Besponsa

(inotuzumab ozogamicin)

BESPONSA™
inotuzumab ozogamicin INJECTION FOR IV INFUSION

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Besponsa
- **Generic name:** Inotuzumab ozogamicin
- **Pharmacological class:** CD22-directed antibody-drug conjugate
- **Strength and Formulation:** 0.9mg/vial; lyophilized powder for IV inj after reconstitution and dilution; preservative-free
- **Manufacturer:** Pfizer
- **How supplied:** Single-dose vial—1
- **Legal Classification:** Rx

Indications

- Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

Dosage & Administration

- See full labeling
- Infuse over 1hr at rate of 50mL/hr
- Pre-medicate with a corticosteroid, antipyretic, and antihistamine prior to dosing; or for cytoreduction: see full labeling.

Dosage & Administration

- **Cycle 1:** 1.8mg/m^2 as 3 divided doses on Day 1 (0.8mg/m^2), Day 8 (0.5mg/m^2), Day 15 (0.5mg/m^2) for 3 weeks; may be extended to 4 weeks (eg, 7-day treatment-free interval starting on Day 21) if complete remission (CR) or complete remission with incomplete hematologic recovery (CRi) achieved, and/or to allow recovery from toxicity

Dosage & Administration

- **Subsequent cycles**
  - **if CR or CRi achieved:** 1.5mg/m^2 as 3 divided doses on Day 1 (0.5mg/m^2), Day 8 (0.5mg/m^2), Day 15 (0.5mg/m^2) for 4 weeks;
  - **if CR or CRi not achieved:** 1.8mg/m^2 as 3 divided doses on Day 1 (0.8mg/m^2), Day 8 (0.5mg/m^2), Day 15 (0.5mg/m^2) for 4 weeks;
- Discontinue if CR or CRi not achieved within 3 cycles

Dosage & Administration

- Patients proceeding to hematopoietic stem cell transplant (HSCT): treat for 2 cycles; may consider 3rd cycle if CR or CRi and minimal residual disease negativity not achieved after 2 cycles; if not proceeding to HSCT: may treat up to max 6 cycles
- Dose modifications for toxicities: see full labeling

Considerations for Special Populations

- **Pregnancy:** Avoid; exclude status prior to initiation; use effective contraception during and for 8 months (females) or 5 months (males w. female partners) after last dose.
- **Nursing mothers:** Not recommended during and for at least 2 months after last dose
- **Pediatric:** Not established
- **Elderly:** No adjustment to starting dose required based on age

Warnings/Precautions

- Risk of **hepatotoxicity**, including **veno-occlusive disease** (VOD); monitor closely; permanently discontinue if VOD occurs
- Increased risk of VOD in those who underwent HSCT after Besponsa treatment, ongoing or prior liver disease, prior HSCT, increased age, later salvage lines, and a greater number of treatment cycles
- **Monitor liver function tests** prior to and after each dose; interrupt, reduce, or permanently discontinue if elevated

Warnings/Precautions

- Increased risk of post-HSCT non-relapse mortality rate; monitor for toxicities (eg, infection, VOD)
- History of or predisposition for **QT prolongation, electrolyte disturbances**; obtain ECGs and electrolytes prior to treatment, after initiation of drug known to prolong QTc, and periodically thereafter as indicated

Warnings/Precautions

- **Monitor CBCs**, for signs/symptoms of infection, bleeding/hemorrhage, or other effects of myelosuppression; interrupt, reduce, or permanently discontinue if develops
- **Monitor for infusion-related reactions** during and for at least 1 hour after infusion ends; interrupt and treat if occurs; permanently discontinue if severe or life-threatening
- Embryo-fetal toxicity

Interactions

- Increased risk of **QT interval prolongation** with concomitant drugs known to prolong the QT interval or induce Torsades de Pointes; avoid, discontinue, or use alternative drugs

Adverse Reactions

- Thrombocytopenia
- Neutropenia
- Infection
- Anemia
- Leukopenia
- Fatigue
- Hemorrhage
- Pyrexia
- Nausea
- Headache
- Febrile neutropenia
- Transaminases increased
- Abdominal pain
- Gamma-glutamyltransferase increased
- Hyperbilirubinemia
- Infusion-related reactions
- Impaired fertility

Mechanism of Action

- Besponsa binds to CD22-expressing tumor cells, eventually leading to cell cycle arrest and apoptosis through DNA breakage

Clinical Studies

- Besponsa was evaluated in **INO-VATE ALL,** a randomized, open-label, international, multicenter study in patients with relapsed or refractory ALL (N=326)

Clinical Studies

- Eligible patients were aged ≥18 years with Philadelphia chromosome-negative or Philadelphia chromosome-positive relapsed or refractory B-cell precursor ALL
- All patients were required to have ≥5% bone marrow blasts and to have received 1 or 2 previous induction chemotherapy regimens for ALL

Clinical Studies

- The efficacy of Besponsa was established on the basis of CR, the duration of CR, and proportion of MRD-negative CR (<1 × 10^{-4} of bone marrow nucleated cells by flow cytometry) in the first 218 patients randomized
- CR, duration of remission (DoR), and MRD results in the initial 218 randomized patients were consistent with those seen in all 326 randomized patients

Clinical Studies

- Among the initial 218 randomized patients:
  - CR/Cri for Besponsa-treated patients was **80.7%** (95% CI, 72.1%-87.7%) vs **29.4%** with chemotherapy (95% CI, 21.0%-38.8%)
  - Among patients achieving CR/CRi, those treated with Besponsa also showed a higher rate of minimal residual disease (MRD) negativity (78.4% [95% CI, 68.4%-86.5%]) vs those treated with chemotherapy (28.1% [95% CI, 13.7%-46.7%])

Clinical Studies

- 48% of Besponsa-treated patients proceeded to HSCT vs 22% treated with chemotherapy
- Median overall survival (OS) for patients treated with Besponsa was **7.7** months (95% CI, 6.0-9.2) and **6.2** months (95% CI, 4.7-8.3) for patients treated with chemotherapy
- Analysis of OS for patients treated with Besponsa vs chemotherapy did not meet the pre-specified boundary for statistical significance (HR 0.75 [97.5% CI, 0.57-0.99])

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/besponsa/drug/34795/