	0.8	3.2	LOW	2

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lymphocytes (10^9/L)	20[redacted] 111	WEEK 17	0.564	0.8	3.2	LOW	2
Lymphocytes (10^9/L)	20[redacted] 142	WEEK 21	1.218	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 169	WEEK 25	1.089	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 258	WEEK 37	1.28	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 335	WEEK 49	1.24	0.8	3.2	NORMAL	0
Neutrophils (10^9/L)	20[redacted] -9	SCREENING	1.29	1.6	6.32	LOW	2
Neutrophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	0.884	1.6	6.32	LOW	3
Neutrophils (10^9/L)	20[redacted] 8	WEEK 2	7.828	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 29	WEEK 5	6.004	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 55	WEEK 9	5.994	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 83	WEEK 13	9.18	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 111	WEEK 17	14.49	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 142	WEEK 21	2.646	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 169	WEEK 25	1.98	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 258	WEEK 37	4.544	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 335	WEEK 49	4.464	1.6	6.32	NORMAL	0
Platelets (10^9/L)	20[redacted] -9	SCREENING	140	140	400	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Platelets (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	178	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 8	WEEK 2	306	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 29	WEEK 5	239	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 55	WEEK 9	222	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 83	WEEK 13	199	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 111	WEEK 17	283	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 142	WEEK 21	121	140	400	LOW	1
Platelets (10^9/L)	20[redacted] 169	WEEK 25	244	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 258	WEEK 37	272	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 335	WEEK 49	267	140	400	NORMAL	0
Potassium (mmol/L)	20[redacted] -9	SCREENING	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	4.1	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 8	WEEK 2	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 29	WEEK 5	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 55	WEEK 9	3.8	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 83	WEEK 13	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 111	WEEK 17	3.6	3.5	4.8	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Potassium (mmol/L)	20[redacted] 142	WEEK 21	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 169	WEEK 25	3.8	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 258	WEEK 37	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 335	WEEK 49	4.1	3.5	4.8	NORMAL	0
Protein (g/L)	20[redacted] -9	SCREENING	62	67	83	LOW	-
Protein (g/L)	20[redacted] 1	WEEK 1 DAY 1	63	67	83	LOW	-
Protein (g/L)	20[redacted] 8	WEEK 2	58	67	83	LOW	-
Protein (g/L)	20[redacted] 55	WEEK 9	60	67	83	LOW	-
Protein (g/L)	20[redacted] 83	WEEK 13	67	67	83	NORMAL	-
Protein (g/L)	20[redacted] 111	WEEK 17	63	67	83	LOW	-
Protein (g/L)	20[redacted] 142	WEEK 21	59	67	83	LOW	-
Protein (g/L)	20[redacted] 169	WEEK 25	62	67	83	LOW	-
Protein (g/L)	20[redacted] 258	WEEK 37	58	67	83	LOW	-
Protein (g/L)	20[redacted] 335	WEEK 49	61	67	83	LOW	-
Sodium (mmol/L)	20[redacted] -9	SCREENING	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 8	WEEK 2	143	136	145	NORMAL	0

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Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Sodium (mmol/L)	20[redacted] 29	WEEK 5	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 55	WEEK 9	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 83	WEEK 13	145	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 111	WEEK 17	143	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 142	WEEK 21	141	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 169	WEEK 25	140	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 258	WEEK 37	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 335	WEEK 49	144	136	145	NORMAL	0
Urate (umol/L)	20[redacted] -9	SCREENING	237.92	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 1	WEEK 1 DAY 1	261.712	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 8	WEEK 2	261.712	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 29	WEEK 5	285.504	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 55	WEEK 9	297.4	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 83	WEEK 13	309.296	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 111	WEEK 17	261.712	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 142	WEEK 21	142.752	178.44	356.88	LOW	0
Urate (umol/L)	20[redacted] 169	WEEK 25	172.492	178.44	356.88	LOW	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urate (umol/L)	20[redacted] 258	WEEK 37	273.608	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 335	WEEK 49	279.556	178.44	356.88	NORMAL	0
Urea Nitrogen (mmol/L)	20[redacted] -9	SCREENING	3.57	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	3.927	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 8	WEEK 2	4.284	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 29	WEEK 5	3.927	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 55	WEEK 9	4.284	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 83	WEEK 13	4.641	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 111	WEEK 17	2.856	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 142	WEEK 21	4.998	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 169	WEEK 25	1.785	2.856	7.14	LOW	-
Urea Nitrogen (mmol/L)	20[redacted] 258	WEEK 37	6.426	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 335	WEEK 49	4.998	2.856	7.14	NORMAL	-

(2) イブルチニブと関連性がない重篤な有害事象

1) 被験者番号 54179060GVH3001-[redacted]

■ REASON FOR NARRATIVE SELECTION

Treatment-emergent serious adverse events (SAEs)

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■ Death

No Death reported

■ Treatment-emergent serious adverse events (SAEs)

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
腎盂腎炎	PYELONEPHRITIS	20[redacted] 20[redacted]	78 14	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	12
敗血症	SEPSIS	20[redacted] 20[redacted]	79 9	Y 4	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	14

Note: Adverse Events are coded using MedDRA 22.1

■ Adverse events (AEs) leading to ibrutinib discontinuation

No Adverse events (AEs) leading to ibrutinib discontinuation reported

■ Other malignancies

No Other malignancies reported

■ Major hemorrhage

No Major hemorrhage reported

■ Demographics, Baseline Characteristics

- Country: JPN
- Race: Asian
- Age: 6[redacted]
- Sex: Male
- Baseline height (cm): [redacted]
- Baseline weight (kg): [redacted]
- Baseline karnofsky/Lansky performance status score: 80
- Overall severity of cGVHD: Moderate
- cGVHD disease state: STEROID REFRACTORY DISEASE
- Month from initial diagnosis date: 41.4
- Number of prior cGVHD treatment regimens: 2
- First study drug intake: 20[redacted] (Study Day 1)
- Last study drug intake: 20[redacted] (Study Day 330)

■ Disposition Information

□ End of treatment: Subject Ongoing on Treatment

□ End of trial: Subject Ongoing on Study

■ Other Adverse Events

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
不眠症	INSOMNIA	20[redacted] 20	1 1	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	6
ざ瘡	ACNE	20 -	15 -	N 1	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	2
便秘	CONSTIPATION	20 -	57 -	N 1	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	3
口内炎	MUCOSITIS ORAL	20 20	57 29	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	7
爪囲炎	PARONYCHIA(RIGHT FINGER)	20 20	71 120	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	9
腎盂腎炎	PYELONEPHRITIS	20 20	76 2	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	11
皮膚擦過傷	ABRASION(LEFT LOWER LIMB)	20 20	76 89	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	1
尿閉	URINARY RETENTION	20 20	79 7	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	19
良性前立腺肥大症	WORSENING PROSTATIC HYPERPLASIA	20 -	83 -	N 2	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	21

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
尿閉	URINARY RETENTION	20[redacted] 20[redacted]	86 7	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	20
腎盂腎炎	PYELONEPHRITIS	20[redacted] 20[redacted]	92 99	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	13
口内炎	MUCOSITIS ORAL	20[redacted] -	141 -	N 2	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	8
下痢	DIARRHEA	20[redacted] 20[redacted]	144 13	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	4
爪囲炎	PARONYCHIA(THE FIRST TOE OF RIGHT)	20[redacted] -	190 -	N 1	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	10
皮膚嚢腫	SKIN ATHEROMA	20[redacted] 20[redacted]	259 21	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	15
皮膚嚢腫	SKIN ATHEROMA	20[redacted] 20[redacted]	280 42	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	16
皮膚嚢腫	SKIN ATHEROMA	20[redacted] -	322 -	N 2	NOT RELATED DOSE NOT CHANGED	Y NOT RECOVERED/NOT RESOLVED	17

Note: Adverse Events are coded using MedDRA 22.1

■ Medical History

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Immune system disorders	Acute graft versus host disease	ACUTE GVHD	BEFORE	-
Cardiac disorders	Pericardial effusion	PERICARDIAL FLUID	BEFORE	-
Respiratory, thoracic and mediastinal disorders	Pleural effusion	PLEURAL FLUID	BEFORE	-

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Reproductive system and breast disorders	Benign prostatic hyperplasia	PROSTATIC HYPERPLASIA	ONGOING	1
Metabolism and nutrition disorders	Dyslipidaemia	DYSLIPIDEMIA	ONGOING	2
Metabolism and nutrition disorders	Hyperuricaemia	HYPERURICEMIA	ONGOING	2
Hepatobiliary disorders	Hepatitis	INTERFACE HEPATITIS	ONGOING	2
General disorders and administration site conditions	Oedema peripheral	LOWER EXTREMITY EDEMA	ONGOING	2
Infections and infestations	Bronchitis	OBSTRUCTIVE BRONCHITIS	ONGOING	2
Endocrine disorders	Secondary adrenocortical insufficiency	SECONDARY ADRENAL INSUFFICIENCY	ONGOING	2
Metabolism and nutrition disorders	Steroid diabetes	STEROID DIABETES	ONGOING	2

Note: Medical History are coded using MedDRA 22.1

■ Transplant History

Transplantation Date	Dictionary-Derived Term	Transplant Type	HLA matching and donor relation to recipient	Sex matching between donor and recipient	Stem Cell Source
20[redacted]	Acute myeloid leukaemia	Myeloablative	Matched unrelated	Matched	Bone Marrow

■ Disease History

Date of Initial Diagnosis	Initial Diagnosis
20[redacted]	CGVHD

■ Study Medication

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 1 DAY 1	20[redacted]	20[redacted]	1	1	420.0	-	-	-
WEEK 1 DAY 2	20[redacted]	20[redacted]	2	7	420.0	-	-	-
WEEK 2	20[redacted]	20[redacted]	8	28	420.0	-	-	-
WEEK 5	20[redacted]	20[redacted]	29	56	420.0	-	-	-
WEEK 9	20[redacted]	20[redacted]	57	76	420.0	-	-	-
WEEK 9	20[redacted]	20[redacted]	77	77	840.0	-	OTHER	-
WEEK 9	20[redacted]	20[redacted]	78	78	0.0	OTHER	-	-

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 9	20[redacted]	20[redacted]	79	84	420.0	-	-	-
WEEK 13	20[redacted]	20[redacted]	85	112	420.0	-	-	-
WEEK 17	20[redacted]	20[redacted]	113	140	420.0	-	-	-
WEEK 21	20[redacted]	20[redacted]	141	163	420.0	-	-	-
WEEK 25	20[redacted]	20[redacted]	164	252	420.0	-	-	-
WEEK 37	20[redacted]	20[redacted]	253	329	420.0	-	-	-
WEEK 49	20[redacted]	20[redacted]	330	330	420.0	-	-	-

■ Prior and Concomitant Medications

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
ACICLOVIR (ACICLOVIR)	- -	Y	- -	PROPHYLAXIS	200 mg	QD ORAL	-
NADIFLOXACIN (ACUATIM)	20[redacted] 190	-	20[redacted] 197	ADVERSE EVENT	1 APPLICATION	BID TOPICAL	2
NADIFLOXACIN (ACUATIM)	20[redacted] 224	-	- -	ADVERSE EVENT	1 APPLICATION	BID TOPICAL	2
ALENDRONATE SODIUM (ALENDRONATE SODIUM HYDRATE)	- -	Y	- -	PROPHYLAXIS	35 mg	EVERY WEEK ORAL	-
SODIUM GUALENATE HYDRATE (AZULENE(SODIUM GUALENATE HYDRATE))	- -	Y	- -	CGVHD	- OTHER	PRN OTHER	-
GUAIAZULENE (AZUNOL OINTMENT(DIMETHLY ISOPROPYLAZULENE))	20[redacted] 141	-	- -	CGVHD	- OTHER	PRN TOPICAL	-
PENTAMIDINE ISETHIONATE (BENAMBAX)	- -	Y	- -	PROPHYLAXIS	100 mg	EVERY 4 WEEKS RESPIRATORY (INHALATION)	-
BEZAFIBRATE (BEZAFIBRATE)	- -	Y	- -	MEDICAL HISTORY	200 mg	QD ORAL	-
CEFACLOR (CEFACLOR CAPSULE)	20[redacted] 259	-	20[redacted] 266	ADVERSE EVENT	250 mg	TID ORAL	1

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
CEFACLOR (CEFACLOR CAPSULE)	20[redacted] 322	-	20[redacted] 336	ADVERSE EVENT	250 mg	TID ORAL	1
FEBUXOSTAT (FEBURIC)	- -	Y	- -	MEDICAL HISTORY	10 mg	QD ORAL	-
FLUCONAZOLE (FLUCONAZOLE)	20[redacted] -2	-	- -	PROPHYLAXIS	400 mg	QD ORAL	-
FUROSEMIDE (FUROSEMIDE)	- -	Y	20[redacted] 28	MEDICAL HISTORY	20 mg	BID ORAL	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 29	-	20[redacted] 63	MEDICAL HISTORY	20 mg	QD ORAL	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 64	-	20[redacted] 77	MEDICAL HISTORY	10 mg	QD ORAL	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 85	-	20[redacted] 85	MEDICAL HISTORY	20 mg	ONCE INTRAVENOUS	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 87	-	20[redacted] 90	MEDICAL HISTORY	20 mg	QD ORAL	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 91	-	20[redacted] 127	MEDICAL HISTORY	10 mg	QD ORAL	-
FUROSEMIDE (FUROSEMIDE)	20[redacted] 128	-	20[redacted] 141	MEDICAL HISTORY	5 mg	QD ORAL	-
GENTAMICIN (GENTAMICIN)	20[redacted] 15	-	- -	ADVERSE EVENT	- OTHER	PRN TOPICAL	2
GENTAMICIN (GENTAMICIN)	20[redacted] 15	-	- -	ADVERSE EVENT	- OTHER	PRN TOPICAL	1
INSULIN GLARGINE (GLARGINE)	- -	Y	20[redacted] 77	MEDICAL HISTORY	6 U	QD SUBCUTANEOUS	-
INSULIN GLARGINE (GLARGINE)	20[redacted] 84	-	20[redacted] 85	MEDICAL HISTORY	6 U	QD SUBCUTANEOUS	-
INSULIN GLARGINE (GLARGINE)	20[redacted] 86	-	20[redacted] 87	MEDICAL HISTORY	4 U	QD SUBCUTANEOUS	-
INSULIN GLARGINE (GLARGINE)	20[redacted] 88	-	20[redacted] 89	MEDICAL HISTORY	2 U	QD SUBCUTANEOUS	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
INSULIN LISPRO (HUMALOG)	- -	Y	20[redacted] 15	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
INSULIN LISPRO (HUMALOG)	20[redacted] 16	-	20[redacted] 42	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
INSULIN LISPRO (HUMALOG)	20[redacted] 43	-	20[redacted] 78	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
INSULIN LISPRO (HUMALOG)	20[redacted] 85	-	20[redacted] 91	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
INSULIN LISPRO (HUMALOG)	20[redacted] 92	-	20[redacted] 99	MEDICAL HISTORY	6 U	TID SUBCUTANEOUS	-
INSULIN LISPRO (HUMALOG)	20[redacted] 100	-	- -	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
INSULIN HUMAN (HUMULIN R)	20[redacted] 80	-	20[redacted] 82	MEDICAL HISTORY	- U	PRN SUBCUTANEOUS	-
HYALURONATE SODIUM (HYALEIN)	- -	Y	- -	CGVHD	- APPLICATION	PRN OPHTHALMIC	-
INFLUENZA VACCINE (INFLUENZA HA VACCINE)	20[redacted] 253	-	20[redacted] 253	PROPHYLAXIS	0.5 mL	ONCE SUBCUTANEOUS	-
ITRACONAZOLE (ITRACONAZOLE)	- -	Y	20[redacted] -3	PROPHYLAXIS	20 mL	QD ORAL	-
LANSOPRAZOLE (LANSOPRAZOLE)	- -	Y	- -	PROPHYLAXIS	15 mg	QD ORAL	-
INSULIN GLARGINE (LANTUS)	20[redacted] 80	-	20[redacted] 83	MEDICAL HISTORY	- U	QD SUBCUTANEOUS	-
LEVOFLOXACIN (LEVOFLOXACIN)	20[redacted] 99	-	20[redacted] 103	ADVERSE EVENT	500 mg	QD ORAL	1
LEVOFLOXACIN (LEVOFLOXACIN)	20[redacted] 113	-	20[redacted] 119	ADVERSE EVENT	500 mg	QD ORAL	1
HYDROCORTISONE BUTYRATE (LOCOIDCREAM(HYDROCORTISONE BUTYRATE))	20[redacted] 64	-	- -	CGVHD	- OTHER	PRN TOPICAL	-
MAGNESIUM OXIDE (MAGMITT)	20[redacted] 57	-	- -	ADVERSE EVENT	- OTHER	PRN ORAL	3

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
CLOSTRIDIUM BUTYRICUM (MIYA-BM)	20[redacted] 148	-	20[redacted] 156	ADVERSE EVENT	3 g	TID ORAL	4
BENZETHONIUM CHLORIDE (NEOSTELIN GREEN(BENZETHONIUM CHLORIDE))	20[redacted] 253	-	- -	ADVERSE EVENT	- OTHER	PRN TOPICAL	8
DIFLUCORTOLONE VALERATE (NERISONA)	- -	Y	- -	CGVHD	- OTHER	PRN TOPICAL	-
INSULIN ASPART (NOVORAPID)	20[redacted] 80	-	20[redacted] 84	MEDICAL HISTORY	- U	TID SUBCUTANEOUS	-
WHITE SOFT PARAFFIN (PROPETO)	20[redacted] 280	-	- -	PROPHYLAXIS	- OTHER	PRN TOPICAL	-
DIPHENHYDRAMINE (RESTAMIN CREAM)	20[redacted] 253	-	- -	CGVHD	- OTHER	PRN TOPICAL	-
BETAMETHASONE VALERATE; GENTAMICIN SULFATE (RINDERON-VG)	20[redacted] 190	-	20[redacted] 322	ADVERSE EVENT	2 APPLICATION	QD TOPICAL	1
RETINOL (SAHNE)	20[redacted] 15	-	- -	PROPHYLAXIS	- OTHER	PRN TOPICAL	-
TOLVAPTAN (SAMSCA)	- -	Y	20[redacted] 113	MEDICAL HISTORY	3.75 mg	QD ORAL	-
TOLVAPTAN (SAMSCA)	20[redacted] 114	-	20[redacted] 253	MEDICAL HISTORY	1.875 mg	QD ORAL	-
TOLVAPTAN (SAMSCA)	20[redacted] 254	-	20[redacted] 282	MEDICAL HISTORY	1.875 mg	QOD ORAL	-
POTASSIUM CHLORIDE; SODIUM CHLORIDE (SOFT SANTEAR)	- -	Y	- -	CGVHD	- APPLICATION	PRN OPHTHALMIC	-
TIOTROPIUM BROMIDE (SPIRIVA)	- -	Y	- -	MEDICAL HISTORY	1 PUFF	QD RESPIRATORY (INHALATION)	-
BUDESONIDE; FORMOTEROL FUMARATE (SYMBICORT)	- -	Y	- -	MEDICAL HISTORY	2 PUFF	BID RESPIRATORY (INHALATION)	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (TAZOPIPE)	20[redacted] 78	-	20[redacted] 78	ADVERSE EVENT	2.25 g	TID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (TAZOPIPE)	20[redacted] 79	-	20[redacted] 91	ADVERSE EVENT	2.25 g	QID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (TAZOPIPE)	20[redacted] 79	-	20[redacted] 91	ADVERSE EVENT	2.25 g	QID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (TAZOPIPE)	20[redacted] 92	-	20[redacted] 92	ADVERSE EVENT	2.25 g	BID INTRAVENOUS	1
TRAZODONE (TRAZODONE)	20[redacted] 1	-	20[redacted] 1	ADVERSE EVENT	25 mg	ONCE ORAL	6
SILODOSIN (URIEF)	20[redacted] 83	-	20[redacted] 86	ADVERSE EVENT	4 mg	QD ORAL	1
SILODOSIN (URIEF)	20[redacted] 83	-	20[redacted] 86	ADVERSE EVENT	4 mg	QD ORAL	2
SILODOSIN (URIEF)	20[redacted] 87	-	- -	ADVERSE EVENT	4 mg	BID ORAL	2
SILODOSIN (URIEF)	20[redacted] 87	-	- -	ADVERSE EVENT	4 mg	BID ORAL	2
URSODEOXYCHOLIC ACID (URSODEOXYCHOLIC ACID)	- -	Y	- -	MEDICAL HISTORY	200 mg	TID ORAL	-
SALBUTAMOL SULFATE (VENETLIN)	- -	Y	- -	OTHER	0.3 mL	EVERY 4 WEEKS RESPIRATORY (INHALATION)	-
LIDOCAINE (XYLOCAINE(LIDOCAINE))	20[redacted] 57	-	20[redacted] 77	ADVERSE EVENT	- OTHER	PRN OTHER	7
EZETIMIBE (ZETIA)	- -	Y	- -	MEDICAL HISTORY	15 mg	QD ORAL	-

■ Karnofsky/Lansky performance status score

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Date of Finding Study Day of Finding	Visit Name	Result
20[redacted] -23	SCREENING	80
20[redacted] 1	WEEK 1 DAY 1	80
20[redacted] 29	WEEK 5	80
20[redacted] 57	WEEK 9	80
20[redacted] 85	WEEK 13	70
20[redacted] 113	WEEK 17	80
20[redacted] 141	WEEK 21	80
20[redacted] 164	WEEK 25	80
20[redacted] 253	WEEK 37	80
20[redacted] 330	WEEK 49	80

■ Laboratory Data

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] -23	SCREENING	64	10	42	HIGH	1
Alanine Aminotransferase (Enzyme U/L)	20[redacted] -2	WEEK 1 DAY 1	48	10	42	HIGH	1
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	30	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	32	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 57	WEEK 9	42	10	42	NORMAL	0

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Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 85	WEEK 13	29	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 113	WEEK 17	19	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	33	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 164	WEEK 25	23	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 253	WEEK 37	35	10	42	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 330	WEEK 49	32	10	42	NORMAL	0
Albumin (g/L)	20[redacted] -23	SCREENING	36	41	51	LOW	1
Albumin (g/L)	20[redacted] -2	WEEK 1 DAY 1	36	41	51	LOW	1
Albumin (g/L)	20[redacted] 8	WEEK 2	33	41	51	LOW	1
Albumin (g/L)	20[redacted] 29	WEEK 5	36	41	51	LOW	1
Albumin (g/L)	20[redacted] 57	WEEK 9	33	41	51	LOW	1
Albumin (g/L)	20[redacted] 85	WEEK 13	26	41	51	LOW	2
Albumin (g/L)	20[redacted] 113	WEEK 17	33	41	51	LOW	1
Albumin (g/L)	20[redacted] 141	WEEK 21	32	41	51	LOW	1
Albumin (g/L)	20[redacted] 164	WEEK 25	34	41	51	LOW	1
Albumin (g/L)	20[redacted] 253	WEEK 37	34	41	51	LOW	1
Albumin (g/L)	20[redacted] 330	WEEK 49	32	41	51	LOW	1

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alkaline Phosphatase (Enzyme U/L)	20[redacted] -23	SCREENING	430	106	322	HIGH	1
Alkaline Phosphatase (Enzyme U/L)	20[redacted] -2	WEEK 1 DAY 1	555	106	322	HIGH	1
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 8	WEEK 2	223	106	322	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 29	WEEK 5	409	106	322	HIGH	1
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 57	WEEK 9	304	106	322	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 85	WEEK 13	348	106	322	HIGH	1
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 113	WEEK 17	328	106	322	HIGH	1
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 141	WEEK 21	300	106	322	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 164	WEEK 25	263	106	322	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 253	WEEK 37	322	106	322	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 330	WEEK 49	349	106	322	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] -23	SCREENING	38	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] -2	WEEK 1 DAY 1	31	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	26	13	30	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 29	WEEK 5	37	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 57	WEEK 9	38	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 85	WEEK 13	24	13	30	NORMAL	0

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Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 113	WEEK 17	25	13	30	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	35	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 164	WEEK 25	34	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 253	WEEK 37	35	13	30	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 330	WEEK 49	33	13	30	HIGH	1
Bilirubin (umol/L)	20[redacted] -23	SCREENING	8.55	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] -2	WEEK 1 DAY 1	10.26	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 8	WEEK 2	11.97	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 29	WEEK 5	8.55	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 57	WEEK 9	6.84	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 85	WEEK 13	11.97	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 113	WEEK 17	10.26	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 141	WEEK 21	8.55	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 164	WEEK 25	10.26	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 253	WEEK 37	10.26	6.84	25.65	NORMAL	0
Bilirubin (umol/L)	20[redacted] 330	WEEK 49	10.26	6.84	25.65	NORMAL	0
Creatinine (umol/L)	20[redacted] -23	SCREENING	80.444	57.46	94.588	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Creatinine (umol/L)	20[redacted] -2	WEEK 1 DAY 1	84.864	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 8	WEEK 2	85.748	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 29	WEEK 5	110.5	57.46	94.588	HIGH	1
Creatinine (umol/L)	20[redacted] 57	WEEK 9	91.936	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 85	WEEK 13	87.516	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 113	WEEK 17	86.632	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 141	WEEK 21	83.096	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 164	WEEK 25	92.82	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 253	WEEK 37	94.588	57.46	94.588	NORMAL	0
Creatinine (umol/L)	20[redacted] 330	WEEK 49	84.864	57.46	94.588	NORMAL	0
Eosinophils (10^9/L)	20[redacted] -23	SCREENING	0	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] -2	WEEK 1 DAY 1	0	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 8	WEEK 2	0	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 29	WEEK 5	0.048	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 57	WEEK 9	0.131	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 85	WEEK 13	0	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 113	WEEK 17	0	0	0.731	NORMAL	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Eosinophils (10^9/L)	20[redacted] 141	WEEK 21	0.4	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 164	WEEK 25	0	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 253	WEEK 37	0.074	0	0.731	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 330	WEEK 49	0	0	0.731	NORMAL	-
Glucose (mmol/L)	20[redacted] -23	SCREENING	6.8277	4.0522	6.0506	HIGH	1
Glucose (mmol/L)	20[redacted] -2	WEEK 1 DAY 1	14.2106	4.0522	6.0506	HIGH	3
Glucose (mmol/L)	20[redacted] 8	WEEK 2	6.3837	4.0522	6.0506	HIGH	1
Glucose (mmol/L)	20[redacted] 29	WEEK 5	12.0457	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 57	WEEK 9	14.3216	4.0522	6.0506	HIGH	3
Glucose (mmol/L)	20[redacted] 85	WEEK 13	13.3224	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 113	WEEK 17	11.324	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 141	WEEK 21	10.4914	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 164	WEEK 25	9.2702	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 253	WEEK 37	10.88	4.0522	6.0506	HIGH	2
Glucose (mmol/L)	20[redacted] 330	WEEK 49	13.4334	4.0522	6.0506	HIGH	2
HIV Antibody	20[redacted] -23	SCREENING	NEGATIVE	-	-	-	-
Hemoglobin (g/L)	20[redacted] -23	SCREENING	142	137	168	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Hemoglobin (g/L)	20[redacted] -2	WEEK 1 DAY 1	138	137	168	NORMAL	0
Hemoglobin (g/L)	20[redacted] 8	WEEK 2	128	137	168	LOW	1
Hemoglobin (g/L)	20[redacted] 29	WEEK 5	134	137	168	LOW	1
Hemoglobin (g/L)	20[redacted] 57	WEEK 9	128	137	168	LOW	1
Hemoglobin (g/L)	20[redacted] 85	WEEK 13	127	137	168	LOW	1
Hemoglobin (g/L)	20[redacted] 113	WEEK 17	139	137	168	NORMAL	0
Hemoglobin (g/L)	20[redacted] 141	WEEK 21	136	137	168	LOW	1
Hemoglobin (g/L)	20[redacted] 164	WEEK 25	139	137	168	NORMAL	0
Hemoglobin (g/L)	20[redacted] 253	WEEK 37	139	137	168	NORMAL	0
Hemoglobin (g/L)	20[redacted] 330	WEEK 49	138	137	168	NORMAL	0
Hepatitis B Virus Core Antibody	20[redacted] -23	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antibody	20[redacted] -23	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antigen	20[redacted] -23	SCREENING	NEGATIVE	-	-	-	-
Hepatitis C Virus Antibody	20[redacted] -23	SCREENING	NEGATIVE	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] -23	SCREENING	2.02	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 85	WEEK 13	2.82	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 164	WEEK 25	3.66	-	-	-	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Immunoglobulin A (g/L)	20[redacted] 253	WEEK 37	4.04	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 330	WEEK 49	4.09	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] -23	SCREENING	5.88	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 85	WEEK 13	8.04	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 164	WEEK 25	8.94	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 253	WEEK 37	9.3	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 330	WEEK 49	8.13	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] -23	SCREENING	1.01	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 85	WEEK 13	0.82	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 164	WEEK 25	0.88	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 253	WEEK 37	0.89	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 330	WEEK 49	0.81	-	-	-	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] -23	SCREENING	266	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] -2	WEEK 1 DAY 1	256	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 8	WEEK 2	248	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 29	WEEK 5	295	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 57	WEEK 9	231	124	222	HIGH	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 85	WEEK 13	307	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 113	WEEK 17	266	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 141	WEEK 21	286	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 164	WEEK 25	372	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 253	WEEK 37	231	124	222	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 330	WEEK 49	258	124	222	HIGH	-
Leukocytes (10^9/L)	20[redacted] -23	SCREENING	7.4	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] -2	WEEK 1 DAY 1	8	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 8	WEEK 2	7.6	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 29	WEEK 5	9.6	3.3	8.6	HIGH	0
Leukocytes (10^9/L)	20[redacted] 57	WEEK 9	8.7	3.3	8.6	HIGH	0
Leukocytes (10^9/L)	20[redacted] 85	WEEK 13	6.4	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 113	WEEK 17	9.7	3.3	8.6	HIGH	0
Leukocytes (10^9/L)	20[redacted] 141	WEEK 21	8	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 164	WEEK 25	9.2	3.3	8.6	HIGH	0
Leukocytes (10^9/L)	20[redacted] 253	WEEK 37	7.4	3.3	8.6	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 330	WEEK 49	5.9	3.3	8.6	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lymphocytes (10^9/L)	20[redacted] -23	SCREENING	2.442	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] -2	WEEK 1 DAY 1	2.64	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 8	WEEK 2	3.306	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 29	WEEK 5	3.312	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 57	WEEK 9	2.828	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 85	WEEK 13	2.048	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 113	WEEK 17	3.783	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 141	WEEK 21	3.12	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 164	WEEK 25	3.68	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 253	WEEK 37	3.404	0.545	4.257	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 330	WEEK 49	2.537	0.545	4.257	NORMAL	0
Neutrophils (10^9/L)	20[redacted] -23	SCREENING	4.292	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] -2	WEEK 1 DAY 1	4.4	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 8	WEEK 2	3.534	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 29	WEEK 5	4.944	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 57	WEEK 9	5.177	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 85	WEEK 13	4.032	1.271	6.923	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Neutrophils (10^9/L)	20[redacted] 113	WEEK 17	5.044	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 141	WEEK 21	3.92	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 164	WEEK 25	5.152	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 253	WEEK 37	3.034	1.271	6.923	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 330	WEEK 49	2.891	1.271	6.923	NORMAL	0
Platelets (10^9/L)	20[redacted] -23	SCREENING	190	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] -2	WEEK 1 DAY 1	223	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 8	WEEK 2	147	158	348	LOW	1
Platelets (10^9/L)	20[redacted] 29	WEEK 5	174	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 57	WEEK 9	185	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 85	WEEK 13	206	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 113	WEEK 17	204	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 141	WEEK 21	155	158	348	LOW	1
Platelets (10^9/L)	20[redacted] 164	WEEK 25	171	158	348	NORMAL	0
Platelets (10^9/L)	20[redacted] 253	WEEK 37	150	158	348	LOW	1
Platelets (10^9/L)	20[redacted] 330	WEEK 49	162	158	348	NORMAL	0
Potassium (mmol/L)	20[redacted] -23	SCREENING	4.5	3.6	4.8	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Potassium (mmol/L)	20[redacted] -2	WEEK 1 DAY 1	4.4	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 8	WEEK 2	4.3	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 29	WEEK 5	4.2	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 57	WEEK 9	4.2	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 85	WEEK 13	3.6	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 113	WEEK 17	4.3	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 141	WEEK 21	3.8	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 164	WEEK 25	4.3	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 253	WEEK 37	4.4	3.6	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 330	WEEK 49	4.3	3.6	4.8	NORMAL	0
Protein (g/L)	20[redacted] -23	SCREENING	60	66	81	LOW	-
Protein (g/L)	20[redacted] -2	WEEK 1 DAY 1	62	66	81	LOW	-
Protein (g/L)	20[redacted] 8	WEEK 2	57	66	81	LOW	-
Protein (g/L)	20[redacted] 29	WEEK 5	61	66	81	LOW	-
Protein (g/L)	20[redacted] 57	WEEK 9	58	66	81	LOW	-
Protein (g/L)	20[redacted] 85	WEEK 13	53	66	81	LOW	-
Protein (g/L)	20[redacted] 113	WEEK 17	62	66	81	LOW	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Protein (g/L)	20[redacted] 141	WEEK 21	60	66	81	LOW	-
Protein (g/L)	20[redacted] 164	WEEK 25	63	66	81	LOW	-
Protein (g/L)	20[redacted] 253	WEEK 37	63	66	81	LOW	-
Protein (g/L)	20[redacted] 330	WEEK 49	61	66	81	LOW	-
Sodium (mmol/L)	20[redacted] -23	SCREENING	143	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] -2	WEEK 1 DAY 1	143	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 8	WEEK 2	141	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 29	WEEK 5	142	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 57	WEEK 9	140	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 85	WEEK 13	142	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 113	WEEK 17	142	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 141	WEEK 21	141	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 164	WEEK 25	142	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 253	WEEK 37	142	138	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 330	WEEK 49	141	138	145	NORMAL	0
Urate (umol/L)	20[redacted] -23	SCREENING	392.568	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] -2	WEEK 1 DAY 1	356.88	220.076	416.36	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urate (umol/L)	20[redacted] 8	WEEK 2	392.568	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 29	WEEK 5	440.152	220.076	416.36	HIGH	1
Urate (umol/L)	20[redacted] 57	WEEK 9	386.62	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 85	WEEK 13	178.44	220.076	416.36	LOW	0
Urate (umol/L)	20[redacted] 113	WEEK 17	321.192	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 141	WEEK 21	368.776	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 164	WEEK 25	333.088	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 253	WEEK 37	297.4	220.076	416.36	NORMAL	0
Urate (umol/L)	20[redacted] 330	WEEK 49	297.4	220.076	416.36	NORMAL	0
Urea Nitrogen (mmol/L)	20[redacted] -23	SCREENING	6.069	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] -2	WEEK 1 DAY 1	6.426	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 8	WEEK 2	5.355	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 29	WEEK 5	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 57	WEEK 9	5.712	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 85	WEEK 13	4.998	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 113	WEEK 17	3.57	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 141	WEEK 21	4.998	2.856	7.14	NORMAL	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urea Nitrogen (mmol/L)	20[redacted] 164	WEEK 25	5.355	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 253	WEEK 37	4.284	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 330	WEEK 49	4.284	2.856	7.14	NORMAL	-

2) 被験者番号 54179060GVH3001-[redacted]

■ REASON FOR NARRATIVE SELECTION

Treatment-emergent serious adverse events (SAEs)

■ Death

No Death reported

■ Treatment-emergent serious adverse events (SAEs)

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
肺炎	PNEUMONIA	20[redacted] 20	32 19	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	14
細菌性肺炎	PNEUMONIA BACTERIAL	20 20	120 15	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	18
肺炎	PNEUMONIA	20 20	227 9	Y 3	DOUBTFUL DOSE NOT CHANGED	Y RECOVERED/RESOLVED	16
白内障	CATARACT OF LEFT EYE	20 20	235 75	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	3

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
白内障	CATARACT OF RIGHT EYE	20[redacted] 20[redacted]	235 56	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	5
アナフィラキシー反応	ANAPHYLAXIS	20[redacted] 20[redacted]	464 9	Y 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	1

Note: Adverse Events are coded using MedDRA 22.1

■ Adverse events (AEs) leading to ibrutinib discontinuation

No Adverse events (AEs) leading to ibrutinib discontinuation reported

■ Other malignancies

No Other malignancies reported

■ Major hemorrhage

No Major hemorrhage reported

■ Demographics, Baseline Characteristics

- Country: JPN
- Race: Asian
- Age: 5[redacted]
- Sex: Female
- Baseline height (cm): [redacted]
- Baseline weight (kg): [redacted]
- Baseline karnofsky/Lansky performance status score: 80
- Overall severity of cGVHD: Severe
- cGVHD disease state: STEROID DEPENDENT DISEASE
- Month from initial diagnosis date: 14.2
- Number of prior cGVHD treatment regimens: 1
- First study drug intake: 20[redacted] (Study Day 1)
- Last study drug intake: 20[redacted] (Study Day 476)

■ Disposition Information

- End of treatment: Subject Ongoing on Treatment
- End of trial: Subject Ongoing on Study

■ Other Adverse Events

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
口内炎	STOMATITIS	20[redacted] 20	9 24	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	21
倦怠感	MALAISE	20 20	17 16	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	12
羞明	PHOTOPHOBIA	20 -	17 -	N 1	NOT RELATED DOSE NOT CHANGED	N NOT RECOVERED/NOT RESOLVED	13
発熱	FEVER	20 20	30 2	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	6
中毒性皮疹	TOXICODERMA	20 20	35 10	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	23
肺炎	PNEUMONIA	20 20	51 16	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	15
全身性浮腫	GENERALISED OEDEMA	20 20	95 7	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	8
インフルエンザ	INFLUENZA A VIRUS INFECTION	20 20	111 10	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	11
中毒性皮疹	TOXICODERMA	20 20	124 14	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	24
細菌性肺炎	PNEUMONIA BACTERIAL	20 20	135 7	N 1	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	19
白内障	CATARACT OF LEFT EYE	20[redacted] 20	148 87	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	2

Dictionary-Derived Term	Reported Term for the Adverse Event	Start Date of Adverse Event End Date of Adverse Event	Study Day of Start of Adverse Event Adverse Event Duration (days)	Serious Event Standard Toxicity Grade	Causality Action Taken with Study Treatment	Concomitant or Additional Treatment Given Outcome of Adverse Event	Sequence Number
白内障	CATARACT OF RIGHT EYE	20[redacted] 20	148 87	N 1	NOT RELATED DOSE NOT CHANGED	N RECOVERED/RESOLVED	4
低カリウム血症	HYPOKALEMIA	20 20	227 7	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	9
嘔吐	VOMITING	20 20	227 3	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	27
肺炎	PNEUMONIA	20 20	236 7	N 1	DOUBTFUL DOSE NOT CHANGED	Y RECOVERED/RESOLVED	17
そう痒症	PRURITUS	20 20	262 11	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	20
食物アレルギー	FOOD ALLERGIES	20 20	391 6	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	7
上気道感染	UPPER RESPIRATORY INFECTION	20 20	444 8	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	25
上気道感染	UPPER RESPIRATORY INFECTION	20 20	464 9	N 2	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	26
低カリウム血症	HYPOKALEMIA	20 20	470 7	N 3	NOT RELATED DOSE NOT CHANGED	Y RECOVERED/RESOLVED	10

Note: Adverse Events are coded using MedDRA 22.1

■ Medical History

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Immune system disorders	Acute graft versus host disease	ACUTE GRAFT VERSUS HOST DISEASE	BEFORE	-

Body System or Organ Class	Dictionary-Derived Term	Reported Term for the Medical History	End Relative to Reference Period	Toxicity Grade
Skin and subcutaneous tissue disorders	Drug eruption	DRUG ERUPTION	BEFORE	-
General disorders and administration site conditions	Pain	CHRONIC PAIN	ONGOING	2
Metabolism and nutrition disorders	Hyperuricaemia	HYPERURICAEMIA	ONGOING	2

Note: Medical History are coded using MedDRA 22.1

■ Transplant History

Transplantation Date	Dictionary-Derived Term	Transplant Type	HLA matching and donor relation to recipient	Sex matching between donor and recipient	Stem Cell Source
20[redacted]	Myelodysplastic syndrome	Myeloablative	Matched related	Matched	Peripheral Stem Cells

■ Disease History

Date of Initial Diagnosis	Initial Diagnosis
20[redacted]	CGVHD

■ Study Medication

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 1 DAY 1	20[redacted]	20[redacted]	1	1	420.0	-	-	-
WEEK 1 DAY 2	20[redacted]	20[redacted]	2	7	420.0	-	-	-
WEEK 2	20[redacted]	20[redacted]	8	31	420.0	-	-	-
WEEK 5	20[redacted]	20[redacted]	32	55	420.0	-	-	-
WEEK 9	20[redacted]	20[redacted]	56	78	420.0	-	-	-
WEEK 9	20[redacted]	20[redacted]	79	79	0.0	OTHER	-	-
WEEK 9	20[redacted]	20[redacted]	80	86	420.0	-	-	-
WEEK 13	20[redacted]	20[redacted]	87	114	420.0	-	-	-
WEEK 17	20[redacted]	20[redacted]	115	140	420.0	-	-	-
WEEK 21	20[redacted]	20[redacted]	141	171	420.0	-	-	-
WEEK 25	20[redacted]	20[redacted]	172	226	420.0	-	-	-
WEEK 25	20[redacted]	20[redacted]	227	227	0.0	OTHER	-	-

Visit Name	Start Date of Treatment	End Date of Treatment	Study Day of Start of Treatment	Study Day of End of Treatment	Dose per Administration (mg)	Reason for Dose Skip	Reason for Dose Adjustment	AE Sequence Number(s)
WEEK 25	20[redacted]	20[redacted]	228	254	280.0	-	CYP3A INHIBITOR	-
WEEK 37	20[redacted]	20[redacted]	255	272	280.0	-	-	-
WEEK 37	20[redacted]	20[redacted]	273	279	0.0	OTHER	-	-
WEEK 37	20[redacted]	20[redacted]	280	286	280.0	-	-	-
WEEK 37	20[redacted]	20[redacted]	287	293	0.0	OTHER	-	-
WEEK 37	20[redacted]	20[redacted]	294	338	280.0	-	-	-
WEEK 49	20[redacted]	20[redacted]	339	391	280.0	-	-	-
WEEK 49	20[redacted]	20[redacted]	392	392	0.0	OTHER	-	-
WEEK 49	20[redacted]	20[redacted]	393	415	280.0	-	-	-
WEEK 61	20[redacted]	20[redacted]	416	464	280.0	-	-	-
WEEK 61	20[redacted]	20[redacted]	465	465	0.0	OTHER	-	-
WEEK 61	20[redacted]	20[redacted]	466	476	280.0	-	-	-

■ Prior and Concomitant Medications

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
PARACETAMOL (ACELIO)	20[redacted] 33	-	20[redacted] 33	ADVERSE EVENT	500 mg	BID INTRAVENOUS	1
PARACETAMOL (ACELIO)	20[redacted] 35	-	20[redacted] 35	ADVERSE EVENT	500 mg	QD INTRAVENOUS	1
PARACETAMOL (ACELIO)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	500 mg	BID INTRAVENOUS	1
FLUTICASONE PROPIONATE; SALMETEROL XINAFOATE (ADOAIR DISKUS)	20[redacted] -208	Y	- -	CGVHD	2 PUFF	BID RESPIRATORY (INHALATION)	-
FEXOFENADINE HYDROCHLORIDE (ALLEGRA)	20[redacted] 233	-	20[redacted] 236	ADVERSE EVENT	60 mg	BID ORAL	1
FEXOFENADINE HYDROCHLORIDE (ALLEGRA)	20[redacted] 233	-	20[redacted] 236	ADVERSE EVENT	60 mg	BID ORAL	1
OLOPATADINE HYDROCHLORIDE (ALLELOCK OD TABLETS)	20[redacted] 124	-	20[redacted] 128	ADVERSE EVENT	5 mg	BID ORAL	2

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
SENNA SPP. (ALOSENN(SENNA SPP.))	20[redacted] 255	-	20[redacted] 268	PROPHYLAXIS	1 g	BID ORAL	-
SENNA SPP. (ALOSENN(SENNA SPP.))	20[redacted] 290	-	20[redacted] 290	PROPHYLAXIS	1 g	QD ORAL	-
AMIKACIN (AMIKACIN INJECTION)	20[redacted] 464	-	20[redacted] 464	ADVERSE EVENT	200 mg	ONCE INTRAVENOUS	2
AMIKACIN SULFATE (AMIKAMYCIN INJECTION)	20[redacted] 32	-	20[redacted] 35	ADVERSE EVENT	200 mg	QD INTRAVENOUS	1
AMIKACIN SULFATE (AMIKAMYCIN INJECTION)	20[redacted] 120	-	20[redacted] 124	ADVERSE EVENT	200 mg	QD INTRAVENOUS	1
AMIKACIN SULFATE (AMIKAMYCIN INJECTION)	20[redacted] 138	-	20[redacted] 138	PROPHYLAXIS	200 mg	ONCE INTRAVENOUS	-
BETAMETHASONE BUTYRATE PROPIONATE (ANTEBATE OINTMENT 0.05%)	20[redacted] 37	-	20[redacted] 44	ADVERSE EVENT	1 FINGERTIP UNIT	PRN TRANSDERMAL	2
BETAMETHASONE BUTYRATE PROPIONATE (ANTEBATE OINTMENT 0.05%)	20[redacted] 124	-	20[redacted] 137	ADVERSE EVENT	- OTHER	PRN TOPICAL	2
SODIUM GUALENATE HYDRATE (AZUNOL [GUAIAZULENE] GARGLE LIQUID)	- -	Y	20[redacted] 172	CGVHD	5 mL	PRN TOPICAL	-
SULFAMETHOXAZOLE; TRIMETHOPRIM (BACTRAMIN)	- -	Y	20[redacted] -75	PROPHYLAXIS	1 TABLET	QOD ORAL	-
SULFAMETHOXAZOLE; TRIMETHOPRIM (BACTRAMIN)	20[redacted] -74	Y	20[redacted] 464	PROPHYLAXIS	1 TABLET	2 TIMES PER WEEK ORAL	-
SULFAMETHOXAZOLE; TRIMETHOPRIM (BACTRAMIN)	20[redacted] 467	-	- -	PROPHYLAXIS	1 TABLET	2 TIMES PER WEEK ORAL	-
OXYBUPROCAINE HYDROCHLORIDE (BENOXIL OPHTHALMIC SOLUTION 0.4%)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	5
OXYBUPROCAINE HYDROCHLORIDE (BENOXIL OPHTHALMIC SOLUTION 0.4%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	3
ALENDRONATE SODIUM (BONALON)	- -	Y	20[redacted] -75	PROPHYLAXIS	5 mg	OTHER ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
ALENDRONATE SODIUM (BONALON)	20[redacted] -74	Y	20[redacted] 138	PROPHYLAXIS	5 mg	2 TIMES PER WEEK ORAL	-
ALENDRONATE SODIUM (BONALON)	20[redacted] 139	-	- -	PROPHYLAXIS	5 mg	EVERY WEEK ORAL	-
EPINEPHRINE (BOSMIN INJECTION)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	1 mg	PRN OPHTHALMIC	5
CALCIUM CHLORIDE DIHYDRATE; GLUCOSE; GLUTATHIONE; MAGNESIUM CHLORIDE; POTASSIUM CHLORIDE; SODIUM BICARBONATE; SODIUM CHLORIDE; SODIUM PHOSPHATE (BSS PLUS 500 INTRAOCULAR IRRIGATING SOLUTION)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	500 mL	PRN OPHTHALMIC	5
CALCIUM CHLORIDE DIHYDRATE; GLUCOSE; GLUTATHIONE; MAGNESIUM CHLORIDE; POTASSIUM CHLORIDE; SODIUM BICARBONATE; SODIUM CHLORIDE; SODIUM PHOSPHATE (BSS PLUS 500 INTRAOCULAR IRRIGATING SOLUTION 0.0184%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	500 mL	PRN OPHTHALMIC	3
PARACETAMOL (CALONAL)	20[redacted] 30	-	20[redacted] 31	ADVERSE EVENT	200 mg	PRN ORAL	6
PARACETAMOL (CALONAL TAB)	20[redacted] 111	-	20[redacted] 120	ADVERSE EVENT	200 mg	PRN ORAL	1
PARACETAMOL (CALONAL TAB.200)	20[redacted] 276	-	20[redacted] 277	ADVERSE EVENT	200 mg	PRN ORAL	5
PARACETAMOL (CALONAL TAB.200)	20[redacted] 290	-	20[redacted] 291	ADVERSE EVENT	200 mg	PRN ORAL	3
CHLORPHENAMINE MALEATE (CHLORPHENIRAMINE MALEATE)	20[redacted] 262	-	20[redacted] 272	ADVERSE EVENT	2 mg	PRN ORAL	2
CHLORPHENAMINE MALEATE (CHLORPHENIRAMINE MALEATE)	20[redacted] 395	-	20[redacted] 396	ADVERSE EVENT	2 mg	QD ORAL	7
CLARITHROMYCIN (CLARITH)	- -	Y	20[redacted] -13	PROPHYLAXIS	400 mg	BID ORAL	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
CODEINE PHOSPHATE (CODEINE PHOSPHATE)	20[redacted] 138	-	20[redacted] 140	ADVERSE EVENT	20 mg	QD ORAL	1
CODEINE PHOSPHATE (CODEINE PHOSPHATE POWDER)	20[redacted] 122	-	20[redacted] 137	ADVERSE EVENT	60 mg	TID ORAL	1
CODEINE PHOSPHATE (CODEINE PHOSPHATE POWDER)	20[redacted] 122	-	20[redacted] 137	ADVERSE EVENT	60 mg	TID ORAL	1
LEVOFLOXACIN (CRAVIT)	20[redacted] 50	-	20[redacted] 52	PROPHYLAXIS	500 mg	QD INTRAVENOUS	-
LEVOFLOXACIN (CRAVIT TABLETS)	20[redacted] 41	-	20[redacted] 52	ADVERSE EVENT	500 mg	QD ORAL	1
LEVOFLOXACIN (CRAVIT TABLETS)	20[redacted] 41	-	20[redacted] 52	ADVERSE EVENT	500 mg	QD ORAL	1
LEVOFLOXACIN (CRAVIT TABLETS)	20[redacted] 134	-	20[redacted] 138	PROPHYLAXIS	500 mg	QD ORAL	-
DEXAMETHASONE (DEXALTIN ORAL OINTMENT)	20[redacted] 24	-	20[redacted] 79	CGVHD	1 FINGERTIP UNIT	PRN TOPICAL	-
FLUCONAZOLE (DIFLUCAN)	- -	Y	20[redacted] 226	PROPHYLAXIS	100 mg	QD ORAL	-
DIQUAFOSOL TETRASODIUM (DIQUAS OPHTHALMIC SOLUTION 3%)	20[redacted] 32	-	- -	CGVHD	1 gtt	QID OPHTHALMIC	-
FAROPENEM SODIUM (FAROM TAB.)	20[redacted] 50	-	20[redacted] 52	ADVERSE EVENT	200 mg	TID ORAL	1
FAROPENEM SODIUM (FAROM TAB.)	20[redacted] 50	-	20[redacted] 52	ADVERSE EVENT	200 mg	TID ORAL	1
FAROPENEM SODIUM (FAROM TAB.)	20[redacted] 134	-	20[redacted] 138	PROPHYLAXIS	200 mg	TID ORAL	-
FEBUXOSTAT (FEBURIC TABLETS)	20[redacted] 74	-	20[redacted] 464	MEDICAL HISTORY	10 mg	QD ORAL	-
FEBUXOSTAT (FEBURIC TABLETS)	20[redacted] 467	-	- -	MEDICAL HISTORY	10 mg	QD ORAL	-
DORIPENEM (FINIBAX)	20[redacted] 227	-	20[redacted] 227	ADVERSE EVENT	1 g	QD INTRAVENOUS	1

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
DORIPENEM (FINIBAX)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	2 g	QD INTRAVENOUS	1
CEFOZOPRAN HYDROCHLORIDE (FIRSTCIN)	20[redacted] 35	-	20[redacted] 49	ADVERSE EVENT	2 g	BID INTRAVENOUS	1
CEFOZOPRAN HYDROCHLORIDE (FIRSTCIN)	20[redacted] 120	-	20[redacted] 123	ADVERSE EVENT	2 g	BID INTRAVENOUS	1
CEFOZOPRAN HYDROCHLORIDE (FIRSTCIN)	20[redacted] 124	-	20[redacted] 124	ADVERSE EVENT	2 g	QD INTRAVENOUS	1
CEFCAPENE PIVOXIL HYDROCHLORIDE (FLOMOX(PIVOXIL HYDROCHLORIDE HYDRATE))	20[redacted] 409	-	20[redacted] 415	PROPHYLAXIS	100 mg	TID ORAL	-
CEFCAPENE PIVOXIL HYDROCHLORIDE (FLOMOX(PIVOXIL HYDROCHLORIDE HYDRATE))	20[redacted] 444	-	20[redacted] 451	ADVERSE EVENT	100 mg	TID ORAL	2
MICAFUNGIN SODIUM (FUNGUARD)	20[redacted] 35	-	20[redacted] 50	ADVERSE EVENT	75 mg	QD INTRAVENOUS	1
GATIFLOXACIN (GATIFLO OPHTHALMIC SOLUTION 0.3%)	20[redacted] 249	-	20[redacted] 275	CGVHD	5 mL	QID OPHTHALMIC	-
GATIFLOXACIN (GATIFLO OPHTHALMIC SOLUTION 0.3%)	20[redacted] 276	-	20[redacted] 277	ADVERSE EVENT	5 mL	QID OPHTHALMIC	5
GATIFLOXACIN (GATIFLO OPHTHALMIC SOLUTION 0.3%)	20[redacted] 290	-	20[redacted] 291	ADVERSE EVENT	5 mL	QID OPHTHALMIC	3
HYALURONATE SODIUM (HYALEIN)	20[redacted] 80	-	20[redacted] 289	CGVHD	1 gtt	PRN OPHTHALMIC	-
HYALURONATE SODIUM (HYALEIN OPHTHALMIC SOLUTION)	20[redacted] 276	-	- -	CGVHD	1 gtt	QID OPHTHALMIC	-
ACICLOVIR (INAVIR DRY POWDER INHALER)	20[redacted] 111	-	20[redacted] 120	ADVERSE EVENT	20 mg	QD ORAL	1
POTASSIUM CHLORIDE (KCL INJECTION)	20[redacted] 228	-	20[redacted] 233	ADVERSE EVENT	- mEq	QD INTRAVENOUS	9
CLOBETASONE BUTYRATE (KINDAVATE OINTMENT)	20[redacted] 121	-	20[redacted] 261	CGVHD	5 g	PRN TOPICAL	-
FUROSEMIDE (LASIX)	20[redacted] 95	-	20[redacted] 101	ADVERSE EVENT	20 mg	QD ORAL	8

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
FUROSEMIDE (LASIX)	20[redacted] 102	-	20[redacted] 135	PROPHYLAXIS	20 mg	QD ORAL	-
CEFDITOREN PIVOXIL (MEIACT)	20[redacted] 24	-	20[redacted] 32	PROPHYLAXIS	100 mg	3 TIMES PER WEEK ORAL	-
CEFDITOREN PIVOXIL (MEIACT)	20[redacted] 138	-	20[redacted] 141	ADVERSE EVENT	100 mg	TID ORAL	1
CEFDITOREN PIVOXIL (MEIACT)	20[redacted] 235	-	20[redacted] 241	ADVERSE EVENT	100 mg	TID ORAL	1
CEFDITOREN PIVOXIL (MEIACT)	20[redacted] 235	-	20[redacted] 241	ADVERSE EVENT	100 mg	TID ORAL	1
DIPHENHYDRAMINE; MENTHOL (MENTHOL RESTAMIN[DIPHENHYDRAMINE] CREAM)	20[redacted] 128	-	20[redacted] 137	ADVERSE EVENT	1 FINGERTIP UNIT	PRN TRANSDERMAL	2
MEROPENEM (MEROPEN)	20[redacted] 32	-	20[redacted] 34	ADVERSE EVENT	1 g	BID INTRAVENOUS	1
MEROPENEM (MEROPEN)	20[redacted] 35	-	20[redacted] 35	ADVERSE EVENT	1 g	QD INTRAVENOUS	1
MEROPENEM (MEROPEN)	20[redacted] 37	-	20[redacted] 37	ADVERSE EVENT	1 g	QD INTRAVENOUS	1
MEROPENEM (MEROPEN)	20[redacted] 464	-	20[redacted] 464	ADVERSE EVENT	1 g	ONCE INTRAVENOUS	2
MINOCYCLINE HYDROCHLORIDE (MINOMYCIN TABLETS)	20[redacted] 138	-	20[redacted] 141	ADVERSE EVENT	50 mg	BID ORAL	1
KETOPROFEN (MOHRUS TAPE)	- -	Y	20[redacted] 24	CGVHD	40 mg	PRN TRANSDERMAL	-
KETOPROFEN (MOHRUS TAPE)	20[redacted] 228	-	20[redacted] 231	CGVHD	40 mg	PRN TRANSDERMAL	-
PHENYLEPHRINE HYDROCHLORIDE; TROPICAMIDE (MYDRIN-P OPHTHALMIC SOLUTION)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	1 gtt	QID OPHTHALMIC	5
PHENYLEPHRINE HYDROCHLORIDE; TROPICAMIDE (MYDRIN-P OPHTHALMIC SOLUTION)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	1 gtt	QID OPHTHALMIC	3

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
PHENYLEPHRINE HYDROCHLORIDE (NEOSYNESIN [PHENYLEPHRINE HYDROCHLORIDE])	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	10 mL	OTHER OPHTHALMIC	5
PHENYLEPHRINE HYDROCHLORIDE (NEOSYNESIN [PHENYLEPHRINE HYDROCHLORIDE])	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	10 mL	QID OPHTHALMIC	3
NEPAFENAC (NEVANAC OPHTHALMIC SUSPENSION 0.1%)	20[redacted] 276	-	20[redacted] 283	ADVERSE EVENT	1 gtt	TID OPHTHALMIC	5
NEPAFENAC (NEVANAC OPHTHALMIC SUSPENSION 0.1%)	20[redacted] 291	-	20[redacted] 297	ADVERSE EVENT	1 gtt	TID OPHTHALMIC	3
NEPAFENAC (NEVANAC OPHTHALMIC SUSPENSION 0.1%)	20[redacted] 310	-	20[redacted] 365	CGVHD	1 gtt	QID OPHTHALMIC	-
AMLODIPINE BESILATE (NORVASC)	- -	Y	20[redacted] 444	PROPHYLAXIS	10 mg	QD ORAL	-
AMLODIPINE BESILATE (NORVASC)	20[redacted] 445	-	20[redacted] 464	PROPHYLAXIS	5 mg	QD ORAL	-
AMLODIPINE BESILATE (NORVASC)	20[redacted] 467	-	- -	PROPHYLAXIS	5 mg	QD ORAL	-
HYALURONATE SODIUM (OPEGAN HI)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	5
HYALURONATE SODIUM (OPEGAN HI)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	0.85 mL	PRN OPHTHALMIC	3
CALCIUM CHLORIDE DIHYDRATE; GLUCOSE; MAGNESIUM SULFATE; POTASSIUM CHLORIDE; SODIUM BICARBONATE; SODIUM CHLORIDE (OPEGUARD-MA INTRAOCULAR IRRIGATING SOLUTION)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	500 mL	PRN OPHTHALMIC	3
HYALURONATE SODIUM (OPELEAD OPHTHALMIC VISCOELASTIC PREPARATION 1%)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	5
HYALURONATE SODIUM (OPELEAD OPHTHALMIC VISCOELASTIC PREPARATION 1%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	0.5 mL	PRN OPHTHALMIC	3

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
OXYCODONE HYDROCHLORIDE (OXINORM [OXYCODONE HYDROCHLORIDE])	- -	Y	- -	MEDICAL HISTORY	10 mg	PRN ORAL	-
OXYGEN (OXYGEN)	20[redacted] 464	-	20[redacted] 464	ADVERSE EVENT	4 L	OTHER OTHER	1
OXYGEN (OXYGEN)	20[redacted] 465	-	20[redacted] 465	ADVERSE EVENT	3 L	OTHER OTHER	1
ALL OTHER NON-THERAPEUTIC PRODUCTS (PHACOEMULSIFICATION AND ASPIRATION AND INTRA OCULAR LENS)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	- -	- -	5
DEXCHLORPHENIRAMINE MALEATE (POLARAMINE)	20[redacted] 464	-	20[redacted] 464	ADVERSE EVENT	5 mg	ONCE INTRAVENOUS	1
DEXCHLORPHENIRAMINE MALEATE (POLARAMINE)	20[redacted] 465	-	20[redacted] 469	ADVERSE EVENT	5 mg	BID INTRAVENOUS	1
DEXCHLORPHENIRAMINE MALEATE (POLARAMINE)	20[redacted] 470	-	20[redacted] 470	ADVERSE EVENT	5 mg	QD INTRAVENOUS	1
POVIDONE-IODINE (POPIYODON SOLUTION 10%)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	20 mL	PRN OPHTHALMIC	5
POVIDONE-IODINE (POPIYODON SOLUTION 10%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	20 mL	PRN OPHTHALMIC	3
POTASSIUM CHLORIDE (POTASSIUM CHLORIDE)	20[redacted] 228	-	20[redacted] 231	ADVERSE EVENT	13.4 mEq	TID ORAL	1
POTASSIUM CHLORIDE (POTASSIUM CHLORIDE)	20[redacted] 470	-	20[redacted] 471	ADVERSE EVENT	13.4 mEq	TID ORAL	1
POTASSIUM CHLORIDE (POTASSIUM CHLORIDE)	20[redacted] 472	-	20[redacted] 472	ADVERSE EVENT	13.4 mEq	BID ORAL	1
METOCLOPRAMIDE HYDROCHLORIDE (PRIMPERAN INJECTION)	20[redacted] 227	-	20[redacted] 227	ADVERSE EVENT	20 mg	ONCE INTRAVENOUS	2
METOCLOPRAMIDE HYDROCHLORIDE (PRIMPERAN INJECTION)	20[redacted] 229	-	20[redacted] 229	ADVERSE EVENT	10 mg	ONCE INTRAVENOUS	2
SENNOSIDE A+B CALCIUM (PURSENNID(SENNOSIDE A+B CALCIUM))	20[redacted] 124	-	20[redacted] 143	PROPHYLAXIS	12 mg	PRN ORAL	-
SENNOSIDE A+B CALCIUM (PURSENNID(SENNOSIDE A+B CALCIUM))	20[redacted] 304	-	20[redacted] 339	PROPHYLAXIS	12 mg	QD ORAL	-

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SENNOSIDE A+B CALCIUM (PURSENNID(SENNOSID A+B CALCIUM)TABLETS)	20[redacted] 468	-	20[redacted] 469	PROPHYLAXIS	12 mg	QD ORAL	-
DIPHENHYDRAMINE (RESTAMIN KOWA CREAM 1%)	20[redacted] 37	-	20[redacted] 44	ADVERSE EVENT	1 FINGERTIP UNIT	PRN TRANSDERMAL	2
BETAMETHASONE (RINDERON)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	2 mg	PRN OPHTHALMIC	5
BETAMETHASONE (RINDERON)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	2 mg	PRN OPHTHALMIC	3
CEFTRIAXONE SODIUM (ROCEPHIN)	20[redacted] 138	-	20[redacted] 138	ADVERSE EVENT	2 g	ONCE INTRAVENOUS	1
CEFTRIAXONE SODIUM (ROCEPHIN)	20[redacted] 444	-	20[redacted] 444	ADVERSE EVENT	1 g	ONCE INTRAVENOUS	2
RUPATADINE FUMARATE (RUPAFIN TABLETS)	20[redacted] 128	-	20[redacted] 134	ADVERSE EVENT	10 mg	QD ORAL	2
TEPRENONE (SELBEX)	20[redacted] -12	-	20[redacted] 464	PROPHYLAXIS	150 mg	TID ORAL	-
TEPRENONE (SELBEX)	20[redacted] 467	-	- -	PROPHYLAXIS	50 mg	TID ORAL	-
MONTELUKAST SODIUM (SINGULAIR)	20[redacted] 467	-	- -	CGVHD	10 mg	QD ORAL	-
MONTELUKAST SODIUM (SINGURAIR)	- -	Y	20[redacted] 464	CGVHD	10 mg	QD ORAL	-
HYALURONATE SODIUM (SODIUM HYALURONATE OPHTHALMIC SOLUTION 0.1%)	20[redacted] 121	-	20[redacted] 121	CGVHD	1 gtt	QID OPHTHALMIC	-
HYALURONATE SODIUM (SODIUM HYALURONATE OPHTHALMIC SOLUTION 0.1%)	20[redacted] 234	-	20[redacted] 234	CGVHD	1 gtt	QID OPHTHALMIC	-
HYALURONATE SODIUM (SODIUM HYALURONATE OPHTHALMIC SOLUTION 0.1%)	20[redacted] 276	-	20[redacted] 276	CGVHD	1 gtt	QID OPHTHALMIC	-

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CYSTEINE; GLYCINE; GLYCYRRHIZIC ACID (STRONGER NEO-MINOPHAGEN C P INJ.)	20[redacted] 465	-	20[redacted] 465	ADVERSE EVENT	40 mL	ONCE INTRAVENOUS	1
CYSTEINE; GLYCINE; GLYCYRRHIZIC ACID (STRONGER NEO-MINOPHAGEN C P INJ.)	20[redacted] 466	-	20[redacted] 469	ADVERSE EVENT	40 mL	BID INTRAVENOUS	1
CYSTEINE; GLYCINE; GLYCYRRHIZIC ACID (STRONGER NEO-MINOPHAGEN C P INJ.)	20[redacted] 470	-	20[redacted] 472	ADVERSE EVENT	40 mL	QD INTRAVENOUS	1
LANSOPRAZOLE (TAKEPRON)	- -	Y	20[redacted] 464	PROPHYLAXIS	30 mg	QD ORAL	-
LANSOPRAZOLE (TAKEPRON)	20[redacted] 467	-	- -	PROPHYLAXIS	30 mg	QD ORAL	-
OSELTAMIVIR PHOSPHATE (TAMIFLU)	20[redacted] 95	-	20[redacted] 99	PROPHYLAXIS	75 mg	BID ORAL	-
OSELTAMIVIR PHOSPHATE (TAMIFLU)	20[redacted] 115	-	20[redacted] 119	ADVERSE EVENT	75 mg	BID ORAL	1
TEICOPLANIN (TARGOCID)	20[redacted] 35	-	20[redacted] 49	ADVERSE EVENT	400 mg	QD INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 36	-	20[redacted] 36	ADVERSE EVENT	400 mg	BID INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	400 mg	QD INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	600 mg	QD INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 229	-	20[redacted] 229	ADVERSE EVENT	600 mg	BID INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 230	-	20[redacted] 230	ADVERSE EVENT	600 mg	QD INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 231	-	20[redacted] 236	ADVERSE EVENT	400 mg	QD INTRAVENOUS	1
TEICOPLANIN (TARGOCID)	20[redacted] 231	-	20[redacted] 236	ADVERSE EVENT	400 mg	QD INTRAVENOUS	1
OFLOXACIN (TARIVID OPHTHALMIC OINTMENT 0.3%)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	1 g	PRN OPHTHALMIC	5

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
OFLOXACIN (TARIVID OPHTHALMIC OINTMENT 0.3%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	1 g	PRN OPHTHALMIC	3
URSODEOXYCHOLIC ACID (URSO [URSODEOXYCHOLIC ACID])	20[redacted] -96	Y	20[redacted] 73	PROPHYLAXIS	100 mg	QD ORAL	-
URSODEOXYCHOLIC ACID (URSO[URSODEOXYCHOLIC ACID])	20[redacted] -603	Y	20[redacted] -97	PROPHYLAXIS	100 mg	TID ORAL	-
MOXIFLOXACIN HYDROCHLORIDE (VEGAMOX OPHTHALMIC SOLUTION 0.5%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	5 mL	PRN OPHTHALMIC	3
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 17	-	20[redacted] 17	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 66	-	20[redacted] 66	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 95	-	20[redacted] 95	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 122	-	20[redacted] 124	CGVHD	5 g	QD INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 144	-	20[redacted] 144	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 178	-	20[redacted] 178	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 227	-	20[redacted] 227	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 228	-	20[redacted] 230	CGVHD	5 g	QD INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 269	-	20[redacted] 269	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 304	-	20[redacted] 304	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 339	-	20[redacted] 339	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 367	-	20[redacted] 367	CGVHD	10 g	ONCE INTRAVENOUS	-

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 409	-	20[redacted] 409	CGVHD	5 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 444	-	20[redacted] 444	CGVHD	10 g	ONCE INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 465	-	20[redacted] 467	CGVHD	5 g	QD INTRAVENOUS	-
IMMUNOGLOBULIN HUMAN NORMAL (VENOGLOBULIN)	20[redacted] 466	-	20[redacted] 472	CGVHD	5 g	QD INTRAVENOUS	-
VORICONAZOLE (VFEND)	20[redacted] 227	-	20[redacted] 227	ADVERSE EVENT	350 mg	ONCE INTRAVENOUS	1
VORICONAZOLE (VFEND)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	200 mg	ONCE INTRAVENOUS	1
VORICONAZOLE (VFEND)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	350 mg	ONCE INTRAVENOUS	1
VORICONAZOLE (VFEND)	20[redacted] 229	-	20[redacted] 231	ADVERSE EVENT	400 mg	QD INTRAVENOUS	1
VORICONAZOLE (VFEND)	20[redacted] 232	-	20[redacted] 235	ADVERSE EVENT	200 mg	BID ORAL	1
VORICONAZOLE (VFEND)	20[redacted] 236	-	20[redacted] 394	PROPHYLAXIS	200 mg	BID ORAL	-
VORICONAZOLE (VFEND)	20[redacted] 395	-	- -	PROPHYLAXIS	100 mg	BID ORAL	-
EPINEPHRINE; LIDOCAINE HYDROCHLORIDE (XYLOCAINE INJECTION 2% WITH EPINEPHRINE)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	3.4 mL	PRN TOPICAL	5
EPINEPHRINE; LIDOCAINE HYDROCHLORIDE (XYLOCAINE INJECTION 2% WITH EPINEPHRINE)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	1.5 mL	PRN TOPICAL	3
BENZALKONIUM CHLORIDE; LIDOCAINE HYDROCHLORIDE; METHYLCELLULOSE (XYLOCAINE OPHTHALMIC SOLUTION 4%)	20[redacted] 276	-	20[redacted] 276	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	5
BENZALKONIUM CHLORIDE; LIDOCAINE HYDROCHLORIDE; METHYLCELLULOSE (XYLOCAINE OPHTHALMIC SOLUTION 4%)	20[redacted] 290	-	20[redacted] 290	ADVERSE EVENT	0.1 mL	PRN OPHTHALMIC	3

Standardized Medication Name Reported Name of Drug, Med, or Therapy	Start Date of Medication Study Day of Start of Medication	Started Before Informed Concent Date	End Date of Medication Study Day of End of Medication	Indication	Dose per Administration Dose Units	Dosing Frequency per Interval Route of Administration	AE Sequence Number(s)
LIDOCAINE (XYLOCAINE[LIDOCAINE] SOLUTION)	20[redacted] 24	-	20[redacted] 80	CGVHD	1 OTHER	PRN TOPICAL	-
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 124	-	20[redacted] 124	ADVERSE EVENT	4.5 g	QD INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 125	-	20[redacted] 125	ADVERSE EVENT	4.5 g	TID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 126	-	20[redacted] 126	ADVERSE EVENT	4.5 g	BID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 228	-	20[redacted] 228	ADVERSE EVENT	4.5 g	BID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 229	-	20[redacted] 235	ADVERSE EVENT	4.5 g	TID INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 236	-	20[redacted] 236	ADVERSE EVENT	4.5 g	ONCE INTRAVENOUS	1
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 465	-	20[redacted] 465	ADVERSE EVENT	2.25 g	BID INTRAVENOUS	2
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 466	-	20[redacted] 471	ADVERSE EVENT	2.25 g	QID INTRAVENOUS	2
PIPERACILLIN SODIUM; TAZOBACTAM SODIUM (ZOSYN)	20[redacted] 472	-	20[redacted] 472	ADVERSE EVENT	2.25 g	TID INTRAVENOUS	2
ACICLOVIR (ZOVIRAX)	- -	Y	20[redacted] -109	PROPHYLAXIS	200 mg	QOD ORAL	-
ACICLOVIR (ZOVIRAX)	20[redacted] -108	Y	20[redacted] -75	PROPHYLAXIS	200 mg	OTHER ORAL	-
ACICLOVIR (ZOVIRAX)	20[redacted] -74	Y	20[redacted] 464	PROPHYLAXIS	200 mg	2 TIMES PER WEEK ORAL	-
ACICLOVIR (ZOVIRAX)	20[redacted] 469	-	- -	PROPHYLAXIS	200 mg	2 TIMES PER WEEK ORAL	-

■ Karnofsky/Lansky performance status score

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Date of Finding Study Day of Finding	Visit Name	Result
20[redacted]-18	SCREENING	80
20[redacted]1	WEEK 1 DAY 1	80
20[redacted]32	WEEK 5	80
20[redacted]56	WEEK 9	90
20[redacted]87	WEEK 13	80
20[redacted]115	WEEK 17	80
20[redacted]141	WEEK 21	80
20[redacted]172	WEEK 25	80
20[redacted]255	WEEK 37	80
20[redacted]339	WEEK 49	90
20[redacted]416	WEEK 61	90

■ Laboratory Data

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted]-18	SCREENING	27	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted]1	WEEK 1 DAY 1	21	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted]8	WEEK 2	22	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted]32	WEEK 5	33	0	34.99	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 56	WEEK 9	20	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 87	WEEK 13	24	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 115	WEEK 17	63	0	34.99	HIGH	1
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	37	0	34.99	HIGH	1
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 172	WEEK 25	24	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 255	WEEK 37	40	0	34.99	HIGH	1
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 339	WEEK 49	15	0	34.99	NORMAL	0
Alanine Aminotransferase (Enzyme U/L)	20[redacted] 416	WEEK 61	19	0	34.99	NORMAL	0
Albumin (g/L)	20[redacted] -18	SCREENING	44	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 1	WEEK 1 DAY 1	40	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 8	WEEK 2	42	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 32	WEEK 5	36	39	48	LOW	1
Albumin (g/L)	20[redacted] 56	WEEK 9	42	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 87	WEEK 13	46	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 115	WEEK 17	40	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 141	WEEK 21	37	39	48	LOW	1
Albumin (g/L)	20[redacted] 172	WEEK 25	42	39	48	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Albumin (g/L)	20[redacted] 255	WEEK 37	44	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 339	WEEK 49	42	39	48	NORMAL	0
Albumin (g/L)	20[redacted] 416	WEEK 61	44	39	48	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] -18	SCREENING	188	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	234	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 8	WEEK 2	201	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 32	WEEK 5	202	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 56	WEEK 9	169	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 87	WEEK 13	128	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 115	WEEK 17	134	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 141	WEEK 21	195	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 172	WEEK 25	116	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 255	WEEK 37	133	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 339	WEEK 49	226	100	310	NORMAL	0
Alkaline Phosphatase (Enzyme U/L)	20[redacted] 416	WEEK 61	152	100	310	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] -18	SCREENING	21	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	16	0	29.99	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 8	WEEK 2	17	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 32	WEEK 5	23	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 56	WEEK 9	15	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 87	WEEK 13	19	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 115	WEEK 17	48	0	29.99	HIGH	1
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 141	WEEK 21	20	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 172	WEEK 25	18	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 255	WEEK 37	25	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 339	WEEK 49	14	0	29.99	NORMAL	0
Aspartate Aminotransferase (Enzyme U/L)	20[redacted] 416	WEEK 61	18	0	29.99	NORMAL	0
Bilirubin (umol/L)	20[redacted] -18	SCREENING	11.97	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 1	WEEK 1 DAY 1	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 8	WEEK 2	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 32	WEEK 5	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 56	WEEK 9	15.39	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 87	WEEK 13	8.55	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 115	WEEK 17	8.55	3.42	18.81	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Bilirubin (umol/L)	20[redacted] 141	WEEK 21	6.84	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 172	WEEK 25	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 255	WEEK 37	10.26	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 339	WEEK 49	5.13	3.42	18.81	NORMAL	0
Bilirubin (umol/L)	20[redacted] 416	WEEK 61	10.26	3.42	18.81	NORMAL	0
Creatinine (umol/L)	20[redacted] -18	SCREENING	83.096	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 1	WEEK 1 DAY 1	76.908	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 8	WEEK 2	77.792	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 32	WEEK 5	73.372	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 56	WEEK 9	63.648	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 87	WEEK 13	66.3	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 115	WEEK 17	75.14	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 141	WEEK 21	76.908	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 172	WEEK 25	74.256	44.2	70.72	HIGH	1
Creatinine (umol/L)	20[redacted] 255	WEEK 37	64.532	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 339	WEEK 49	65.416	44.2	70.72	NORMAL	0
Creatinine (umol/L)	20[redacted] 416	WEEK 61	73.372	44.2	70.72	HIGH	1

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Deoxyribonucleic Acid	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 56	WEEK 9	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 87	WEEK 13	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 172	WEEK 25	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 269	WEEK 37 UNSCHEDULED 01	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 353	WEEK 49 UNSCHEDULED 01	NEGATIVE	-	-	-	-
Deoxyribonucleic Acid	20[redacted] 416	WEEK 61	NEGATIVE	-	-	-	-
Eosinophils (10^9/L)	20[redacted] -18	SCREENING	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	0.18	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 8	WEEK 2	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 32	WEEK 5	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 56	WEEK 9	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 87	WEEK 13	0.05	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 115	WEEK 17	0.16	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 141	WEEK 21	0.293	0.04	0.32	NORMAL	-
Eosinophils (10^9/L)	20[redacted] 172	WEEK 25	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 255	WEEK 37	0.14	0.04	0.32	NORMAL	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Eosinophils (10^9/L)	20[redacted] 339	WEEK 49	0	0.04	0.32	LOW	-
Eosinophils (10^9/L)	20[redacted] 416	WEEK 61	0.31	0.04	0.32	NORMAL	-
Glucose (mmol/L)	20[redacted] -18	SCREENING	6.3281	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	6.8832	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 8	WEEK 2	7.8269	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 32	WEEK 5	5.2179	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 56	WEEK 9	8.3265	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 87	WEEK 13	5.329	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 115	WEEK 17	6.9943	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 141	WEEK 21	6.3837	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 172	WEEK 25	4.9404	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 255	WEEK 37	4.6073	3.8857	6.1061	NORMAL	0
Glucose (mmol/L)	20[redacted] 339	WEEK 49	6.3837	3.8857	6.1061	HIGH	1
Glucose (mmol/L)	20[redacted] 416	WEEK 61	6.9388	3.8857	6.1061	HIGH	1
HIV Antibody	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Hemoglobin (g/L)	20[redacted] -18	SCREENING	136	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 1	WEEK 1 DAY 1	113	115	155	LOW	1

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Hemoglobin (g/L)	20[redacted] 8	WEEK 2	121	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 32	WEEK 5	117	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 56	WEEK 9	117	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 87	WEEK 13	125	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 115	WEEK 17	138	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 141	WEEK 21	118	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 172	WEEK 25	123	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 255	WEEK 37	126	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 339	WEEK 49	126	115	155	NORMAL	0
Hemoglobin (g/L)	20[redacted] 416	WEEK 61	131	115	155	NORMAL	0
Hepatitis B Virus Core Antibody	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Hepatitis B Virus Surface Antibody	20[redacted] -12	SCREENING	POSITIVE	-	-	-	-
Hepatitis B Virus Surface Antigen	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Hepatitis C Virus Antibody	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] -12	SCREENING	0.19	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 87	WEEK 13	0.2	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 172	WEEK 25	0.23	-	-	-	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Immunoglobulin A (g/L)	20[redacted] 255	WEEK 37	0.16	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 339	WEEK 49	0.14	-	-	-	-
Immunoglobulin A (g/L)	20[redacted] 416	WEEK 61	0.14	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] -12	SCREENING	5.28	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 87	WEEK 13	5.19	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 172	WEEK 25	4.68	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 255	WEEK 37	4.98	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 339	WEEK 49	3.68	-	-	-	-
Immunoglobulin G (g/L)	20[redacted] 416	WEEK 61	5.39	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] -12	SCREENING	0.14	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 87	WEEK 13	0.1	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 172	WEEK 25	0.27	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 255	WEEK 37	0.11	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 339	WEEK 49	0.1	-	-	-	-
Immunoglobulin M (g/L)	20[redacted] 416	WEEK 61	0.15	-	-	-	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] -18	SCREENING	327	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 1	WEEK 1 DAY 1	289	110	219	HIGH	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 8	WEEK 2	330	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 32	WEEK 5	313	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 56	WEEK 9	288	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 87	WEEK 13	312	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 115	WEEK 17	295	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 141	WEEK 21	321	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 172	WEEK 25	289	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 255	WEEK 37	272	110	219	HIGH	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 339	WEEK 49	180	110	219	NORMAL	-
Lactate Dehydrogenase (Enzyme U/L)	20[redacted] 416	WEEK 61	160	110	219	NORMAL	-
Leukocytes (10^9/L)	20[redacted] -18	SCREENING	7.7	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	6	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 8	WEEK 2	11.5	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 32	WEEK 5	15.4	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 56	WEEK 9	13.8	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 87	WEEK 13	10	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 115	WEEK 17	8	4	8	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Leukocytes (10^9/L)	20[redacted] 141	WEEK 21	11.7	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 172	WEEK 25	9	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 255	WEEK 37	7	4	8	NORMAL	0
Leukocytes (10^9/L)	20[redacted] 339	WEEK 49	8.5	4	8	HIGH	0
Leukocytes (10^9/L)	20[redacted] 416	WEEK 61	6.2	4	8	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] -18	SCREENING	0.308	0.8	3.2	LOW	3
Lymphocytes (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	0.6	0.8	3.2	LOW	2
Lymphocytes (10^9/L)	20[redacted] 8	WEEK 2	0.92	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 32	WEEK 5	0.231	0.8	3.2	LOW	3
Lymphocytes (10^9/L)	20[redacted] 56	WEEK 9	0.966	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 87	WEEK 13	0.25	0.8	3.2	LOW	3
Lymphocytes (10^9/L)	20[redacted] 115	WEEK 17	0.24	0.8	3.2	LOW	3
Lymphocytes (10^9/L)	20[redacted] 141	WEEK 21	0.936	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 172	WEEK 25	0.45	0.8	3.2	LOW	3
Lymphocytes (10^9/L)	20[redacted] 255	WEEK 37	0.91	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 339	WEEK 49	1.615	0.8	3.2	NORMAL	0
Lymphocytes (10^9/L)	20[redacted] 416	WEEK 61	1.24	0.8	3.2	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Neutrophils (10^9/L)	20[redacted] -18	SCREENING	7.161	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	4.8	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 8	WEEK 2	10.235	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 32	WEEK 5	14.168	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 56	WEEK 9	11.868	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 87	WEEK 13	9.25	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 115	WEEK 17	6.88	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 141	WEEK 21	9.243	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 172	WEEK 25	7.65	1.6	6.32	HIGH	0
Neutrophils (10^9/L)	20[redacted] 255	WEEK 37	5.32	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 339	WEEK 49	6.205	1.6	6.32	NORMAL	0
Neutrophils (10^9/L)	20[redacted] 416	WEEK 61	4.092	1.6	6.32	NORMAL	0
Platelets (10^9/L)	20[redacted] -18	SCREENING	141	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 1	WEEK 1 DAY 1	120	140	400	LOW	1
Platelets (10^9/L)	20[redacted] 8	WEEK 2	122	140	400	LOW	1
Platelets (10^9/L)	20[redacted] 32	WEEK 5	153	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 56	WEEK 9	181	140	400	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Platelets (10^9/L)	20[redacted] 87	WEEK 13	175	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 115	WEEK 17	143	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 141	WEEK 21	178	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 172	WEEK 25	166	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 255	WEEK 37	153	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 339	WEEK 49	177	140	400	NORMAL	0
Platelets (10^9/L)	20[redacted] 416	WEEK 61	184	140	400	NORMAL	0
Potassium (mmol/L)	20[redacted] -18	SCREENING	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	4.1	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 8	WEEK 2	4.4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 32	WEEK 5	4.7	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 56	WEEK 9	4.1	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 87	WEEK 13	4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 115	WEEK 17	3.8	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 141	WEEK 21	3.8	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 172	WEEK 25	4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 227	WEEK 25 UNSCHEDULED 01	3	3.5	4.8	LOW	2

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Potassium (mmol/L)	20[redacted] 233	WEEK 25 UNSCHEDULED 02	4.4	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 255	WEEK 37	4.2	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 339	WEEK 49	3.9	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 416	WEEK 61	3.6	3.5	4.8	NORMAL	0
Potassium (mmol/L)	20[redacted] 470	WEEK 61 UNSCHEDULED 01	2.7	3.5	4.8	LOW	3
Potassium (mmol/L)	20[redacted] 476	WEEK 61 UNSCHEDULED 02	4.1	3.5	4.8	NORMAL	0
Protein (g/L)	20[redacted] -18	SCREENING	69	67	83	NORMAL	-
Protein (g/L)	20[redacted] 1	WEEK 1 DAY 1	63	67	83	LOW	-
Protein (g/L)	20[redacted] 8	WEEK 2	64	67	83	LOW	-
Protein (g/L)	20[redacted] 32	WEEK 5	70	67	83	NORMAL	-
Protein (g/L)	20[redacted] 56	WEEK 9	69	67	83	NORMAL	-
Protein (g/L)	20[redacted] 87	WEEK 13	70	67	83	NORMAL	-
Protein (g/L)	20[redacted] 115	WEEK 17	67	67	83	NORMAL	-
Protein (g/L)	20[redacted] 141	WEEK 21	64	67	83	LOW	-
Protein (g/L)	20[redacted] 172	WEEK 25	65	67	83	LOW	-
Protein (g/L)	20[redacted] 255	WEEK 37	67	67	83	NORMAL	-
Protein (g/L)	20[redacted] 339	WEEK 49	65	67	83	LOW	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Protein (g/L)	20[redacted] 416	WEEK 61	67	67	83	NORMAL	-
Ribonucleic Acid	20[redacted] -12	SCREENING	NEGATIVE	-	-	-	-
Ribonucleic Acid	20[redacted] 87	WEEK 13	NEGATIVE	-	-	-	-
Ribonucleic Acid	20[redacted] 172	WEEK 25	NEGATIVE	-	-	-	-
Ribonucleic Acid	20[redacted] 353	WEEK 49 UNSCHEDULED 01	NEGATIVE	-	-	-	-
Sodium (mmol/L)	20[redacted] -18	SCREENING	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	143	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 8	WEEK 2	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 32	WEEK 5	140	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 56	WEEK 9	141	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 87	WEEK 13	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 115	WEEK 17	139	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 141	WEEK 21	144	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 172	WEEK 25	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 255	WEEK 37	142	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 339	WEEK 49	143	136	145	NORMAL	0
Sodium (mmol/L)	20[redacted] 416	WEEK 61	144	136	145	NORMAL	0

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urate (umol/L)	20[redacted] -18	SCREENING	333.088	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 1	WEEK 1 DAY 1	303.348	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 8	WEEK 2	356.88	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 32	WEEK 5	327.14	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 56	WEEK 9	392.568	178.44	356.88	HIGH	1
Urate (umol/L)	20[redacted] 87	WEEK 13	285.504	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 115	WEEK 17	327.14	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 141	WEEK 21	315.244	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 172	WEEK 25	279.556	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 255	WEEK 37	249.816	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 339	WEEK 49	261.712	178.44	356.88	NORMAL	0
Urate (umol/L)	20[redacted] 416	WEEK 61	303.348	178.44	356.88	NORMAL	0
Urea Nitrogen (mmol/L)	20[redacted] -18	SCREENING	7.14	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 1	WEEK 1 DAY 1	7.854	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 8	WEEK 2	9.639	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 32	WEEK 5	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 56	WEEK 9	4.998	2.856	7.14	NORMAL	-

Parameter	Date of Specimen Collection Study Day of Specimen Collection	Visit Name	Result	LLN	ULN	Reference Range Indicator	Analysis Toxicity Grade
Urea Nitrogen (mmol/L)	20[redacted] 87	WEEK 13	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 115	WEEK 17	6.426	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 141	WEEK 21	4.998	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 172	WEEK 25	5.355	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 255	WEEK 37	5.712	2.856	7.14	NORMAL	-
Urea Nitrogen (mmol/L)	20[redacted] 339	WEEK 49	7.497	2.856	7.14	HIGH	-
Urea Nitrogen (mmol/L)	20[redacted] 416	WEEK 61	5.355	2.856	7.14	NORMAL	-

2.7.6.3 海外臨床第 I/II 相試験（PCYC-1146-IM，評価資料：5.3.5.2.3）

2.7.6.3.1 概要

2.7.6.3.1.1 計画

(1) 治験の標題

慢性移植片対宿主病（cGVHD）を有する小児患者を対象に，イブルチニブの安全性及び有効性を評価する第 I/II 相用量設定試験

(2) 治験実施医療機関

海外 12 施設（韓国 3 施設，米国，オーストラリア及びロシア各 2 施設，イギリス，イタリア及びカナダ各 1 施設）

(3) 公表文献（引用文献）

なし

(4) 治験実施期間

2018 年 12 月 12 日（最初の被験者の同意取得日）～20[redacted]年[redacted]月[redacted]日（中間解析のデータベースロック日）

(5) 開発の相

第 I/II 相

(6) 目的

本試験は，2 つのパート（パート A 及びパート B）で構成される。各パートの試験の目的は以下のとおりである。

主要目的

パート A：薬物動態（PK）データ［及び薬力学（PD）データ］をもとに，1～11 歳の cGVHD 被験者におけるイブルチニブの小児推奨用量（RPED）を決定する。

パート B：1～21 歳の cGVHD 被験者におけるイブルチニブの PK 及び安全性を評価する。

副次目的

パート A

・ イブルチニブの安全性の検討

・ イブルチニブの PD［ブルトン型チロシンキナーゼ（BTK）結合部位占有率］の検討

パート A 継続コホート（イブルチニブを漸増後，継続投与している被験者）及びパート B

- National Institutes of Health（NIH）Consensus Development Project Criteria（2014）に基づく 24 週時の奏効率の評価
- 奏効持続期間の評価
- 全生存率の評価
- 晩期合併症（成長，発達及び免疫再構築への影響を含む）へのイブルチニブの潜在的影響の評価による安全性の検討

探索的目的

- イブルチニブ RPED を投与した cGVHD 被験者における PD［BTK 及びインターロイキン-2 誘導型 T 細胞キナーゼ（ITK）結合部位占有率］の評価
- 未治療 cGVHD 被験者における NIH Consensus Development Project Criteria（2014）に基づく 48 週時の奏効率の評価
- 1～11 歳の cGVHD 被験者における Pediatric stem cell QL questionnaire（PedsQL™ Stem Cell Transplant Module）を指標とした生活の質（QOL）の評価
- 12～21 歳の cGVHD 被験者における Lee cGVHD 症状評価尺度による症状負荷の変化の評価

(7) 治験方法

本試験は，中等症又は重症の小児の cGVHD 患者を対象に，イブルチニブの安全性及び有効性を評価する非盲検，多施設，国際共同第 I/II 相試験であり，パート A 及びパート B から構成される。

パート A では，1 種類以上の全身療法で効果不十分な 1～11 歳の中等症又は重症の cGVHD 患者を対象に，RPED 及び安全性を検討した。被験者にイブルチニブを漸増投与し，PK データに基づいて，イブルチニブ 420 mg/日を投与された成人 cGVHD 被験者と同程度の曝露量となるよう 1～11 歳の RPED を決定した。RPED 決定後，パート A で漸増投与を受けた被験者は RPED を継続投与することとした。

パート B は，パート A と並行して開始し，未治療又は 1 種類以上の全身療法で効果不十分な 12～21 歳の中等症又は重症の cGVHD 患者を対象に，イブルチニブの PK，安全性及び有効性を評価することとした。RPED 決定後は，1～21 歳の被験者の登録を可能とした。12 歳以上の被験者には，成人用量のイブルチニブ 420 mg/日［副作用，肝機能障害又はチトクローム P450（CYP）3A 阻害薬併用により用量調節］を経口投与した。未治療の被験者には，cGVHD の一次治療としてステロイド（prednisone 0.5～1 mg/kg/日）及びイブルチニブを併用投与することとした。

(8) 被験者数（計画時及び解析時）

計画時

パート A では，1～11 歳の被験者を 12 例以上，そのうち少なくとも 3 例は 1～5 歳の被験者を組み入れる計画とした。

パート B では，1～21 歳の被験者を 10～32 例組み入れる計画とした。

解析時

20[redacted]年[redacted]月[redacted]日までにパート B に登録されイブルチニブの投与を受けた 12～21 歳の被験者 18 例のデータで中間解析を行った。

(9) 診断及び主な組入れ基準

パート A は，1 種類以上の全身療法で効果不十分な 1～11 歳の中等症又は重症の cGVHD 患者を対象とした。

パート B は，未治療又は 1 種類以上の全身療法で効果不十分な 12～21 歳の中等症又は重症の cGVHD 患者を対象とした。RPED 決定後は，1～11 歳の cGVHD 患者も登録の対象とした。

(10) 被験薬，用量及び投与方法

パート A：開始用量として，イブルチニブ 120 mg/m^2（カプセル，錠剤又は懸濁液）を 1 日 1 回経口投与し，14 日後に 240 mg/m^2 へ漸増することとした。

パート B：12～21 歳の被験者には，イブルチニブ 420 mg（カプセル，錠剤又は懸濁液）を 1 日 1 回経口投与することとした。未治療の被験者には，cGVHD の一次治療としてステロイド（prednisone 0.5～1 mg/kg/日）及びイブルチニブを併用投与することとした。1～11 歳の被験者には，パート A で決定した RPED を投与することとした。

イブルチニブの用量減量基準として，副作用に伴う基準，肝機能障害に伴う基準及び CYP3A 阻害薬との併用時の基準を設定した。

12 歳以上の被験者に対する用量調節基準を以下に示す。

1) 副作用に伴う用量調節

以下のいずれかの毒性が認められた場合は，表 2.7.6.3-1 及び表 2.7.6.3-2 に従い，イブルチニブの用量を変更することとした。

- 7 日間を超えて持続する Grade 4 の好中球減少症（好中球絶対数<500/μL）
- 臨床的に重大な出血事象を伴う Grade 3 の血小板減少症（血小板数＜50,000/μL）
- Grade 4 の血小板減少症（血小板数＜25,000/μL）
- 適切な制吐薬及び/又は止瀉薬による治療にもかかわらず持続する，Grade 3 又は 4 の悪心，嘔吐又は下痢
- その他の Grade 4 の毒性又は管理できない Grade 3 の毒性

表 2.7.6.3-1 副作用に伴うイブルチニブの用量調節

発現回数	対処方法
初回	Grade 1 以下又はベースラインに回復するまでイブルチニブを中断し，開始用量で再開する
2 回目	Grade 1 以下又はベースラインに回復するまでイブルチニブを中断し，開始用量から 1 レベル減量して再開する（開始用量が 420 mg/日の場合，280 mg/日に減量して再開する）
3 回目	Grade 1 以下又はベースラインに回復するまでイブルチニブを中断し，開始用量から 2 レベル減量して再開する（開始用量が 420 mg/日の場合，140 mg/日に減量して再開する）
4 回目	イブルチニブを中止する

表 2.7.6.3-2 副作用に伴うイブルチニブの用量減量レベル

開始用量	420 mg	280 mg	140 mg
用量減量レベル 1	280 mg	140 mg	70 mg
用量減量レベル 2	140 mg	70 mg	中止
用量減量レベル 3	中止	中止	--

2) 肝機能障害に伴う用量調節

肝機能障害を有する被験者に対しては，表 2.7.6.3-3 に従い，ベースラインの総ビリルビン値と試験期間中の総ビリルビン値に応じて，イブルチニブの用量を変更することとした。総ビリルビン値の上昇の原因が肝臓由来ではない場合又はジルベール症候群による場合は，用量調節は不要とした。

表 2.7.6.3-3 肝機能障害に伴うイブルチニブの用量調節

開始用量	ベースラインの総ビリルビン値 ≦1.5 × ULN : 420 mg	ベースラインの総ビリルビン値 ＞1.5 - 3 × ULN : 140 mg
試験期間中の総ビリルビン値：≦1.5 × ULN	420 mg を継続	420 mg に増量
試験期間中の総ビリルビン値：＞1.5-3 × ULN	140 mg に減量	140 mg を継続
試験期間中の総ビリルビン値：＞3 × ULN	総ビリルビン値が＞1.5-3 × ULN となるまで中断し*，140 mg で再開 総ビリルビン値が≦1.5 × ULN となった時点で，420 mg で再開	総ビリルビン値が＞1.5-3 × ULN となるまで中断し*，140 mg で再開 総ビリルビン値が≦1.5 × ULN となった時点で，420 mg で再開

ULN = 基準値上限
* 肝機能障害のため 28 日を超えて中断した後，治験担当医師が再開を希望する場合は，メディカルモニターに連絡して承認を得ることとした。

3) CYP3A 阻害薬併用時の用量調節

CYP3A 阻害薬併用時は，表 2.7.6.3-4 に従い，イブルチニブの用量を変更することとした。

表 2.7.6.3-4 CYP3A 阻害薬併用時のイブルチニブの用量調節

併用する CYP 阻害薬	イブルチニブの投与量
軽度の CYP3A 阻害薬	1 日 1 回 420 mg（用量調節不要）
中程度の CYP3A 阻害薬	1 日 1 回 420 mg（用量調節不要）
ボリコナゾール* 又は ポサコナゾール（懸濁液 1 日 2 回 200 mg 以下 又は徐放錠 1 日 1 回 300 mg 以下）	1 日 1 回 280 mg
他の強力な CYP3A 阻害薬 又は ポサコナゾール（上記より高い用量）	1 日 1 回 140 mg 又は CYP3A 阻害能がより低い代替薬への変更を検討する

* 被験者に対してイトラコナゾール及びケトコナゾールを使用する場合はボリコナゾールで代用することとした。

(11) 対照薬，用量及び投与方法

なし

(12) 投与期間

被験者は，cGVHD の進行，許容できない毒性の発現，基礎悪性腫瘍の進行又は再発，cGVHD に対する新たな全身療法の開始，同意撤回，試験終了，又はその他の投与中止基準に合致するまで，イブルチニブの投与を受けることとした。

(13) 評価基準及び評価項目

主要評価項目

パート A：イブルチニブの RPED 決定のための 1～11 歳の cGVHD 被験者における PK（AUC）

パート B：12～21 歳の cGVHD 被験者における PK（AUC）及び安全性（治験薬投与後に発現した有害事象及び臨床検査値異常）

副次評価項目

パート A：安全性（治験薬投与後に発現した有害事象及び臨床検査値異常）及び PD（BTK 結合部位占有率）

パート A 継続コホート及びパート B：24 週時の奏効率［完全奏効（CR）及び部分奏効（PR）］，奏効持続期間，全生存率，小児の成長及び発達（身長，体重，Tanner Stage，3 歳未満の被験者の頭囲など）並びに免疫再構築データ

探索的評価項目

PD（BTK 及び ITK 結合部位占有率），未治療 cGVHD 被験者における 48 週時の奏効率，QOL の変化（2～11 歳：PedsQL^{TM} Stem Cell Transplant Module，1 歳：general PedsQL），12 歳以上の被験者における Lee cGVHD 症状評価尺度の変化

(14) 統計手法

被験者の内訳，人口統計学的特性，曝露量，PK（血漿中濃度）及び安全性パラメータの記述統計量及び／又は一覧を示した。有害事象は，イブルチニブの初回投与から最終投与 30 日後又は cGVHD に対する別の治療開始の前日のいずれか早い日まで収集した。治験薬と関連性があると判断された有害事象は，有害事象の発現日にかかわらず，治験薬投与後に発現したものと判断した。

2.7.6.3.1.2　結果

本項には，パート B に組み入れられ，20[redacted]年[redacted]月[redacted]日までにイブルチニブ（カプセル又は錠剤）420 mg/日の経口投与を開始した 12～21 歳の 18 例における安全性及び PK に関する中間解析の結果を要約する。PK，安全性及び有効性の主要解析は全被験者が 24 週の投与を終了した後に実施する。最終解析は，全被験者が 60 カ月の追跡調査を終了した後に実施する。

(1) 対象集団

被験者の内訳：中間解析時点（データベースロック日：20[redacted]年[redacted]月[redacted]日）で，12～21 歳の被験者 18 例［12～17 歳は 17 例，18 歳以上は 1 例（1[redacted]歳）］をパート B に登録し，全例にイブルチニブ（錠剤又はカプセル）420 mg/日を投与した。

中間解析時点で，8 例（44.4%）はイブルチニブの投与を継続しており，10 例（55.6%）は投与を中止していた。最も多い主たる投与中止理由は，同意撤回（4 例，22.2%）であった。1 例（5.6%）は主たる投与中止理由が有害事象（下気道感染）であった。観察期間の中央値（範囲）は 4.98 カ月（3.61～15.38 カ月）であった。イブルチニブの投与期間の中央値（範囲）は 2.74 カ月（0.2～7.9 カ月）であった。

治験対象集団：ベースライン時の被験者の年齢の中央値（範囲）は 16.0 歳（12～1[redacted]歳）で，12 例（66.7%）が男性であった。移植から cGVHD の初回診断までの期間の中央値（範囲）は 7.75 カ月（3.4～25.6 カ月），cGVHD の初回診断から試験組入れまでの期間の中央値（範囲）は 16.07 カ月（0.4～131.0 カ月）であった。移植理由は 13 例（72.2%）が悪性腫瘍，5 例（27.8%）が悪性腫瘍以外の基礎疾患であった。cGVHD の重症度は，12 例（66.7%）が重症，6 例（33.3%）が中等症であった。18 例中 2 例は未治療の cGVHD 患者であった。16 例は cGVHD の治療歴を有し，そのうち 14 例（87.5%）は prednisone 等のステロイドの全身療法を受けていた。18 例中 12 例（66.7%）は，ミコフェノール酸モフェチル（6 例，33.3%），タクロリムス（4 例，22.2%），シクロスポリン（3 例，16.7%）などの prednisone 以外の免疫抑制剤を 1 種類以上併用していた。

試験期間中に少なくとも 1 剤の CYP3A 阻害薬を併用した患者は 18 例中 14 例（77.8%）であった。強力な CYP3A 阻害薬を併用した被験者は 9 例（50.0%）で，最も多かったのはポサコナゾール（7 例，38.9%）であった。中程度の CYP3A 阻害薬を併用した被験者は 7 例（38.9%）で，最も多かったのはフルコナゾール（5 例，27.8%），次いでイマチニブ（3 例，16.7%）であった。

(2) 薬物動態

12～21 歳の cGVHD 被験者に成人用量のイブルチニブ 420 mg/日（強力な CYP3A 阻害薬併用時にはイブルチニブを減量）を投与したときのイブルチニブ及び代謝物 PCI-45227 の血漿中濃度を測定した。12～21 歳の cGVHD 被験者にイブルチニブ 420 mg/日を投与したときの定常状態（Week 3 Day 1 の投与前）における血漿中イブルチニブのトラフ濃度の平均値（± 標準偏差）は 13.1 ± 13.6 ng/mL であり，PCYC-1129-CA 試験で成人 cGVHD 被験者にイブルチニブ 420 mg/日を投与したときに確認された血漿中濃度の範囲内であった。

(3) 安全性

18 例全例に 1 件以上の有害事象が認められた。

- 20%以上の被験者に認められた有害事象は，腹痛，下痢，悪心及び口内炎（各 4 例，22.2%）であった。これらの事象の重症度は主に Grade 1 又は Grade 2 であった。
- Grade 3 以上の有害事象は，11 例（61.1%）に認められた。2 例以上に認められた Grade 3 以上の有害事象は，下気道感染，気胸，発熱及び口内炎（各 2 例，11.1%）であった。
- イブルチニブと関連性がある有害事象は，12 例（66.7%）に認められた。15%以上の被験者に認められたイブルチニブと関連性がある有害事象は，点状出血及び口内炎（各 3 例，16.7%）であった。
- 重篤な有害事象は，11 例（61.1%）に認められた。2 例以上に認められた重篤な有害事象は，インフルエンザ，下気道感染，気胸及び発熱（各 2 例，11.1%）であった。
- 死亡に至った有害事象は認められなかった。
- 投与中止に至った有害事象は 2 例（11.1%）に認められ，急性骨髄性白血病及び下気道感染が各 1 例であった。このうち急性骨髄性白血病は基礎悪性腫瘍の悪化であった。
- 大出血事象が認められた被験者はいなかった。
- 心房細動は認められなかった。その他の不整脈［ICH 国際医薬用語集の標準検索式（SMQ）の不整脈，広域及び狭域］は 2 例（11.1%）に認められた。内訳は，Grade 1 の洞性頻脈及び Grade 3 の失神が各 1 例であった。
- 二次性悪性腫瘍が認められた被験者はいなかった。
- 間質性肺疾患が認められた被験者はいなかった。
- 臨床検査値において，Grade 3 又は Grade 4 のヘモグロビン及び血小板数の減少が各 1 例（5.6%）に認められた。また，Grade 3 又は Grade 4 のアラニンアミノトランスフェラーゼの増加が 3 例（16.7%）に認められた。

2.7.6.3.1.3　結論

中央値 2.74 カ月の投与期間において，12～21 歳の cGVHD 被験者に強力な CYP3A 阻害薬併用時に減量基準を設けてイブルチニブ 420 mg/日を投与したときの安全性及び忍容性プロファイル

は許容可能であった。また，同用法用量における 12～21 歳の cGVHD 被験者の血漿中イブルチニブのトラフ濃度は，成人 cGVHD 被験者にイブルチニブ 420 mg/日を投与した場合と同程度だった。イブルチニブの既知の安全性プロファイルと比較して，新たな安全性のシグナルは特定されなかった。

2.7.6.3.2 有害事象

PCYC-1146-IM 試験開始から中間解析のデータベースロック日（20[redacted]年[redacted]月[redacted]日）までに発現した，全ての有害事象の発現状況を表 2.7.6.3-5 に，イブルチニブと関連性がある有害事象の発現状況を表 2.7.6.3-6 に示す。

表 2.7.6.3-5 全ての有害事象の発現状況（PCYC-1146-IM 試験，安全性解析対象集団）

System Organ Class MedDRA Preferred Term	All (N=18) n(%) Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
Subjects with any TEAE	18 (100.0)	11 (61.1)	0
血液およびリンパ系障害	3 (16.7)	0	0
貧血	1 (5.6)	0	0
内出血発生の増加傾向	1 (5.6)	0	0
白血球増加症	1 (5.6)	0	0
心臓障害	1 (5.6)	0	0
洞性頻脈	1 (5.6)	0	0
内分泌障害	1 (5.6)	0	0
クッシング症候群	1 (5.6)	0	0
眼障害	2 (11.1)	0	0
眼瞼炎	1 (5.6)	0	0
眼痛	1 (5.6)	0	0
胃腸障害	15 (83.3)	3 (16.7)	0
腹痛	4 (22.2)	0	0
下痢	4 (22.2)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 1 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%)		
	Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
悪心	4 (22.2)	0	0
口内炎	4 (22.2)	2 (11.1)	0
口腔粘膜紅斑	2 (11.1)	0	0
嘔吐	2 (11.1)	0	0
齲歯	1 (5.6)	1 (5.6)	0
消化不良	1 (5.6)	0	0
胃炎	1 (5.6)	0	0
歯肉出血	1 (5.6)	0	0
舌痛	1 (5.6)	0	0
口唇出血	1 (5.6)	0	0
口腔内潰瘍形成	1 (5.6)	0	0
口腔内痛	1 (5.6)	0	0
口の錯感覚	1 (5.6)	0	0
一般・全身障害および投与部位の状態	4 (22.2)	2 (11.1)	0
発熱	2 (11.1)	2 (11.1)	0
胸痛	1 (5.6)	0	0
非心臓性胸痛	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 2 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%)		
	Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
免疫系障害	3 (16.7)	0	0
低γグロブリン血症	2 (11.1)	0	0
薬物過敏症	1 (5.6)	0	0
感染症および寄生虫症	14 (77.8)	6 (33.3)	0
インフルエンザ	2 (11.1)	1 (5.6)	0
下気道感染	2 (11.1)	2 (11.1)	0
肺炎	2 (11.1)	0	0
せつ	1 (5.6)	0	0
胃腸炎	1 (5.6)	0	0
ノロウイルス性胃腸炎	1 (5.6)	1 (5.6)	0
潜伏結核	1 (5.6)	0	0
メタニューモウイルス感染	1 (5.6)	0	0
口腔カンジダ症	1 (5.6)	0	0
爪囲炎	1 (5.6)	0	0
歯周炎	1 (5.6)	0	0
歯髄炎	1 (5.6)	1 (5.6)	0
気道感染	1 (5.6)	0	0
真菌性気道感染	1 (5.6)	0	0
副鼻腔炎	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 3 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%)		
	Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
スフィンゴモナス・パウシモビリス性菌血症	1 (5.6)	1 (5.6)	0
上気道感染	1 (5.6)	0	0
傷害、中毒および処置合併症	4 (22.2)	1 (5.6)	0
偶発的過量投与	1 (5.6)	0	0
足関節部骨折	1 (5.6)	0	0
挫傷	1 (5.6)	0	0
関節損傷	1 (5.6)	0	0
口腔内損傷	1 (5.6)	0	0
各種物質毒性	1 (5.6)	1 (5.6)	0
臨床検査	3 (16.7)	0	0
Ｂリンパ球数減少	1 (5.6)	0	0
心電図ＳＴ－Ｔ部分異常	1 (5.6)	0	0
ヘモグロビン増加	1 (5.6)	0	0
肝機能検査値上昇	1 (5.6)	0	0
代謝および栄養障害	3 (16.7)	0	0
低アルブミン血症	1 (5.6)	0	0
低カルシウム血症	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 4 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%)		
	Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
低ナトリウム血症	1 (5.6)	0	0
低蛋白血症	1 (5.6)	0	0
栄養障害	1 (5.6)	0	0
筋骨格系および結合組織障害	7 (38.9)	1 (5.6)	0
筋痙縮	2 (11.1)	0	0
骨壊死	2 (11.1)	1 (5.6)	0
関節痛	1 (5.6)	0	0
骨痛	1 (5.6)	0	0
四肢痛	1 (5.6)	0	0
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 (5.6)	0	0
急性骨髄性白血病	1 (5.6)	0	0
神経系障害	5 (27.8)	1 (5.6)	0
頭痛	2 (11.1)	0	0
手根管症候群	1 (5.6)	0	0
神経痛	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 5 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%)		
	Any Grade n(%)	Grade 3 + 4 n(%)	Grade 5 n(%)
末梢性感覚ニューロパチー	1 (5.6)	0	0
失神	1 (5.6)	1 (5.6)	0
精神障害	1 (5.6)	0	0
うつ病	1 (5.6)	0	0
腎および尿路障害	1 (5.6)	0	0
排尿困難	1 (5.6)	0	0
呼吸器、胸郭および縦隔障害	10 (55.6)	2 (11.1)	0
咳嗽	3 (16.7)	0	0
口腔咽頭痛	2 (11.1)	0	0
気胸	2 (11.1)	2 (11.1)	0
呼吸困難	1 (5.6)	0	0
鼻出血	1 (5.6)	0	0
気縦隔症	1 (5.6)	1 (5.6)	0
湿性咳嗽	1 (5.6)	0	0
呼吸不全	1 (5.6)	0	0
鼻漏	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 6 of 7

System Organ Class MedDRA Preferred Term	All (N=18) n(%) Any Grade n(%)	 Grade 3 + 4 n(%)	 Grade 5 n(%)
皮膚および皮下組織障害	9 (50.0)	1 (5.6)	0
点状出血	3 (16.7)	0	0
皮膚乾燥	2 (11.1)	0	0
皮膚潰瘍	2 (11.1)	0	0
ざ瘡様皮膚炎	1 (5.6)	0	0
爪の障害	1 (5.6)	0	0
皮下気腫	1 (5.6)	1 (5.6)	0
血管障害	2 (11.1)	0	0
高血圧	1 (5.6)	0	0
静脈炎	1 (5.6)	0	0

Safety analysis population includes all Part B subjects age >= 12 years old years who received ibrutinib at the adult cGVHD dose using capsule or tablet formulation prior to 01JAN2020. Adverse events are coded by MedDRA Version 22.1.
N = number of subjects in the specified population. Percentages are calculated by100*n/N. Treatment emergent period is the time interval from the date of the first dose of ibrutinib to either 30 days after the last dose of ibrutinib or the day before initiation of subsequent cGVHD therapy whichever earlier. One exception is if the AE is deemed related to ibrutinib, then regardless of the AE start date it is treatment-emergent. Subjects with multiple events for a given preferred term and overall are counted once only using maximum severity for each preferred term and overall, respectively.
Events are sorted by decreasing frequency of preferred term by Any Grade column.
SAS-PROD: BTK/PCYC-1146-IM/Interim unicorn/Programs/t teae socpt maxsev.sas ab 27APR2020:15:33 Page 7 of 7

表 2.7.6.3-6 イブルチニブと関連性がある有害事象の発現状況（PCYC-1146-IM 試験，安全性解析対象集団）

	Ibrutinib	
	AEs	>=Grade 3 AEs
Analysis Set: Safety analysis population	18	
Avg duration of follow-up (month)	6.47	
Avg exposure (month)	3.21	
Subjects with one or more TEAE	12 (66.7%)	5 (27.8%)
System organ class MedDRA Preferred term		
胃腸障害	8 (44.4%)	2 (11.1%)
口内炎	3 (16.7%)	2 (11.1%)
悪心	2 (11.1%)	0
口腔粘膜紅斑	2 (11.1%)	0
嘔吐	2 (11.1%)	0
腹痛	1 (5.6%)	0
下痢	1 (5.6%)	0
消化不良	1 (5.6%)	0
胃炎	1 (5.6%)	0
歯肉出血	1 (5.6%)	0
舌痛	1 (5.6%)	0
口腔内潰瘍形成	1 (5.6%)	0
感染症および寄生虫症	4 (22.2%)	2 (11.1%)
下気道感染	2 (11.1%)	2 (11.1%)
口腔カンジダ症	1 (5.6%)	0
爪囲炎	1 (5.6%)	0
真菌性気道感染	1 (5.6%)	0
皮膚および皮下組織障害	4 (22.2%)	1 (5.6%)
点状出血	3 (16.7%)	0
爪の障害	1 (5.6%)	0
皮下気腫	1 (5.6%)	1 (5.6%)
血液およびリンパ系障害	3 (16.7%)	0
貧血	1 (5.6%)	0
内出血発生の増加傾向	1 (5.6%)	0
白血球増加症	1 (5.6%)	0
神経系障害	3 (16.7%)	0
手根管症候群	1 (5.6%)	0
頭痛	1 (5.6%)	0
末梢性感覚ニューロパチー	1 (5.6%)	0
呼吸器、胸郭および縦隔障害	3 (16.7%)	1 (5.6%)
鼻出血	1 (5.6%)	0
口腔咽頭痛	1 (5.6%)	0
気縦隔症	1 (5.6%)	1 (5.6%)
気胸	1 (5.6%)	1 (5.6%)
傷害、中毒および処置合併症	2 (11.1%)	1 (5.6%)
偶発的過量投与	1 (5.6%)	0
各種物質毒性	1 (5.6%)	1 (5.6%)
臨床検査	2 (11.1%)	0
Ｂリンパ球数減少	1 (5.6%)	0
ヘモグロビン増加	1 (5.6%)	0

	Ibrutinib	
	AEs	>=Grade 3 AEs
代謝および栄養障害	2 (11.1%)	0
低アルブミン血症	1 (5.6%)	0
低カルシウム血症	1 (5.6%)	0
栄養障害	1 (5.6%)	0
眼障害	1 (5.6%)	0
眼瞼炎	1 (5.6%)	0
筋骨格系および結合組織障害	1 (5.6%)	0
骨痛	1 (5.6%)	0

Key: TEAE: treatment-emergent adverse event, Avg = average
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event.
Adverse events are coded using Medical Dictionary for Regulatory Activities Version 22.1

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2.7.6.3.3 死亡及び重篤な有害事象の個別症例の詳細

PCYC-1146-IM 試験開始から中間解析のデータベースロック日（20[redacted]年[redacted]月[redacted]日）までに死亡及び重篤な有害事象を発現した被験者の詳細を示す。

2.7.6.3.3.1 死亡例

該当なし

2.7.6.3.3.2 重篤な有害事象

(1) イブルチニブと関連性がある重篤な有害事象

1) 被験者番号[redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian boy
Study treatment:	Part B: Ibrutinib 280 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 7
Reason(s) for narrative:	Serious adverse event: 口内炎 (Grade 3)

Subject [redacted] was a 1[redacted]-year-old Asian boy diagnosed with cGVHD approximately 11 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was immunodeficiency congenital. Eight previous systemic cGVHD treatment regimens had been received: 5 courses of prednisone, prednisolone/ciclosporin, and 2 courses of extracorporeal photopheresis. The subject had no history of acute GVHD. At baseline, cGVHD staging was severe and the Karnofsky Performance Status score was 90%. The ongoing medical history included osteopenia, body height below normal, delayed puberty, and spinal compression. At study entry, the subject was receiving no cGVHD prophylactic treatment. The baseline laboratory results included white blood cell count 7.48 x 10^9/L, neutrophils 5.89 x 10^9/L, hemoglobin 110 g/L, platelets 247 x 10^9/L, and creatinine 46 µmol/L. The baseline physical exam showed abnormal cGVHD features of both hands and feet and sclerotic changes in glans penis area.

Medications received within 30 days prior to the event included itraconazole, phenoxymethylpenicillin, lansoprazole, loperamide, aciclovir, co-trimoxazole, calcium folinate, colecalciferol, calcium, cetirizine, posaconazole, potassium, and iron.

2) 被験者番号[redacted]

Subject No.:	[redacted]

Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian/White girl
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 234
Reason(s) for narrative:	Serious adverse events: ノロウイルス性胃腸炎 (Grade 3); 各種物質毒性 (Grade 3; 2 events)

Subject [redacted] was a 1[redacted]-year-old Asian/White girl diagnosed with cGVHD approximately 2 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was acute myeloid leukemia. One previous systemic cGVHD treatment regimen had been received: tacrolimus. The subject had a history of acute GVHD. At baseline, cGVHD staging was severe and the Lansky Performance Status score was 90%. The ongoing medical history included obliterative bronchiolitis, bronchiectasis, diabetes, and diarrhea (Grade 1). At study entry, cGVHD prophylactic treatment included tacrolimus. The baseline laboratory results included white blood cell (WBC) count 6.1 x 10^9/L, neutrophils 2.99 x 10^9/L, hemoglobin 130 g/L, and platelets 267 x 10^9/L.

Medications received within 30 days prior to the event included paraffin cream, sulfamethoxazole/trimethoprim, valaciclovir, tacrolimus, magnesium, azithromycin, fluticasone/salmeterol, and carmellose.

Medications received within 30 days prior to the event included posaconazole, paracetamol, and the same medications listed above.

3) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old White boy
Study treatment:	Part B: Ibrutinib 280 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 48
Reason(s) for narrative:	Serious adverse event: 偶発的過量投与 (Grade 1)

Subject [redacted] was a 1[redacted]-year-old White boy diagnosed with cGVHD approximately 2 years prior to study enrollment. The underlying indication for stem cell transplant was sickle cell disease. No previous systemic cGVHD treatment regimens had been received and the subject had no history of acute GVHD. At baseline, cGVHD staging was moderate and the Karnofsky Performance Status score was

80%. The past medical history included hemolysis, acute chest syndrome, iron overload, hypertension, and hypertriglyceridemia. The ongoing medical history included vitamin D deficiency and osteoporosis. At study entry, cGVHD prophylactic treatment included budesonide and mycophenolate mofetil.

Medications received within 30 days prior to the event included vitamin D, ursodeoxycholic acid, mycophenolate mofetil, budesonide, emollients and protectives (ceramol), and mometasone.

4) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian/White boy
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	Ibrutinib was ongoing at the time of this report
Reason(s) for narrative:	Serious adverse event: 下気道感染 (Grade 3)

Subject [redacted] was a 1[redacted]-year-old Asian/White boy diagnosed with cGVHD approximately 2 years prior to study enrollment. The underlying indication for bone marrow transplant was acute myeloid leukemia. Three previous systemic cGVHD treatment regimens had been received: budesonide, ciclosporin/rituximab, and rituximab. The subject had a history of acute GVHD. At baseline, cGVHD staging was moderate and the Karnofsky Performance Status score was 100%. No relevant ongoing medical history was reported. At study entry, cGVHD prophylactic treatment included ciclosporin. The baseline laboratory results included white blood cell count 7.2 x 10^9/L, neutrophils 4.46 x 10^9/L, hemoglobin 137 g/L, and platelets 269 x 10^9/L. Baseline pulmonary function test showed FEV1 78%.

Medications received within 30 days prior to the event included magnesium, paracetamol, sodium bicarbonate, dexamethasone mouthwash, ciclosporin, and sodium chloride.

5) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refectory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian boy
Study treatment:	Part B: Ibrutinib 280 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 63

Reason(s) for narrative:	Serious adverse event/Adverse event leading to treatment discontinuation: 下気道感染 (Grade 3) Serious adverse events: 気縦隔症 (Grade 3); 気胸 (Grade 3); 皮下気腫 (Grade 3)

Subject [redacted] was a 1[redacted]-year-old Asian boy diagnosed with cGVHD approximately 1 year prior to study enrollment. The underlying indication for peripheral stem cell transplant was acute lymphocytic leukemia. Two previous systemic cGVHD treatment regimens had been received: hydrocortisone/prednisolone/tacrolimus with extracorporeal photopheresis, and rituximab. The subject had a history of acute GVHD. At baseline, cGVHD staging was moderate and the Karnofsky Performance Status score was 100%. The ongoing medical history included urinary tract infection. At study entry, cGVHD prophylactic treatment included tacrolimus. The baseline laboratory results included white blood cell (WBC) count 3.3 x 10^9/L, neutrophils 1.29 x 10^9/L, hemoglobin 102 g/L, and platelets 95 x 10^9/L. Baseline pulmonary function test showed FEV1 54%.

Medications received within 30 days prior to the event included ondansetron, aciclovir, omeprazole, gabapentin, posaconazole, carmellose, white paraffin, magnesium, amoxicillin, dexamethasone mouthwash, sulfamethoxazole/trimethoprim, methylprednisolone, and tacrolimus.

Medications received within 30 days prior to the event included amoxicillin sodium/clavulanate potassium, chloramphenicol, fluticasone, azithromycin, montelukast, ceftriaxone, ciprofloxacin, and tramadol, in addition to the medications listed above (not including methylprednisolone).

(2) イブルチニブと関連性がない重篤な有害事象

1) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old girl (race not reported)
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 106
Reason(s) for narrative:	Serious adverse event: インフルエンザ (Grade 3)

Subject [redacted] was a 1[redacted]-year-old girl (race not reported) diagnosed with cGVHD approximately 2 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was acute myeloid leukemia. Five previous systemic cGVHD treatment regimens had been received: prednisone, extracorporeal photopheresis, methylprednisolone, tacrolimus/rituximab, and ruxolitinib. The subject had a history of acute GVHD. At baseline, cGVHD staging was severe and the Lansky Performance Status score was 80%. The past medical history included hypertension. The ongoing medical history included adrenal insufficiency, renal impairment (creatinine increased), chronic kidney disease, and fatigue. At study entry,

the subject was receiving no cGVHD prophylactic treatment. The baseline laboratory results included white blood cell count 4.2 x 10^9/L, neutrophils 2.28 x 10^9/L, hemoglobin 112 g/L, and platelets 316 x 10^9/L.

Medications received within 30 days prior to the event included ranitidine, phenoxymethylpenicillin, aciclovir, sodium fluoride/vitamins NOS, fluconazole, calcium, ergocalciferol, ruxolitinib, pentamidine, fluticasone/salmeterol, ondansetron, diphenhydramine, and levofloxacin.

2) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	New onset of Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old White boy
Study treatment:	Part B: Ibrutinib 140 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	Ibrutinib was ongoing at the time of this report
Reason(s) for narrative:	Serious adverse events: 腹痛 (Grade 1); 発熱 (Grade 1); スフィンゴモナス・パウシモビリス性菌血症 (Grade 3); 発熱 (Grade 3)

Subject [redacted] was a 1[redacted]-year-old White boy diagnosed with cGVHD approximately 1 year prior to study enrollment. The underlying indication for peripheral stem cell transplant was adrenoleukodystrophy (X-linked adrenoleukodystrophy). Four previous systemic cGVHD treatment regimens had been received: azathioprine/imatinib, methylprednisolone/extracorporeal photopheresis, ruxolitinib, and ruxolitinib/bortezomib/extracorporeal photopheresis. The subject had a history of acute GVHD. At baseline, cGVHD staging was severe and the Lansky Performance Status score was 70%. The past medical history included Addison's disease and herpes zoster. The ongoing medical history included osteonecrosis. At study entry, the subject was receiving no cGVHD prophylactic treatment. The baseline laboratory results included white blood cell count 5.49 x 10^9/L, neutrophils 3.5 x 10^9/L, hemoglobin 99 g/L, and platelets 460 x 10^9/L.

Medications received within 30 days prior to the event included hydrocortisone, ondansetron, sulfamethoxazole/trimethoprim, vitamin D, haloperidol, posaconazole, calcium, zoledronic acid, bortezomib, omeprazole, pregabalin, vitamin B complex, and ceftriaxone.

3) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian boy
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD,

	progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	The last dose of ibrutinib was administered on Day 124
Reason(s) for narrative:	Serious adverse events: 口腔内痛 (Grade 1); 骨壊死 (Grade 3); 急性骨髄性白血病 (Grade 2)

Subject [redacted] was a 1[redacted]-year-old Asian boy diagnosed with cGVHD approximately 1 year prior to study enrollment. The underlying indication for peripheral stem cell transplant was acute myeloid leukemia. Four previous systemic cGVHD treatment regimens had been received: ciclosporin, prednisolone/mycophenolate mofetil, methotrexate, and prednisolone/tacrolimus. The subject had no history of acute GVHD. At baseline, cGVHD staging was severe and the Karnofsky Performance Status score was 70%. The ongoing medical history included Grade 3 osteonecrosis (hip) and osteoporosis. At study entry, the subject received no cGVHD prophylactic treatment. The baseline laboratory results included white blood cell count 3.42 x 10^9/L, neutrophils 62.9%, hemoglobin 10^9 g/L, and platelets 174 x 10^9/L.

Medications received within 30 days prior to the event included ondansetron, deferasirox, calcium carbonate, mycophenolate mofetil, pethidine, colecalciferol, fluconazole, magnesium, morphine, fentanyl, and lorazepam.

4) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian girl
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	Ibrutinib was ongoing at the time of this report
Reason(s) for narrative:	Serious adverse event: 肺炎 (Grade 2)

Subject [redacted] was a 1[redacted]-year-old Asian girl diagnosed with cGVHD approximately 5 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was precursor B-lymphoblastic lymphoma. Three previous systemic cGVHD treatment regimens had been received: prednisolone, imatinib/mycophenolate mofetil, and tacrolimus/methotrexate. The subject had a history of acute GVHD. At baseline, cGVHD staging was severe and the Karnofsky Performance Status score was 60%. The ongoing medical history included osteonecrosis (femoral head). At study entry, cGVHD prophylactic treatment included mycophenolate mofetil and tacrolimus.

Medications received within 30 days prior to the event included sulfamethoxazole/trimethoprim, magnesium oxide, magnesium/pyridoxin, tacrolimus, mycophenolate mofetil, dexamethasone, fentanyl, nystatin, paraffin wool fat, alendronic acid/colecalciferol, and diquafosol.

5) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian boy
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)
Study treatment end:	Ibrutinib was ongoing at the time of this report
Reason(s) for narrative:	Serious adverse events: 発熱 (Grade 1 and 3); 四肢痛 (Grade 2); インフルエンザ (Grade 2)

Subject [redacted] was a 1[redacted]-year-old Asian boy diagnosed with cGVHD approximately 3 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was B-precursor type acute leukemia. Two previous systemic cGVHD treatment regimens had been received: ciclosporin/prednisolone and mycophenolate mofetil/imatinib. The subject had a history of acute GVHD. At baseline, cGVHD staging was severe and the Karnofsky Performance Status score was 60%. No relevant medical history was reported. At study entry, cGVHD prophylactic treatment included mycophenolate mofetil and imatinib.

Medications received within 30 days prior to the event included mycophenolate mofetil, imatinib, testosterone, nystatin, sulfamethoxazole/trimethoprim, mupirocin, paracetamol, calcium/vitamin D, paraffin wool fat, and ciclosporin.

Medications received within 30 days prior to the event included mycophenolate mofetil, imatinib, testosterone, mupirocin, paraffin wool fat, ciclosporin, and sulfamethoxazole/trimethoprim.

6) 被験者番号 [redacted]

Subject No.:	[redacted]
Diagnosis:	Refractory Chronic Graft Versus Host Disease (cGVHD)
Demographics:	1[redacted]-year-old Asian boy
Study treatment:	Part B: Ibrutinib 420 mg daily PO starting Day 1 of Week 1 until no longer requires treatment, subject begins a new systemic treatment for cGVHD, progression of cGVHD, recurrence of underlying disease, or unacceptable toxicity
Study treatment start:	Ibrutinib started on [redacted] 20[redacted] (Day 1)

Study treatment end:	The last dose of ibrutinib was administered on Day 47
Reason(s) for narrative:	Serious adverse events: 気胸 (Grade 3; 2 events)

Subject [redacted] was a 1[redacted]-year-old Asian boy diagnosed with cGVHD approximately 5 years prior to study enrollment. The underlying indication for peripheral stem cell transplant was chronic granulomatous disease. Three previous systemic cGVHD treatment regimens had been received: prednisolone, prednisone/mycophenolate mofetil/imatinib, and mycophenolate mofetil/imatinib. The subject had no history of acute GVHD. At baseline, cGVHD staging was severe and the Karnofsky Performance Status score was 60%. The ongoing medical history included hypothyroidism, hyperuricemia, and proteinuria. At study entry, cGVHD prophylactic treatment included imatinib and mycophenolate mofetil. The baseline laboratory results included white blood cell count 8.17 x 10^9/L, neutrophils 53.9%, hemoglobin 156 g/L, and platelets 229 x 10^9/L.

Medications received within 30 days prior to the event included tiotropium, fluticasone/salmeterol, imatinib, mycophenolate mofetil, levothyroxine, azithromycin, hyaluronate, fluticasone/vilanterol, benzbromarone, and erdosteine.

2.7.6.4　国際共同第 III 相試験（PCYC-1140-IM，参考資料：5.3.5.1.1）

2.7.6.4.1　概要

2.7.6.4.1.1　計画

(1) 治験の標題

未治療の慢性移植片対宿主病（cGVHD）患者を対象として，イブルチニブにコルチコステロイドを併用した場合とプラセボにコルチコステロイドを併用した場合を比較するランダム化，二重盲検，第 III 相試験

(2) 治験実施医療機関

66 施設（米国 21 施設，日本 8 施設及びその他の国 37 施設）

(3) 公表文献（引用文献）

なし

(4) 治験実施期間

2017 年 5 月 11 日（最初の被験者の同意取得日）～2020 年 3 月 30 日（主要解析のデータベースロック日）

(5) 開発の相

第 III 相

(6) 目的

主要目的

未治療の中等症から重症の cGVHD 患者を対象として，イブルチニブに prednisone を併用した場合（イブルチニブ群）とプラセボに prednisone を併用した場合（プラセボ群）の有効性を，National Institutes of Health（NIH）Consensus Development Project Criteria（2014）に基づく 48 週時の奏効率［完全奏効（CR）及び部分奏効（PR）の割合］により比較検証する。

副次目的

以下について，両群を比較する。

有効性

- NIH Consensus Development Project Criteria（2014）に基づく 24 週時の奏効率（CR 及び PR）
- 奏効持続期間
- 24 週時のステロイド用量が 0.15 mg/kg/日未満の被験者の割合

・ 全ての免疫抑制剤（イブルチニブ及びプラセボを除く）を中止するまでの期間

・ 全生存期間

・ Lee cGVHD 症状評価尺度のスコアの改善

安全性

・ 安全性及び忍容性

・ ステロイド関連疾患の罹患率の差（高血糖，高血圧など）

(7) 治験方法

本試験は，未治療の cGVHD 患者を対象に，イブルチニブと prednisone の併用投与とプラセボと prednisone の併用投与を比較する，多施設共同，国際共同，ランダム化，二重盲検第 III 相試験である。NIH Consensus Development Project Criteria（2014）に基づく中等症又は重症の cGVHD 患者を，イブルチニブ群又はプラセボ群に 1 : 1 の比でランダム化した。ランダム化の層別因子は，年齢（12～21 歳／22 歳以上），NIH Global Severity グレード（中等症／重症）並びに急性 GVHD（aGVHD）の治療又は予防目的での全身性免疫抑制剤の継続使用（あり／なし）とした。

被験者は，イブルチニブ 420 mg 又はプラセボを，cGVHD の進行，基礎悪性腫瘍の進行又は再発，cGVHD に対する他の全身療法の開始又は許容できない毒性の発現まで，1 日 1 回経口投与された。本試験では，イブルチニブ及びプラセボの用量調節基準として，チトクローム P450（CYP）3A 阻害薬との併用時の基準及び肝機能障害に伴う基準を設定した。全ての免疫抑制剤が中止された後に奏効が維持されている場合，イブルチニブ又はプラセボの投与を中止できることとした。Prednisone は，開始用量として 1 mg/kg/日（高用量に対する忍容性がない場合は 0.5 mg/kg/日まで減量可能）を，許容できない毒性の発現又は prednisone の漸減の成功まで，継続的に経口投与した。

奏効は NIH Consensus Development Project Criteria（2014）に基づき定義し，cGVHD に対する新たな全身療法の開始，移植の適応とされた基礎悪性腫瘍の進行，移植後リンパ増殖症又は死亡がないことを必須とした。基礎悪性腫瘍の進行は，各悪性腫瘍の標準的な臨床基準を用いて定義した。全ての被験者は，イブルチニブ又はプラセボの投与期間中，cGVHD 進行時評価の来院時（該当する場合）及び投与終了時の来院時に cGVHD の治療効果の評価を受けた。cGVHD の進行又は基礎悪性腫瘍の進行以外の理由でイブルチニブ又はプラセボの投与を中止した被験者に対しては，cGVHD の疾患評価を継続した。cGVHD の進行又は基礎悪性腫瘍の進行が認められた被験者に対しては，生存確認及び cGVHD の治療について追跡調査した。cGVHD の効果判定には，NIH Consensus Panel Response criteria（2014）に基づく治験担当医師の評価を用いた。

成人被験者に対しては最初の被験者のランダム化から約 3 年後まで，ランダム化時に 22 歳未満であった青年期被験者に対してはランダム化後最長 5 年間追跡調査することとした。ただし，18 歳未満の最後の被験者が本試験を終え，参加中の全ての被験者が最低 1 年間の追跡調査を実施済みである場合は，本試験は終了できることとした。また，被験者は長期追跡調査のために長期継続投与試験に移行できることとした。

本試験では，被験者の安全性を確保するため，並びに中間解析により無益性を評価し試験チームに助言するために，独立データモニタリング委員会が継続的にデータを監視した。中間解析による無益性評価に際して，独立データモニタリング委員会に薬物動態データを提供した。

(8) 被験者数（計画時及び解析時）

計画時

約 186 例をランダム化する計画とした。

解析時

193 例がランダム化され，190 例（98.4%）がイブルチニブ又はプラセボを 1 回以上投与された。有効性評価とベースライン時の特性の要約には intent-to-treat 集団（193 例）を用いた。安全性評価には安全性解析対象集団（190 例）を用いた。

(9) 診断及び主な組入れ基準

主な選択基準

- NIH Consensus Development Project Criteria（2014）で定義される未治療の中等症又は重症の cGVHD 患者
- 同種造血細胞移植の既往がある患者
- cGVHD に対してステロイドによる全身療法が必要な患者
- cGVHD に対する全身療法による治療歴（体外循環光療法を含む）がない患者
- 被験者は aGVHD の予防又は治療のために他の免疫抑制剤の投与を受けていてもよいが，aGVHD の予防又は治療のために prednisone を投与している場合は 0.5 mg/kg/日以下であること
- 12 歳以上の患者
- Karnofsky performance status 又は Lansky Performance status（16 歳未満）スコアが 60 以上の患者
- 適切な腎機能，肝機能及び血液機能を有する患者

主な除外基準

- cGVHD に対する全身療法（同意取得前 72 時間以内の cGVHD に対するステロイドの投与を除く）による治療歴がある患者
- cGVHD の治療として 0.5 mg/kg/日以上の prednisone 投与を開始できない患者
- cGVHD による臓器病変が泌尿生殖器の単一器官のみの患者

(10) 被験薬，用量及び投与方法

イブルチニブは，経口投与用の 70 mg 又は 140 mg の硬ゼラチンカプセルを用いた。イブルチニブ群の被験者に，イブルチニブ 420 mg 及び prednisone 1 mg/kg（漸減の成功まで）を 1 日 1 回経口投与した。イブルチニブの用量調節基準として，副作用に伴う基準，CYP3A 阻害薬との併用時の基準及び肝機能障害に伴う基準を設定した。

(11) 対照薬，用量及び投与方法

プラセボは，経口投与用の硬ゼラチンカプセルを用いた。プラセボのカプセルの外見は，イブルチニブのカプセルと同一とした。プラセボ群の被験者に，プラセボ及び prednisone 1 mg/kg（漸減の成功まで）を 1 日 1 回経口投与した。

(12) 治験薬の用量調節基準

1) 副作用に伴う用量調節

以下のいずれかの毒性が認められた場合は，表 2.7.6.4-1 及び表 2.7.6.4-2 に従い，治験薬（イブルチニブ又はプラセボ）の用量を変更することとした。

- 7 日間を超えて持続する Grade 4 の好中球減少症（好中球絶対数<500/μL）
- 臨床的に重大な出血事象を伴う Grade 3 の血小板減少症（血小板数＜50,000/μL）
- Grade 4 の血小板減少症（血小板数＜25,000/μL）
- 適切な制吐薬及び/又は止瀉薬による治療にもかかわらず持続する，Grade 3 又は 4 の悪心，嘔吐又は下痢
- その他の Grade 4 の毒性又は管理できない Grade 3 の毒性

表 2.7.6.4-1 副作用に伴う治験薬の用量調節

発現回数	対処方法
初回	Grade 1 以下又はベースラインに回復するまで治験薬を中断し，開始用量で再開する
2 回目	Grade 1 以下又はベースラインに回復するまで治験薬を中断し，開始用量から 1 レベル減量して再開する（開始用量が 420 mg/日の場合，280 mg/日に減量して再開する）
3 回目	Grade 1 以下又はベースラインに回復するまで治験薬を中断し，開始用量から 2 レベル減量して再開する（開始用量が 420 mg/日の場合，140 mg/日に減量して再開する）
4 回目	治験薬を中止する

表 2.7.6.4-2 副作用に伴う治験薬の用量減量レベル

開始用量	420 mg	280 mg	140 mg
用量減量レベル 1	280 mg	140 mg	70 mg
用量減量レベル 2	140 mg	70 mg	中止
用量減量レベル 3	中止	中止	--

2) 肝機能障害に伴う用量調節

肝機能障害を有する被験者に対しては，表 2.7.6.4-3 に従い，ベースラインの総ビリルビン値と試験期間中の総ビリルビン値に応じて，治験薬の用量を変更することとした。総ビリルビン値の上昇の原因が肝臓由来ではない場合又はジルベール症候群による場合は，用量調節は不要とした。

表 2.7.6.4-3 肝機能障害に伴う治験薬の用量調節

開始用量	ベースラインの総ビリルビン値 ≦1.5 × ULN : 420 mg	ベースラインの総ビリルビン値 ＞1.5 - 3 × ULN : 140 mg
試験期間中の総ビリルビン値：≦1.5 × ULN	420 mg を継続	420 mg に増量
試験期間中の総ビリルビン値：＞1.5-3 × ULN	140 mg に減量	140 mg を継続
試験期間中の総ビリルビン値：＞3 × ULN	総ビリルビン値が＞1.5-3 × ULN となるまで中断し*，140 mg で再開 総ビリルビン値が≦1.5 × ULN となった時点で，420 mg で再開	総ビリルビン値が＞1.5-3 × ULN となるまで中断し*，140 mg で再開 総ビリルビン値が≦1.5 × ULN となった時点で，420 mg で再開

ULN = 基準値上限
* 肝機能障害のため 28 日を超えて中断した後，治験担当医師が再開を希望する場合は，メディカルモニターに連絡して承認を得ることとした。

3) CYP3A 阻害薬併用時の用量調節

CYP3A 阻害薬併用時は，表 2.7.6.4-4 に従い，治験薬の用量を変更することとした。

表 2.7.6.4-4 CYP3A 阻害薬併用時の治験薬の用量調節

併用する CYP 阻害薬	治験薬の投与量
軽度の CYP3A 阻害薬	1 日 1 回 420 mg（用量調節不要）
中程度の CYP3A 阻害薬	1 日 1 回 420 mg（用量調節不要）
ボリコナゾール* 又は ポサコナゾール（懸濁液 1 日 2 回 200 mg 以下又は徐放錠 1 日 1 回 300 mg 以下）	1 日 1 回 280 mg
他の強力な CYP3A 阻害薬 又は ポサコナゾール（上記より高い用量）	1 日 1 回 140 mg 又は CYP3A 阻害能がより低い代替薬への変更を検討する

* 被験者に対してイトラコナゾール及びケトコナゾールを使用する場合はボリコナゾールで代用することとした。

(13) 投与期間

両群の被験者は，cGVHD の進行，基礎悪性腫瘍の進行又は再発，cGVHD に対する他の全身療法の開始又は許容できない毒性の発現まで，イブルチニブ又はプラセボの投与を継続した。また，被験者は，許容できない毒性の発現又は prednisone の漸減の成功まで，prednisone の投与を継続した。cGVHD の治療のための全身性免疫抑制剤（生理的副腎機能の補充のみを目的とした極低用量のステロイドの継続使用は許容される）を全て中止し，cGVHD の奏効が全ての免疫抑制剤の中止後 12 週間維持され，イブルチニブ又はプラセボを 48 週間以上投与した場合，被験者はイブルチニブ又はプラセボの投与を中断できることとした。

(14) 評価基準及び評価項目

主要評価項目は，NIH Consensus Panel Chronic GVHD Activity Assessment（2014）に基づく 48 週時の奏効率（治験担当医師の評価による CR 及び PR）とした。副次評価項目は，cGVHD 治療のための全てのステロイドを中止するまでの期間，ステロイドを含む全ての免疫抑制剤（イブルチニブ及びプラセボを除く）を中止するまでの期間，24 週時の奏効率，Lee cGVHD 症状評価尺度のスコアの改善（2 回の来院時に連続して 7 点以上の低下），24 週時点で 30 日間以上連続してステロイド用量が 0.15 mg/kg/日未満であった被験者の割合，全生存期間，奏効持続期間，イブルチニブと prednisone の併用投与の安全性及び忍容性並びにステロイド関連疾患の罹患率の差（高血糖，高血圧など）とした。

(15) 統計手法

主要評価項目及び副次評価項目は，両側有意水準を 0.05 とし，直列型ゲートキーピング法を用いて以下の階層順で検定することとした：（1）48 週時の奏効率，（2）cGVHD 治療のための全てのステロイドを中止するまでの期間，（3）cGVHD 治療のためのステロイドを含む全ての免疫抑制剤（イブルチニブ及びプラセボを除く）を中止するまでの期間，（4）24 週時の奏効率，（5）2 回連続した来院時における Lee cGVHD 症状評価尺度のスコアの改善，（6）24 週時点で 30 日間以上連続してステロイド用量が 0.15 mg/kg/日未満であった被験者の割合。

主要評価項目である 48 週時の奏効率は，非層別化カイ二乗検定を用いて検定し，両群間の奏効率を有意水準 5%で比較した。また，24 週時の奏効率，Lee 症状評価尺度のスコアの改善及び 24 週時点で 30 日間以上連続してステロイド用量が 0.15 mg/kg/日未満であった被験者の割合の解析にもカイ二乗検定を用いた。全てのステロイドの投与中止までの期間及び全ての免疫抑制剤の投与中止までの期間の解析には，競合リスクを調整した Gray のカイ二乗検定を用いた。

全生存期間の正式な解析は最終解析時に実施するが，主要解析時に得られていたデータに基づき，全生存期間の要約を示した。Kaplan-Meier 法を用いて各投与群の全生存期間を要約した。奏効持続期間は，奏効評価のため Kaplan-Meier 法を用いて要約した。有害事象の主要解析はイブルチニブ又はプラセボの投与後に発現した有害事象に基づき実施し，安全性評価項目の記述統計量及び一覧を示した。

2.7.6.4.1.2　結果

本項には，主要解析（データベースロック日：2020 年 3 月 30 日，最後の被験者のランダム化から約 1 年後）の結果を示した。

(1) 対象集団

被験者の内訳：193 例（イブルチニブ群 95 例，プラセボ群 98 例）がランダム化された。両群の観察期間の中央値（範囲）は 19.0 カ月（0.03～34.2 カ月）で，イブルチニブ群で 19.8 カ月（0.59～34.2 カ月），プラセボ群で 18.4 カ月（0.03～32.9 カ月）であった。

190 例（98.4%）がイブルチニブ又はプラセボの投与を 1 回以上受け，その内訳はイブルチニブ群 94 例（98.9%），プラセボ群 96 例（98.0%）であった。イブルチニブの投与期間の中央値

（範囲）は 5.4 カ月（0～31 カ月），相対用量強度の中央値は 100%，プラセボの投与期間の中央値（範囲）は 6.4 カ月（0～31 カ月），相対用量強度の中央値は 99.3%であった。

イブルチニブ群では，29 例（30.5%）がイブルチニブの投与を継続しており，42 例（44.2%）が prednisone の投与を継続していた。イブルチニブの投与を中止した被験者は 65 例（68.4%）であり，主な投与中止理由（5%以上）は，cGVHD の進行（21 例，22.1%）が最も多く，次いで cGVHD の進行に関連しない有害事象（18 例，18.9%），治験担当医師の判断（11 例，11.6%）及び被験者による同意撤回（9 例，9.5%）であった。Prednisone の投与を中止した被験者は 52 例（54.7%）であり，主な投与中止理由（5%以上）は，cGVHD の進行（13 例，13.7%）が最も多く，次いで cGVHD に対する他の治療の開始（10 例，10.5%），治験担当医師の判断及び被験者による同意撤回（各 8 例，8.4%），cGVHD の進行に関連しない有害事象（6 例，6.3%）並びに死亡（5 例，5.3%）であった。被験者の 43.2%（41 例）が治療期を継続中，34.7%（33 例）がフォローアップ期を継続中で，22.1%（21 例）が試験を中止していた。試験中止の主な理由（5.0%以上）は死亡（17 例，17.9%）であった。

プラセボ群では，20 例（20.4%）がプラセボの投与を継続しており，33 例（33.7%）が prednisone の投与を継続していた。プラセボの投与を中止した被験者は 76 例（77.6%）であり，主な投与中止理由（5%以上）は，cGVHD の進行（30 例，30.6%）が最も多く，次いで cGVHD の進行に関連しない有害事象（14 例，14.3%），治験担当医師の判断（12 例，12.2%），cGVHD に対する他の治療の開始（7 例，7.1%），被験者による同意撤回（6 例，6.1%）並びに基礎悪性腫瘍の進行又は再発（5 例，5.1%）であった。Prednisone の投与を中止した被験者は 63 例（64.3%）であり，主な投与中止理由（5%以上）は，cGVHD の進行（21 例，21.4%）が最も多く，次いで cGVHD に対する他の治療の開始（19 例，19.4%），治験担当医師の判断（8 例，8.2%），基礎悪性腫瘍の進行又は再発並びに被験者による同意撤回（各 5 例，5.1%）であった。被験者の 33.7%（33 例）が治療期を継続中，43.9%（43 例）がフォローアップ期を継続中で，22.4%（22 例）が試験を中止していた。試験中止の主な理由（5%以上）は，死亡（16 例，16.3%）及び追跡調査の同意撤回（5 例，5.1%）であった。

治験対象集団：ベースライン時の年齢の中央値（範囲）は 55.0 歳（1[redacted]～76 歳）であり，1.0%（2 例）が 18 歳未満，18.1%（35 例）が 65 歳以上であった。被験者の 65.3%が男性，54.4%が白人であり，59.1%が欧州，アジア，オーストラリア及びカナダを含む米国以外の被験者であった。

移植理由は基礎悪性腫瘍が 98.4%であった。移植から cGVHD の初回診断までの期間の中央値（範囲）は 8.0 カ月（1.3～88.1 カ月），cGVHD の初回診断から試験組入れまでの期間の中央値（範囲）は 0.4 カ月（0.0～39.8 カ月）であった。被験者の 52.3%が骨髄破壊的前処置を受けており，50.8%は非血縁ドナーからの移植を受けていた。被験者の 76.7%はドナーとレシピエントの間でヒト白血球抗原が適合していた。幹細胞ソースは 90.2%が末梢血幹細胞であった。

ベースライン時には，全ての被験者がクレアチニンクリアランス 30 mL/min 以上であり，41.5%が National Cancer Institute organ dysfunction working group の肝機能分類に基づく肝機能障害を有していた。cGVHD の重症度は中等症が 57.5%（111 例），重症が 42.5%（82 例）であった。臓器病変が最も多く認められた臓器は口腔（155 例，80.3%），次いで皮膚（148 例，76.7%），眼（122 例，63.2%）であった。Karnofsky performance status 又は Lansky Performance status スコア

の中央値は 80.0 であり，被験者の 88.1%が 80 以上であった。被験者の 54.4%に aGVHD の既往歴が，89.6%に GVHD の予防的治療歴があった。ベースライン時に被験者の 54.9%が全身性免疫抑制剤による治療を受けていた。

(2) 有効性

観察期間の中央値は 19.0 カ月（イブルチニブ群 19.8 カ月，プラセボ群 18.4 カ月）であった。

主要評価項目

- 48 週時の奏効率（CR 及び PR）は，イブルチニブ群で 41.1%（39/95 例），プラセボ群で 36.7%（36/98 例）であった（p = 0.5384）。

副次評価項目

主要評価項目の統計的有意性が示されなかったため，副次評価項目の検定は実施しなかった。

- 奏効が認められた被験者（いずれかの時点で CR 又は PR が得られた被験者）の奏効持続期間の中央値は，イブルチニブ群で 19.8 カ月［95%信頼区間（CI）：7.4 カ月，推定不能］，プラセボ群で 10.0 カ月（95%CI：6.5 カ月，13.1 カ月）であり，群間のハザード比は 0.697（95%CI：0.451，1.076）であった。
- 全てのステロイドの投与を中止した被験者は，イブルチニブ群で 40 例（42.1%），プラセボ群で 36 例（36.7%）であった。
- ステロイドを含む全ての免疫抑制剤の投与を中止した被験者は，イブルチニブ群で 29 例（30.5%），プラセボ群で 24 例（24.5%）であった。
- 24 週時の奏効率（CR 又は PR）は，イブルチニブ群で 47.4%（45/95 例），プラセボ群で 54.1%（53/98 例）であり，群間差は－0.067（95%CI：－0.208，0.074）であった。
- イブルチニブ又はプラセボ投与により Lee cGVHD 症状評価尺度の総合要約スコアが改善（2 回の来院時に連続して 7 点以上の低下）した被験者の割合は，イブルチニブ群で 38.9%（37/95 例），プラセボ群で 26.5%（26/98 例）であり，群間差は 0.124（95%CI：－0.007，0.256）であった。
- 24 週時点で，30 日間以上継続してステロイド用量が 0.15 mg/kg/日未満であった被験者の割合は，イブルチニブ群で 40.0%（38/95 例），プラセボ群で 45.9%（45/98 例）であり，群間差は－0.059（95%CI：－0.199，0.080）であった。
- 全生存期間は両群で同程度であり（死亡：イブルチニブ群 17 例，プラセボ群 17 例），ハザード比は 0.994（95%CI：0.507，1.949）であった。全生存期間は両群とも中央値に達しなかった。

追加の事後解析

- 無イベント生存期間（ランダム化から cGVHD の進行，cGVHD の他の治療の開始，基礎悪性腫瘍の再発又は死亡のいずれか早い時点までの期間と定義した。イベントが認められな

かった被験者は最終評価日で打ち切りとした。）を事後解析として評価した。無イベント生存期間の中央値は，イブルチニブ群で 14.2 カ月（95%CI：5.6 カ月，推定不能），プラセボ群で 8.2 カ月（95%CI：6.0 カ月，12.0 カ月）であった。無イベント生存期間のハザード比は 0.723（95%CI：0.500，1.044）であった。

・ イブルチニブ又はプラセボを 1 回以上投与された被験者の基礎悪性腫瘍の再発率は，イブルチニブ群で 6.4%（6/94 例），プラセボ群で 11.5%（11/96 例）であった。

(3) 安全性

イブルチニブと prednisone の併用投与は，未治療の中等症から重症の成人及び青年期の cGVHD 被験者において良好な忍容性を示した。新たな安全性のシグナルは特定されなかった。

イブルチニブの投与期間の中央値は 5.4 カ月（平均値：8.7 カ月），プラセボの投与期間の中央値は 6.4 カ月（平均値：8.6 カ月）であった。イブルチニブ又はプラセボの投与期間中の prednisone の投与期間の中央値（範囲）は，イブルチニブ群で 4.9 カ月（0～26 カ月），プラセボ群で 5.2 カ月（0～31 カ月）であった。イブルチニブ又はプラセボの投与期間中に認められた有害事象は以下であった。

・ 有害事象はイブルチニブ群の被験者の 98.9%（93/94 例）に，プラセボ群の被験者の 99.0%（95/96 例）に発現した。20%以上の被験者に認められた有害事象は，イブルチニブ群では末梢性浮腫及び不眠症（各 25 例，26.6%），咳嗽（20 例，21.3%），プラセボ群では咳嗽（29 例，30.2%）であった。

・ Grade 3 以上の有害事象は，イブルチニブ群の被験者の 62.8%（59/94 例）に，プラセボ群の被験者の 66.7%（64/96 例）に発現した。5%以上の被験者に認められた Grade 3 以上の有害事象は，イブルチニブ群では血小板減少症（8 例，8.5%），肺炎（7 例，7.4%），高血圧及び低カリウム血症（各 5 例，5.3%），プラセボ群では血小板減少症，肺炎及び高血糖（各 7 例，7.3%），アラニンアミノトランスフェラーゼ増加，貧血及び高血圧（各 5 例，5.2%）であった。

・ 重篤な有害事象は，イブルチニブ群の被験者の 46.8%（44/94 例）に，プラセボ群の被験者の 47.9%（46/96 例）に発現した。5%以上の被験者に認められた重篤な有害事象は，両群ともに肺炎（イブルチニブ群 6 例，6.4%，プラセボ群 8 例，8.3%）であった。

・ 死亡に至った有害事象は，イブルチニブ群の被験者の 9.6%（9/94 例）に，プラセボ群の被験者の 6.3%（6/96 例）に認められた。2 例以上に認められた死亡に至った有害事象はなかった。

・ イブルチニブ又はプラセボの減量に至った有害事象は，イブルチニブ群の被験者の 9.6%（9/94 例）に，プラセボ群の被験者の 13.5%（13/96 例）に認められた。2%以上の被験者に認められたイブルチニブ又はプラセボの減量に至った有害事象は，イブルチニブ群では疲労（2 例，2.1%），プラセボ群ではアラニンアミノトランスフェラーゼ増加（3 例，3.1%）及び疲労（2 例，2.1%）であった。

- イブルチニブ又はプラセボの投与中止の主たる理由になった有害事象は，イブルチニブ群の被験者の 19.1%（18/94 例）に，プラセボ群の被験者の 12.5%（12/96 例）に認められた。2%以上の被験者に認められたイブルチニブ又はプラセボの投与中止の主たる理由になった有害事象は，イブルチニブ群では心房細動及び肺炎（各 2 例，2.1%），プラセボ群では疲労（2 例，2.1%）であった。
- 大出血事象はイブルチニブ群で 3 例（3.2%），プラセボ群で 4 例（4.2%）に認められた。イブルチニブ群で認められた大出血事象は，血尿（2 例，2.1%）及びメレナ（1 例，1.1%）であり，いずれも死亡には至らなかった。プラセボ群で認められた大出血事象は，胃腸出血（2 例，2.1%），出血性膀胱炎，鼻出血，下部消化管出血及び不正子宮出血（各 1 例，1.0%）（1 例に胃腸出血及び下部消化管出血が認められ，別の 1 例に胃腸出血及び不正子宮出血が認められた）であり，いずれも死亡には至らなかった。
- 心房細動は，イブルチニブ群で 5 例（5.3%），プラセボ群で 3 例（3.1%）に発現し，いずれも死亡には至らなかった。Grade 3 以上の心房細動は両群で各 2 例（2.1%）に発現した。
- 高血圧は，イブルチニブ群で 10 例（10.6%），プラセボ群で 13 例（13.5%）に発現した。Grade 3 以上の高血圧は，両群で各 5 例（イブルチニブ群 5.3%，プラセボ群 5.2%）に発現した。

2.7.6.4.1.3　結論

本試験は主要評価項目を達成しなかった。副次評価項目の一部では，プラセボ群と比較してイブルチニブ群で良好な傾向が認められ，特に Lee cGVHD 症状評価尺度の総合要約スコアの改善，奏効持続期間，事後解析として実施した無イベント生存期間で改善傾向が認められた。追跡期間が長いほど奏効持続期間の群間差が大きかったことから，主要評価項目である 48 週時の奏効率は，有効性を評価するには時期が早かった可能性がある。最終解析時に副次評価項目の長期評価を実施する予定である。イブルチニブと prednisone との併用投与は，未治療の中等症から重症の cGVHD を有する成人及び青年期の被験者において良好な忍容性を示し，新たな安全性のシグナルは特定されなかった。