Brentuximab vedotin for the treatment of older patients (>60 years) - core data
Brentuximab vedotin is indicated for the treatment of adult patients with relapsed or refractory (R/R) CD30+ Hodgkin lymphoma (HL):¹

1. following autologous stem cell transplant (ASCT)
2. following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option
3. at increased risk of relapse or progression following ASCT

The dosing recommendations for brentuximab vedotin in patients aged 65 and older are the same as for adults¹

1. Brentuximab vedotin (ADCETRIS) Summary of Product Characteristics
Brentuximab vedotin in patients aged 60 years or older with relapsed or refractory (R/R) CD30-positive lymphomas: a retrospective evaluation of safety and efficacy

**Design:** Retrospective, comparative analysis across seven prospective clinical studies

**Objective:** To characterise the safety and efficacy of targeted therapy with brentuximab vedotin in older patients with R/R CD30+ lymphomas

**Patients:** 40 brentuximab vedotin treatment courses identified among 38 patients aged 60 years or older

- 16 patients had Hodgkin lymphoma (HL), 22 had anaplastic large cell lymphoma and two had another CD30+ lymphoma subtype
- Median age: 66 years (range 60–82)
- Median prior cancer-related systemic therapies: 2.0 (range 1–6)

Most patients in the analysis set received single-agent brentuximab vedotin (1.8 mg/kg) administered intravenously q3wk (licensed dose). The only exception was a phase I study, where patients received brentuximab vedotin once weekly for each 3-week cycle (q1wk), at doses ranging from 0.6 to 1.4 mg/kg (unlicensed dose).

Brentuximab vedotin in patients aged 60 years or older with R/R CD30-positive lymphomas: a retrospective evaluation of safety and efficacy

**Response:** Brentuximab vedotin showed substantial antitumour activity in heavily pre-treated HL patients ≥60 years of age

- ORR was 56%, while 38% of patients achieved CR\(^1\)

<table>
<thead>
<tr>
<th>Response data for patients ≥60 years of age with R/R HL(^1)</th>
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<tbody>
<tr>
<td><strong>N=16</strong></td>
</tr>
<tr>
<td>ORR, %</td>
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<tr>
<td>CR, %</td>
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<tr>
<td>Estimated median OS (All patients; 95% CI)</td>
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<td>Estimated 2 year OS rate, %</td>
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- In the pivotal phase II study of brentuximab vedotin in patients with R/R HL (n=102; median age: 31, range 15-77), ORR was 75% with 34% of patients achieving CR\(^2\)

CI, confidence intervals; CR, complete remission; ORR, objective response rate; OS, overall survival

Brentuximab vedotin in patients aged 60 years or older with R/R CD30-positive lymphomas: a retrospective evaluation of safety and efficacy

**Safety:** Brentuximab vedotin appeared to be generally well tolerated in the older population

- Older patients experienced a significantly higher rate of treatment-emergent anaemia (30% vs 10%), and a trend towards higher rates of treatment-emergent peripheral sensory neuropathy (60% vs 46%) and fatigue (58% vs 43%)

- Incidence of treatment-related serious adverse events (AEs) appeared to be similar among older and younger patients (20% vs 16% respectively)

- Peripheral sensory neuropathy was the most common AE of any grade, occurring in 60% of patients ≥60 years. It was also the leading cause of dose delays (23%)

- There were no episodes of Grade 4 or 5 peripheral sensory neuropathy

![Bar chart showing the most common grade 3 AEs (in >10% of patients ≥60 years old)]

AE, adverse events

Italian real life experience with brentuximab vedotin: results of a national observational study in R/R HL

**Design:** A large Italian observational, retrospective study was conducted to examine the use of brentuximab vedotin in everyday clinical practice

**Dosing and schedule:** Patients (n=234) with CD30+ HL were treated with brentuximab vedotin (1.8 mg/kg IV every 3 weeks)
- 49% were relapsed and 51% refractory

**Response:** Best response was observed after a median of four cycles in 59.8% of patients (140/234)
- CR was achieved in 31.6% of patients (74/234)
- PR was achieved in 28.2% of patients (66/234)

- Analysis of the elderly subgroup (>60 years) showed:
  - CR was achieved in 50% patients (14/28)
  - PR was achieved in 17.8% of patients (5/28)

- Overall response rate at end of treatment was 48.3% (62 CR; 51 PR)

**Safety:** Brentuximab vedotin was well tolerated and the toxicity profile was similar to previous clinical trial data

CR, complete remission; IV, intravenous; PR, partial remission

Summary

• In a retrospective comparative analysis across several prospective clinical studies, brentuximab vedotin appeared to be generally well-tolerated in the elderly (≥60 years) population; a population that represents an unmet need\(^1\)

• Elderly patients experienced higher rates of treatment-emergent anaemia, peripheral sensory neuropathy and fatigue. Incidence of treatment-related serious adverse events appeared to be similar among older and younger patients (20% vs 16% respectively)\(^1\)

• In a large observational retrospective analysis, an elderly subgroup (age ≥60 years) achieved higher CR rates (50%) than the overall population\(^2\)

• Brentuximab vedotin showed substantial anti-tumour activity in R/R HL patients ≥60 years of age\(^1,2\)

CR, complete remission

Please refer to the summary of product characteristics for details on the full side-effect profile and drug interactions of brentuximab vedotin. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda UK Ltd. on 01628 537900
Adcetris® (brentuximab vedotin)
(Refer to Summary of Product Characteristics (SmPC) before prescribing)

Presentation: 50 mg powder for concentrate for solution for infusion. Indication: treatment of adult patients with relapsed or refractory (R/R) CD30+ Hodgkin lymphoma (HL) following autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option; treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT; treatment of adult patients with R/R systemic anaplastic large cell lymphoma (sALCL); treatment of adult patients with R/R anaplastic large cell lymphoma (ALCL) or systemic anaplastic large cell lymphoma (sALCL). Dosage & Administration: Administration should be under the supervision of a physician experienced in the use of anti-cancer agents. Recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks (If R/R, may be repeated after ≥1 month of stable disease or partial response (PR)) to the patient who has not developed Grade 3 or 4 anaemia, thrombocytopenia and neutropenia which is reversible in most cases. Patients should be managed for symptoms of neutropenia. Patients experiencing new or worsening peripheral neuropathy may require delay and dose reduction or discontinuation of further infusions. Management of neutropenia

Men being treated with Adcetris are advised not to father a child during treatment and for up to 6 months following the last dose. Drug Interactions: Co-administration of Adcetris: with strong CYP3A4 and P-gp inhibitors, such as ketoconazole, may increase the incidence of neutropenia; with ritampin, a strong CYP34A inducer, did not alter the plasma exposure to Adcetris however, it appeared to reduce plasma concentrations of MMAE metabolites. Adcetris is not expected to alter the exposure to medicines that are metabolized by CYP34A enzymes e.g. midazolam. Adverse Effects: Very common (≥10%): Infection, upper respiratory tract infection, neutropenia, peripheral sensory neuropathy, peripheral motor neuropathy, cough, dyspnoea, diarrhoea, nausea, vomiting, constipation, abdominal pain, rash, pruritus, myalgia, arthralgia, fatigue, pyrexia, infusion-related reactions, weight decreased. Common (1/100 to <1/10): Herpes zoster, pneumonia, herpes simplex, oral candidiasis, anaemia, thrombocytopenia, hyperglycaemia, dizziness, alanine transaminase (ALT) and aspartate aminotransferase (AST) increased, alopecia, back pain, chills. Uncommon (1/1000 to <1/100): Pneumocystis jiroveci pneumonia, staphylococcal bacteraemia, tumour lysis syndrome, demyelinating polyneuropathy, pancreatitis, acute, cytomegalovirus infection or reactivation, sepsis, septic shock. Rare (≥1/10000): Adcetris should not be used in patients with a prior history of epidermal necrolysis. Frequency not known (cannot be estimated from the available data): Progressive multifocal leukoencephalopathy. Please refer to the SmPC for full details on full side effect profile and interactions. Pharmacological Precautions: Store vial in a cool place. The following table lists the more important drug interactions of Adcetris:

Please refer to the summary of product characteristics for details on the full side-effect profile and drug interactions of Adcetris. Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk. Adverse events should also be reported to Takeda UK Ltd 01628 537900 Fax: 01628 526617. Adcetris® is a registered trademark.

Adcetris has received a conditional marketing authorisation in Europe. A conditional marketing authorisation is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are required. The European regulatory agency will review new information on Adcetris at least every year and the summary of product characteristics will be updated as necessary.