Health Technology Briefing
October 2025

Nivolumab with brentuximab vedotin for treating relapsed or refractory CD30+ classical Hodgkin lymphoma in people aged 5 years and older

Company/Developer	Bristol-Myers Squibb Pharmaceuticals Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 36336	NICE ID: Not Available	UKPS ID: 675176

Licensing and Market Availability Plans

Currently in phase II clinical trials.

Summary

Nivolumab with brentuximab vedotin is being developed for treating relapsed/refractory (R/R) CD30+ classical Hodgkin lymphoma (cHL) after failure of first-line therapy in patients aged 5 years and older. This disease sub-type (cHL) makes up about two-thirds of Hodgkin lymphoma cases and is the most frequently occurring cancer in adolescents. Relapsed means that the disease has returned after responding to treatment and refractory means it no longer responds to a specific treatment. Symptoms of cHL can include swelling of the lymph nodes (part of the immune system), fever, abdominal pain and weight loss. Current standard treatment involves highly toxic chemotherapy, which is not well tolerated in the target age group.

Nivolumab and brentuximab vedotin are both administered intravenously (into a vein) and have anti-tumour mechanisms that destroy cancer cells. Nivolumab prevents the cancer cells from disabling the body's defences. Brentuximab vedotin targets a protein called CD30+ that is expressed on cHL cells, which causes these cells to die. If approved, nivolumab with brentuximab vedotin will offer an additional treatment option for patients aged five years and older with R/R CD30+ cHL.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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The treatment of relapsed or refractory (R/R) CD30+ classical Hodgkin lymphoma (cHL) in adults and paedatrics aged 5 years and older after failure of first-line therapy.[a,1]

Technology

Description

Nivolumab (Opdivo, BMS-936558) is a monoclonal antibody, a type of protein that has been designed to attach to a receptor called PD-1 found on cells of the immune system called T cells. Cancer cells can produce proteins (PD-L1 and PD-L2) that attach to this receptor and switch off the activity of the T cells, preventing them from attacking the cancer. By attaching to the receptor, nivolumab prevents PD-L1 and PD-L2 from switching off the T cells, thereby increasing the ability of the immune system to kill cancer cells.[1,2] Brentuximab vedotin (Adcetris) is an antibody-drug conjugate that delivers an antineoplastic agent that results in apoptotic cell death selectively in CD30-expressing tumour cells through inducing cell cycle arrest.[3]

Nivolumab plus brentuximab vedotin is in clinical development for the treatment of R/R cHL in patients five years and older. In the phase II clinical trial (CheckMate 744; NCT02927769), all eligible participants received 3mg/kg intravenous nivolumab on day eight of cycle one and the same dose again on day one of each subsequent cycle, up to a maximum of six cycles. Likewise, 1.8mg/kg (up to a maximum of 180mg) intravenous brentuximab vedotin was administered on day one of each cycle.[4] For patients with a suboptimal response, brentuximab vedotin with bendamustine (a chemotherapy drug) was administered instead.[1]

Key Innovation

Standard of care treatment for patients with R/R cHL involves second line therapy followed by high dose chemotherapy and autologous stem cell transplant (HDCT/ASCT) and carries with it toxicities to the patient.[5] Alternate therapies that minimise these toxicities are needed. Nivolumab with brentuximab vedotin omits HDCT/ASCT and therefore may prove less toxic.[5] Children, adolescents and young adults with R/R cHL without complete metabolic response have suboptimal outcomes. Biomarkers associated with these poor outcomes include PD-L1 overexpression and tumour-associated macrophages, which have also been reported to express high PD-L1 levels.[6] Nivolumab, a checkpoint inhibitor that blocks PD-1, may increase CMR outcomes. This efficacy may be enhanced when combined with brentuximab vedotin, which selectively targets CD30-expressing tumour cells and induces apoptosis.[3]

If licensed, nivolumab with brentuximab vedotin will provide an additional treatment option for adults and paediatrics aged five years and older with R/R CD30+ cHL.

Regulatory & Development Status

Nivolumab currently has Marketing Authorisation in the EU/UK as a combination therapy for the treatment of adult patients with R/R cHL after autologous stem cell transplant and treatment with brentuximab vedotin.[7]

Nivolumab is currently marketed in the EU/UK in combination with other technologies for the following indications:[7]

- Gastric/gastroesophageal adenocarcinoma
- Hepatocellular carcinoma
- Oesophageal carcinoma
- Colorectal cancer

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- Pleural mesothelioma
- Melanoma
- Non-small cell lung cancer (NSCLC)
- Renal cell carcinoma
- Urothelial carcinoma

Nivolumab is currently marketed in the EU/UK as a monotherapy for the treatment of:[7]

- Oesophageal carcinoma
- Urothelial carcinoma
- Head and neck cancer
- Melanoma
- Renal cell carcinoma

Brentuximab vedotin is currently marketed in the EU/UK as a monotherapy for the treatment of:[3]

- Adult patients with R/R CD30+ Hodgkin lymphoma
- Systemic anaplastic large cell lymphoma
- Cutaneous T-cell lymphoma

Nivolumab plus brentuximab vedotin is not in late stage clinical development for any other indication.

Patient Group

Disease Area and Clinical Need

Hodgkin lymphoma (HL) is a type of blood cancer that develops when white blood cells called lymphocytes grow out of control. Lymphocytes are part of the immune system, and travel around the lymphatic system, helping fight infections.[8] The causes of HL is not fully understood but a person's risk of developing the condition increases if they are genetically pre-disposed, have a pre-existing medical condition which has compromised the immune system, take immunosuppressant medication(s), or have previously been infected with the Epstein-Barr virus.[8,9] Symptoms commonly include painless enlargement or swelling of lymph nodes in the neck, armpit, or groin; other symptoms can include itching, fever, cough, shortness of breath, abdominal pain and weight loss.[10] Relapsed means that the disease has returned after responding to treatment and refractory means it no longer responds to a specific treatment.[11]

HL is an uncommon cancer, accounting for less than 1% of all new cancer cases between 2017-2019 in the UK. There are around 2,200 new HL cases in the UK every year (2017-2019).[12] The age-standardised one-year and five-year net survival rates for HL (2016-2020) are 91.3% and 92.3% respectively for men, and 82.3% and 85.6% respectively for women.[13] In England (2024-2025), there were 4,929 finished consultant episodes (FCE) for HL (ICD-10 code: C81.9) with 4,691 hospital admissions that resulted in 4,153 FCE bed days and 4,201 FCE day cases.[14]

Recommended Treatment Options

The National Institute of Health and Care Excellence (NICE) recommend the following treatments for R/R cHL:

- Pembrolizumab is recommended as an option for treating R/R cHL in people aged three and older. It is recommended if they have had an ASCT that has not worked or they have had at least two previous therapies and an autologous stem cell transplant is not an option.[15,16]
- Nivolumab is recommended, within its marketing authorisation, as an option for treating R/R cHL in adults after autologous stem cell transplant and treatment with brentuximab vedotin.[17]

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NICE also recommends the following treatments for R/R CD30+ HL:

- Brentuximab vedotin is recommended as an option for treading CD30-positive Hodgkin lymphoma in adults with R/R disease only if they have already had ASCT or at least two previous therapies.[18]

Clinical Trial Information	
Trial	**CheckMate 744**; NCT02927769, 2016-002347-41; Risk-based, Response-adapted, Phase II Open-label Trial of Nivolumab + Brentuximab Vedotin (N + Bv) for Children, Adolescents, and Young Adults With Relapsed/Refractory (R/R) CD30 + Classic Hodgkin Lymphoma (cHL) After Failure of First-line Therapy, Followed by Brentuximab + Bendamustine (Bv + B) for Participants With a Suboptimal Response (CheckMate 744: CHECKpoint Pathway and Nivolumab Clinical Trial Evaluation) **Phase II –** Completed **Location(s):** Eight EU countries, UK, USA, and other countries **Completion date:** May 2024
Trial Design	Non-randomised, parallel assignment, open-label
Population	N=72 (actual); subjects with cHL that have relapsed or are refractory to first line treatment; aged five to 30 years old
Intervention(s)	3mg/kg nivolumab (intravenous) + 1.8mg/kg brentuximab vedotin (intravenous).[4]
Comparator(s)	Brentuximab vedotin + 90mg/m^2 bendamustine for participants with suboptimal response.[4]
Outcome(s)	Primary outcome measures: Cohort 1: • Complete metabolic response (CMR) rate at any time prior to radiation therapy by blinded independent centralised review (BICR) [Time Frame: From first dose to CMR or the completion of six cycles of therapy (up to approximately 18 weeks)] • Event-free survival rate at three years by BICR [Time Frame: At three years post first dose of study therapy] Cohort 2: • CMR rate at any time prior to high dose chemotherapy followed by autologous stem cell treatment by BICR [Time Frame: Form first dose to CMR or the completion of six cycles of therapy (up to approximately 18 weeks)] See trial record for full list of all outcomes.
Results (efficacy)	Of 28 included patients treated in the low-risk cohort, 18 (64%) were female, and the median age was 17 (6-27) years. At a median follow-up of 31.9 (2.2-55.3) months, CMR per BICR any time before involved-site radiotherapy was 93% (26 of 28; 90% CI, 79.2-98.7; objective response rate [ORR], 100%), and 23 of 28 (82%) achieved CMR per BICR after 4 cycles of nivolumab plus

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	brentuximab vedotin (objective response rate, 96.4%). Kaplan-Meier estimates of event-free survival and progression-free survival rates at 3 years were 87% (3 of 18; 90% CI, 69.5-94.7) and 95% (1 of 18; 90% CI, 76.7-99.0), respectively.[19]
Results (safety)	During the induction phase, 22 patients (79%) experienced 1 or more treatment-related adverse events (TRAE), most frequently increased alanine aminotransferase (ALT) (6 [21%]). A total of 7 patients (25%) experienced 1 or more grade 3 or 4 TRAEs, including maculopapular rash (1 [4%]), increased ALT (1 [4%]), increased aspartate aminotransferase (2 [7%]), decreased lymphocyte count (1 [4%]), febrile neutropenia (1 [4%]), and soft tissue infection (1 [4%]). During the intensification phase, 2 patients (33%) had TRAEs; none were grade 3 or 4. During the consolidation phase, 3 patients (14%) had 1 or more TRAE of any grade and 2 (9%) had grade 3 or 4 TRAEs. Few patients experienced haematologic TRAEs of any grade (anaemia, 2 [7%]; febrile neutropenia, 1 [4%]; leukopenia, 1 [4%]; neutropenia, 1 [4%]; thrombocytopenia, 1 [4%]). Five patients (18%) had infusion-related reactions; all were grade 1 or 2 and occurred during induction. Treatment-related immune mediated AEs occurred in 6 patients (21%) during induction and 1 (17%) during intensification. A total of 5 patients (18%) had 1 or more serious TRAEs during induction, including grade 3 or 4 rash, urticaria, and febrile neutropenia (1 each). One patient had serious TRAEs of pyrexia and acute kidney injury during intensification. During consolidation, 1 patient had a serious grade 3 or 4 TRAE of enteritis (not in the radiation field). Overall, 2 patients experienced serious AEs leading to discontinuation (1 with rash in the induction phase; 1 with pyrexia and acute kidney injury in the intensification phase). There were no deaths while taking the study treatment.[19]

Estimated Cost

The cost of nivolumab 100mg/10ml concentrate for solution for infusion vials has a NHS indicative price of £1,097.[20]

The cost of brentuximab vedotin 50mg powder for concentrate for solution for infusion vials has a NHS indicative price of £2,500.[21]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma in people 3 years and over (TA967). May 2024.
- NICE technology appraisal guidance. Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies (TA772). February 2022.
- NICE technology appraisal guidance. Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma (TA524). June 2018.
- NICE technology appraisal guidance. Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma (TA462). July 2017.

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- NICE quality standard. Haematological Cancers (QS150). June 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy Statement: Bendamustine for relapsed/refractory classical Hodgkin lymphoma (all ages). 200701P. July 2020
- NHS England. 2013/14 Standard Contract for Cancer: Chemotherapy (Adult), B15/S/a.

Other Guidance

- EuroNet Paediatric Hodgkin Lymphoma Group. Risk and Response Adapted Treatment Guidelines for Managing First Relapsed and Refractory Classical Hodgkin Lymphoma in Children and Young People. 2020.[22]

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