Health Technology Briefing
September 2022

Teclistamab with daratumumab for previously treated relapsed or refractory multiple myeloma

Company/Developer	Janssen-Cilag Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34006	NICE ID: 11798	UKPS ID: 665250

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Teclistamab, in combination with daratumumab, is in clinical development for the treatment of adults with relapsed or refractory multiple myeloma (MM) who have had previous treatment. MM is a form of cancer that occurs in immune cells found in bone marrow. The disease occurs due to uncontrolled duplication of these immune cells, known as plasma cells. In relapsed or refractory MM (RRMM), the patient has gone into complete or partial remission but then the disease has returned ('relapsed') or the patient stops responding to treatment ('refractory'). Despite many different treatment options being available to patients with RRMM, many patients do not respond to treatment or the disease returns following treatment. Therefore, there is need to develop additional treatment options for these patients.

Teclistamab is a bispecific antibody, a type of protein that attaches to two targets at the same time. Teclistamab attaches to a protein on the surface of the MM cells, and a protein on the cells of the immune system at the same time, thereby activating the immune cells to kill the MM cells. Daratumumab is a monoclonal antibody currently used to treat adults with MM. Teclistamab and daratumumab are administered through subcutaneous (SC) injection. If licensed, this novel combination of teclistamab and daratumumab will offer an additional treatment option for previously treated RRMM patients.

Proposed Indication

Treatment of relapsed or refractory multiple myeloma (RRMM) adult patients who have received one or more prior treatments including proteasome inhibitor (PI) and Immuno-Modulatory drugs (IMiDs). Patients who have received only 1 prior line of therapy must be lenalidomide refractory[1]

Technology

Description

Teclistamab (JNJ-64007957) is a humanised bispecific antibody that targets the B-cell maturation antigen (BCMA), a member of the tumour necrosis factor family of receptors which is highly expressed on the plasma cell of MM patients.[2] Teclistamab also binds to the CD3 receptors on T cells of the immune system; and by attaching to BCMA and CD3 at the same time, teclistamab activates an immune response against the MM cells.[3,4]

Teclistamab, in combination with daratumumab, is in clinical development for the treatment of patients with relapsed or refractory MM who have received 1 to 3 prior line(s) of antimyeloma therapy including a PI and lenalidomide. In the phase III clinical trial (MajesTEC-3; NCT05083169), participants will receive teclistamab and daratumumab by subcutaneous (SC) injection. Step-up doses of teclistamab will be given prior to the first full dose.[1]

Key Innovation

Patients with relapsed/refractory MM after prior therapy with a PI and IMiDs (such as lenalidomide) are challenging to treat. Different combination therapies have been approved for patients with RRMM, however, disease control could be further improved, hence the need for new therapeutic options with different modes of action.[5] Teclistamab, in combination with daratumumab (a CD38 monoclonal antibody) in a previous study (NCT04108195) was well-tolerable with no overlapping toxicities, and provides a novel immunotherapy approach that may yield improved efficacy in heavily pre-treated patients.[6]

If licensed, teclistamab in combination with daratumumab will offer an additional treatment option for previously treated RRMM.

Regulatory & Development Status

Teclistamab, in combination with daratumumab, does not have Marketing Authorisation in the UK/EU for any indication.

Teclistamab was granted the following regulatory designations/awards:[4,7]

- PRIME status for treatment of adult patients with RRMM, who previously received ≥3 prior lines of therapy by the EMA in January 2021.
- Breakthrough therapy by the US FDA for the treatment of RRMM in June 2021.

Patient Group

Disease Area and Clinical Need

Multiple Myeloma (MM) is a haematological malignancy that is characterised by a clonal expansion of malignantly transformed plasma cells in the bone marrow. These cells produce an excess of monoclonal immunoglobulins, which are secreted into the blood and urine.[8] Myeloma can develop anywhere there is bone marrow, so can affect lots of different bones in the body.[9,10] Symptoms of MM can include broken bones, bone pain, fatigue, persistent infections, nausea and spinal cord compression.[8] Relapsed MM is a stage of disease where a patient has gone into complete or partial remission but then the disease has come back.[11] Refractory MM is a stage of disease where a patient stops responding to treatment.[12]

MM is the 19th most common cancer in the UK, accounting for 2% of all new cancer cases (2016-18). The age standardised incidence rate of MM in England is 12.4 and 7.6 per 100,000 amongst males and females respectively.[13] In UK, there was an average of 5,951 new cases of myeloma each year (2016-2018), and around 3,100 myeloma deaths every year (2017-2019).[14] For patients diagnosed in England between 2013 and 2017, the 1-year and 5-year survival rates were 82.7% and 52.3% respectively.[15] In England (2020-21), there were 107,457 finished consultant episodes (FCEs) and 103,209 admissions for MM (ICD-10 code C90.0), which resulted in 92,913 day cases and 66,906 FCE bed days.[16]

Recommended Treatment Options

For previously treated MM, NICE recommends the following treatment options:[17-26]

- Daratumumab
- Carfilzomib with lenalidomide and dexamethasone
- Carfilzomib with dexamethasone
- Daratumumab with bortezomib and dexamethasone
- Bortezomib
- Pomalidomide with dexamethasone
- Panobinostat with bortezomib and dexamethasone
- Ixazomib with lenalidomide and dexamethasone
- Lenalidomide with dexamethasone
- Isatuximab with pomalidomide and dexamethasone

Clinical Trial Information

Trial	**MajesTEC-3; NCT05083169, 2020-004742-11;** A Phase 3 Randomised Study Comparing Teclistamab in Combination With Daratumumab SC (Tec-Dara) Versus Daratumumab SC, Pomalidomide, and Dexamethasone (DPd) or Daratumumab SC, Bortezomib, and Dexamethasone (DVd) in Participants With Relapsed or Refractory Multiple Myeloma **Phase III** – recruiting **Location(s):** 10 EU countries, UK, USA, Canada and other countries **Primary completion date:** July 2024
Trial Design	Randomised, parallel assignment, open label
Population	N=560 (estimated); aged 18 years and older; Subjects who have received 1 to 3 prior line(s) of antimyeloma therapy including a proteasome inhibitor (PI) and lenalidomide; subjects who have received only 1 line of prior line of antimyeloma therapy must be lenalidomide refractory.

Intervention(s)	• Teclistamab (SC) and daratumumab (SC)
Comparator(s)	• Daratumumab (SC), Pomalidomide (oral), Dexamethasone (oral or IV) • Daratumumab (SC), Bortezomib (SC), Dexamethasone (oral or IV)
Outcome(s)	Progression Free Survival [Time Frame: Up to 5 years and 2 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of teclistamab is not yet known.

Daratumumab is already marketed in the UK; a 1800mg/15ml vial costs £4,320; a 100mg/5ml vial costs £360; and a 400mg/20ml vial costs £1,440.[27]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. REGN5458 for treating relapsed or refractory multiple myeloma (GID-TA11052). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies (GID-TA10672). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma. (GID-TA10646). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Teclistamab for treating relapsed or refractory multiple myeloma after 3 therapies. (GID-TA10968). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Talquetamab for treating relapsed or refractory multiple myeloma after 3 therapies. (GID-TA10969). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Ciltacabtagene autoleucel for treating relapsed or refractory multiple myeloma (GID-TA10806). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Venetoclax with dexamethasone for treating relapsed or refractory t(11;14)-positive multiple myeloma after lenalidomide and a proteasome inhibitor. (GID-TA10926). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma. (GID-TA10646). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Elranatamab for treating refractory multiple myeloma after 3 standard therapies (GID-TA10918). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies (GID-TA10568). Expected date of issue to be confirmed.

- NICE technology appraisal in development. Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma. (GID-TA10579). Expected October 2022.
- NICE technology appraisal. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (TA783). April 2022.
- NICE technology appraisal. Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma. (TA695). April 2021.
- NICE technology appraisal. Carfilzomib for previously treated multiple myeloma. (TA657). November 2020.
- NICE technology appraisal. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma. (TA658). November 2020.
- NICE technology appraisal. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies. (TA171). Last updated: June 2019.
- NICE technology appraisal. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (TA573). April 2019.
- NICE technology appraisal. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (TA510). March 2018.
- NICE technology appraisal. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (TA505). February 2018.
- NICE technology appraisal. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib. (TA427). January 2017.
- NICE technology appraisal. Panobinostat for treating multiple myeloma after at least 2 previous treatments. (TA380). January 2016.
- NICE technology appraisal. Bortezomib monotherapy for relapsed multiple myeloma. (TA129). October 2007.
- NICE guideline. Myeloma: diagnosis and management. (NG53). Last updated: October 2018.
- NICE technology appraisal in development. Melphalan flufenamide with dexamethasone for treating relapsed or refractory multiple myeloma. (GID-TA10744). Suspended.
- NICE technology appraisal in development. Ciltacabtagene autoleucel for treating relapsed or refractory multiple myeloma. (GID-TA10806). Suspended.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Second allogeneic haematopoietic stem cell transplant for relapsed disease (all ages). 2017. 16068/P
- NHS England. Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT)(All Ages): Revised. 2015. B04/P/a.
- 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.
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Other Guidance

- Sive J, Cuthill K, Hunter H, Kazmi M, Pratt G et al. Guidelines on the diagnosis, investigation and initial treatment of myeloma: a British Society for Haematology/UK Myeloma Forum Guideline. 2021.[28]
- Dimopoulos MA, Moreau P, Terpos E, Mateos MV, Zweegman S et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.[29]

Additional Information

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