אוגוסט 2021

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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Table 5: Adverse reactions to ADCETRIS

System organ class	Adverse reactions (monotherapy)	Adverse reactions (combination therapy)
Immune system disorders		
Uncommon:	Anaphylactic reaction	Anaphylactic ~~transfusion~~ reaction

5.1 Pharmacodynamic properties

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Study SGN35-005

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As of study closure, approximately 10 years after enrollment of the first patient, PFS per investigator continued to show a benefit (HR = 0.51 [95% CI (0.37, 0.71)]). Overall survival

Takeda Israel Ltd.
25 Efal st., P.O.B 4140, Petach-Tikva 4951125
Tel:+972-3-3733140 Fax (local) : + 972-3-3733150

results were consistent with those reported at the time of primary analysis (HR = 1.11 [95% CI (0.72, 1.70)]). Figure 3 shows PFS per investigator in the ITT population as of study closure

Figure 3: Kaplan-Meier Plot of PFS per investigator (ITT, study closure)

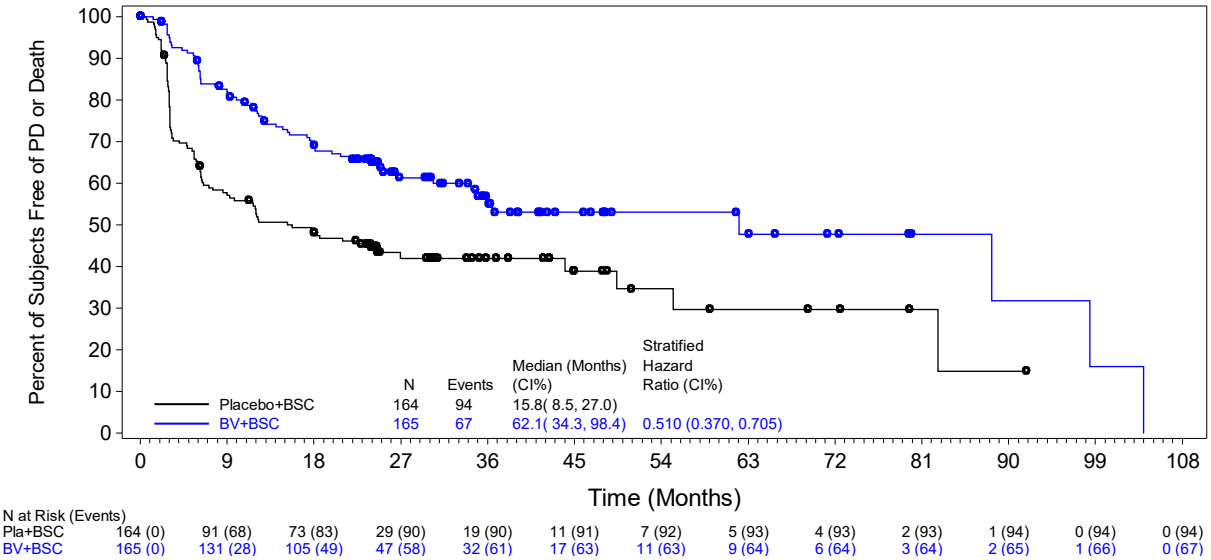

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Figure 5: Kaplan-Meier Plot of PFS per Investigator in Patients with ≥ 2 Risk Factors (3-year follow-up)

As of study closure, approximately 10 years after enrollment of the first patient, the hazard ratio for PFS per investigator for patients with 2 or more risk factors was 0.41 (95% CI [0.29, 0.58]). The hazard ratio for PFS per investigator for patients with 3 or more risk factors was 0.38 (95% CI [0.25, 0.59]). Overall survival results remained consistent with those observed as of the primary analysis.

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Study C25007

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A phase 4 single-arm study was conducted in patients with relapsed or refractory HL (n=60) who had received at least one prior chemotherapeutic regimen and at the time of treatment initiation with ADCETRIS were not considered candidates for SCT or multi-agent chemotherapy. Eligible patients were not to have received a prior SCT.

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Study SGN35-014

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Patients were treated with 1.8 mg/kg of ~~for 6 to 8 cycles~~ ADCETRIS administered as an intravenous infusion over 30 minutes on day 1 of each 21-day cycle + CHP (cyclophosphamide 750 mg/m2 every 3 weeks by IV infusion; doxorubicin 50 mg/m2 every 3 weeks by IV infusion; and prednisone 100 mg on Days 1 to 5 of each 3-week cycle, orally) for 6 to 8 cycles.

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6.6 Special precautions for disposal and other handling

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Table 20: Sample calculations for patients receiving the recommended dose of 1.8 mg/kg, 1.2 mg/kg or 0.9 mg/kg of ADCETRIS for weights ranging from 60 kg to 120 kg

~~Patient weight (kg)~~	~~Total dose = patient weight multiplied by recommended dose [1.8 mg/kg[a]])~~	~~Total volume to be diluted[b] = total dose divided by reconstituted vial concentration [5 mg/mL])~~	~~Number of vials needed = total volume to be diluted divided by total volume per vial [10 mL/vial])~~
~~60 kg~~	~~108 mg~~	~~21.6 mL~~	~~2.16 vials~~
~~80 kg~~	~~144 mg~~	~~28.8 mL~~	~~2.88 vials~~
~~100 kg~~	~~180 mg~~	~~36 mL~~	~~3.6 vials~~
~~120 kg[c]~~	~~180 mg[d]~~	~~36 mL~~	~~3.6 vials~~

Recommended dose	Patient weight (kg)	Total dose = patient weight multiplied by recommended dose	Total volume to be diluted[a] = total dose divided by reconstituted vial concentration (5 mg/mL)	Number of vials needed = total volume to be diluted divided by total volume per vial (10 mL/vial)
1.8 mg/kg (up to a maximum of 180 mg)	60 kg	108 mg	21.6 mL	2.16 vials
	80 kg	144 mg	28.8 mL	2.88 vials
	100 kg	180 mg	36 mL	3.6 vials
	120 kg[b]	180 mg	36 mL	3.6 vials
1.2 mg/kg (up to a maximum of 120 mg)	60 kg	72 mg	14.4 mL	1.44 vials
	80 kg	96 mg	19.2 mL	1.92 vials
	100 kg	120 mg	24 mL	2.4 vials
	120 kg[b]	120 mg	24 mL	2.4 vials
0.9 mg/kg (up to a maximum of 90 mg)	60 kg	54 mg	10.8 mL	1.08 vials
	80 kg	72 mg	14.4 mL	1.44 vials
	100 kg	90 mg	18 mL	1.8 vials

	120 kg[b]	90 mg	18 mL	1.8 vials

~~For a reduced dose, use 1.2 mg/kg for the calculation~~

a. To be diluted in 150 mL of diluent and administered by intravenous infusion over 30 minutes ~~every 3 weeks~~.
b. If patient's weight is more than 100 kg, the dose calculation should use 100 kg.
c. ~~The maximal recommended dose is 180 mg~~

~~Table 21: Sample calculations for patients receiving the recommended dose of 1.2 mg/kg of ADCETRIS for weights ranging from 60 kg to 120 kg as combination therapy or when a reduced dose is required~~

~~Patient weight (kg)~~	~~Total dose = patient weight multiplied by recommended dose [1.2 mg/kga])~~	~~Total volume to be dilutedb = total dose divided by reconstituted vial concentration [5 mg/mL])~~	~~Number of vials needed = total volume to be diluted divided by total volume per vial [10 mL/vial])~~
~~60 kg~~	~~72 mg~~	~~14.4 mL~~	~~1.44 vials~~
~~80 kg~~	~~96 mg~~	~~19.2 mL~~	~~1.92 vials~~
~~100 kg~~	~~120 mg~~	~~24 mL~~	~~2.4 vials~~
~~120 kgc~~	~~120 mg d~~	~~24 mL~~	~~2.4 vials~~

~~For a reduced dose, use 0.9 mg/kg for the calculation.~~

~~To be diluted in 150 mL of diluent and administered by intravenous infusion over 30 minutes every 2 weeks as combination therapy or every 3 weeks when a reduced dose of the monotherapy is required.~~

~~If patient's weight is more than 100 kg, the dose calculation should use 100 kg.~~

~~The maximal recommended dose for combination therapy is 120 mg.~~

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העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פניה לחברת טקדה ישראל בע"מ, רח' אפעל 25, פתח תקוה, 03-3733140

בברכה,

אנה מורביוב
רוקחת ממונה
טקדה ישראל בע"מ

Takeda Israel Ltd.
25 Efal st., P.O.B 4140, Petach-Tikva 4951125
Tel:+972-3-3733140 Fax (local) : + 972-3-3733150