

Statistical Analysis Plan

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Title: General Drug Use Surveillance Protocol General Drug Use Surveillance for ADCETRIS Intravenous Infusion 50 mg "Untreated CD30-Positive Hodgkin's Lymphoma"

Study Number: C25018

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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

| Statistical Analysis Plan (Final Analysis) | |
|---|--|
| Product name : Adcetris for Intravenous Infusion 50 mg Study title : General use-results surveillance [Untreated CD30 positive Hodgkin's lymphoma] | |
| Statistical Analysis Plan (Final Analysis) Product name : Adcetris for Intravenous Infusion 50 mg Study title : General use-results surveillance (Untreated CD30 positive Hodgkin's lymphoma) S p o n s o r : Takeda Pharmaceutical Company Limited. S p o n s o r : Takeda Pharmaceutical Company Limited. Takeda Pharmaceutical Company Limited. Cather and Science | |
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version 1.0 : January 26, 2023

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Definitions of terms 1

List of Terms and Abbreviations 1.1

- In this statistical analysis plan, the term "adverse drug reactions/infections" will be used in the term "adverse drug reactions/infections" will be used in the term "Serious adverse arts"
- Serious adverse events: Adverse events assessed as "serious" by the investigator. Events listed in the MedDRA code list (PT code) using the Takeda Medically Significant AE List as the Important Medical Events List will be handled as serious events, even if the assessment by the investigator is "non-serious.
- Related to this product: An adverse event not related to Adcetris
- Not related to this product: Adverse events assessed as not related to Adcetris.
- Summary statistics: A general term for number of subjects, mean, standard deviation, maximum, minimum, and quartiles.
- Patients whose survey form was not collected: Patients whose survey form was not collected among registered patients.
- CRF collected patients: Patients whose CRF has been collected among registered patients.
- Days after treatment: Day-Us defined as the day before the start of treatment with Adcetris, and Day 1 is defined as the day of the start of treatment with Adcetris.
- Duration of Adcetris treatment (days): End date of Adcetris treatment start date of Adcetris treatment +1
- Timing of onset of adverse events (or adverse drug reactions, etc.): Calculated as the date of onset of adverse events (or adverse drug reactions, etc.) – the start date of the first dose of Adcetris +1.
- Time from diagnosis of Hodgkin's lymphoma to first dose of Adcetris:
 - Actual number (unit: months) = (Year of the first administration of Adcetris Year of the diagnosis of Hodgkin's lymphoma) ×12+ (Month of the first administration of Adcetris – Month of the diagnosis of Hodgkin's lymphoma) If the month of the diagnosis is unknown, it should be calculated as January of the year described.

- Patients complicated with renal impairment: Patients for whom Takeda MedDRA query (Hereinafter referred to as TMQ) (Renal Disease) is entered in the disease name column.
- Terms of Use Patients complicated with hepatic impairment: Patients with a complication corresponding to • MedDRA standard query (hereinafter referred to as SMQ) code 20000005 (liver disorder SMQ [scope: narrow]) described in the disease name column.
- BMI(kg/m²): Calculated as weight (kg)/height (m)² (rounded off to the first decimal place). ٠
- Treatment status •
- Early treatment: G-CSF formulations administered within 5 days of the first dose of Adcetris. •
 - Non-early administration: Administration of G-CSF on or after Day 6 of the first • administration of Adcetris. хO
- ation anistration a and sub-and sub-and sub-anison and sub-anison anison and sub-anison anison and sub-anison anison aniso No early administration: Cases without administration of G-CSF preparations and cases • with administration only other than early administration

1.2 **Analysis Sets**

The "safety evaluation population" and "efficacy evaluation population" will be set as the analysis

Sourced as "Patients treated with Adcetris who had no major protocol violations and whose safety can be evaluated". Specifically, patients with locked CRFs who meet the following conditions will control to the Adcetris not administered
Registration prior to the will. will. applicable applicable thr

- Enrollment after Day 31 of Adcetris treatment
- Unknown adverse event

<text> In this statistical analysis plan, "Patients evaluable for efficacy with no major protocol violations among patients evaluable for safety" is defined as "patients included in efficacy evaluation." Patients eligible for the safety evaluation who meet the following conditions will be excluded from the

1.3 Number of digits to be displayed

• Percentage (%)

Incidence of adverse events or adverse drug reactions: Round the second decimal place and display to the second decimal place. Other than the above: Round the second decimal place and display to the first decimal place.

• Summary statistics

Mean, 1st quantiles, median, 3rd quantiles: The source data will be rounded to the first decimal place and displayed.

Standard deviation:

The data will be rounded to the second decimal place of the source data. Min, Max:

The same number of digits as that of the source data will be displayed.

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

applicable terms of Use

- Important identified risks
- Bone marrow depression: Events corresponding to McdDRA PT code 10029366 (neutrophil count decreased) or 10016288 (tebrile neutropenia). Among events corresponding to bone marrow depression, Grade ≥ 3 adverse events were collected in this study.

2 Number of medical institutions surveyed and the number and composition of patients enrolled

2.1 Disposition of patients

| | 2.1 Disposition | of patients | rolled) tothe applicable | SO |
|------------|-----------------|--|---|-----|
| | Survey for | General use-results survey | | L'S |
| | analysis : | | G | ,0` |
| | Subjects for | All enrolled patients (patients enr | rolled) | F |
| | analysis : | | <u> </u> | |
| | Analysis item : | Patients enrolled | 00 | |
| | | Study sites | ···CO·· | |
| | | CRF not collected | | |
| | | Case report forms collected | | |
| | | Patients excluded from safety | | |
| | | evaluation ^{**} | ×~0 | |
| | | Reason for exclusion | [Non-treatment with Adcetris, enrollment | |
| | | (duplicate counting) | before the contract period, enrollment after | |
| | | | the start date of treatment with Adcetris 31 | |
| | | | days, unknown presence or absence of | |
| | | 2 | adverse events, withdrawal of consent] | |
| | | Safety analysis set | | |
| | | Patients excluded from efficacy | | |
| | | evaluation* | | |
| | | Reason for exclusion | [Off-label use, violation of inclusion criteria, | |
| | | (duplicate counting) | violation of exclusion criteria] | |
| | | Efficacy analysis set | | |
| | Method of | | s, the following analyses will be performed to | |
| | Analysis : | prepare a case composition diagra | | |
| | 401 | | tutions surveyed will be shown for patients | |
| | à. | 0 | with a different department in the survey will be | |
| | N COL | counted as 1 medical institution. | | |
| ~ | SE | | the reason for exclusion, 0 subject will be | |
| S. | | displayed. | | |
| (by | | For patients excluded from safety evaluation and patients excluded from efficacy | | |
| 001 | | - | s by reason for exclusion will be tabulated and a | |
| 0101 | | list will be prepared. | | |
| Propertyof | | | evaluation " refer to patients excluded | |
| | | | evaluation " among patients whose survey form | |
| | | was conected. Similarly, "patient | s excluded from efficacy evaluation" refers to | |
| | | 7 | | |

Property of Takeda, For non-commercial use only and subject to the applicable terms of use patients excluded from the "patients eligible for efficacy evaluation" among the

3 Patient characteristics

3.1 Patient characteristics

Analysis Safety analysis population population :

Sex

Analysis item :

Age (years)

Time from diagnosis of Hodgkin's lymphoma to first dose of Adcetris (months) Lesion site (multiple counting)

Clinical Stage (Ann Arbor [Stage I, II, III, IV, unknown] 3 Classification) Presence or absence of B symptoms [Absent, present] [0, 1, 2, 3, 4]ECOG Performance Status Treatment category (at the start of [Outpatient/inpatient] treatment with Adcetris) Complications [Absent, present] Presence or absence of concomitant [Absent, present] renal impairment Presence or absence of concomitant [Absent, present] hepatic impairment Presence or absence of medical history [Absent, present, unknown] $\int Min \le -40.0, 40.0 \le -50.0,$ Body weight (kg) $50.0 \le -60.0, 60.0 \le -70.0,$ 70.0 <= - <= Max, not measured] $Min \le - < 18.5, 18.5 \le - < 25.0,$ BMI (kg/m^2) 25.0 <= - < 30.0, 30.0 <= - <=Max] Pregnancy [Absent, present] Breastfeeding (females only) [Absent, present]

[Male, female]

months]

[Min <= - < 18, 18 <= - < 30, 30 <= -

< 40, 40 <= - < 50, 50 <= - < 60, 60

- < 70, 70 <= - < 80, 80 <= - <= Max] [From the current month, the following

month, and the second and subsequent

bone, central nervous system, bone

[Lymph nodes, spleen, liver, lung,

marrow, skin, others]

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For the above analytical variables, frequency tabulation of discrete data and summary statistics of continuous data will be calculated.

Treatment 4

Administration status of Adcetris 4.1

Analysis Safety analysis population population : Analysis item : Adcetris initial dose (mg/kg)

> Mean dose of Adcetris per administration (mg/kg) Adcetris dose per 2 weeks (mg/kg/2 weeks) Maximum number of doses Reasons for Discontinuation of Adcetris (Multiple Count)

..., 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] 1, 2, 3, 4, 5, 6, 7, 8 ° [The treatment goal was achieved., Onset of Grade ≥ 3 "neutropenia" or "febrile neutropenia", The patient stopped visiting the hospital due to transfer, pregnancy, Due to lack of efficacy, Others

For the above analytical variables, frequency tabulation of discrete data and Method of Analysis : summary statistics of continuous data will be calculated.

4.2 **AVD** exposure

| | Analysis | Safety analysis population | |
|------------------------------------|-----------------|---|--|
| | population : | | |
| | Analysis item : | Initial dose of doxorubicin hydrochloride (mg/m^2) | |
| | | Mean dose of doxorubicin hydrochloride per administration (mg/m^2) | |
| | | Vinblastine sulfate initial dose (mg/ m ²) | |
| | , di | Mean dose of vinblastine sulfate per dose (mg/m^2) | |
| | .< | Dacarbazine initial dose (mg/m^2) | |
| | 90. | Mean single dose of dacarbazine (mg/m^2) | |
| | Method of | Summary statistics of continuous data will be calculated for the above analytical | |
| × × | Analysis : | variables. | |
| 0 | | | |
| oroperty of | 4.3 Administrat | tion status of G-CSF preparations | |
| | Analysis | Safety analysis population | |
| $\mathcal{S}_{\ell_{\mathcal{L}}}$ | population : | | |
| Ť | Analysis item : | Presence/absence of administration of [Absent, present] | |

Analysis item : Presence/absence of administration of [Absent, present] **G-CSF** preparations

Treatment status

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Safety analysis 5

Occurrence of adverse events, adverse drug reactions, and infections 5.1

5.1.1 Incidence of adverse events

- Analysis
- population :

Analysis item :

(1) Number of patients with adverse events (2) Number of adverse events (3) T med applicable Analytical

method :

- (3) Incidence of adverse events
- (4) Type of adverse event
- The method of accounting for each analysis is as follows.

[Number of patients with adverse events]

Number of patients with adverse events.

Number of adverse events

Number of adverse events experienced. 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]

Calculate as the number of patients with adverse events/the number of patients evaluable for safety ×100.

[Type of adverse event]

- AEs will be coded using MedDRA/J. The data will be broadly classified by SOC and tabulated by PT. Note that cases in the SOC of "Investigations" will be summarized by HLGT (HLGT codes are sorted in ascending order, but not output) and by PT.
- Property of Takeda. For non In the SOC, the number and percentage of patients with adverse events are presented in internationally agreed order of SOC. If the same SOC occurs more than once in the same subject, the subject will be counted as 1 subject in the SOC.
 - For PTs, the number of patients with adverse events and the incidence will be presented in ascending order of PT codes. If the same PT occurs more than once in the same patient, the patient will be counted as 1 patient for the PT.

| | 5.1.2 Occurren | nce Status of Adverse Reactions/Infections |
|------|-----------------|---|
| | Analysis | Safety analysis population |
| | population : | S |
| | Analysis item : | Adverse reactions |
| | Analytical | For the above analytical variables, the following analyses should be performed. |
| | method : | |
| | | Safety analysis population Adverse reactions For the above analytical variables, the following analyses should be performed. (1) Number of patients with adverse drug reactions (2) Number of adverse drug reactions (3) Incidence of adverse drug reactions (4) Types of adverse drug reactions, etc. The method of accounting for each analysis is as follows. [Number of patients with adverse drug reactions] |
| | | (2) Number of adverse drug reactions |
| | | (3) Incidence of adverse drug reactions |
| | | (4) Types of adverse drug reactions, etc. |
| | | The method of accounting for each analysis is as follows. |
| | | [Number of patients with adverse drug reactions] |
| | | Number of patients with adverse drug reactions |
| | | [Number of adverse drug reactions] |
| | | • Number of adverse drug reactions. If the same adverse drug reaction, etc. |
| | | occurs multiple times in the same patient, the total number of events will be |
| | | tabulated. |
| | | [Incidence of ADRs] |
| | | Calculate as the number of patients with adverse drug reactions/number of |
| | | patients evaluable for safety $\times 100$. |
| | | [Types of adverse reactions] |
| | | Adverse drug reactions will be coded using MedDRA/J. The data will be |
| | | broadly classified by SOC and tabulated by PT. Note that cases in the SOC |
| | | of "Investigations" will be summarized by HLGT (HLGT codes are sorted |
| | | in ascending order, but not output) and by PT. |
| | | In the SOC, the number of patients with adverse drug reactions/infections |
| | 1 de | and the incidence of them are described in internationally agreed order of |
| | .~~ | SOC. If the same SOC occurs more than once in the same subject, the |
| | 20. | subject will be counted as 1 subject in the SOC. |
| | X | • For PTs, the number of patients with adverse drug reactions/infections and |
| S. | | the incidence of them will be described in ascending order of PT codes. If |
| 0, | | the same PT occurs more than once in the same patient, the patient will be |
| oets | 5.1.3 Adverse e | counted as 1 patient for the PT. |
| RKOL | 5.1.3 Adverse c | events, adverse reactions, and infections included in the safety specifications |
| | 5.1.3.1 Advers | se events included in safety specifications |
| 1 | | |

5.1.2 Occurrence Status of Adverse Reactions/Infections

Adverse events included in safety specifications 5.1.3.1

Analysis Safety analysis population

| | population : | | |
|------------|------------------|--|--|
| | Analysis item : | Adverse events included in safety specifications (important identified risks) | |
| | Stratification | Seriousness [Serious, non-serious] | |
| | item : | | |
| | Method of | For the above analysis set, analyses should be performed in the same manner as | |
| | Analysis : | Seriousness [Serious, non-serious] For the above analysis set, analyses should be performed in the same manner as in Section 5.1.1 for each of the subgroups of stratification factors by risk. If the | |
| | | same SOC/PT occurs more than once in the same patient, the patient will be | |
| | | counted as 1 patient in the SOC/PT. However, if the seriousness is different. | |
| | | case shall be counted for each of serious and non-serious cases. The risks | |
| | | covered should also follow the definition provided in the important identified | |
| | | risks. | |
| | | *he | |
| | | t Status of Adverse Reactions/Infections Included in Safety Specifications | |
| | Analysis | Safety analysis population | |
| | population : | | |
| | Analysis item : | Adverse reactions corresponding to safety specifications (important identified | |
| | | risks) | |
| | | - Hora | |
| | Stratification | Seriousness [Serious, non-serious] | |
| | item : | SO | |
| | Method of | For the above analysis set, analyses should be performed in the same manner as | |
| | Analysis : | in Section 5.1.2 for each of the subgroups of stratification factors by risk. If the | |
| | | same SOC/PT occurs more than once in the same patient, the patient will be | |
| | | counted as 1 patient in the SOC/PT. However, if the seriousness is different, 1 | |
| | | case shall be counted for each of serious and non-serious cases. The risks | |
| | | covered should also follow the definition provided in the important identified | |
| | , or | risks. | |
| | 5.2 Occurrence | status of adverse events, adverse reactions, and infections in patients | |
| | excluded fro | om safety evaluation | |
| | 5.2.1 Adverse ev | vents in patients excluded from safety evaluation | |
| Š. | Subjects | Subjects excluded from safety evaluation | |
| oropertyof | analyzed : | | |
| der. | Analysis item : | Adverse events | |
| Pro: | Method of | For the above analytical variable, analyses should be performed in the same | |
| * | Analysis : | manner as in Section 5.1.1. | |
| | | | |
| | | | |

| Subjects | Subjects excluded from safety evaluation |
|------------------|---|
| analyzed : | |
| Analysis item : | Adverse reactions |
| Method of | For the above analytical variable, analyses should be performed in the same |
| Analysis : | manner as in Section 5.1.2. |
| | \checkmark^{\odot} |
| 5.3 Seriousness, | CTCAE Grade (worst value), timing of onset, outcome, occurrence of |

5.2.2 Data on adverse reactions and infections in patients excluded from safety evaluation

Seriousness, CTCAE Grade (worst value), timing of onset, outcome, occurrence of 5.3 adverse events and adverse drug reactions/infections by causal relationship with Adcetris

5.3.1 Seriousness, CTCAE Grade (worst value), timing of onset, outcome, occurrence of cu gubject to the at st adverse events by causal relationship with Adcetris

Safety analysis population

population :

Analysis

Analysis item : Adverse events

Stratification Total

item :

Seriousness CTCAE Grade(worst) Time of onset (days)

, commer

Time of onset (number of doses)

[Serious, non-serious] [Grade3, Grade4, Grade5] [1 <= - <= 14, 15 <= - <= 28, 29 <= - <= 56, 57 <= - <= 112, 113 <= - <= Max][After the first dose to before the second dose, after the second dose to before the third dose, after the third dose to before the fifth dose, after the fifth dose to before the ninth dose, and after the ninth dose

Recovered/resolved,

[Related, not related]

recovering/resolving, not recovered/not resolved, recovered/resolved with sequelae, death (due to the event), unknown]

Relationship to Adcetris

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For the above analysis sets, analyses should be performed in the same manner as in Section 5.1.1 for each of the subgroups of the stratification factors. If the same SOC/PT occurs more than once in the same patient, the patient will be counted as 1 patient in the SOC/PT. However, for the same SOC, one case will be adopted in the following order of priority, and the same PT will be adopted as one case for the content of any of the stratification items in the following order of priority.

Seriousness : serious \rightarrow non-serious

CTCAE Grade (worst) : Grade5→Grade4→Grade3

Time of onset (days) : 1 to 14 days \rightarrow 15 to 28 days \rightarrow 29 to 56 days \rightarrow 57 to 112 days $\rightarrow \geq 113$ days

ims of Use

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Time of onset (number of doses) : After the first dose to before the second dose \rightarrow After the second dose to before the third dose \rightarrow After the third dose to \bigcirc before the fifth dose \rightarrow After the fifth dose to before the ninth dose -→ After the ninth dose and thereafter Outcome: death (due to the event) \rightarrow recovered with sequelae not recovered \rightarrow recovering \rightarrow recovered \rightarrow unknown

Causal relationship with Adcetris: Related \rightarrow Not related

5.3.2 Occurrence Status of Adverse Reactions/Infections by Seriousness, CTCAE Grade (Worst Value), Time of Onset, and Outcome

| Analysis | Safety analysis population | |
|-----------------|--|--|
| population : | | Ĩ |
| Analysis item : | Adverse reactions | |
| Stratification | Total | |
| item : | Safety analysis population Adverse reactions Total | |
| | Seriousness | [Serious, non-serious] |
| | CTCAE Grade (worst) | [Grade3, Grade4, Grade5] |
| | Time of onset (days) | [1 <= - <= 14, 15 <= - <= 28, 29 <= - <= |
| | , c ^o ` | 56, 57 <= - <= 112, 113 <= - <= Max] |
| | Time of onset (number of doses) | [After the first dose to before the second |
| | | dose, after the second dose to before the |
| .40 | | third dose, after the third dose to before |
| 80. | | the fifth dose, after the fifth dose to |
| Xee | | before the ninth dose, and after the |
| ~~·~ | | ninth dose] |
| of Takeda. For | Outcome | [Recovered/resolved, |
| | | recovering/resolving, not recovered/not |
| | | resolved, recovered/resolved with |
| | | sequelae, death (due to the event), |
| | | unknown] |
| | | 1 111 0 11 1 |

Method of

For the above analysis sets, analyses should be performed in the same manner as

Analysis : in Section 5.1.2 for each of the subgroups of the stratification factors. If the same -3720 Terms of Use SOC/PT occurs more than once in the same patient, the patient will be counted as 1 patient in the SOC/PT.However, for the same SOC, one case will be adopted in the following order of priority, and the same PT will be adopted as one case for the content of any of the stratification items in the following order of priority. Seriousness: serious \rightarrow non-serious CTCAE Grade (worst value) : Grade5→Grade4→Grade3 Time of onset (days): 1 to 14 days \rightarrow 15 to 28 days \rightarrow 29 to 56 days 112 days $\rightarrow \geq 113$ days Timing of onset (number of doses): After the first dose to before the second dose \rightarrow After the second dose to before the third dose \rightarrow After the third dose to before the fifth dose \rightarrow After the fifth dose to before the ninth dose \rightarrow After the ninth dose and thereafter Outcome: death (due to the event) \rightarrow recovered with sequelae \rightarrow not recovered \rightarrow recovering \rightarrow recovered \rightarrow unknown

5.4 Occurrence Status of Adverse Reactions/Infections by Patient Background and Treatment Factors

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

AnalysisSafety analysis populationpopulation :Analysis item :Analysis item :Adverse reactionsStratificationSex

item : Roperty of Takeda. For

Age (years)

(months)

[Male, female]

[Min <= - < 18, 18 <= - < 30, 30 <= -< 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, 80 <= - <= Max]

[From the current month, the following month, and the second and subsequent months]

[Lymph nodes, spleen, liver, lung, bone, central nervous system, bone marrow, skin, others]

[Stage I, II, III, IV, unknown]

Clinical Stage (Ann Arbor

Time from diagnosis of Hodgkin's

lymphoma to first dose of Adcetris

Lesion site (multiple counting)

| | Classification) | |
|--|---|--|
| | Presence or absence of B symptoms | [Absent, present] |
| | ECOG Performance Status | |
| | Treatment classification (at the start of treatment with Adcetris) | [Outpatient/inpatient] |
| | Presence or absence of complications | [Absent, present] |
| | Presence or absence of concomitant renal impairment | [Absent, present] [0, 1, 2, 3, 4] [Outpatient/inpatient] [Absent, present] [Absent, present] [Absent, present] [Absent, present] |
| | Presence or absence of concomitant hepatic impairment | [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/m^2) | [Min] = - < 18.5, 18.5 <= - < 25.0, |
| | | $25.0 \le -30.0, 30.0 \le - \le Max$ |
| | Adcetris initial dose (mg/kg) | 25.0 <= - < 30.0, 30.0 <= - <= Max] [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] |
| | (the second s | <= - < 1.2, 1.2, 1.2 < - <= Max] |
| | | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 |
| | administration (mg/kg) | <= - < 1.2, 1.2, 1.2 < - <= Max] |
| | $\cdot \alpha$ | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9] |
| | (mg/kg/2weeks) | <= - < 1.2, 1.2, 1.2 < - <= Max] |
| | G-CSF Early administration | [Absent, present] |
| Method of | -0' | lowing analyses should be performed for |
| Analysis : | each of the subgroups of the stratification | |
| 4 | Number of patients with adverse drug rea | actions |
| , o ^r | Incidence of adverse drug reactions | |
| .X- | The method of accounting for each analy | |
| 00 | Number of patients with adverse drug | reactions |
| Xe | • Number of patients with adverse dr | ug reactions |
| 4 V | [Incidence of ADRs] | |
| ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ | Calculate as the number of patients with | adverse drug reactions/number of |
| petty of takeda. For s.4.2 Occurrence | patients evaluable for safety ×100. | |
| 5.4.2 Occurrent | ce Status of ADRs and Infections by Gen | ıder |
| Analysis | Safety analysis population | |
| 1 11111 / 515 | | |

5.4.2 Occurrence Status of ADRs and Infections by Gender

| population : | | |
|-----------------|---|-----------------------------------|
| Analysis item : | Adverse reactions | |
| Stratification | Sex [] | Male, female] |
| item : | | , V ³ |
| Method of | For the above analysis sets, analyses should be | e performed in the same manner as |
| Analysis : | in Section 5.1.2 for each of the subgroups of the | the stratification factors. |
| | | X ON |
| 5.4.3 Occurrenc | ce Status of Adverse Reactions and Infections | s by Age Group |
| Analysis | Safety analysis population | 20 |

5.4.3 Occurrence Status of Adverse Reactions and Infections by Age Group

| Analysis | Safety analysis population | |
|-----------------|--------------------------------------|--|
| population : | | NOC STREET |
| Analysis item : | Adverse reactions | 2× |
| Stratification | Age (years) | [Min <= - < 18, 18 <= - < 30, 30 |
| item : | | [Min <= - < 18, 18 <= - < 30, 30] <= - < 40, 40 <= - < 50, 50 <= - < 60, 60 <= - < 70, 70 <= - < 80, |
| | | < 60, 60 <= - < 70, 70 <= - < 80, |
| | | 80 <= - <= Max] |
| Mathad of | For the above analysis gets analyses | chauld be norformed in the same manner of |

| Method of | For the above analysis sets, analyses should be performed in the same manner as |
|----------------|---|
| Analysis : | in Section 5.1.2 for each of the subgroups of the stratification factors. |
| | |
| 5 1 1 Occurren | the Status of Adverse Departions/Difference by Presence/Absence of |

5.4.4 Occurrence Status of Adverse Reactions/Infections by Presence/Absence of

| Complicat | ion Renal Impairment | |
|-----------------|---|--------------------------------------|
| Analysis | Safety analysis population | |
| population : | | |
| Analysis item : | Adverse reactions | |
| Stratification | Presence or absence of concomitant renal | |
| item : | impairment | [Absent, present] |
| Method of | For the above analysis sets, analyses should | l be performed in the same manner as |
| Analysis : | in Section 5.1.2 for each of the subgroups of | f the stratification factors. |

5.4.5 Occurrence Status of Adverse Reactions/Infections by Presence/Absence of Complication of Hepatic Impairment

| Complication of Hepatic Impairment | | | |
|------------------------------------|--|--|--|
| Analysis | Safety analysis population | | |
| population : | | | |
| Analysis item : | Adverse reactions | | |
| Stratification | Presence or absence of concomitant | [Absent, present] | |
| item : | hepatic impairment | [Absent, present] | |
| Method of | For the above analysis sets, analyses should | d be performed in the same manner as | |
| Analysis : | in Section 5.1.2 for each of the subgroups of | of the stratification factors. | |
| | Analysis population : Analysis item : Stratification item : Method of | AnalysisSafety analysis populationpopulation :Analysis item :Analysis item :Adverse reactionsStratificationPresence or absence of concomitantitem :hepatic impairmentMethod ofFor the above analysis sets, analyses should | |

5.4.6 Occurrence Status of Adverse Reactions/Infections by Presence/Absence of Early **G-CSF Administration**

| Analysis | Safety analysis population | | |
|-----------------|---|-------------------|--------|
| population : | | | \sim |
| Analysis item : | Adverse reactions | | 0 |
| Stratification | Presence or absence of early G-CSF | [Abcont procent] | ms |
| item : | administration | [Absent, present] | KON. |
| Method of | For the above analysis sets, analyses should be performed in the same manner as | | |
| Analysis : | in Section 5.1.2 for each of the subgroups of the stratification factors. | | |

5.4.7 Occurrence Status of Adverse Reactions/Infections by Presence/Absence of Early G-CSF Administration, Seriousness, CTCAE Grade (Worst Value), Time of Onset, and Outcome

5.4.7.1 Occurrence Status of Adverse Reactions/Infections by Presence/Absence of Early **G-CSF Administration and by Seriousness**

| | | | S |
|------------|-------------------------------|---|--|
| | Analysis | Safety analysis population | ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ |
| | population : | | 1 million and a mi |
| | Analysis item : | Adverse reactions | |
| | Stratification item | Presence/absence of early G-CSF | [Absent, present] |
| | 1: | administration | |
| | Stratification item | Seriousness | [Serious, non-serious] |
| | 2: | Colo Colo | |
| | Method of | For the above analysis sets, the sam | he analyses as those in Section 5.1.2 will be |
| | analysis : | performed for each stratum of Strat | ification Item 2 after stratifying for |
| | | Stratification Item 1. If the same SC | DC/PT occurs more than once in the same |
| | × < | patient, the patient will be counted | as 1 patient in the SOC/PT. However, for the |
| | $\langle \circ \rangle$ | same SOC, one case will be adopte | d in the following order of priority, and for |
| | 20. | the same PT, one case will be adopt | ted for the content of any of the stratification |
| | Vec. | items 2 in the following order of pr | iority. |
| oropertyof | $\langle \mathcal{O} \rangle$ | Seriousness: serious \rightarrow non-seriou | 15 |
| Ŏ | | | |
| (they | 5.4.7.2 Occurr | ence Status of Adverse Reactions/I | nfections by Presence/Absence of Early |
| JOC' | G-CSF A | Administration and CTCAE Grade | e (Worst) |
| Drui | Analysis | Safety analysis population | |
| | population : | | |
| | Analyzia itam : | A | |

Analysis item : Adverse reactions

| | Stratification item | Presence/absence of early G-CSF | [Absent, present] |
|------------------|--|--|---|
| | 1: | administration | |
| | Stratification item 2 : | CTCAE Grade (worst) | [Grade3, Grade4, Grade5] hould be performed in the same manner as occurs more than once in the same |
| | Method of | For the above analysis sets, analyses sh | hould be performed in the same manner as |
| | Analysis : | in Section 5.4.7.1.If the same SOC/PT | occurs more than once in the same |
| | | patient, the patient will be counted as 1 | patient in the SOC/PT.However, for the |
| | | same SOC, one case will be adopted in | the following order of priority, and for |
| | | the same PT, one case will be adopted f | for the content of any of the stratification |
| | | items 2 in the following order of priorit | ty. |
| | | CTCAE Grade (worst) : Grade5→Grad | de4→Grade3 |
| | 5.4.7.3 Occurre | nce Status of Adverse Reactions/Infect | tions by Presence/Absence of Early |
| | G-CSF A | Administrationand Onset Time (Day) | |
| | Analysis | Safety analysis population | NOT NOT |
| | population : | | SUN |
| | Analysis item : | Adverse reactions | 6 |
| | Stratification item | Presence/absence of early G-CSF | [Absent, present] |
| | 1: | administration | |
| | Stratification item | Time of onset (days) | [1 <= - <= 14, 15 <= - <= 28, 29 |
| | 2: | 115 | <= - <= 56, 57 <= - <= 112, 113 |
| | | | <= - <= Max] |
| | Method of | For the above analysis sets, analyses sh | hould be performed in the same manner as |
| | Analysis : | in Section 5.4.7.1. If the same SOC/PT | occurs more than once in the same |
| | | patient, the patient will be counted as 1 | patient in the SOC/PT.However, for the |
| | | same SOC, one case will be adopted in | the following order of priority, and for |
| | al al | the same PT, one case will be adopted f | for the content of any of the stratification |
| | 5.4.7.4 Occurre G-CSF A Analysis | items 2 in the following order of priorit | ty. |
| | Leo | Time of onset (days): 1 to 14 days $\rightarrow 1$ | 5 to 28 days \rightarrow 29 to 56 days \rightarrow 57 to |
| Å | 01 | 112 days $\rightarrow \geq 113$ days | |
| , Õ | | | |
| (th) | 5.4.7.4 Occurre | nce Status of Adverse Reactions/Infect | tions by Presence/Absence of Early |
| Rei | G-CSF A | Administration and Onset Time (Dose) | |
| 8 ⁽⁰⁾ | Analysis | Safety analysis population | |
| v | population : | | |
| | Analysis item : | Adverse reactions | |
| | | | |
| | | 21 | |

| | Stratification item | Presence/absence of early G-CSF | [Absent, present] |
|---|---------------------|---|---|
| | 1: | administration | |
| | Stratification item | Time of onset (number of doses) | [After the first dose to before the second dose, after the second dose to before the third dose, after the third dose to before the |
| | 2: | | second dose, after the second |
| | | | dose to before the third dose, |
| | | | |
| | | | fifth dose, after the fifth dose to |
| | | | before the ninth dose, and after |
| | | | the ninth dose] |
| | Method of | For the above analysis sets, analyses should | be performed in the same manner as |
| | Analysis : | in Section 5.4.7.1.If the same SOC/PT occu | rs more than once in the same |
| | | patient, the patient will be counted as 1 patient | ent in the SOC/PT.However, for the |
| | | same SOC, one case will be adopted in the | following order of priority, and for |
| | | the same PT, one case will be adopted for the | ne content of any of the stratification |
| | | items 2 in the following order of priority. Tin | ming of onset (number of doses): |
| | | After the first dose to before the second dos | $e \rightarrow$ After the second dose to |
| | | before the third dose \rightarrow After the third dos | se to before the fifth dose \rightarrow After |
| | | the fifth dose to before the ninth dose $\rightarrow A$ | fter the ninth dose and thereafter |
| | | 06 | |
| | | nce Status of Adverse Reactions/Infections | by Presence/Absence of Early |
| | G-CSF A | Administration and Outcome | |
| | Analysis | Safety analysis population | |
| | population : | n ^o . | |
| | Analysis item : | Adverse reactions | |
| | | Presence/absence of early G-CSF | [Absent, present] |
| | 1: | administration | |
| | Stratification item | Outcome | [Recovered/resolved, |
| | 2: | | recovering/resolving, not |
| | 90. | | recovered/not resolved, |
| | X | | recovered/resolved with |
| , And | | | sequelae, death (due to the |
| 0' | | | event), unknown] |
| all a | Method of | For the above analysis sets, analyses should | be performed in the same manner as |
| 90 | Analysis : | in Section 5.4.7.1.If the same SOC/PT occu | rs more than once in the same |
| Propertyof | | patient, the patient will be counted as 1 patient | ent in the SOC/PT.However, for the |
| | | same SOC, one case will be adopted in the | following order of priority, and for |
| | | the same PT, one case will be adopted for the | ne content of any of the stratification |

items 2 in the following order of priority.

Outcome: death (due to the event) \rightarrow recovered with sequelae \rightarrow not recovered \rightarrow recovering \rightarrow recovered \rightarrow unknown

Administration status of Adcetris and AVD by outcome at the onset of adverse drug 5.5 reactions/infections

| | Outcome: death (due to the event) \rightarrow re | covered with sequence \rightarrow not |
|-----------------|--|--|
| | recovered \rightarrow recovering \rightarrow recovered | \rightarrow unknown |
| 5.5 Administra | ntion status of Adcetris and AVD by outco | $\rightarrow \text{ unknown}$ $\rightarrow \text{ unknown}$ $\text{ome at the onset of adverse drug}$ $[Absent, present] \qquad OPIICADIE$ |
| reactions/ir | ifections | in's |
| Analysis | Safety analysis population | X ON |
| population : | | × × |
| Analysis item : | Adverse reactions | |
| Stratification | Presence or absence of change due to | |
| item 1 : | this event | [Absent, present] |
| | Breakdown of changes | [Dose reduction, drug cessation [dose |
| | Dreakdown of changes | delay], discontinuation] |
| Stratification | Outcome | [Recovered/resolved, |
| item 2 : : | | recovering/resolving, not |
| | | recovered/not resolved, |
| | | recovered/resolved with sequelae, |
| | 10 | fatal, unknown] |
| | Total | |

The subjects in the above analysis will be stratified with Stratification Item 1 (this product), and the frequency of the number of adverse drug reactions/infections will be tabulated for each stratum in Stratification Item 2. san inblasti connon connon connon connon connon The same tabulation will be performed for AVD (Doxorubicin hydrochloride,

vinblastine sulfate, and dacarbazine).

Method of

Analysis :

6 Efficacy analysis

6.1 Antitumor response after the end of frontline therapy

| 6.1 Antitumor | response after the end of frontline therapy | | | |
|---|---|--|--|----------------|
| Analysis | Patients in the efficacy analysis population for whom antitumor response was assessed Antitumor effect [With PET assessment, without PET assessment, total] For each of the above analysis items, frequency of assessment results will be | | | |
| population : | assessed | | | |
| Analysis item : | Antitumor effect [With PET assessment, without PET | | | |
| | assessment, total] | | | |
| Method of | For each of the above analysis items, frequency of assessment results will be \checkmark | | | |
| Analysis : | tabulated for patients in the efficacy evaluation set for whom antitumor response | | | |
| has been assessed to calculate the response rate. In addition, a band graph will be prepared for the above analysis results. This tabulation will be performed for the entire population and patients excluding those who received a dose exceeding the | | | | |
| | | | | approved dose. |
| | | | | |

6.2 Antitumor effect after the end of frontline therapy by patient background factor and ,10 treatment factor lucia act for

| | Analysis | Patients in the efficacy analysis set for w | hom antitumor response was assessed |
|----------|-----------------|--|--|
| | population : | | 2 |
| | Analysis item : | Antitumor effect Sex Age (years) | [With PET assessment, without PET |
| | | OL. | assessment, total] |
| | Stratification | Sex S | [Male, female] |
| | item : | | |
| | | Age (years) | [Min <= - < 18, 18 <= - < 30, 30 <= - |
| | | ACT IN A REAL OF | <40, 40 <= -<50, 50 <= -<60, 60 |
| | | anti. | <= - < 70, 70 <= - < 80, 80 <= - <= |
| | | ~~ ^{CO} | Max] |
| | | Time from diagnosis of Hodgkin's | [From the current month, the following |
| | (or | lymphoma to first dose of Adcetris | month, and the second and subsequent |
| | | (months) | months] |
| | 9.9. | Lesion site (multiple counting) | [Lymph nodes, spleen, liver, |
| | X | | lung,bone,central nervous system, |
| × | | | bone marrow, skin, others] |
| 0 | | Clinical Stage (Ann Arbor | [Stage I, II, III, IV, unknown] |
| | | Classification) | |
| .090 | | Presence or absence of B symptoms | [Absent, present] |
| Property | | ECOG Performance Status | [0, 1, 2, 3, 4] |
| | | Treatment classification (at the start of | |
| | | treatment with Adcetris) | [Outpatient/inpatient] |
| | | | |

| Presence or absence of complications | [Absent, present] |
|--|---|
| Presence or absence of concomitant renal impairment | [Absent, present] |
| Presence or absence of concomitant hepatic impairment | [Absent, present] [Absent, present] [Absent, present, unknown] |
| Presence or absence of medical history | [Absent, present, unknown] |
| Body weight (kg) | [Min <= - < 40.0, 40.0 <= - < 50.0, 🖉 |
| | 50.0 <= - < 60.0, 60.0<= - < 70.0, |
| | 70.0 <= - <= Max, Not measured] |
| BMI (kg/m ²) | [Min <= - < 18.5, 18.5 <= - < 25.0, |
| | 25.0 <= - < 30.0, 30.0 <= - <= |
| | Max] |
| Adcetris initial dose (mg/kg) | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] |
| | <= - < 1.2, 1.2, 1.2 < - <= Max] |
| mean dose of Adcetris per | [Min < = - < 0.6, 0.6 < = - < 0.9, 0.9] |
| administration (mg/kg) | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9] $[Min <= - < 0.6, 0.6 <= - < 0.9, 0.9]$ |
| Adcetris dose per 2 weeks | Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 |
| (mg/kg/2weeks) | <= - < 1.2, 1.2, 1.2 < - <= Max] |
| Presence or absence of early G-CSF | [Absent, present] |
| administration | |
| For each of the above avaluate items, the | frequency of accomment regults will be |

Method of Analysis :

For each of the above analysis items, the frequency of assessment results will be tabulated by stratum of the stratification items for patients who have been assessed for antitumor effect among the patients evaluable for efficacy, and the property of Takeda. response rate will be calculated. This tabulation will be performed for the entire population and patients excluding those who received a dose exceeding the

7 Adverse reactions and infections in the additional pharmacovigilance plan

7.1 Adverse reactions and infections included under the additional pharmacovigilance plan (Attached Form 12)

| 7.1 Adverse rea | actions and infections inclue | ded under the additional pharma | covigilance plan |
|--------------------------|-------------------------------|---|---------------------|
| (Attached F | Form 12) | | Se |
| Analysis | Safety analysis population | | |
| population : | A 1 | | S |
| Analysis item : | risks) | nding to safety specifications (impo | ortant identified |
| Stratification item : | Seriousness | [Serious, non-serious] | |
| Analytical | For the above analytical var | riable, the following analyses shoul | ld be performed for |
| method : | each of the subgroups of the | e stratification factors, in accordance | ce with (Note) 1~4 |
| | of Form 12 in the Attachme | nt of PSEHB/PED Notification No | 0. 0325 No. 10 |
| | dated March 25, 2020. | <u></u> 0 | |
| | (1) Number of subjects | with events and the incidence of the | em |
| | | the risk name and risk name shall b | be in accordance |
| | with the definition describe | d in Important Identified Risks. | |
| Property of Takeda. For | with the definition describe | Bours | |

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8 Case summary in post-marketing surveillance

Case summary in post-marketing surveillance (Attached form 16) 8.1

sct to the applicable terms of Use Subjects to be CRF collected cases analyzed : Analysis item : Case No. Name of medical institution Sex Age Reason for use (Disease code, disease name) Concomitant conditions (Disease code, disease name) Route of administration Maximum dose Mean dose Unit Duration of use (duration of treatment with Adcetris) Concomitant medicinal products (Drug Code, Drug Name) Degree of effect Adverse Reactions (Disease code, disease name, and outcome) CRF number withdrawal Reason for withdrawal G-CSF Early administration of drug product For the above analysis items, a list will be prepared in accordance with the Analytical Guidelines for Preparation of the Reexamination Data Entry File issued by method : PSEHB/PED Notification No. 1119 No. 3 dated November 19, 2020.

Preparation history (version control)

| | version | date | Author/reviewer | comment | l co |
|------------|----------------|------------|-----------------|----------------------------------|--------|
| | Version 1.0 | 2023.01.26 | | Preparation of the first version | son US |
| Propertyof | (akeda | Fornom | commercialus | reparation of the first version | erms |

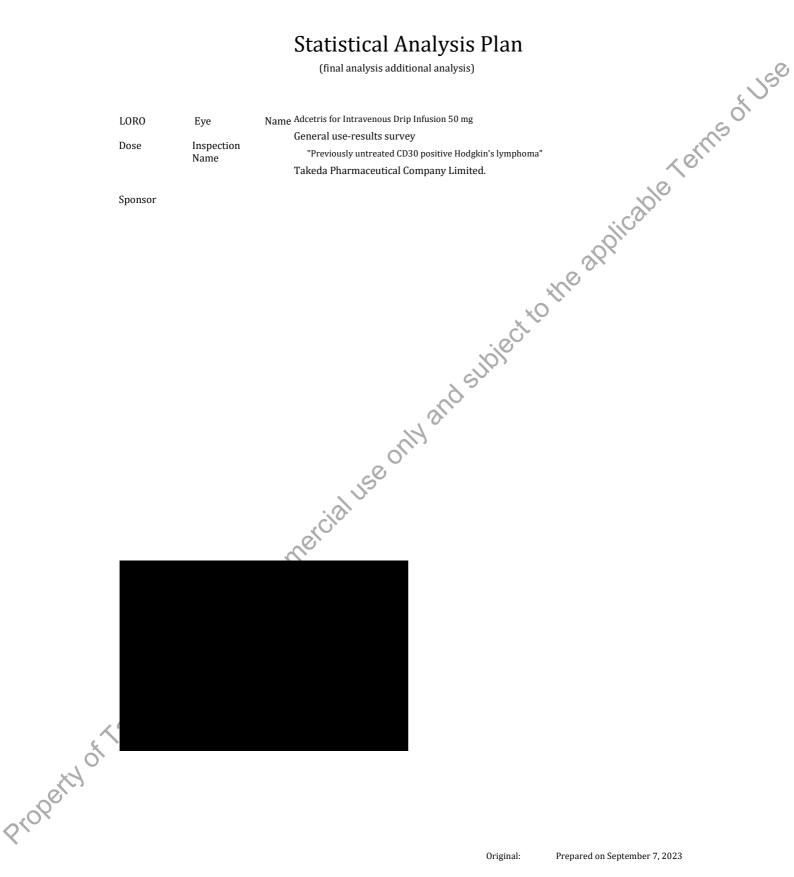


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| | |
| 3.1 Data on adverse drug reactions/infections | |
| 3.1.1 Occurrence Status of Adverse Reactions • Infections by the Presence or Absence of Early Administration or Prophylactic Administration of G-CSF Preparations (This | |
| Adverse reactions, etc. that occurred within 14 days after the start of administration of the drug) | 3 |
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| 3.2. 1 Occurrence Status of Adverse Reactions • Infections by Patient Background Factor and Treatment Factor (Start of this drug | |
| Treatment) | |
| Adverse reactions, etc. that occurred within 14 days after the start of study treatment |) |
| 3.22 Occurrence Status of Adverse Reactions • Infections by Sex (Adverse Reactions that Occurred within 14 Days after the Start of thi | S |
| drug Treatment) | |
| Use, etc.) |) |
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| ADVERSE REACTIONS, etc11 | |
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| drug treatment) | |
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| drug treatment) | |
| Adverse reactions, etc. that occurred by the time of onset) | L |
| 3.3 Occurrence Status of ADRs • Infections by Seriousness, CTCAE Grade (Worst Value), and Outcome (Administration of this drug | |
| Adverse reactions, etc. that occurred by 14 days after the start of administration) | |
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| Property of Takeda. For non- | |
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| | |

1 Definition 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.

Linuxerse events that are not "not related" to this drug as Linuxysis plan, the title is Linuxerse events: Adverse events assessed as "serious" by the investigator. Takeda The Important Medical Events List is used as the Medically Significant AE List, and events listed in the MedDRA code list (PT code) are handled as serious even if the investigator's assessment is "non-serious." ated 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. •Adverse reactions, etc.: An abbreviation of the term "adverse reactions • infections." Adverse events that are not "not related" to this drug as

•Serious adverse events: Adverse events assessed as "serious" by the investigator. Takeda

•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 11:100 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. С

•Duration of treatment with this drug (days): end date of treatment with this drug (day): start date of treatment with this drug +1

•Timing of onset of an adverse event (or adverse drug reaction, etc.): The date of onset of the adverse event (or adverse drug reaction, etc.) will be calculated as the start date of the first administration of one drug +1.

•Time from Hodgkin's lymphoma diagnosis to first dose of this drug:

•Actual number (months) = (Year of the first administration of this drug-Year of the diagnosis of Hodgkin's lymphoma) X12+ (Month of the first administration of this drug - Month of the diagnosis of Hodgkin's lymphoma) If the month of the diagnosis is unknown, January of the year will be used for calculation. Ø

(Renal

•Patients complicated with renal impairment: Takeda MedDRA query (Hereinafter referred to as TMQ) in the field of disease name

Complications applicable to "Disease " are listed.

•Patients complicated with hepatic impairment; Patients in whom a complication corresponding to MedDRA standard query (Hereinafter referred to as SMQ) code 20000005 (liver disorder SMQ [scope: narrow]) is entered in the disease name field.

.ated a . For horn BMI (kg/m 2): Calculated as weight (kg)/height (m) 2 (rounded to the first decimal place).

- ٠ Early dose: G-CSF is administered within 5 days of the first dose of this drug.
- ٠ Non-early dose: G-CSF is administered on or after Day 6 of the first dose of this drug.
- •
- •
- ٠
- •
- Property of Takeda. For non-commercial use on wand and a state of the second of the se this drug +1 However, G-CSF preparations should be administered from the first dose of this drug to before the second dose.

3

1.2 Populations for Analyses

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:.

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propend of takeds, for non-commercial use only and subject to the applicable terms of use

(2) Patient characteristics

2.1 Patient characteristics by early use or prophylactic use of G-CSF preparations

| 2.1 Patient characteristic | cs by early use or prophylactic use of G-CSF preparations | |
|--|---|--|
| Analysis population: Analysis item: Sex | Subjects evaluable for safety | |
| Апатуыз пени. зел | Age (years) | [Male, female] [Min <=- < 18,18 <= - < 30, 30 <=-< 40, 40 <= - < 50, 50 <= - < 60, 60 <=-< 70, 70 <= - < 80, 80 <=- <=Max] [Min <= - < 65, 65 <= - <= Max][From the current month, the following month, and the |
| | Time from diagnosis of Hodgkin's lymphoma | month after next] [Lymph nodes, spleen, liver, lung, bone, CNS, |
| | to first dose of this drug (months) Disease site (multiple counting) | bone marrow, skin, others] [Oral stage, stage B, stage B, stage B unknown] [Absent, present] |
| | Clinical stage (Ann Arbor staging) Presence or absence of B symptoms ECOG Performance Status Treatment category (at the start of this drug | [0,1,2, 3, 4] [Outpatient/inpatient] Absent, Present] Absent, Present] Absent, Present] Absent] |
| | treatment) Complications Presence or absence of concurrent renal impairment | [Absent, present, unknown] [Min <= - < 40.0, 40.0 <= - < 50.0,50.0 <= - < 60.0, 60.0<= - < 70.0,70.0 <= - <= Max, not measured] |
| | Presence or absence of concurrent hepatic impairment Presence or absence of medical history Weight (kg) | [Min <=- < 18.5, 18.5 <= - < 25.0,25.0 <= - < 30.0, 30.0 <=- <=Max] Absent, Present] Absent, Present] Absent, Present] Absent, Present] Absent] |
| | BMI(kg/m2) | |
| Stratification item- | | |
| | Pregnancy (females only) | |
| 80. | Breastfeeding status (females only) | |
| Stratification item: | Presence or absence of early administration of G-CSF preparations | |
| x 10 | Presence or absence of prophylactic administration of G-CSF preparations | |
| Analytical method: | For the above analytical variables, in each of the subgroup preparations | os of stratification factors (early administration of G-CSF |
| Stratification item: Stratification item: Analytical method: | Frequency tabulation of discrete data and summary statist or absence of and the presence or absence of prophylactic | |

(3) Matters related to safety

3.1 Occurrence status of adverse reactions/infections

| 3.1 | 1 | Occurrence s | tatus of adverse reactions/infections |
|-----------------|----------|-------------------------------|---|
| 3.1 | 1.1 | Occurrence Sta | tus of Adverse Reactions • Infections by Presence or Absence of Early Administration or Prophylactic |
| | | Administration | Adverse Reactions • Infections by Presence of Absence of Early Administration of Prophylactic a of G-CSF Preparations (e.g., Adverse Reactions that Occurred within 14 Days after the Start of this drug Subjects evaluable for safety Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug |
| | | Treatment) | 1/2- |
| An | alysis | population: | Subjects evaluable for safety |
| Ana | alysis i | item: | Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug |
| Stra | atifica | tion item: | Presence or absence of early administration of G-CSF preparations [Absent, present] Presence or absence of prophylactic administration of G-CSF preparations [Absent, present] |
| Ana | alytica | l method: | The above analysis items were analyzed by the presence or absence of early administration of G-CSF preparations 🕜 |
| and | d by th | e presence or ⁱ at | sence of early administration of G-CSF preparations. |
| | | | The following analyses will be performed by the presence or absence of prophylactic |
| | | | administration of the drug product. |
| | | | (1) Number of patients with adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug |
| | | | (2) Number of adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug |
| | | | (3) Incidence of adverse drug reactions, etc. that occurred within 14 days after the start of administration of this drug |
| | | | (4) Types of adverse drug reactions, etc. that occurred within 14 days after the start of administration of this |
| | | | drug 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.] |
| | | | • Calculate with the number of patients with adverse drug reactions/number of patients evaluated for safety X100. [Types of adverse reactions] |
| | | | 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 |
| Property of the | | • | ascending order of PT codes. A subject who experienced the same PT more than once should be counted as 1 subject with the PT. |
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3.2 Occurrence Status of Adverse Reactions/Infections by Patient Background and Treatment Factor

3.2. 1 Occurrence of adverse drug reactions/infections by patient background factor and treatment factor (e.g., adverse drug reactions that occurred within 14 days after the start of administration of this drug)

| that occurred v | within 14 days after the start of administration of this drug) | | С |
|-------------------------|--|---|-------|
| Analysis population | Subjects evaluable for safety | | otUse |
| Analysis item: | Adverse reactions, etc. that occurred within 14 days after the | start of administration of this drug | 0 |
| Stratification item: Se | ex | [Male, female] | |
| | Age (years) | [Min <=- < 18,18 <= - < 30, 30 <=- | |
| | | < 40, 40 <= - < 50, 50 <= - < 60, 60<=-< 70.70 | |
| | | <= - < 80, 80 <=- <=Max] | |
| | | [Min <= - < 65, 65 <= - <= Max][From the | |
| | | current month, the following month, and the | |
| | | month after next] | |
| | Time from diagnosis of Hodgkin's lymphoma | *// [©] | |
| | to first dose of this drug (months) | [Lymph nodes, spleen, liver, lung, bone, CNS, | |
| | Disease site (multiple counting) | bone marrow, skin, others] | |
| | | [Oral stage, stage B, stage B, stage B unknown] | |
| | Clinical stage (Ann Arbor staging) | [Absent, present] | |
| | Presence or absence of B symptoms | [0,1,2, 3, 4] | |
| | ECOG Performance Status Treatment category (at the start of this drug | [Outpatient/inpatient] | |
| | treatment) | [Absent, present] [Absent, present] | |
| | Complications | Absent, Present] | |
| | Presence or absence of concurrent renal | Absent, present, unknown] | |
| | impairment | [Min <= - < 40.0, 40.0 <= - < 50.0, 50.0 <= - < 60.0, | |
| | Presence or absence of concurrent hepatic | 60.0<= - < 70.0,70.0 <= - <= Max, not measured] | |
| | impairment | [Min <=- < 18.5, 18.5 <= - < 25.0,25.0 <= - < 30.0, | |
| | Presence or absence of medical history | 30.0 <=- <=Max] | |
| | Weight (kg) | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= | |
| | | - < 1.2, 1.2,1.2 < - <= Max] | |
| | CONT. | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= | |
| | | - < 1.2, 1.2,1.2 < - <= Max] | |
| | ~0` | [Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= | |
| à | BMI (kg/m2) | - < 1.2, 1.2,1.2 < - <= Max] | |
| <0. | | Absent, Present] | |
| S. | | | |
| (BOC | | | |
| XOL | This drug loading dose (mg/kg) | | |
| operty of Takeda. For | Mean dose of this drug per administration (mg/kg) | | |
| (C) | This drug dose per 2 weeks (mg/kg/2 weeks) | | |
| 001 | Presence or absence of early administration of G-CSF | | |
| 07 | preparations | | |
| * | | | |
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Analytical method:

For the above analytical variable, the following analyses should be performed for each stratum of the stratification factor.

Number of patients with adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug

Incidence of adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug The ternsoiuse method of counting in each analysis is as follows.

[Number of patients with adverse reactions, etc.]

• Number of patients with adverse reactions, etc. [Incidence of adverse reactions, etc.] Calculate with the number of patients with adverse drug reactions/number of patients evaluated for safety X100.

3.2. 2 Occurrence status of ADRs • Infections by sex (ADRs that occurred within 14 days after the start of administration of this drug, etc.)

Subjects evaluable for safety

Analysis population:

Analytical method: stratification factor.

Analysis item:

Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug Stratification item: Sex [Male, female]

For the above analysis set, the following analyses will be performed for each stratum of the

Number of patients with adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug

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Number of adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug Incidence of adverse drug reactions, etc. that occurred within 14 days after the start of administration of this drug Type of adverse drug reactions, etc. that occurred by 14 days after the start of administration of this drug The method of counting in 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.]

Calculate with the number of patients with adverse drug reactions/number of patients evaluated for safety X100. [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.

y PT, order of PT. C PT. C PT. C PT. C PT. C 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

| | 323 Onset status of ADRs | • infections by age group (ADRs, etc. that occurred within 14 days after the start of administration of this |
|------------|--|--|
| | drug) | |
| | Analysis population: | Subjects evaluable for safety |
| | Analysis item: | Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug |
| | Stratification item: | Age (years) [Min <=- < 18,18 <= - < 30, 30 <=- |
| | | < 40, 40 <= - < 50, 50 <= - < 60, 60 |
| | | Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug Age (years) $\begin{bmatrix} Min <=- < 18, 18 <= - < 30, 30 <=- \\< 40, 40 <=- < 50, 50 <= - < 60, 60 \\<=- < 70, 70 <= - < 80, 80 <=- <=Max \end{bmatrix}$ [Min <= - < 65, 65 <= - <= Max] |
| | : | [Min <= - < 65, 65 <= - <= Max] |
| | Analytical method: | For the above analytical variable, the same analyses as those described in Section 3.2.2 were performed for each |
| | stratum of the stratificatio | |
| | | Perform. |
| | | NO. |
| | | |
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| | | Solution (Solution (Soluti |
| | 3.2.4 Incidence of ADRs | Infections by presence or absence of concurrent renal impairment (ADRs, etc. that occurred within 14 days |
| | | f administration of this drug) |
| | Analysis population: | Subjects evaluable for safety |
| | Analysis item: | Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug |
| | Stratification item: | Presence or absence of concurrent renal impairment [Absent, present] |
| | Analytical method: | For the above analysis set, the same analyses as those described in Section 3.2.2 were performed for each stratum of |
| | the stratification factor. | 8 |
| | | Perform. |
| | | |
| | | |
| | | |
| | | ^o |
| | 3. 2.5 Occurrence status | of ADRs • Infections by presence or absence of concurrent hepatic impairment (ADRs, etc. that occurred |
| | within 14 days | after the start of administration of this drug) |
| | Analysis population: | Subjects evaluable for safety |
| | Analysis item: | Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug |
| | Stratification item: | Presence or absence of concurrent hepatic impairment [Absent, present] |
| | Analytical method: | For the above analysis set, the same analyses as those described in Section 3.2.2 were performed for each stratum of |
| | the stratification factor. | O_{1} |
| | | Perform. |
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| * | the stratification factor | |
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3.3 Occurrence Status of Adverse Reactions • Infections by Seriousness, CTCAE Grade (Worst Value), and Outcome (Adverse Reactions, etc. that Occurred within 14 Days after the Start of this drug Treatment) Analysis Set: Subjects evaluable for safety Analysis item: Adverse reactions, etc. that occurred within 14 days after the start of administration of this drug

Stratification item: Total

| Seriousness | [Serious, non-serious] | | |
|---|--|--|--|
| CTCAE Grade (worst value) | [Grade3, Grade4, Grade5] | | |
| Outcome | [recovered/resolved, recovering/resolving, not | | |
| recovered/not resolved. recovered/resolved but later] | | | |

ermsonuse Presence of residual disease, death (due to this event), In the above analysis

population, subjects with or without early administration of G-CSF preparations and subjects with G-CSF

unknown] Analysis method:

For each of the stratification factors with or without prophylactic administration of the product, the same analyses as those in Section 3.1.1 will be performed. 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 2° according to the following order of priority for any of the stratification factors.

Seriousness: Serious - Non-serious

ropety of Takeda. For non-commercial use on want subject is a large on the subject is a large of ._____ uvurst value): Grade5—Grade4—Grade3 Outcome: Death (due to this event) Recovered once with sequelae 1 Not recovered/Not resolved T Recovering/Resolving T Unknown

[4] Re-output of the final analysis figures/tables (replacement)

4.1 Patient characteristics

Analysis population: Subjects evaluable for safety Analysis item: Sex

Age (years)

insof Use [Male, female] [Min <=- < 18,18 <= - < 30, 30 <=-< 40, 40 <= - < 50, 50 <= - < 60, 60 <=-< 70, 70 <= - < 80, 80 <=- <=Max] [From the current month, the following month? and the month after next]

Time from diagnosis of Hodgkin's lymphoma to first dose of this drug (months) Disease site (multiple counting)

Clinical stage (Ann Arbor staging) Presence or absence of B symptoms ECOG Performance Status

Treatment category (at the start of this drug treatment)

Complications

Presence or absence of concurrent renal impairment

Presence or absence of concurrent hepatic

Presence or absence of medical history

[Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others] [Oral stage, stage B, stage B, stage B unknown] [Absent, present] [0,1,2,3,4] [Outpatient/inpatient] [Absent, present] [Absent, present] [Absent, present] Absent, present, unknown] Min <= - < 40.0, 40.0 <= - < 50.0,50.0 <= - < 60.0, 60.0<= - < 70.0,70.0 <= - <= Max, not measured] [Min <=- < 18.5, 18.5 <= - < 25.0, 25.0 <= - < 30.0, 30.0 <=- <= Max]

. of medical k. BMI(kg/m2) P Absent, Present] Breastfeeding status (females Absent, Present] only. For the above analytical variables, frequency tabulation of discrete data and continuous data

Analysis Methods:

Summary statistics will be calculated.

4.2 Occurrence Status of Adverse Drug Reactions/Infections by Patient Background Factor and Treatment Factor

Analysis population: Subjects evaluable for safety Analysis item: Adverse reactions, etc.

Stratification item: \$ex

Age (years)

[Male, female] [Min <=- < 18,18 <= - < 30, 30 <=-

< 40, 40 <= - < 50, 50 <= - < 60, 60

<=-< 70, 70 <= - < 80, 80 <=- <=Max] [From the current month, the following month, and the month after next]

Time from diagnosis of Hodgkin's lymphoma to first dose of this drug (months) Disease site (multiple counting)

Clinical stage (Ann Arbor staging)
Presence or absence of B symptoms
ECOG Performance Status
Treatment category (at the start of this drug treatment)
Complications
Presence or absence of concurrent renal impairment
Presence or absence of concurrent hepatic impairment
Presence or absence of medical history
Weight (kg)

icable terms of Use [Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others] stage B, stage B, stage B, unknown [Absent, present] [0,1,2, 3, 4] [Outpatient/inpatient] Absent, Present] Absent, Present] Absent, Present] [Absent, present, unknown] [Min <= - < 40.0, 40.0 <= - < 50.0, 50.0 <= - < 60.0, 60.0<= - < 70.0,70.0 <= <= Max, not measured] [Min <=- < 18.5, 18.5 <=- < 25.0,25. <= - < 30.0, 30. <= - <= Max] [Min <= < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= onlyand - < 1.2, 1.2,1.2 < - <= Max] Min <= - < 0.6, 0.6 <= - < 0.9, 0.9 <= - < 1.2, 1.2, 1.2 < - <= Max] Absent, Present]

BMI(kg/m2)

This drug loading dose (mg/kg) Mean dose of this drug per administration (mg/kg)

5°

This drug dose per 2 weeks (mg/kg/2 weeks) Presence or absence of early administration of G-CSF preparations

Analytical method: Analytical method: Analytical method: Analytical method: Analytical method: Analytical method:

For the above analytical variable, the following analyses should be performed for each stratum of the stratification factor.

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, etc.]

•Number of patients with adverse reactions, etc.

[Incidence of adverse reactions, etc.]

Calculate with the number of patients with adverse drug reactions/number of patients evaluated for safety X100.

4.3 Antitumor effect after the end of frontline therapy by patient demographics and treatment factors

Analysis population: Patients whose antitumor effect was assessed among the patients evaluated for efficacy

Analysis item: Antitumor effect

Stratification item: Sex

Age (years)

< 40, 40 v= - v 50, 50 v= - v 60, 60 times of US® , 80 v= - v= honth *' [With PET assessment, without PET assessment, total] [Male, female] [Mln v=- < 18,18 v= - < 30, 30 v=

v= - v 70, 70 v= - v 80, 80 v= - v=

Max] [From the current month, the following month, Time from diagnosis of Hodgkin's lymphoma and the month after next]

to first dose of this drug (months) Disease site (multiple counting)

Clinical stage (Ann Arbor staging) Presence or absence of B symptoms **ECOG Performance Status**

Treatment category (at the start of this drug treatment) Complications

Presence or absence of concurrent renal impairment Presence or absence of concurrent hepatic impairment

Presence or absence of medical history

Mean dose of this drug per administration (mg/kg)

This drug dose per 2 weeks (mg/kg/2 weeks) Presence or absence of early administration of G-CSF

[Lymph nodes, spleen, liver, lung, bone, CNS, bone marrow, skin, others] [Oral stage, stage B, stage B, stage B unknown] Absent, Present] [0,1,2,3,4] [Outpatient/inpatient] Absent, Present] Absent, Present] Absent, Present] [Absent, present, unknown] [Min v= - v 40.0, 40.0 v= - v 50.0,

50.0 v= - v 60.0, 60.0v= - v 70.0, 70.0 v= -v= Max, not measured [Min v= - v 18.5, 18.5 v= - v 25.0,

25., v= -v 30.0, 30. v= - v=Max] [Min v= - v 0.6, 0.6 v= - v 0.9, 0.9 v=-v 1.2, 1.2,1.2 v - v= Max] Min v= - v 0.6, 0.6 v= - v 0.9, 0.9 v= -v 1.2, 1.2, 1.2 v - v= Max] Min v= - v 0.6, 0.6 v= - v 0.9, 0.9 v= -v 1.2, 1.2,1.2 v - v= Max] Absent, Present]

For each of the above analysis items, the tumor response was assessed in the efficacy analysis set. Frequency tabulation of assessment results by stratum of stratification items in patients who were assessed

propend of takeds, for non-commercial use only and subject to the applicable terms of use will be performed to calculate the response rate. This tabulation will be performed for the overall population and the

Preparation history (version control)

| | Version | Date | Author/Reporter | Comments | e e e e e e e e e e e e e e e e e e e |
|------------|---------------------|----------|-----------------|---|---------------------------------------|
| | Original Version | 2023.9.7 | | from the diagnosis of Hodgkin's lymphoma to the first dose of this drug" at | erms of Use |
| Propertyof | 24000 | Fornon | ommercialus | the final analysis. Therefore, correction of the derivation method and reported to the derivation method and reported to the additional states and tables were planned. | |