Statistical Analysis Plan

NCT Number: NCT04213209

Title: Specified drug use Surveillance for ADCETRIS Intravenous Infusion 50 mg "Relapsed or refractory CD30 positive peripheral T-cell lymphoma and Hodgkin lymphoma (pediatric only)"

Study Number: C25021

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Certain information within this document has been redacted (ie, specific content is masked irreversibly from view) to protect either personally identifiable information or company confidential information.

Note; This document was translated into English as the language on original version was Japanese.

Statistical Analysis Plan

(final analysis)Pri

Adcetris for Intravenous Drip Infusion 50 mg Special drug use-results survey "Relapsed or refractory CD30 positive peripheral T-cell lymphoma and Hodgkin lymphoma (children only)"

Sponsor: Takeda Pharmaceutical Company Limited.

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1 Definitions of Terms, etc.

1.1 List of Terms and Abbreviations

- This drug: Adcetris for Intravenous Drip Infusion 50 mg is abbreviated as this drug.
- Adverse Event: AE occurred after administration of this drug.
- Adverse reactions, etc.: An abbreviation for the term “adverse reactions/infections.” Adverse events that are not "not related" to this drug as assessed by the managing physician. This statistical analysis plan uses “adverse drug reactions/infections ” in the title and“ adverse drug reactions, etc. ” in the text and tables.
- Serious adverse events: Adverse events assessed as "serious" by the investigator. Using the Important Medical Events List, events listed in the MedDRA code list (PT code) will be handled as serious even if the investigator's assessment is “non-serious.”
- Related to this drug: An AE that is not related to this drug.
- Not related to this drug: An AE that is not related to this drug.
- Summary statistics: A collective term for sample size, mean, standard deviation, maximum, minimum, and quartiles.
- Patients whose CRFs were not collected: Registered patients whose CRFs were not collected.
- Patients whose CRFs were collected: Registered patients whose CRFs were collected.
- Days after administration: Day -1 is defined as the day before the start date of this drug treatment and Day 1 is defined as the start date of this drug treatment.
- Duration of treatment with this drug (days): The end date of treatment with this drug − the start date of treatment with this drug +1
- Children: Patients aged < 18 years at the start of treatment.
- Adults: Patients aged 18 years or older at the start of treatment.
- Timing of onset of an adverse event (or adverse drug reaction, etc.): Calculated as the date of onset of the adverse event (or adverse drug reaction, etc.) - the start date of the first dose of this drug +1.
- Duration of disease:
    - Actual number (months) = (Year of the first administration of this drug - Year of the diagnosis of peripheral T-cell lymphoma or Hodgkin's lymphoma) ×12+ (Month of the first administration of this drug - Month of the diagnosis of peripheral T-cell lymphoma or Hodgkin's lymphoma)
      If the month of diagnosis is unknown, it should be calculated as January of the year of diagnosis.
- Time from the last day of treatment immediately before administration of this drug to the first administration of this drug (days): The first day of administration of this drug − the last day of treatment immediately before administration of this drug +1

- BMI (kg/m ^{2}): Calculated as weight (kg)/height (m) ^{2} (rounded to the first decimal place).
- Approved dose of this drug: 1.8 mg/kg per dose.
- Overall survival: Time from the start date of this drug treatment to the date of confirmation of survival (the last observation date entered in the survey form) or the date of assessment of the outcome of adverse event as death.
    - Overall survival (date of death or confirmation of survival) (days) = date of death or confirmation of survival − start date of this drug treatment +1

1.2 Analysis Sets

As the analysis population of the general drug use-results survey, the "subjects for safety evaluation" and the "subjects for efficacy evaluation" will be defined. This analysis set will be defined as follows:.

Subjects evaluable for safety

Defined as "Patients receiving this drug who had no major protocol violations and whose safety could be evaluated."
Specifically, patients with locked CRFs who meet any of the following criteria will be excluded from the safety analysis set.

- This drug naïve
- Presence/absence of adverse event unknown
- Withdrawal of consent

Patients eligible for efficacy evaluation

In this statistical analysis plan, the "Patients evaluable for efficacy with no major protocol deviations among patients evaluated for safety" will be defined as the patients evaluated for efficacy. Patients who meet the following conditions among the patients evaluated for safety will be excluded from the patients evaluated for efficacy.

- Other than target disease [revealed after the fact]
- Violation of inclusion criteria [revealed after the fact]
  - Patients who do not meet the following inclusion criteria will be excluded from the efficacy analysis set as violation of the inclusion criteria.
    - Patients with relapsed or refractory disease
    - Patients who are positive for CD30

1.3 Number of digits to be displayed

- Percentage (%)
  Incidence of adverse events or adverse drug reactions:
  Round and display to 2 decimal places.
  Other than the above:
  Round off to one decimal place.

- Summary statistics
  Mean, 14 percentile, median, 34 percentile:
  Rounded to one digit below the source data.
  Standard deviation:
  Round off to the second digit below the source data.
  Min, Max:
  Display the same number of digits as displayed in the source data.

- confidence interval
  Rounded to the second digit below the source data.

1.4 Important identified risks, important potential risks, and important missing information

- Important identified risks
    - Peripheral neuropathy: events with SMQ code 20000034 (peripheral neuropathy [broad]).
    - Bone marrow depression: Events corresponding to MedDRA PT codes 10029354 (neutropenia), 10029366 (neutrophil count decreased), and 10016288 (febrile neutropenia).
    - Lung disorder: Events coded to SMQ 20000042 (Interstitial lung disease [Broad]).

2 Number of study sites and patients enrolled and patient composition

2.1 Disposition of subjects

Analysis population:	Specified use-results survey	
Analysis population:	All enrolled patients (patients enrolled)	
Analysis item:	Patients enrolled	
	Medical institution inspected	
	CRF not collected	
	CRF collected	
	Patients excluded from safety evaluation *	
	Reason for exclusion (multiple counting)	[this drug was not administered, presence or absence of adverse events was unknown, and consent was withdrawn.]
	Subjects evaluable for safety	
	Patients excluded from efficacy evaluation *	
	Reason for exclusion (multiple counting)	[Other than the target disease [Found after the fact], Violation of inclusion criteria [found out after the fact]
	Patients eligible for efficacy evaluation	
Analytical method:	For the above analytical variables, the following analyses will be performed to prepare the patient composition chart.	
	For registered patients, the number of study sites is also shown. The same medical institution with different departments in the survey shall be counted as one medical institution.	
	If there is no subject applicable to the reason for exclusion, 0 subject is displayed.	
	For patients excluded from the safety evaluation and efficacy evaluation, the number of patients by reason for exclusion will be tabulated and listed.	
	*"Patients excluded from safety evaluation" refers to patients who were excluded from the "patients eligible for safety evaluation" among patients whose CRFs were collected. Similarly, "patients excluded from efficacy evaluation" refer to "patients excluded from efficacy evaluation" among the "patients evaluated for safety."	
	（1） Frequency tabulations	

3 Patient characteristics

3.1 Patient characteristics

Analysis population:	Subjects evaluable for safety	
Analysis item:	Gender	[Male, female]
	Age (years)	[Min <= - < 18, 18 <= - < 30, 30 <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]
	Disease duration (months)	
	Diagnosis	[Peripheral T-cell lymphoma (PTCL), Hodgkin lymphoma (HL)]
	Type of PTCL	[Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), adult T-cell leukemia/lymphoma (ATLL), ALK-positive anaplastic large cell lymphoma (ALK+ ALCL) [for patients aged < 18 years], ALK-negative anaplastic large cell lymphoma (ALK-ALCL) [for patients aged < 18 years], other]
	(details on adult T-cell leukemia/lymphoma [ATLL])	[Acute type, lymphoma type, others]
	Disease site (multiple counting)	[Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others]
	Clinical stage	
	Ann Arbor Classification	[Stage I, II, III, IV, unknown]
	Murphy classification	[Stage I, II, III, IV, unknown]
	Presence or absence of B symptoms	[Absent, present]
	Relapsed/refractory status	[Relapsed/refractory]
	ECOG Performance Status	[0, 1, 2, 3, 4]
	Treatment category (at the start of this drug treatment)	[Outpatient/inpatient]
	Complications	[Absent, present]
	Presence or absence of medical history	[Absent, present, unknown]
	Smoking history	[Never smoked, current smoker, former smoker but not current smoker, unknown]

Weight (kg)	[Min <= - < 40.0, 40.0 <= - < 50.0, 50.0 <= - < 60.0, 60.0<= - < 70.0, 70.0 <= - <= Max, not measured]
BMI(kg/m2)	[Min <= - < 18.5, 18.5 <= - < 25.0, 25.0 <= - < 30.0, 30.0 <= - <= Max]
Pregnancy (females only)	[Absent, present]
Breastfeeding status (females only)	[Absent, present]
Treatment for PTCL or HL before the start of this drug	
Number of regimens	[0, 1, 2, 3, 4, ≥ 5, unknown]
Drug therapy	[(1) A+CHP, (2) CHOP, (3) ABVD, (4) mLSG15, (5) GDP, (6) OEPA/OPPA, (7) ALCL99, others, unknown]
Radiotherapy	[Absent, present, unknown]
Hematopoietic stem cell transplantation	[Absent, present, unknown]
(With haematopoietic stem cell transplant)	[Autologous transplant, allogeneic transplant]
Time from the last day of treatment immediately before administration of this drug to the first administration of this drug (days)	

Analytical method: For the above analytical variables, frequency tabulation of discrete data and summary statistics of continuous data will be calculated. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

4 Details of treatment

4.1 Administration status of this drug

Analysis population:	Subjects evaluable for safety	
Analysis item:	This drug loading dose (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
	Mean dose of this drug per administration (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
	This drug dose per 3 weeks (mg/kg/3 weeks)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
	Maximum number of doses	[1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17]
	Reasons for Discontinuation of this drug (Multiple Count)	[The treatment goal was achieved, the patient did not visit the hospital due to the onset of adverse events, transfer to another hospital, etc., pregnancy, disease progression, hematopoietic stem cell transplantation, follow-up observation, patient's or family's wish, etc.]
Analytical method:	For the above analytical variables, frequency tabulation of discrete data and summary statistics of continuous data will be calculated. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).	

5 Matters related to safety

5.1 Status of Occurrence of Adverse Events and Adverse Drug Reactions/Infections

5.1.1 Occurrence of adverse events

Analysis population: Subjects evaluable for safety

Analysis item: Adverse Events

Analytical method: For the above analytical variable, the following analyses should be performed. This tabulation will be performed for all patients, adults (PTCL-NOS, AITL, ATLL, others), and children (PTCL, HL).

（1） Number of subjects with adverse events

（2） Number of AEs

（3） Incidence of adverse events

（4） Type of Adverse Event

The calculation method for each analysis is as follows.

[Number of subjects with adverse events]

- Number of patients with adverse events.

[Number of adverse events]

- Number of AEs that occurred. If the same adverse event occurs more than once in the same patient, the total number of events will be tabulated.

[Incidence of adverse events]

- Calculated as the number of patients with adverse events/number of patients evaluated for safety ×100.

[Type of adverse event]

- AEs will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- Within SOC, the number of patients with adverse events and the incidence rate will be described using internationally agreed SOC order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.
- By PT, the number of patients with adverse events and the incidence will be described in ascending order of PT codes. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.1.2 Occurrence status of adverse reactions/infections

Analysis population: Subjects evaluable for safety

Analysis item: Adverse reactions, etc.

Analytical method: For the above analytical variable, the following analyses should be performed. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

（1） Number of patients with adverse reactions, etc.

（2） Number of adverse drug reactions

（3） Incidence of adverse drug reactions

（4） Types of adverse reactions, etc.

The calculation method for each analysis is as follows.

[Number of patients with adverse reactions]

- Number of patients with adverse reactions, etc.

[Number of adverse reactions]

- Number of adverse drug reactions, etc. that occurred. If the same adverse drug reaction, etc. occurs multiple times in the same patient, the total number of events will be tabulated.

[Incidence of adverse reactions]

- Number of patients with adverse drug reactions/Number of patients evaluated for safety ×100.

[Types of adverse reactions, etc.]

- Adverse drug reactions will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- In SOC, the number of patients with adverse drug reactions, etc. and the incidence will be described in SOC internationally agreed order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.
- By PT, the number of patients with adverse drug reactions, etc. and the incidence will be described in ascending order of PT codes. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.1.3 Incidences of adverse events and adverse drug reactions/infections included in the safety specifications

5.1.3.1 Incidences of adverse events included in the safety specifications

Analysis population: Subjects evaluable for safety

Analysis item: Adverse events included in the safety specifications (important identified risks)

Stratification item: Seriousness [Serious, non-serious]

Analytical method: For the above analysis set, analyses should be performed in the same manners as in Section 5.1.1 for each risk and each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL). A subject who experienced the same SOC/PT more than once should be counted as 1 subject in the SOC/PT. However, if the seriousness differs, 1 subject will be counted for each of serious and non-serious. The target risks shall follow the definitions described in the important identified risks.

5.1.3.2 Incident Status of Adverse Reactions/Infections Included in Safety Specifications

Analysis population: Subjects evaluable for safety

Analysis item: Adverse reactions, etc. corresponding to safety specifications (important identified risks)

Stratification item: Seriousness [Serious, non-serious]

Analytical method: For the above analysis set, analyses should be performed in the same manners as in Section 5.1.2 for each risk and each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL). A subject who experienced the same SOC/PT more than once should be counted as 1 subject in the SOC/PT. However, if the seriousness differs, 1 subject will be counted for each of serious and non-serious. The target risks shall follow the definitions described in the important identified risks.

5.2 Status of occurrence of adverse events, adverse drug reactions, and infections in patients excluded from safety evaluation

5.2.1 Status of adverse events in patients excluded from safety evaluation

Analysis population: Patients excluded from safety evaluation

Analysis item: Adverse Events

Analytical method: For the above analytical variable, the following analyses should be performed.

（1） Number of subjects with adverse events

（2） Number of AEs

（3） Incidence of adverse events

（4） Type of Adverse Event

The calculation method for each analysis is as follows.

[Number of subjects with adverse events]

- Number of patients with adverse events.

[Number of adverse events]

- Number of AEs that occurred. If the same adverse event occurs more than once in the same patient, the total number of events will be tabulated.

[Incidence of adverse events]

- Number of patients with adverse events/Number of patients excluded from safety evaluation ×100.

[Type of adverse event]

- AEs will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- Within SOC, the number of patients with adverse events and the incidence rate will be described using internationally agreed SOC order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.

- By PT, the number of patients with adverse events and the incidence will be described in ascending order of PT codes. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.2.2 Occurrence Status of Adverse Reactions/Infections in Patients Excluded from Safety Evaluation

Analysis population: Patients excluded from safety evaluation

Analysis item: Adverse reactions, etc.

Analytical method: For the above analytical variable, the following analyses should be performed.

（1） Number of patients with adverse reactions, etc.

（2） Number of adverse drug reactions

（3） Incidence of adverse drug reactions

（4） Types of adverse reactions, etc.

The calculation method for each analysis is as follows.

[Number of patients with adverse reactions, etc.]

- Number of patients with adverse reactions, etc.

[Number of adverse reactions]

- Number of adverse drug reactions, etc. that occurred. If the same adverse drug reaction, etc. occurred multiple times in the same patient, the total number of events will be tabulated.

[Incidence of adverse reactions, etc.]

- Number of patients with adverse drug reactions/Number of patients excluded from safety evaluation ×100.

[Types of adverse reactions, etc.]

- Adverse drug reactions will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- In SOC, the number of patients with adverse drug reactions, etc. and the incidence will be described in SOC internationally agreed order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.
- By PT, the number of patients with adverse drug reactions, etc. and the incidence will be described in ascending order of PT codes. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.3 Occurrence status of adverse events and adverse drug reactions/infections by seriousness, CTCAE Grade (worst value), timing of onset, outcome, and causal relationship with this drug

5.3.1 Occurrence of adverse events by seriousness, CTCAE Grade (worst value), timing of onset, outcome, and causal relationship with this drug

Analysis population: Subjects evaluable for safety

Analysis item:	Adverse Events	
Stratification item:	Total	
	Seriousness	[Serious, non-serious]
	CTCAE Grade (worst value)	[Grade1, Grade2, Grade3, Grade4, Grade5]
	Timing of onset (day)	[1 <= - <= 21, 22 <= - <= 84, 85 <= - <= 168, 169 <= - <= 252, 253 <= - <= 336, 337 <= - <= Max]
	Timing of onset (number of doses)	[From after the 1st dose to before the 2nd dose, from after the 2nd dose to before the 5th dose, from after the 5th dose to before the 9th dose, from after the 9th dose to before the 13th dose, from after the 13th dose to before the 17th dose, from after the 17th dose]
	Outcome	[Recovered/resolved, resolving, not recovered, recovered with sequelae, fatal (due to this event), unknown]
	Relationship to this drug	[Related, Not Related]

Analytical method: For the above analysis set, analyses similar to those in Section 5.1.1 will be performed for each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL). A subject who experienced the same SOC/PT more than once should be counted as 1 subject in the SOC/PT. However, 1 subject within the same SOC will be included in the study according to the following order of priority, and 1 subject within the same PT will be included in the study according to the following order of priority for any of the stratification factors.

Seriousness: Serious → Non-serious

CTCAE Grade (worst value): Grade5→Grade4→Grade3→Grade2→Grade1

Timing of onset (days): 1 to 21 days →22 to 84 days →85 to 168 days →169 to 252 days →253 to 336 days → ≥ 337 days

Timing of onset (number of doses): After the first dose to before the second dose → After the second dose to before the fifth dose → After the fifth dose to before the ninth dose → After the ninth dose to before the thirteenth dose → After the thirteenth dose to before the seventeenth dose → After the seventeenth dose and thereafter

Outcome: Death (due to this event) → recovered with sequelae → not recovered → recovering → recovered → unknown

Causal relationship with this drug: Related → Not related

5.3.2 Occurrence status of adverse drug reactions/infections by seriousness, CTCAE Grade (worst value), timing of onset, and outcome

Analysis population:	Subjects evaluable for safety	
Analysis item:	Adverse reactions, etc.	
Stratification item:	Total	
	Seriousness	[Serious, non-serious]
	CTCAE Grade (worst value)	[Grade1, Grade2, Grade3, Grade4, Grade5]
	Timing of onset (day)	[1 <= - <= 21, 22 <= - <= 84, 85 <= - <= 168, 169 <= - <= 252, 253 <= - <= 336, 337 <= - <= Max]
	Timing of onset (number of doses)	[From after the 1st dose to before the 2nd dose, from after the 2nd dose to before the 5th dose, from after the 5th dose to before the 9th dose, from after the 9th dose to before the 13th dose, from after the 13th dose to before the 17th dose, from after the 17th dose onwards]
	Outcome	[Recovered/resolved, resolving, not recovered, recovered with sequelae, fatal (due to this event), unknown]
Analytical method:	For the above analysis set, analyses similar to those in Section 5.1.2 will be performed for each stratum of the stratification factor.This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL). A subject who experienced the same SOC/PT more than once should be counted as 1 subject in the SOC/PT. However, 1 subject within the same SOC will be included in the study according to the following order of priority, and 1 subject within the same PT will be included in the study according to the following order of priority for any of the stratification factors. Seriousness: Serious → Non-serious CTCAE Grade (worst value): Grade5→Grade4→Grade3→Grade2→Grade1 Timing of onset (days): 1 to 21 days →22 to 84 days →85 to 168 days →169 to 252 days →253 to 336 days → ≥ 337 days Timing of onset (number of doses): After the first dose to before the second dose → After the second dose to before the fifth dose → After the fifth dose to before the ninth dose → After the ninth dose to before the thirteenth dose → After the thirteenth dose to before the seventeenth dose → After the seventeenth dose and thereafter Outcome: Death (due to this event) → recovered with sequelae → not recovered → recovering → recovered → unknown	

5.4 Onset status of adverse reactions/infections by patient background and treatment factors

5.4.1 Onset status of adverse reactions/infections by patient background factor and treatment details factor

Analysis population:	Subjects evaluable for safety	
Analysis item:	Adverse reactions, etc.	
Stratification item:	Gender	[Male, female]
	Age (years)	[Min <= - < 18, 18 <= - < 30, 30 <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]
	Diagnosis	[Peripheral T-cell lymphoma (PTCL), Hodgkin lymphoma (HL)]
	Type of PTCL	[Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), adult T-cell leukemia/lymphoma (ATLL), ALK-positive anaplastic large cell lymphoma (ALK+ ALCL) [for patients aged < 18 years], ALK-negative anaplastic large cell lymphoma (ALK-ALCL) [for patients aged < 18 years], other]
	(details on adult T-cell leukemia/lymphoma [ATLL])	[Acute type, lymphoma type, others]
	Disease site (multiple counting)	[Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others]
	Clinical stage	
	Ann Arbor Classification	[Stage I, II, III, IV, unknown]
	Murphy classification	[Stage I, II, III, IV, unknown]
	Presence or absence of B symptoms	[Absent, present]
	Relapsed/refractory status	[Relapsed/refractory]
	ECOG Performance Status	[0, 1, 2, 3, 4]
	Treatment category (at the start of this drug treatment)	[Outpatient/inpatient]
	Complications	[Absent, present]
	Presence or absence of medical history	[Absent, present, unknown]

Weight (kg)	[Min <= - < 40.0, 40.0 <= - < 50.0, 50.0 <= - < 60.0, 60.0<= - < 70.0, 70.0 <= - <= Max, not measured]
BMI(kg/m2)	[Min <= - < 18.5, 18.5 <= - < 25.0, 25.0 <= - < 30.0, 30.0 <= - <= Max]
Treatment for PTCL or HL before the start of this drug	
Drug therapy	[(1) A+CHP, (2) CHOP, (3) ABVD, (4) mLSG15, (5) GDP, (6) OEPA/OPPA, (7) ALCL99, others, unknown]
Radiotherapy	[Absent, present, unknown]
Hematopoietic stem cell transplantation	[Absent, present, unknown]
(With haematopoietic stem cell transplant)	[Autologous transplant, allogeneic transplant]
This drug loading dose (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
Mean dose of this drug per administration (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
This drug dose per 3 weeks (mg/kg/3 weeks)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]

Analytical method: For the above analytical variable, the following analyses will be performed for each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

Number of patients with adverse reactions, etc.

Incidence of adverse drug reactions

The calculation method for each analysis is as follows.

[Number of patients with adverse reactions]

- Number of patients with adverse reactions, etc.

[Incidence of adverse reactions]

Number of patients with adverse drug reactions/Number of patients evaluated for safety ×100.

5.4.2 Occurrence Status of Adverse Reactions/Infections by Gender

Analysis population: Subjects evaluable for safety

Analysis item: Adverse reactions, etc.

Stratification item: Gender [Male, female]

Analytical method: For the above analysis set, analyses similar to those in Section 5.1.2 will be performed for each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

5.4.3 Occurrence Status of Adverse Reactions/Infections by Age Group

Analysis population: Subjects evaluable for safety

Analysis item: Adverse reactions, etc.

Stratification item:

Age (years) (all subjects)	[Min <= - < 12, 12 <= - < 18, 18 <= - < 30, 30 <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]
Age (years) (adult)	[Min <= - < 18, 18 <= - < 30, 30 <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]
Age (years) (children)	[Min <= - < 12, 12 <= -<= Max]

Analytical method: For the above analysis set, analyses similar to those in Section 5.1.2 will be performed for each stratum of the stratification factor. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

5.5 Occurrence Status of Adverse Events and Adverse Drug Reactions/Infections for which Action Taken with this drug was Discontinuation

5.5.1 Incidences of adverse events leading to discontinuation of this drug

Analysis population: Subjects evaluable for safety

Analysis item: AEs leading to discontinuation of this drug

Analytical method: For the above analytical variable, the following analyses should be performed. This tabulation will be performed for all patients, adults (PTCL-NOS, AITL, ATLL, others), and children (PTCL, HL).

（1） Number of patients with adverse events leading to discontinuation of this drug

（2） Number of AEs leading to this drug discontinuation

（3） Incidence of AEs leading to discontinuation of this drug

（4） Adverse event type for which action taken with this drug was discontinuation

The calculation method for each analysis is as follows.

[Number of patients with adverse events for which this drug treatment was discontinued]

- Number of subjects with AEs leading to discontinuation of this drug.

[Number of adverse events for which this drug was discontinued]

- Number of adverse events for which the action taken with this drug was discontinuation. If the same adverse event occurs more than once in the same patient, the total number of events will be tabulated.

[Incidence of adverse events for which action taken with this drug was discontinuation]

- Calculate the number of patients with adverse events whose action taken with this drug is discontinuation/the number of patients included in the safety evaluation ×100.

[Action taken with this drug was treatment discontinuation due to type of adverse event]

- AEs leading to discontinuation of this drug will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- For SOC, the number of patients with adverse events whose action taken with this drug is treatment discontinuation and the incidence are described in SOC internationally agreed order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.
- By PT, the number of patients with adverse events whose action taken with this drug was treatment discontinuation and the incidence thereof will be entered in ascending order of PT code. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.5.2 Occurrence Status of Adverse Reactions/Infections for which Action Taken with this drug was Discontinuation

Analysis population:	Subjects evaluable for safety
Analysis item:	Adverse reactions, etc. for which the action taken with this drug is discontinuation of administration
Analytical method:	For the above analytical variable, the following analyses should be performed. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).

（1） Number of patients with adverse drug reactions, etc. for which this drug treatment was discontinued

（2） Number of ADRs leading to discontinuation of this drug

（3） Incidence of adverse drug reactions/infections leading to discontinuation of this drug

（4） Type of adverse drug reaction, etc. for which action taken with this drug is discontinuation

The calculation method for each analysis is as follows.

[Number of patients with adverse drug reactions, etc. for which this drug was discontinued]

- Action taken with this drug was number of patients with adverse drug reactions.

[Action taken with this drug was number of adverse drug reactions requiring treatment discontinuation]

- Number of adverse drug reactions, etc. for which action taken with this drug was discontinuation. If the same adverse drug reaction, etc. occurs multiple times in the same patient, the total number of events will be tabulated.

[Incidence of adverse drug reactions, etc. for which treatment with this drug was discontinued]

- Calculate the number of patients with adverse drug reactions, etc. for which actions taken for this drug are discontinuation/the number of patients included in the safety evaluation ×100.

[Action taken with this drug was treatment discontinuation due to type of adverse reactions, etc.]

- Adverse drug reactions, etc. for which this drug treatment is discontinued will be coded using MedDRA/J. It will be roughly classified by SOC and tabulated by PT. SOC of "investigations" will be summarized by HLGT (Sort in ascending order of HLGT code, but do not output) and PT.
- In SOC, the number of patients with adverse drug reactions, etc. for which the action taken with this drug is treatment discontinuation and the incidence are described in SOC internationally agreed order. A subject with multiple occurrences of an event within an SOC should be counted only once for that SOC.
- By PT, action taken with this drug was treatment discontinuation Describe the number of patients with adverse reactions, etc. and the incidence in ascending order of PT code. A subject who experienced the same PT more than once should be counted as 1 subject with the PT.

5.6 Status of administration of this drug by outcome at the onset of adverse reactions/infections

Analysis population:	Subjects evaluable for safety	
Analysis item:	Number of adverse drug reactions	
Stratification item 1:	Presence or absence of changes due to this event	[Absent, present]
	Details of changes (duplicate counting) [*] [*]	[Dose reduction, dose interruption [dose delay], discontinuation]
Stratification item 2:	Outcome	[Recovered/resolved, resolving, not recovered, recovered with sequelae, fatal, unknown]
	Total	

Analytical method: For the above analysis set, the number of adverse drug reactions, etc. will be tabulated for each stratum of Stratification Item 1 and the number of events will be tabulated for each stratum of Stratification Item 2. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL). The denominator for the incidence rate per Stratum Item 1 will be the number of events per stratum in Stratum Item 2.

5.7 Status of administration of this drug due to adverse events and adverse drug reactions/infections included in the safety specifications

5.7.1 Administration status of this drug due to adverse events included in the safety specifications

Analysis population: Subjects evaluable for safety

Analysis item:	Adverse events included in the safety specifications (Important identified risks: peripheral neuropathy, bone marrow depression)	
Stratification item:	Presence or absence of changes due to this event	[Absent, present]
	Details of changes (duplicate counting)	[Dose reduction, dose interruption [dose delay], discontinuation]
Analytical method:	For the above analysis subjects, the number of adverse events will be tabulated by frequency by CTCAE Grade (worst value) of adverse events falling under each risk and stratified by stratification item. For the incidence rate for each stratification factor, the denominator will be the number of events for each CTCAE Grade (worst value). This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).	

5.7.2 Status of administration of this drug due to adverse reactions/infections included in the safety specifications

Analysis population:	Subjects evaluable for safety	
Analysis item:	Adverse reactions, etc. corresponding to safety specifications (Important identified risks: peripheral neuropathy, bone marrow depression)	
Stratification item:	Presence or absence of changes due to this event	[Absent, present]
	Details of changes (duplicate counting)	[Dose reduction, dose interruption [dose delay], discontinuation]
Analytical method:	In the above analysis population, the number of adverse drug reactions, etc. will be tabulated for frequency by stratification item by CTCAE Grade (worst value) of adverse drug reactions, etc. corresponding to each risk. For the incidence rate for each stratification factor, the denominator will be the number of events for each CTCAE Grade (worst value). This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others) and children (PTCL, HL).	

6 Efficacy

6.1 Tumor response during the first 12 months of this drug therapy

Analysis population:	Patients whose antitumor effect was assessed among the patients evaluated for efficacy	
Analysis item:	Antitumor effect	
Stratification item:	PTCL or HL other than adult T-cell leukemia/lymphoma (ATLL) *Data will be tabulated in adults (PTCL-NOS, AITL, others), and children (PTCL, HL) and separately. ATLL	[With PET assessment, without PET assessment, total]
	Pediatric PTCL or HL (JPLSG version)	[For PTCL, For HL]
Analytical method:	For each of the above analysis items, the frequency of assessment results will be tabulated for each stratum of the stratification item in patients whose antitumor effect has been assessed among the patients evaluated for efficacy, and the response rate will be calculated. In addition, a band graph will be prepared for the above analysis results.	

6.2 Antitumor effect in 12 months from the start of this drug by patient demographics and treatment factors

6.2.1 Antitumor effect in 12 months from the start of this drug by patient demographics and treatment factors (adult)

Analysis population:	Patients whose antitumor effect was assessed among the patients evaluated for efficacy (adults)	
Analysis item:	Antitumor effect	
Stratification item 1:	PTCL or HL other than adult T-cell leukemia/lymphoma (ATLL) *To be tabulated separately for PTCL-NOS, AITL, and others ATLL	[With PET assessment, without PET assessment, total]
Stratification item 2:	Gender	[Male, female]
	Age (years)	[Min <= - < 18, 18 <= - < 30, 30 <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]
	Diagnosis	[Peripheral T-cell lymphoma (PTCL), Hodgkin lymphoma (HL)]
	Type of PTCL	[Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), adult T-cell leukemia/lymphoma (ATLL), ALK-positive

	anaplastic large cell lymphoma (ALK+ ALCL) [for patients aged < 18 years], ALK-negative anaplastic large cell lymphoma (ALK-ALCL) [for patients aged < 18 years], other]
(details on adult T-cell leukemia/lymphoma [ATLL])	[Acute type, lymphoma type, others]
Disease site (multiple counting)	[Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others]
Clinical stage	
Ann Arbor Classification	[Stage I, II, III, IV, unknown]
Murphy classification	[Stage I, II, III, IV, unknown]
Presence or absence of B symptoms	[Absent, present]
Relapsed/refractory status	[Relapsed/refractory]
ECOG Performance Status	[0, 1, 2, 3, 4]
Treatment category (at the start of this drug treatment)	[Outpatient/inpatient]
Complications	[Absent, present]
Presence or absence of medical history	[Absent, present, unknown]
Weight (kg)	[Min <= - < 40.0, 40.0 <= - < 50.0, 50.0 <= - < 60.0, 60.0<= - < 70.0, 70.0 <= - <= Max, not measured]
BMI(kg/m2)	[Min <= - < 18.5, 18.5 <= - < 25.0, 25.0 <= - < 30.0, 30.0 <= - <= Max]
Treatment for PTCL or HL before the start of this drug	
Number of regimens	[0, 1, 2, 3, 4, ≥ 5, unknown]
Drug therapy	[(1) A+CHP, (2) CHOP, (3) ABVD, (4) mLSG15, (5) GDP, (6) OEPA/OPPA, (7) ALCL99, others, unknown]
Radiotherapy	[Absent, present, unknown]
Hematopoietic stem cell transplantation	[Absent, present, unknown]
(With haematopoietic stem cell transplant)	[Autologous transplant, allogeneic transplant]

	This drug loading dose (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
	Mean dose of this drug per administration (mg/kg)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
	This drug dose per 3 weeks (mg/kg/3 weeks)	[Min <= - < 0.9, 0.9 <= - < 1.2, 1.2 <= - < 1.8, 1.8, 1.8 < - <= Max]
Analytical method:	For each of the above analysis items, frequency will be tabulated by stratification item 1 and then by stratum of stratification item 2 in patients (adults) whose antitumor effect has been assessed among the efficacy evaluation set.	

6.2.2 Antitumor effect in 12 months from the start of this drug by patient demographics and treatment factors (children)

Analysis population:	Efficacy analysis set with tumor response assessment (children)	
Analysis item:	Antitumor effect	
Stratification item 1:	PTCL	[With PET assessment, without PET assessment, total]
	HL	[With PET assessment, without PET assessment, total]
	Pediatric PTCL or HL (JPLSG version)	[For PTCL, For HL]
Analytical method:	For each of the above analysis items, data will be tabulated in the same manner as in Section 6.2.1 in patients (children) whose antitumor effect has been assessed among the efficacy evaluation set, stratified by stratification item 1.	

6.3 Overall survival

Analysis population:	Patients eligible for efficacy evaluation
Analysis item:	Overall survival
Analytical method:	For the above analysis set, the survival rate at 12 months will be estimated by the Kaplan-Meier method, and Kaplan-Meier plots will be prepared. This tabulation will be performed for cases of overall, adults (PTCL-NOS, AITL, ATLL, others), and children (PTCL, HL).

7 Occurrence Status of Adverse Reactions/Infections in Additional Pharmacovigilance Plan

7.1 Incidences of ADRs and infections included in additional pharmacovigilance plan (Attached Form 12)

Analysis population:	Subjects evaluable for safety
Analysis item:	Adverse reactions, etc. corresponding to safety specifications (important identified risks)
Stratification item:	Seriousness [Serious, non-serious]
Analytical method:	For the above analytical variables, the following analyses should be performed for each of the subgroups of the stratification factors in accordance with (Note) 1~4 in Attached Form 12 to PSEHB/PED Notification No. 0325- 10 dated March 25, 2020.

（1） Number of patients with events and incidence

The order of description of risk names and risk names shall follow the definitions described in Important Identified Risks.

8 Case Summary for Post-marketing Surveillance, etc.

8.1 Case summary in post-marketing surveillance, etc. (Attached Form 16)

Analysis population:	CRF collected
Analysis item:	Case No.
	Name of medical institution
	Gender
	Age
	Reason for use (Disease code, disease name)
	Comorbidity (Disease code, disease name)
	Route of administration
	Maximum dose
	Mean dose
	Unit
	Duration of use (duration of this drug treatment)
	Concomitant medications (Drug code, drug name)
	Degree of effect
	Adverse reactions (Disease code, disease name, outcome)
	CRF No.
	Dropout
	Reason for dropout
	Name of disease (other than target disease)
Analytical method:	A list of the above analysis items will be prepared in accordance with the reexamination data entry file preparation guideline specified in the Notification No. 1119 (3) of the Pharmaceutical Evaluation Division, PSEHB dated November 19, 2020.

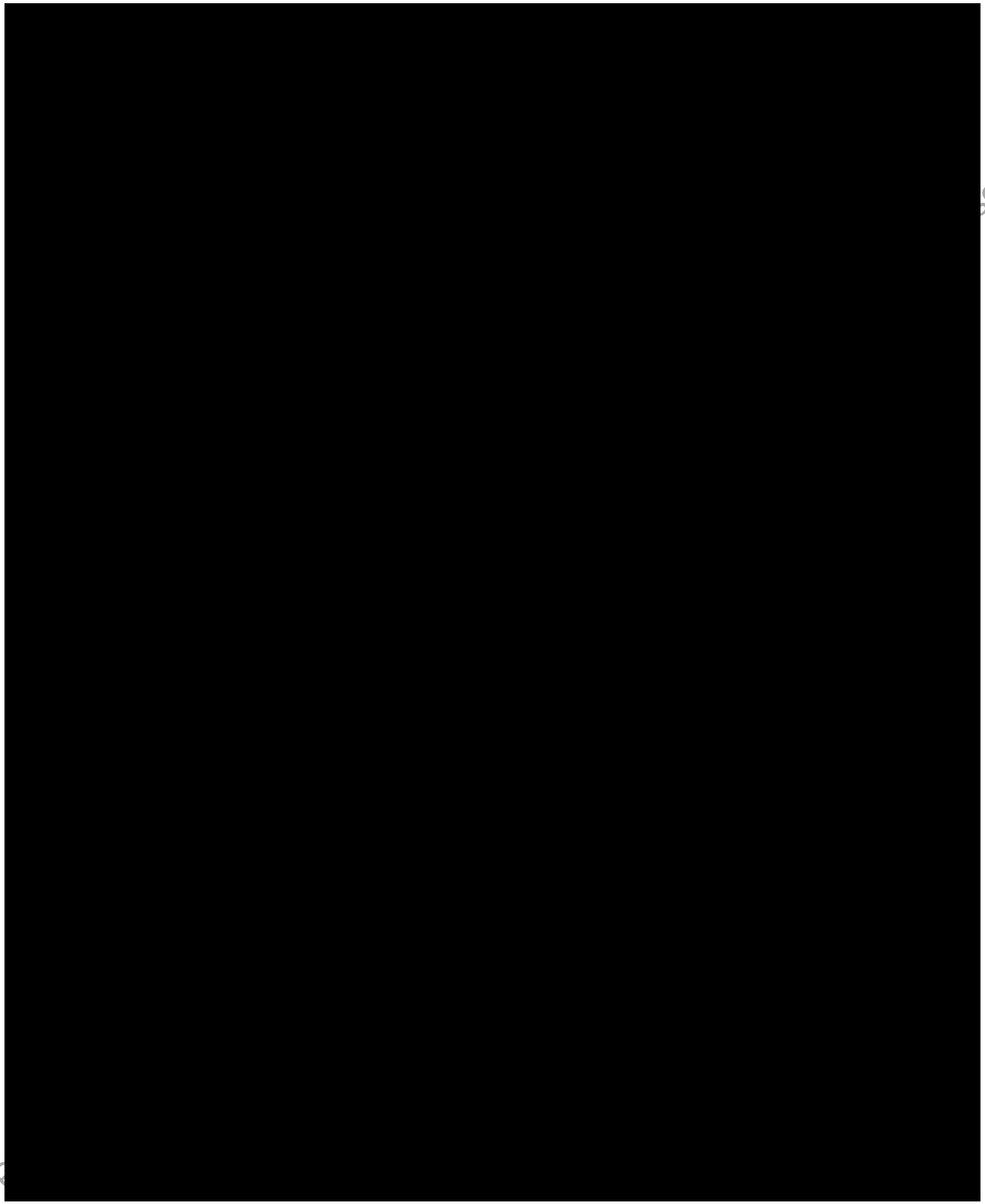
Preparation history (version control)

Version	Date	Author/Reporter	Comments
Original Version	2023.10.30	[redacted]	Preparation of initial version
Version 2	2023.11.21	[redacted]	Version 2 prepared Changes from Version 1 are described in Appendix 1.

[Appendix 1] Comparison table of changes

Statistical Analysis Plan (Version 1, prepared on October 30, 2023 → Version 2, prepared on 21/11/2023)

Page	Before amendment	After amendment	Reason for change
22		5.6 Status of this drug administration by outcome at the onset of adverse drug reactions/infections Addition of description about the incidence rate	Description adjustment.
22		5.7 Status of administration of this drug due to adverse events and adverse drug reactions/infections included in the safety specifications Item added	Due to addition of tabulation.



[redacted]