26/07/2024

Re:	Clinical Trial Application
Product:	Anitocabtagene Autoleucel
Universal Trial No:	KT-US-679-0788
EU Clinical Trial -Nr.:	2024-511188-26
Title:	A Phase 3, Randomized, Open-Label Study to Compare the Efficacy and Safety of Anitocabtagene Autoleucel Versus Standard of Care Therapy in Participants With Relapsed/Refractory Multiple Myeloma
Kite Submission number:	DT001

Dear Sir/Madam,

Please find enclosed a complete Clinical Trial Application with supporting documentation for Kite Study KT-US-679-0788.

Kite proposes Germany as reference member state.

Study KT-US-679-0788 (iMMagine-3) is a Phase 3, randomized, open-label, multicenter study evaluating the safety and efficacy of anitocabtagene autoleucel (previously referred to as CART-ddBCMA) versus investigator's choice from 4 standard of care therapy (SOCT) options in participants with relapsed/refractory multiple myeloma (RRMM) who have received 1 to 3 prior lines of therapy including an immunomodulatory drug (IMiD) and an anti-CD38 monoclonal antibody (mAb).

Participants will be randomized in a 1:1 ratio to receive either anitocabtagene autoleuceol or SOCT. Prior to randomization, the investigator will select the SOCT regimen for the participant from among the following 4 treatment regimens:

- Pomalidomide, bortezomib, and dexamethasone (PVd)
- Daratumumab, pomalidomide, and dexamethasone (DPd)
- Carfilzomib, daratumumab, and dexamethasone (KDd)
- Carfilzomib and dexamethasone (Kd)

If the participant is assigned to the SOCT arm, they will receive the selected regimen. If the participant is assigned to the anitocabtagene autoleucel arm, the SOCT regimen initially selected may be used as optional bridging therapy, if required per the investigator's discretion.

Both safety and efficacy data will be assessed. Response assessments will be timed from randomization for both arms and will continue until progression as per IMWG criteria, even if the treatment cycles on the SOCT arm are discontinued due to other reasons, such as unacceptable toxicity.

The primary objective of this study is as follows:

- To compare the efficacy of anitocabtagene autoleucel versus SOCT in participants with RRMM as measured by progression-free survival (PFS) per blinded independent review committee (IRC)

Study KT-US-679-0788 (iMMagine-3) is considered by the Sponsor to be a Category Two clinical trial.

Reviewers' notes:

Protocol: It is noted that the KT-US-679-0788 protocol dated 07 March 2024 is the original protocol and it contains all the information on the design of this study.

IMP/IMPD:

The IMPs in the study are:

- Anitocabtagene autoleucel (115×10^6 [$\pm$ 10×10^6] CAR+ viable T cells, dispersion for infusion)

Anitocabtagene autoleucel is a genetically modification organism (GMO). The complete quality information for this IMP is included in the IMPD. All non-clinical and clinical information related to anitocabtagene autoleucel is included in the Investigator Brochure Edition 1.5, dated 01 December 2023.

In the comparator arm of the study, IMPs to be used as part of the PVd, DPd, KDd or Kd regimens are:

- Bortezomib
- Carfilzomib
- Daratumumab
- Dexamethasone
- Pomalidomide

These comparator IMPs are defined only by the active ingredients in the protocol and are not fixed to particular products (the investigative sites may use any IMP that is authorised in the Member State concerned). Generic products may be used in the study. The comparator IMPs will be sourced by each investigative site. They will be used in accordance with their current product

labels and institutional guidelines. The sponsor has selected one valid summary of product characteristics (SmPC) for inclusion in this application as equivalent to the IMPD/IB for all comparator IMPs that contain the active substances listed above and are used at any clinical trial site.

The IMPs to be used in the study are not classified as a narcotic, psychotropic or radiopharmaceutical.

AxMP:

The Auxiliary Medicinal Product (AxMP) in the study are listed below

- Cyclophosphamide, Fludarabine, Mesna, Acetaminophen (Paracetamol), Diphenhydramine, Tocilizumab, Dexamethasone, Methylprednisolone, Acylclovir, Famiciclovir, Levofloxacin, Posaconazole, Amphotericin B, Isavucanazole, Cefepime, Piperacillin, Tazobactam, Meropenem, Vancomycin

These medicinal products are classified as AxMPs in accordance with the Guidance on Auxiliary Medicinal Products in Clinical Trials (28 June 2017). Other concomitant medications that are considered optional and thus not relevant for the design of the clinical trial are not included as AxMPs. As per the new recommendations on the use of AxMPs in Clinical trials by the Clinical Trials Coordination and Advisory Group (CTAG), the AxMPs stated above are unmodified and authorised therefore, no SmPC is submitted within our application. The AxMPs to be used in the study are not classified as a narcotic, psychotropic or radiopharmaceutical.

Risk/Benefit assessment for the study: The benefit/risk assessment for the study is presented in the clinical trial protocol, section 1.5 which complements the IMPDs for this study.

Reference Safety Information: The RSI for each product is noted below:

- Anitocabtagene autoleucel: Section 6.7 of the anitocabtagene autoleucel IB (Edition 01 December 2023)
- Bortezomib: Section 4.8 of the Bortezomib Fresenius Kabi SmPC
- Carfilzomib: Section 4.8 of the Kyprolis SmPC
- Daratumumab: Section 4.8 of the Darzalex SmPC
- Dexamethasone: Section 4.8 of the Neofordex SmPC
- Pomalidomide: Section 4.8 of the Imnovid SmPC

Data Safety Monitoring Board (DSMB): The most recent version of the DSMB Charter is provided with this submission.

GLP Studies: Kite confirms that the GLP studies included in the Investigator's Brochure for anitocabtagene autoleucel were conducted in, or inspected by, a country that has implemented the OECD Mutual Acceptance of Data (MAD) system.

Scientific Advice: This study has received scientific advice relating to this clinical trial and the investigational medicinal product by EMA. A summary of scientific advice can be found as a standalone document within this application.

This study has also received scientific advice relating to quality aspects by (PEI) and ANSM (Simultaneous National Scientific Advice). A summary of scientific advice can be found as a standalone document within this application.

In addition, the study has received a Type B scientific advice meeting with the FDA relating to this clinical trial and the investigational medicinal product. A summary of scientific advice can be found as a standalone document within this application.

PIP: There is no PIP involved with this study.

Orphan Designation: The IMPs in this study do not have an orphan designation.

Additional Comments:

All Counties

Considerations on GMO submissions: Applications for the contained use or deliberate release of GMOs in context of this clinical trial will be performed in each member state concerned according to the national requirements.

Germany

Request for a consenting opinion according to § 36 StrlSchG

Please note that the consenting opinion of the ethics committee must indicate that the requirements of § 36 StrlSchG have been taken into account.

Since radioactive substances or ionizing radiation are used on patients for the purpose of medical research, there is an obligation to obtain an approval or to notify the Federal Office for Radiation Protection (BfS) according to §§ 31 ff. StrISchG.

Please send your statement according to § 36 StrlSchG to: CASGermany.SM@ppd.com

Italy

Name: Comitato Etico Nazionale per le sperimentazioni cliniche relative alle terapie avanzate ("ATMP")

Postal Address: Via del Tritone, 181 00187 Roma, Italy

Email: segr.cen.atmp@aifa.gov.it

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Duty Stamps virtually paid pursuant to art.15 DPR 642/72 with authorization N. 28877/2015 dated 5 February 2015 by the Tax Agency – Ufficio Territoriale Milano 2

Netherlands

For The Netherlands, the proposed Medical Research Ethics Committee to review this submission is CCMO. As this is a study with a GMO as investigational product, it is required to be reviewed by this ethics committee.

Name: Centrale Commissie Mensgebonden Onderzoek (CCMO)

Postal address: Postbus 16302, 2500 BH Den Haag, The Netherlands

Visiting address: Bezuidenhoutseweg 30, 2594 AV Den Haag, The Netherlands

Email: tc@ccmo.nl

Spain

Name: CEIm Provincial de Sevilla

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Czech Republic

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Yours faithfully,

The Applicant

Cover Letter Annex II – List of Submitted Documents for Czech Republic Part II

Document	Version / Date
K1_KT-US-679-0788_Recruitment_Informed-Consent-Procedure_CZ_13Jun2024_Public	13Jun2024
L1_KT-US-679-0788_GDPR ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_GDPR ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Main ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_Main ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Optional Biopsy ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_Optional Biopsy ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Optional Future Research ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_Optional Future Research ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Pregnant Participant FUL_ ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_Pregnant Participant FUL_ ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Pregnant Partner FUL_ ICF_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L1_KT-US-679-0788_Pregnant Partner FUL_ ICF_CZ_Czech_v1.0_19Jun2024_NotPublic	V1.0_19Jun2024
L1_KT-US-679-0788_Scout ICF_CZ_Czech_v1.0_09Jul2024_Public	V1.0_09Jul2024
L1_KT-US-679-0788_Scout ICF_CZ_Czech_v1.0_09Jul2024_NotPublic	V1.0_09Jul2024
L1_KT-US-679-0788_Scout Telephone Data ICF_CZ_Czech_v1.0_09Jul2024_Public	V1.0_09Jul2024

L1_KT-US-679-0788_Scout Telephone Data ICF_CZ_Czech_v1.0_09Jul2024_NotPublic	V1.0_09Jul2024
L2_KT-US-679-0788_Table of Visits and Procedures_CZ_Czech_v1.0_19Jun2024_Public	V1.0_19Jun2024
L2_KT-US-679-0788_Table of Visits and Procedures_CZ_Czech_19Jun2024_NotPublic	V1.0_19Jun2024
M1_CV_PI_Hajek-Roman_FN-Ostrava_CZ_04Jul2024	04Jul2024
M1_CV_PI_Pour-Ludek_FN-Brno_CZ_08Jul2024	08Jul2024
M2_KT-US-679-0788_Declaration-of-interest_Hajek-Roman_PI_FN-Ostrava_CZ_04Jul2024	04Jul2024
M2_KT-US-679-0788_Declaration-of-interest_Pour-Ludek_PI_FN-Brno_CZ_08Jul2024	08Jul2024
N1_KT-US-679-788_Statement-of-Suitability_CZ_Hajek_04Jul2024	04Jul2024
N1_KT-US-679-788_Statement-of-Suitability_CZ_Pour_08Jul2024	08Jul2024
N2_KT-US-679-788_List_of_participating sites_CZ_01Jul2024	01Jul2024
O1_KT-US-679-0788_Insurance-Certificate_CZ_21Jun2024	21Jun2024
O2_KT-US-679-0788_Insurance_Sponsor_Statement_CZ_01Jul2024	01Jul2024
O2_KT-US-679-0788_Insurance_Terms-Conditions_CZ_Czech_01Jan2020	01Jan2020
P1_KT-US-679-0788_Compensation_for_Trial_Participants_v1_0_CZ_24May2024	v1.0_24May2024
P1_KT-US-679-0788_Financial_Coverage_sponsor_Statement_CZ_01Jul2024	01Jul2024
R1_KT-US-679-0788_Data-Protection-Declaration_CZ_01Jul2024	01Jul2024
S1_KT-US-679-0788_Use-of-Biological-Samples-Declaration_CZ_v1.0_17Jun2024	v1.0_17Jun2024