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Newcastle University

Health Technology Briefing
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Mosunetuzumab (subcutaneous injection) for treating relapsed or refractory follicular lymphoma

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 38557	NICE ID: Not Available	UKPS ID: 674561

Licensing and Market Availability Plans

Currently in phase I/II clinical development.

Summary

Mosunetuzumab is in clinical development for the treatment of relapsed or refractory follicular lymphoma (FL). FL is a type of blood cancer originating in the lymph nodes of the immune system, and it is the most common type of low-grade Non-Hodgkin's Lymphoma in the UK. A relapsed or refractory cancer is one that has come back after a successful treatment regimen or has not responded to a previous regimen, meaning a new interventional approach is required in both cases. Although the survival rates for FL are relatively high compared to some other cancers, the disease can cause a range of issues that decrease patient quality of life. There are currently limited options for the second-line or greater treatments required for relapsed and refractory patients with FL. This indicates that there remains an unmet need to treat relapsed or refectory FL.

Mosunetuzumab is a monoclonal antibody (proteins that bind to specific targets, such as certain proteins that exist on the surface of cancerous cells) that stimulates the body's immune system by triggering T-cells (a type of white blood cell) to find and kill cancer cells. Mosunetuzumab can be administered intravenously or subcutaneously. If licensed, mosunetuzumab would provide another option for treatment of relapsed or refractory FL.

Proposed Indication

For the treatment of relapsed or refractory B-cell non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukaemia (CLL).[1]

Technology

Description

Mosunetuzumab (BTCT4465A, Lunsumio[1,2]) is an anti-CD20/CD3 T-cell antibody which binds to CD20-expressing B-cells. Mosunetuzumab is a conditional agonist, meaning bound B-cells are only killed when it simultaneously binds to CD20 on B-cells and CD3 on T-cells. Since this antibody recognises two different antigens it is known as a bispecific antibody. This simultaneous binding of mosunetuzumab causes the formation of an immunologic synapse between a target B cell and a cytotoxic T-cell, which in turn induces T-cell activation. Activated T-cells then release perforin and granzymes, which travel through the immunologic synapse causing B-cell lysis and death.[3]

Mosunetuzumab is currently in clinical development for the treatment of relapsed or refractory B-cell NHL (of which FL is a common form) and CLL. In a phase I/II clinical trial (NCT02500407), participants with FL are given mosunetuzumab via intravenous (IV) or subcutaneous (SC) injection as part of a dose escalation (administered in 21-day cycles with cycle 1 step-up dosing: 1 mg on cycle 1 day 1, 2 mg on cycle 1 day 8, 60 mg on cycle 1 day 15 and cycle 2 day 1, and 30 mg on day 1 of cycle 3 and onwards).[4] Participants assigned to an atezolizumab combination group will also receive 1200 mg of intravenous (IV) atezolizumab in combination with mosunetuzumab.[1]

Key Innovation

Treatment options for relapsed or refractory FL are limited and there is no standard of care.[5] IV mosunetuzumab is currently licensed for the treatment of relapsed or refractory FL, with initial infusions being administered over a minimum of 4 hours.[3] SC injections of mosunetuzumab may be preferable to IV infusions for some patients due to the lack of needing to penetrate a vein and the potentially reduced timescale of the process, as has been suggested in trials investigating other FL treatments.[6]

If licensed, SC mosunetuzumab will provide an additional treatment option for patients with relapsed or refractory B-cell NHL and CLL.

Regulatory & Development Status

Mosunetuzumab as a monotherapy is indicated for the treatment of adult patients with relapsed or refractory FL who have received at least two prior systemic therapies.[3]

Mosunetuzumab is also in phase II and III clinical development for diffuse large B-cell lymphoma.[7]

Patient Group

Disease Area and Clinical Need

Lymphoma is a type of blood cancer affecting the white blood cells of the lymphatic system. It begins in the lymph nodes where lymphocytes begin to divide abnormally and collect in the nodes. These affected

lymphocytes lose their infection-fighting properties, increasing the risk of infection.[8,9] NHL can cause a variety of symptoms which range from painful and/or disruptive through to fatal. Symptoms include swelling of the lymph nodes, night sweats, unintentional weight gain, breathlessness and excessive itching sensations.[10] Several risk factors are associated with an increased risk of developing NHL, such as living with a compromised immune system, being an older adult, and certain infections such as helicobacter pylori, human immunodeficiency virus (HIV) and T cell lymphoma virus 1.[11] NHL can be divided into low grade or high grades depending on how quickly the NHL is likely to grow and spread within the body. About 90% of people diagnosed with NHL have a B-cell lymphoma, of which the most common types are diffuse large B-cell lymphoma (DLBCL) and FL.[12]

NHL is the 6th most common cancer in the UK, accounting for 4% of all new cancer cases (2016-2018)[13]. The age standardised incidence rate of follicular NHL in England is 4.5 and 3.9 per 100,000 amongst males and females respectively[14]. In England (2022-23) there were 20,913 finished consultant episodes (FCEs) and 20,199 admissions for FL (ICD-10 code C82), which resulted in 18,719 day cases and 12,302 FCE bed days[15]. In England (2020), there were 2172 patients diagnosed with NHL[14]. For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates were 79.4% and 65.6% respectively[16].

Recommended Treatment Options

NICE recommends the following treatment options for relapsed or refractory FL:[17]

- Obinutuzumab with bendamustine for treating FL that did not respond or progressed up to 6 months after treatment with rituximab or a rituximab-containing regimen[18]
- Rituximab, as a monotherapy or in combination with chemotherapy, for the treatment of relapsed or refractory stage III/IV follicular NHL when all alternative treatment options have been exhausted[19]
- Lenalidomide with rituximab for adults with previously treated FL (grade 1 to 3A)[20]

Clinical Trial Information

Trial	NCT02500407, An Open-Label, Multicenter, Phase I/II Trial Evaluating the Safety, Efficacy, and Pharmacokinetics of Escalating Doses of Mosunetuzumab (BTCT4465A) as a Single Agent and Combined with Atezolizumab in Patients with Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia **Phase 1/2:** Active, not recruiting **Location(s):** two EU countries, UK, USA, Canada, Australia and Republic of Korea **Primary completion date:** November 2025
Trial Design	Non-randomised, sequential assignment, open label
Population	N = 836 (estimated); aged 18 years and older; Eastern Cooperative Oncology Group performance status of 0 or 1; relapsed after or failed to respond to at least one prior treatment regimen and for whom there is no available therapy expected to improve survival
Intervention(s)	• IV monotherapy: mosunetuzumab via IV infusion • Atezolizumab combination group: 1200 mg IV atezolizumab combined with mosunetuzumab • SC monotherapy: mosunetuzumab via SC injection

Comparator(s)	
Outcome(s)	Primary outcome measures: • Maximum tolerated dose of mosunetuzumab for 1 cycle (21 days) • Percentage of participants with adverse events up to approximately 14 months • Mosunetuzumab serum concentration up to approximately 12 months • Atezolizumab serum concentration up to approximately 12 months • Percentage of participants with complete response as assessed using standard criteria for NHL up to approximately 4 years
Results (efficacy)	Complete response was recorded in 60% of patients, this was significantly higher than the historical control complete response rate with copanlisib of 14% (p<0·0001).[4]
Results (safety)	Cytokine release syndrome was the most common adverse event (44% of patients) and was predominantly grade 1 (26% of patients) and grade 2 (17% of patients), and primarily confined to cycle 1. The most common grade 3-4 adverse events were neutropenia or decreased neutrophil count (27% of patients), hypophosphataemia (17%), hyperglycaemia (8%), and anaemia (8%). Serious adverse events occurred in 47% of patients. No treatment-related grade 5 (i.e,, fatal) adverse event occurred.[4]

Estimated Cost

Mosunetuzumab costs £220 per 1 mg/1 ml concentrate for a solution for infusion vial, and £6,600 per 30 mg/30 ml concentrate for solution for infusion vial. Depending on the length of the course of treatment the total cost of treatment is £66,660 for 8 cycles or £126,600 for 17 cycles.[21]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Ibrutinib for treating relapsed or refractory follicular lymphoma (ID1251). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tazemetostat for treating relapsed or refractory follicular lymphoma after 2 or more treatments (ID6349). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Epcoritamab for treating relapsed or refractory follicular lymphoma after 2 or more treatments (ID6338). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Zanubrutinib with obinutuzumab for treating relapsed or refractory B-cell follicular lymphoma after 2 or more treatments (TSID 11915). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tafasitamab with lenalidomide and rituximab for treating relapsed or refractory follicular or marginal zone lymphoma after 1 or more anti-CD20 treatments (ID6413). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Lisocabtagene maraleucel for treating relapsed or refractory diffuse large B-cell lymphoma, high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma or follicular lymphoma grade 3B after first-line chemotherapy (ID3887). Expected date of issue December 2024.

- NICE technology appraisal. Mosunetuzumab for treating relapsed or refractory follicular lymphoma in adults who have had 2 or more systemic therapies. May 2023,
- NICE technology appraisal. Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab (TA629). May 2020.
- NICE technology appraisal. Lenalidomide with rituximab for previously treated follicular lymphoma (TA627). April 2020.
- NICE technology appraisal. Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma (TA306). February 2014.
- NICE technology appraisal. Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (TA137). February 2008.
- NICE guideline. Non-Hodgkin's lymphoma: diagnosis and management (NG52). July 2016.
- NICE quality standard. Haematological cancers (QS150). June 2017.

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 Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Teenagers & Young Adults. B17/S/a.

Other Guidance

- European Society of Medical Oncology. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.[22]
- British Society for Haematology. The investigation and management of follicular lymphoma. 2020.[23]
- European Society of Medical Oncology. ESMO Consensus conferences: guidelines on malignant lymphoma. Part 2: marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma. 2013. [24]

Additional Information

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