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Newcastle University

Health Technology Briefing
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Tafasitamab with lenalidomide as add-on therapy for previously treated follicular lymphoma or marginal zone lymphoma

Company/Developer	Incyte Corp

☐ New Active Substance ☒ Significant Licence Extension (SLE)

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Licensing and Market Availability Plans

Tafasitamab with lenalidomide as add-on therapy for previously treated follicular lymphoma or marginal zone lymphoma is in phase 3 clinical development in the 2020 trial, InMIND.[1]

Summary

Tafasitamab with lenalidomide (as an add-on to rituximab) is in clinical development for treating relapsed or refractory follicular lymphoma (FL) of any grade except 3B, or marginal zone lymphoma (MZL). These are slow-growing types of cancer that develop when white blood cells, called B lymphocytes, grow out of control. Common symptoms include painless swellings in the neck, armpit or groin, night sweats, weight loss or high temperatures. MZL may cause these or additional symptoms. These lymphomas often respond well to initial treatment but later return (relapsed cancer). Cancer that does not respond to treatment is called refractory. Most people with FL or MZL live for many years but may have multiple relapses requiring treatment. Relapsed disease often responds less well to treatment so there is a need for additional therapy options.

Tafasitamab and rituximab are manufactured antibodies, similar to those made by the immune system, and are given intravenously. Tafasitamab binds to proteins on the surface of B lymphocytes called CD-19, which can trigger cell death or help the immune system recognise and kill the cells. Rituximab binds a different protein, CD-20, with similar effects and lenalidomide (taken orally) complements this. If licensed, tafasitamab with lenalidomide and rituximab will provide a new targeted immunotherapy option for patients with relapsed/refractory FL or MZL.

Proposed Indication

Relapsed/refractory (R/R) follicular lymphoma (FL) or marginal zone lymphoma (MZL) in adults after previous treatment with systemic anti-CD20 immunotherapy or chemo-immunotherapy.[1]

Technology

Description

Tafasitamab (minjuvi) is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes, a type of white blood cell that usually aids in fighting infection, but proliferates abnormally in FL, MZL and some other lymphoma types).[2,3,4] Upon binding to CD19, tafasitamab mediates B-cell lysis directly by inducing cell death (apoptosis) or indirectly by engagement of immune effector cells like natural killer cells, γδ T-cells and phagocytes. The Fc modification enhances the antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis.[2]

Tafasitamab, in combination with lenalidomide as an add-on to rituximab, is in development for treatment of adults with R/R MZL or grade 1, 2 or 3a FL.[1,5] In the phase III clinical trial (NCT04680052), patients were administered tafasitamab intravenously (IV) alongside lenalidomide (given orally) for 12 cycles, plus rituximab IV on cycles 1-5.

Key Innovation

There is a need for improved therapies to target 'indolent' B-cell FL or MZL, as relapsed disease is common and most people need several different treatments over the course of the disease.[6,7,8,9,10] Patients with FL generally live for extended periods of time, often experiencing multiple relapses requiring several lines of therapy.[11] Exposure over time to multiple treatments is thought to have a cumulative effect in the relapsed setting.[12] There is a particular unmet need for effective treatments for FL that relapses within two years of initial treatment (20% of cases) as early relapse is a predictor of worse outcomes.[11]

Tafasitamab is one of the first therapeutic monoclonal antibodies to target the CD19 ligand to promote B-cell death.[13] Lenalidomide and rituximab also promote immune-cell mediated B-cell death.[5,6] Lenalidomide further limits tumour growth also by inhibiting B-cell proliferation and the formation of new blood vessels, and it may have a synergistic action with immunotherapy (rituximab).[14,15]

Tafasitamab plus lenalidomide as an add-on to rituximab is a new combination in clinical development for second-line treatment of FL or MZL.[1,5] Treatment of these low-grade B-cell lymphoma types is a new indication for tafasitamab in any combination.[15] If licensed, tafasitamab with lenalidomide and rituximab will offer a new treatment option for R/R MZL or FL.

Regulatory & Development Status

Tafasitamab in combination with lenalidomide and rituximab does not have marketing authorisation in the UK for any indication.

Tafasitamab in combination with lenalidomide and continued as monotherapy currently has Marketing Authorisation in the EU/UK for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant.[2]

Tafasitamab in combination with lenalidomide and rituximab is in phase II/III clinical development for the treatment of DLBCL.[16]

Patient Group

Disease Area and Clinical Need

MZL and FL are cancers of type B white blood cells, and sub-types of non-Hodgkin's lymphoma (NHL). Aside from grade 3B FL, they are slow-growing (indolent) low grade lymphomas.[4,7] The grade describes the degree of changes seen in the abnormal B cells.[4] FL develops when abnormal B lymphocytes are produced and start to build up in lymph nodes or other organs.[3] For many it is a chronic, relapsing, indolent condition with long overall survival, however, over time and multiple treatments the disease can become refractory to treatment.[17,18,19] MZL is lymphoma that starts in lymphoid tissue called the marginal zone, commonly in the mucosa tissue of organs such as the stomach or saliva glands[4] Like FL, it can be asymptomatic for some time but require treatment when symptoms develop.[20] Most people diagnosed with NHL are over 55 but it can develop at any age.[10]

The most common sign of symptomatic FL and nodal MZL is painless swellings in the neck, armpit or groin.[7,6] Symptoms of other MZL types depend on the location.[8,9] General symptoms can include heavy night sweats, weight loss, episodic high temperatures, frequent infections or difficulty getting over infections, and fatigue.[3,7] Most people with FL or MZL live many years, with several periods where treatment is not required.[7,6,8,9]

NHL accounts for 4% of cancer cases in the UK (2016-2018).[21] Of these 19% are FL, and 5-10% MZL.[3,20] The age standardised incidence rate of NHL in England is 19.6 and 27.8 per 100,000 amongst females and males, respectively.[21] The five-year survival rate is approximately 90% for FL and 80% for MZL.[22] For FL (ICD-10 code C82) in England (2021-22), there were 20,913 finished consultant episodes (FCEs) and 20,199 admissions, which resulted in 18,719 day cases and 12,302 FCE bed days.[23] In England (2017), there were 2,168 patients diagnosed with FL and 202 deaths registered where follicular lymphoma was the underlying cause.[24] Hospital admission figures specific for MZL are not available.[23]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following for treating R/R FL :

- 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. (2020).[25]
- Lenalidomide with rituximab as an option for previously treated FL (grade 1 to 3A) in adults. (2020).[26]
- Rituximab in combination with chemotherapy for the induction of remission of relapsed stage 3 or 4 follicular NHL (2008).[27]
- Rituximab monotherapy for the maintenance therapy of relapsed stage 3 or 4 follicular NHL following remission induced with chemotherapy with or without rituximab (2008).[27]
- Rituximab monotherapy for treating relapsed or refractory stage 3 or 4 follicular NHL, if there is resistance to or intolerance of chemotherapy (2008).[27]

There are currently no NICE recommended treatment options for indolent MZL.

Clinical Trial Information

Trial	**InMIND**, NCT04680052, EudraCT-2020-004407-13A; Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Tafasitamab Plus Lenalidomide in Addition to Rituximab Versus Lenalidomide in Addition to Rituximab in Patients With Relapsed/Refractory (R/R) Follicular Lymphoma Grade 1 to 3a or R/R Marginal Zone Lymphoma **Phase III** – active not recruiting **Locations:** 14 EU countries, UK, USA, Canada, and other countries **Primary completion date** August 2024
Trial Design	Randomised, parallel assignment, double blind
Population	N=654 (actual); adults with R/R FL Grade 1 to 3a or R/R MZL
Intervention(s)	• tafasitamab IV for 12 cycles • lenalidomide PO for 12 cycles • rituximab IV on cycles 1-5.
Comparator(s)	• placebo IV for 12 cycles • lenalidomide PO for 12 cycles • rituximab IV on cycles 1-5.
Outcome(s)	Progression Free Survival (PFS) in FL population (up to 6 years) PFS in FL and MZL populations (up to 6 years) See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Tafasitamab is already marketed in the UK for R/R DLBCL.[15] One 200mg vial costs £705.00.[28]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Zanubrutinib for treating relapsed or refractory marginal zone lymphoma. (GID-TA10962). Expected publication date: 17 July 2024.
- NICE technology appraisal guidance. Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab. (TA629). May 2020.
- NICE technology appraisal guidance. Lenalidomide with rituximab for previously treated follicular lymphoma. (TA627). April 2020.
- NICE guideline. Non-Hodgkin's lymphoma: diagnosis and management. (NG52). July 2016.
- NICE guideline. Haematological cancers: improving outcomes. (NG47). May 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

- British Society for Haematology. The investigation and management of follicular lymphoma. 2020.[17]
- European Society of Medical Oncology. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.[29]
- European Society of Medical Oncology. Marginal zone lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020.[30]
- 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.[31]

Additional Information

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