מאי 2023

רופא/ה, רוקח/ת נכבד/ה,

הנדון: ADCETRIS® 50mg (brentuximab vedotin)
עדכון העלון לרופא

חברת טקדה ישראל בע"מ מבקשת לידע כי העלון לרופא של התכשיר שבנדון עודכן לאחרונה.

התוויות הרשומות לתכשיר זה:

1. **ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL):**
    1) **following autologous stem cell transplant (ASCT) or**
    2) **following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option.**
2. **ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma (sALCL).**
3. **ADCETRIS is indicated for the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT.**
4. **ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy.**
5. **ADCETRIS is indicated for the treatment of adult patients with previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine.**
6. **ADCETRIS is indicated for the treatment of adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone.**

מרכיב פעיל: **brentuximab vedotin 50 mg/vial**

להלן פירוט השינויים העיקריים בעלון לרופא (טקסט שנוסף מסומן בכחול, טקסט שהושמט מסומן כטקסט אדום עם קו חוצה, טקסט המהווה החמרה מודגש בצהוב):

4.8 Undesirable effects

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Monotherapy

In the pooled dataset of ADCETRIS as monotherapy across HL, sALCL and CTCL studies (SG035-0003, SG035-0004, SGN35-005, SGN35-006, C25001, C25006 and C25007, see section 5.1) the most frequent adverse reactions (≥10%) were infections, peripheral sensory neuropathy, nausea, fatigue, diarrhoea, pyrexia, neutropenia, upper respiratory tract infection, arthralgia, ~~neutropenia~~, rash, cough, vomiting, pruritus, ~~arthralgia,~~ peripheral motor neuropathy, infusion-related reactions, ~~pruritus,~~ constipation, dyspnoea, myalgia, weight decreased, ~~myalgia~~ and abdominal pain.

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Description of selected adverse reactions

Neutropenia and febrile neutropenia

Monotherapy

In clinical trials, neutropenia led to dose delays in ~~14~~13% of patients. Grade 3 neutropenia was reported in 13% and Grade 4 neutropenia was reported in 5% of patients. ~~No~~ One patient~~s~~ required dose reduction ~~or~~ and one patient discontinued treatment for neutropenia.

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Peripheral neuropathy

Monotherapy

In clinical trials treatment emergent neuropathy occurred in ~~59~~ 57 % of the population, peripheral motor neuropathy occurred in ~~14~~13% of patients. Peripheral neuropathy led to treatment discontinuation in 15%, dose reductions in 15%, and dose delays in ~~17~~16% of patients.

For patients who experienced peripheral neuropathy the median time of onset of peripheral neuropathy was 12 weeks. The median duration of treatment for patients who discontinued due to peripheral neuropathy was ~~12~~ 11 cycles.

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Combination therapy

Among patients who experienced peripheral neuropathy, the median follow up time from end of treatment until last evaluation was approximately ~~91~~ 286 weeks. At the time of last evaluation, most of the patients (~~76~~86%) who experienced peripheral neuropathy had resolution or improvement of their peripheral neuropathy symptoms. The median time from onset to resolution or improvement of peripheral neuropathy events was ~~10~~ 17 weeks (ranged from 0 weeks to ~~139~~ 283 weeks).

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Infusion-related reactions

Monotherapy

IRRs, such as headache, rash, back pain, vomiting, chills, nausea, dyspnoea, pruritus and cough were reported in ~~13~~ 12 % of patients.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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As of a 01 June 2021 cut-off date, approximately 5 years after enrolment of the last patient, the results in the ITT population showed a statistically significant

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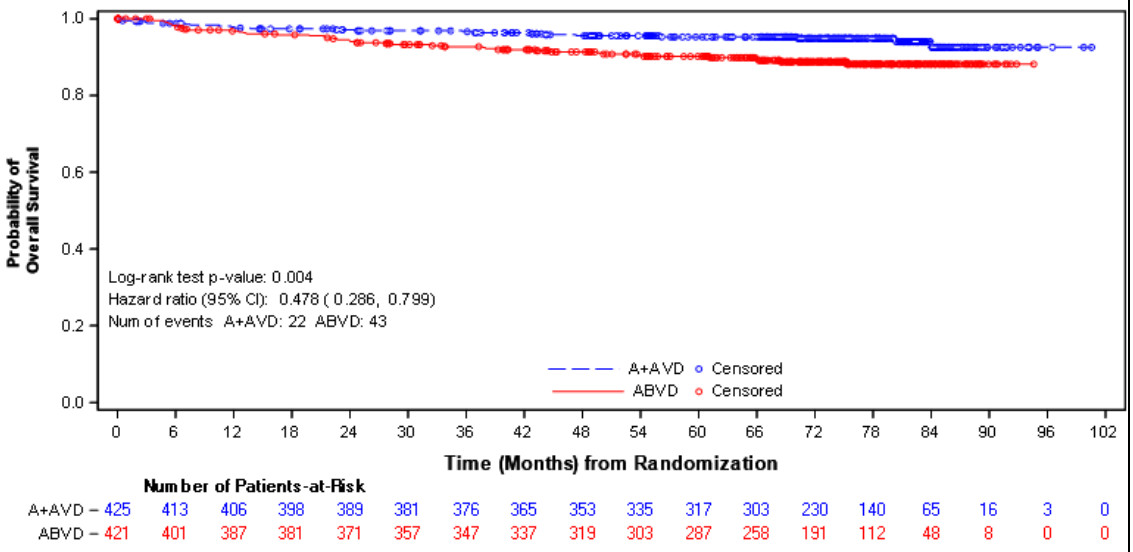
improvement in OS in the ADCETRIS + AVD arm compared with patients treated with ABVD [HR = 0.59, 95% CI (0.396, 0.879)]. In the stage IV population a hazard ratio of 0.48 [95% CI (0.286, 0.799)] was observed for OS in favour of the ADCETRIS + AVD arm compared with patients treated with ABVD, see Figure 3.

Median OS was not reached for either A+AVD or ABVD patients [95%◦CI (NE, NE)].

Figure 3: Overall survival in patients with Stage IV disease (ADCETRIS + AVD vs. ABVD) (6 years median follow up)



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Study C25006

The efficacy and safety of ADCETRIS as a single agent were also evaluated in a phase 4 open-label, single-arm multicenter study in 50 patients with relapsed or refractory sALCL. The ORR per IRF assessment was 64% (32 of 50 patients in the ITT set). The median DOR per IRF was not reached (95% CI 19.71 months, NE). The CR rate was 30% (15 of 50 patients in the ITT set), and tumour reduction (of any degree) was achieved in 93% of evaluable patients. The median DOCR per IRF was not reached (95% CI 10.61 months, NE). Response assessments were generally consistent between IRF and investigator. Of the patients treated, 13 patients went on to receive a haematopoietic stem cell transplant.

Pooled data from studies C25006 and SG035-0004 (N=108) show an ORR per IRF of 76% (82 of 108 patients in the ITT set). The median DOR per IRF was 17.0 months (95% CI 12.62, 32.46). CR was 45% (49 of 108 patients in the ITT set) and tumour reduction (of any degree) was achieved in 96% of evaluable patients. The median DOCR per IRF was 26.3 months (95% CI 16.16, NE). Response assessments per IRF and investigator were generally consistent.

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