NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
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Epcoritamab for treating relapsed or refractory follicular lymphoma

Company/Developer	AbbVie

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 31063	NICE TSID: N/A	UKPS ID: 663553

Licensing and Market Availability Plans

Currently in phase I/II clinical trials.

Summary

Epcoritamab is currently in development for treatment of relapsed or refractory follicular lymphoma (FL). FL is a type of non-Hodgkin's lymphoma (NHL) which affects white blood cells. In FL, the affected white blood cells start to multiply in an abnormal way and begin to aggregate in certain parts of the body such as the lymph nodes. Some FL patients may experience no symptoms. Some symptoms that may occur include painless swelling of the lymph nodes, shortness of breath, fatigue, night sweats and weight loss. A recurrence of lymphoma after going into complete remission is known as a relapse. Lymphoma that is unresponsive to therapy is called refractory lymphoma. The condition can become more difficult to treat if it is relapsed or refractory, as treatment options are limited and often not very effective.

Epcoritamab is an antibody designed to simultaneously attach to a protein (CD3) found on T cells (a type of white blood cell) and a second protein (CD20) found on B cells (another type of white blood cell) within the body. By attaching to the two proteins, the medicine is expected to trigger an immune response which will eventually kill the cancerous B cells. This treatment will allow patients with FL to utilise the body's own T-cells against cancerous B cells. Therefore, it could provide an additional treatment option for relapsed or refractory FL, where previous treatments have failed.

Proposed Indication

For treatment of adult patients with relapsed or refractory follicular lymphoma (FL).[1]

Technology

Description

Epcoritamab (DuoBody®-CD3xCD20, GEN3013) is a subcutaneously administered, bispecific antibody which directly targets cytotoxic T cells by simultaneously binding to CD3 on T-cells and CD20 on B cells. This elicits an immune response, whereby T cells are redirected and activated to kill CD20-expressing malignant lymphoma B cells.[2] In preclinical evaluation, epcoritamab resulted in potent and selective T-cell–mediated cytotoxic activity against CD20+ malignant B cells.[2,3]

Epcoritamab is in development for treatment of patients with relapsed or refractory follicular lymphoma. In the phase I/II clinical trial (EPCORE™NHL-1; NCT03625037), epcoritamab will be administered in 28-day cycles (once weekly step-up doses in weeks 1-3 of cycle 1, then full doses once weekly through cycle 3, once every 2 weeks in cycles 4-9, and once every 4 weeks in cycle 10 and thereafter) until disease progression or unacceptable toxicity. [1,3]

Key Innovation

Several CD20 mAbs are in development for the treatment of B-cell NHL, often in combination with chemotherapy.[4] Nonetheless, a high incidence of disease relapse occurs after treatment with currently available CD20-targeting mAbs, urging the development of more innovative therapies targeting CD20.[3] While conventional mAbs can eliminate target cells via several mechanisms, they do not exploit the cytotoxic machinery of T-cells. Epcoritamab is a novel full-length IgG1 bispecific antibody redirecting CD3+ T-cells to CD20 expressing cells which has been shown to induce T-cell activation and T-cell-mediated cytotoxicity towards malignant B cells.[2,3,5] If licensed, epcoritamab will offer an additional treatment option for patients with relapsed or refractory FL.

Regulatory & Development Status

Epcoritamab does not currently have marketing authorisation in the EU/UK for any indication.

Epcoritamab is currently in Phase II/III clinical trials as both monotherapy and in combination with other therapies, and at different lines of treatment for various types of NHL, including relapsed/refractory diffuse large B cell lymphoma (DLBCL) and FL.[6]

Patient Group

Disease Area and Clinical Need

NHL is a cancer of the lymphatic system. This is the system that helps protect your body from infection and disease.[7] NHL occurs when a type of white blood cell (lymphocytes) start to divide abnormally. Such lymphocytes don't have a resting time, and therefore divide continuously. If lymphocytes divide before reaching maturity, they cannot fight infection as normal lymphocytes do. The abnormal lymphocytes instead, collect in the lymph nodes, or in other places such as the bone marrow or spleen. They can then grow into tumours and begin to cause problems in the lymphatic system.[8] NHL can affect people at any age but is more common over the age of 50. Epstein Barr virus (EBV) infection, which causes glandular fever, may slightly increase the risk of developing some types of NHL.[9] The most common symptom of lymphoma is a painless swelling in the lymph nodes in the neck, armpit or groin.[7] About nine out of 10 people diagnosed with NHL (90%) have a B-cell lymphoma. The most common types of B-cell lymphoma are diffuse large B-cell lymphoma (DLBCL) and FL.[10]

Nearly 14,000 people are diagnosed with a type of NHL every year in the UK. Roughly 20% of people with NHL (two in ten) are diagnosed with follicular lymphoma.[11] According to the 2021-22 Hospital Episodes Statistics data, for FL, there were 21,163 FCE, resulting in 20,446 admissions, 18,999 -day cases and 11,593 FCE bed days. (ICD-10 code C82).[12]

Recommended Treatment Options
NICE recommends the following pharmacological therapies for adult patients with relapsed/ refractory FL:[13-15] • Rituximab subcutaneous injection in combination with chemotherapy for induction or rituximab monotherapy in maintenance or where other treatment options have been exhausted. • Lenalidomide with rituximab. • Obinutuzumab with bendamustine followed by obinutuzumab maintenance for those who do not respond or progress up to six months after treatment with rituximab or a rituximab-containing regimen.

Clinical Trial Information

Trial	**(EPCORE™ NHL-1); NCT03625037; EudraCT; 2017-001748-36** A Phase 1/2, Open-Label Safety Trial of GEN3013 in Patients With Relapsed, Progressive or Refractory B-Cell Lymphoma **Phase I/II:** Recruiting **Location(s):** 9 EU countries, UK, USA, Canada, and other countries. **Primary completion date**: January 2025
Trial Design	Sequential assignment, open label
Population	N= 700 participants (estimated) with CD20+ mature B cell-neoplasm; adults aged 18 years and older; relapsed, progressive and/or refractory disease following treatment with an anti-CD20 monoclonal antibody potentially in combination with chemotherapy and/or relapsed after autologous stem cell rescue. There are three subgroups in the phase 2 part of the study: responsive rate (R/R) aggressive NHL, R/R indolent NHL and R/R mantle cell lymphoma (MCL).
Intervention(s)	Epcoritamab will be administered by subcutaneous injections in cycles of 28 days
Comparator(s)	No comparator
Outcome(s)	Primary Outcome Measure(s): • Escalation part: Incidence of Dose Limiting Toxicities (DLTs) [time frame: during the first cycle (28 days) in each cohort] To determine the recommended phase 2 dose (RP2D) and the maximum dose • Escalation part: Incidence and severity of Adverse Events (AEs) [time frame: from first dose until the end of the safety follow-up period (4 weeks after last dose)] Treatment-emergent AEs (TEAEs) as assessed by CTCAE v5.0. Abnormal laboratory values are reported as AEs per protocol • Expansion part: Objective Response Rate (ORR) [time frame: from first dose until up to 1 year after the last participant's first dose] Defined as proportion of participants who have a partial or complete response (PR or CR) following treatment with Epcoritamab. Determined by the Lugano response criteria, assessed by the Independent Review Committee (IRC) See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	**(EPCORE™ NHL-2)**; NCT04663347; **EduraCT:** 2020-000845-15 A Phase 1b/2, Open-Label Trial to Assess the Safety and Preliminary Efficacy of Epcoritamab (GEN3013; DuoBody®-CD3xCD20) in Combination With Other Agents in Subjects With B-cell Non-Hodgkin Lymphoma (B-NHL) **Phase I/II:** Recruiting **Location(s):** 10 EU countries, UK, USA, and Australia **Primary completion date:** March 2029
Trial Design	Non-randomised, parallel assignment, open label
Population	N = 662 (estimated) with CD20-positive NHL; adults aged 18 and older
Intervention(s)	Epcoritamab (SC) alongside one of the following dependent on study arm and indication: • Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) • Rituximab and lenalidomide (R2) • Rituximab and bendamustine (RB) • Rituximab, cytarabine, dexamethasone, and oxaliplatin/carboplatin (R-DHAX/C) • Gemcitabine and oxaliplatin • Rituximab and lenalidomide • Epcoritamab maintenance • R-mini-CHOP
Comparator(s)	No comparator
Outcome(s)	Primary Outcome Measures: • Number of participants with DLTs [time frame: DLTs are evaluated during the first cycle (28 days) in each cohort] • Number of AEs [time frame: from first dose up to safety follow-up (60 days after last trial treatment)] • Preliminary anti-tumour activity [time frame: up to approximately 3 years after the last subject's first treatment] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of epcoritamab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab [TA629]. May 2020.
- NICE technology appraisal. Idelalisib for treating refractory follicular lymphoma [TA604]. October 2019.
- NICE technology appraisal. Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma [TA137]. February 2008.

- NICE clinical guideline. Non-Hodgkin's lymphoma: diagnosis and management (NG52). July 2016.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Haematopoietic Stem Cell Transplantation (Adult). B04/S/a.
- NHS England. Interim Clinical Commissioning Policy Statement: Use of Plerixafor for Stem Cell Mobilisation. B04/PS/a. September 2013.
- NHS Commissioning Board. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. NHSCB/B04/P/a. April 2013.

Other Guidance

- European Society for Medical Oncology (ESMO). Diffuse Large B-Cell Lymphoma (DLBCL), Follicular Lymphoma (FL) and Chronic Lymphocytic Leukaemia (CLL). March 2023. [16]
- European Society for Medical Oncology (ESMO). Consensus Conference on malignant lymphoma: management of 'ultra-high-risk' patients. 2018.[17]
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Hodgkin's Lymphomas. 2015.[18]

Additional Information

References

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