21-11-2023

Request for Assessment of a New Initial Clinical Trial Application

EU Trial Number	2023-506906-38-00
Investigational Medicinal Product	Epcoritamab
Study Number	M22-003
Study Title	A Phase 3, Multicenter, Randomized, Open-Label Trial to Evaluate the Safety and Efficacy of Epcoritamab + Rituximab and Lenalidomide (R2) Compared to Chemoimmunotherapy in Previously Untreated Follicular Lymphoma (EPCORE™FL-2)
Study Phase	3
Sponsor	AbbVie Deutschland GmbH & Co. KG
First in Humans	No
Scientific Advice	Yes
PIP Study	No
Orphan Designation	Yes
Resubmission	No
Low Interventional Clinical Trial	No
Participating Countries	Belgium, Bulgaria, Croatia, Czechia, Denmark, France, Germany, Greece, Hungary, Italy, Netherlands, Poland, Portugal, Romania, Slovakia, Spain, Sweden.
Proposed Reporting Member State	Spain

Dear Sir/Madam,

The Applicant AbbVie authorized on behalf of the Sponsor, AbbVie Deutschland GmbH & Co. KG, hereby requests the assessment of the enclosed initial Clinical Trial Authorisation (CTA) application.

The following information is provided within this Covering Letter in support of the request for Authorisation of an Initial CTA:

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1.0 Brief Summary of Study M22-003

This is an open-label, randomized, global, Phase 3 trial, evaluating the safety and efficacy of three treatment arms. Eligible subjects will be randomized (2:2:1) to:

- Arm A: ER2
- Arm B: Investigator's choice CIT
- Arm C: R2

The total treatment duration will be 120 weeks for all treatment arms (approximately 2.5 years). After the completion of therapy, all subjects will be followed in the Post-Treatment Follow-up Period until disease progression. After disease progression, subjects will be followed for survival. Response to therapy and monitoring for disease progression will be assessed using Lugano 2014 criteria with PET-CT imaging. After subjects achieve 2 consecutive assessments of Complete Metabolic Response, disease assessments may be performed by CT only, with the exception of the 120-week assessment which will require mandatory PET-CT for all subjects. Any new occurrence of PD or CR assessed by CT alone must be confirmed by PET.

Scientific advice: On 30 May 2023 the EMA - Scientific Advice Working Party (SAWP) provided the final scientific advice letter to AbbVie's request for the design of a first line (1L) Phase 3 study of epcoritamab (M22-003) in combination with Rituximab followed by epcoritamab in combination with lenalidomide and epcoritamab monotherapy maintenance treatment in previously untreated CD20+ follicular lymphoma (FL). A summary of the advice is enclosed in Section 5 of this application.

Information Relating to the IMPs, Auxiliary IMPs.

The study includes the following IMP's:

IMP	Narcotic	Psychotropic	Radiopharmaceutical	Contains a genetically-modified organism(s)	Regulatory Status
Epcoritamab	No	No	No	No	Authorised, but Clinical supply will be used.
Rituximab	No	No	No	No	Authorised
Lenalidomide	No	No	No	No	Authorised
Doxorubicin HCL	No	No	No	No	Authorised
Vincristine	No	No	No	No	Authorised
Cyclophosphamide	No	No	No	No	Authorised
Obinutuzumab	No	No	No	No	Authorised
Bendamustine Hydrochloride	No	No	No	No	Authorised

Prednisone	No	No	No	No	Authorised

The study includes the following Auxiliary IMP's:

AIMP	Narcotic	Psychotropic	Radiopharmaceutical	Contains a genetically-modified organism(s)	Regulatory Status
Tocilizumab	No	No	No	No	Authorised

Please note, clinical trial packaging and labelling of Epcoritamb, Rituximab, Lenalidomide, Doxorubicin HCL, Vincristine, Cyclophosphamide, Obinutuzumab, Bendamustine Hydrochloride and Prednisone, as well as EU QP release, will be performed by AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany.

A full Investigational Medicinal Product Dossier is enclosed for Epcoritamab as per the "Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial" March 2010 (Revision 3).

SUSAR Reporting

The sponsor will be responsible for Suspected Unexpected Serious Adverse Reactions (SUSAR) reporting for the Investigational Medicinal Products (IMPs) in accordance with the Clinical Trials Regulation (EU) No 536/2014.

Appendix A of the IB will serve as the reference safety information (RSI) for Epcoritamab. Section 4.8 Tabulated list of adverse events of the SmPC will serve as the reference safety information (RSI) for Rituximab, Lenalidomide, Doxorubicin HCL, Vincristine, Cyclophosphamide, Obinutuzumab, Bendamustine Hydrochloride and Prednisone in trial M22-003. Please note, the enclosed SmPCs will only be used for the RSI purposes in this study.

Please do not hesitate to contact us if you require any further clarification on this study.

Yours faithfully,

AbbVie

Confirmation of stamp duty for Italy, AIFA:

Stamp duty €16

The payment of stamp duty is absolved in virtual mode (AUT. Agenzia entrate 7169/13) according to art. 35 of Presidential Decree 642/1972

Details of the Ethics Committees:

1. **Ethics Committee for Italy:**
   Comitato Etico Territoriale (CET) delle Marche

2. **Central Ethics Committee for Bulgaria:**
   Ethics Committee for Clinical Trials
   8 Damyan Gruev street
   Sofia 1303
   Bulgaria

3. **Ethics Committee for Spain**
   CEIm Regional de la Comunidad de Madrid

4. **Germany**
   In Germany, approval by BfS (Federal Office for Radiation Protection) is required. Therefore, the ethics committee in Germany should also review the application in this respect to determine whether the clinical trial is ethically justifiable according to § 36 of the Radiation Protection Act.