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מרץ 2024

רופא/ה, רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלון לרופא (עלון לצרכן במתכונת עלון לרופא) של התכשיר:

Besponsa

<u>המרכיב הפעיל:</u>

Inotuzumab Ozogamicin 1 MG/VIAL

<u>Indicated for:</u>
BESPONSA is indicated as monotherapy for the treatment of adults with relapsed or refractory CD22-positive B cell precursor acute lymphoblastic leukaemia (ALL). Adult patients with Philadelphia chromosome positive (Ph+) relapsed or refractory B cell precursor ALL should have failed treatment with at least 1 tyrosine kinase inhibitor (TKI).

<u>להלן העדכונים העיקריים בעלון לרופא:</u>

4.2 Posology and method of administration

Paediatric population

The safety and efficacy of BESPONSA in children aged 0 to <18 years have not been established. ~~No data are available~~. <u>Currently available data are described in sections 4.8, 5.1 and 5.2 but no recommendation on a posology can be made</u>.

4.8 Undesirable effects

<u>Immunogenicity</u>

In clinical studies of inotuzumab ozogamicin in <u>adult</u> patients with relapsed or refractory ALL, 7/236 (3%) patients tested positive for anti-inotuzumab ozogamicin antibodies (<u>ADA</u>). No patients tested positive for neutralising ~~anti-inotuzumab-ozogamicin antibodies~~ ADA. In patients who tested positive for ~~anti-inotuzumab-ozogamicin antibodies~~ <u>ADA</u>, no effect on clearance of BESPONSA was detected based on population-pharmacokinetic analysis. The number of patients <u>with positive ADA</u> was too small to assess the impact of ~~anti-inotuzumab-ozogamicin antibodies~~ ADA on efficacy and safety.

<u>In clinical study ITCC-059 of inotuzumab ozogamicin in paediatric patients with relapsed or refractory ALL (N=51), the incidence of ADA against inotuzumab ozogamicin was 0%.</u>

<u>Paediatric population</u>

<u>BESPONSA has been evaluated in 53 paediatric patients ≥ 1 and < 18 years of age with relapsed or refractory CD22-positive B cell precursor ALL in Study ITCC-059 (see section 5.1).</u>

<u>The most common adverse reactions (> 30%) in the paediatric study ITCC-059 were thrombocytopenia (60%), pyrexia (52%), anaemia (48%), vomiting (48%) neutropenia (44%), infection (44%), haemorrhage (40%), febrile neutropenia (32%), nausea (32%), abdominal pain (32%) in the Phase 1 Cohort and pyrexia (46%), thrombocytopenia (43%), anaemia (43%), vomiting (43%), neutropenia (36%), leukopenia (36%), nausea (32%), infection (32%), transaminase increased (32%), and haemorrhage (32%) in the Phase 2 Cohort.</u>

<u>In the Phase 1 Cohort, 2/25 (8.0%) patients had VOD (neither received transplant) and 6/28 (21.4%) patients in the Phase 2 Cohort had VOD, with a post-HSCT VOD rate of 5/18 (27.8% [95% CI: 9.69-53.48]). In the Phase 1 Cohort, 8/25 patients (32%) and 18/28 (64%) in the Phase 2 Cohort had a follow-up HSCT. The post-HSCT non-relapse mortality rate was 2/8 (25%) and 5/18 (28%) in the Phase 1 Cohort and the Phase 2 Cohort, respectively.</u>

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic and immunomodulating agents, ~~other Antineoplastic agents~~, monoclonal antibodies and antibody drug conjugates, CD22 (Clusters of Differentiation 22) inhibitors, ATC code: ~~L01XC26~~ L01FB01.

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Paediatric population

~~The European Medicines Agency has deferred the obligation to submit the results of studies with BESPONSA in 1 or more subsets of the paediatric population for the treatment of relapsed or refractory ALL (see section 4.2 for information on paediatric use).~~

Study ITCC-059 has been performed in compliance with the agreed Paediatric Investigation Plan (see section 4.2 for information on paediatric use).

Study ITCC-059 was a Phase 1/2 multicentre, single-arm, open-label study conducted in 53 paediatric patients ≥ 1 and < 18 years of age with relapsed or refractory CD22-positive B-cell precursor ALL to identify a recommended Phase 2 Dose (Phase 1) and to further evaluate the efficacy, safety, and tolerability of the selected BESPONSA dose as a monotherapy agent (Phase 2). The study also evaluated the Pharmacokinetics and Pharmacodynamics of BESPONSA as monotherapy (see section 5.2).

In the Phase 1 Cohort (N=25), two dose levels were examined (initial dose of 1.4 mg/m2 per cycle and an initial dose of 1.8 mg/m2 per cycle). In the Phase 2 Cohort (N=28), patients were treated at the initial dose of 1.8 mg/m2 per cycle (0.8mg/m2 on Day 1, 0.5mg/m2 on Days 8 and 15) followed by a dose reduction to 1.5mg/m2 per cycle for patients in remission. In both Cohorts, patients received a median of 2 cycles of therapy (range: 1 to 4 cycles). In the Phase 1 Cohort, the median age was 11 years (range: 1-16 years), and 52% of patients had second or greater relapsed B-cell precursor ALL. In the Phase 2 Cohort, the median age was 7.5 years (range: 1-17 years), and 57% of patients had second or greater relapsed B-cell precursor ALL.

Efficacy was evaluated on the basis of Objective Response Rate (ORR), defined as the rate of patients with CR+CRp+CRi. In the Phase 1 Cohort, 20/25 (80%) patients had CR, the ORR was 80% (95% CI: 59.3-93.2), and the median Duration of Response (DoR) was 8.0 months (95% CI: 3.9-13.9). In the Phase 2 Cohort, 18/28 (64%) patients had CR, the ORR was 79% (95% CI: 59.0-91.7), and the DoR was 7.6 months (95% CI: 3.3-NE). In the Phase 1 Cohort, 8/25 patients (32%) and 18/28 (64%) in the Phase 2 Cohort had a follow-up HSCT.

5.2 Pharmacokinetic properties

Pharmacokinetics in specific groups of subjects or patients

Paediatric population

At the adult recommended dose, the median exposure in paediatric patients with ALL (aged ≥1 and < 18 years) was 25% higher than those in adults. The clinical relevance of the increased exposure is unknown.

השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה.

העלון המעודכן נשלח למשרד הבריאות לצורך פרסומו במאגר התרופות שבאתר משרד הבריאות:
https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h

לחילופין, לקבלת עלונים מלאים מודפסים ניתן לפנות לחברת פייזר פרמצבטיקה ישראל בע"מ
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בברכה,
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