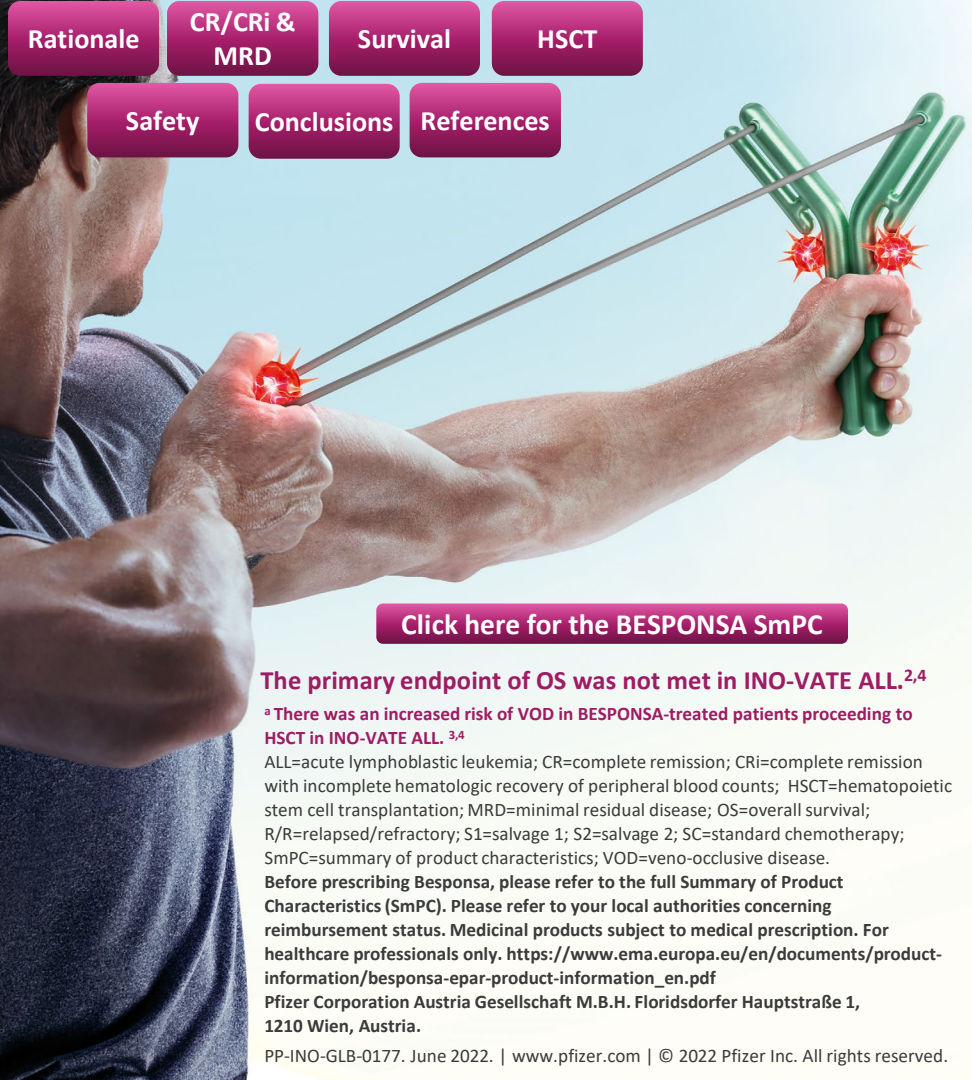

BESPONSA™ inotuzumab ozogamicin INJECTION FOR IV INFUSION

IMPACT OF SALVAGE TREATMENT PHASE ON BESPONSA TREATMENT FOR R/R B-CELL ALL: AN UPDATE FROM THE INO-VATE FINAL STUDY DATABASE

For the full post hoc analysis see:
Jabbour E, *et al. Leuk Lymphoma* 2020

Rates of CR/CRi and MRD negativity in BESPONSA-treated patients were greater in first salvage

CR/CRi: 78.4% in S1 vs. 64.7% in S2[1]

MRD negativity: 77.0% in S1 vs. 72.7% in S2[1]

Improvements in long-term survival were more pronounced in patients treated with BESPONSA in first salvage

25.9% in S1 vs. 16.8% in S2 at 24 months[1]

More patients proceeded to HSCT with BESPONSA when treated in first salvage[a]

52.3% in S1 vs. 39.2% in S2[1]

VOD incidence with BESPONSA appeared greater in second salvage

Post-HSCT VOD: 19.0% in S1 vs. 35.0% in S2[1]

Click here for the BESPONSA SmPC

The primary endpoint of OS was not met in INO-VATE ALL.[2,4]

[a] There was an increased risk of VOD in BESPONSA-treated patients proceeding to HSCT in INO-VATE ALL.[3,4]

ALL=acute lymphoblastic leukemia; CR=complete remission; CRi=complete remission with incomplete hematologic recovery of peripheral blood counts; HSCT=hematopoietic stem cell transplantation; MRD=minimal residual disease; OS=overall survival; R/R=relapsed/refractory; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; SmPC=summary of product characteristics; VOD=veno-occlusive disease.

Before prescribing Besponsa, please refer to the full Summary of Product Characteristics (SmPC). Please refer to your local authorities concerning reimbursement status. Medicinal products subject to medical prescription. For healthcare professionals only. https://www.ema.europa.eu/en/documents/product-information/besponsa-epar-product-information_en.pdf

Pfizer Corporation Austria Gesellschaft M.B.H. Floridsdorfer Hauptstraße 1, 1210 Wien, Austria.

Indication: 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).

INO-VATE ALL: Rationale for the Post Hoc Analysis of INO-VATE ALL Outcomes by Salvage Line

- The prognosis of adults with R/R B-cell ALL is poor; however, outcomes are generally improved among first salvage patients with a longer duration of first complete remission (CR1)[1]
- INO-VATE ALL, the pivotal phase 3 registration study for BESPONSA, was an open-label, randomized trial in adults (N = 326) with R/R B-cell ALL[1,2]
  - **CR/CRi and OS were the two primary endpoints[2]**
    - **Patients treated with BESPONSA had significantly higher rates of remission** compared with those treated with SC (CR/CRi: 80.7% vs. 29.4%, $P < 0.001$)[2,a]
    - **The primary endpoint of OS was not met[2,4]**
- **This post hoc analysis provides an updated, in-depth analysis of the final INO-VATE ALL study outcomes by salvage line[1]**

For the full post hoc analysis see:
Jabbour E, et al. *Leuk Lymphoma.* 2020

[a] Results are from the phase 3 INO-VATE ALL study remission-analysis population, which included the first 218 patients who underwent randomization in the intention-to-treat population. [2]

ALL=acute lymphoblastic leukemia; CR=complete remission; CRi=complete remission with incomplete hematologic recovery of peripheral blood counts; OS=overall survival; R/R=relapsed/refractory; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy.

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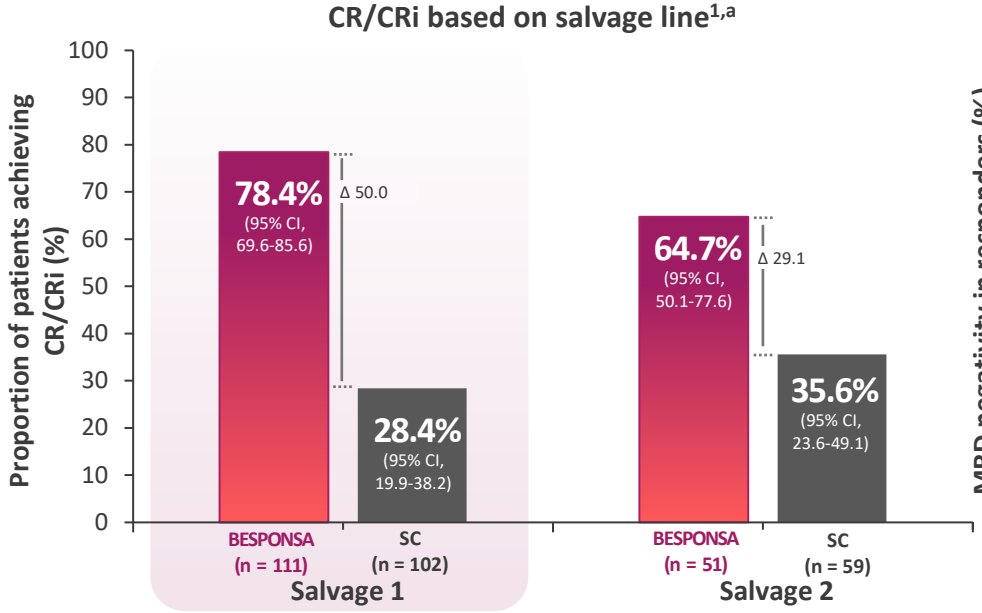
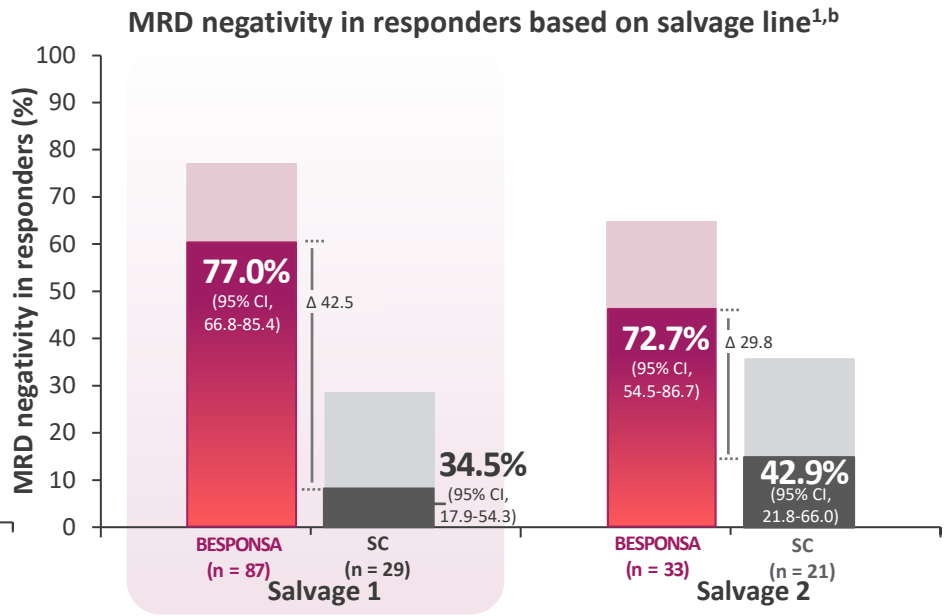
Rates of CR/CRi and MRD Negativity in BESPONSA-treated Patients Were Greater in First Salvage





- CR/CRi rates were also improved in S1 patients with a pre-study extended CR1 ≥ 12 months treated with BESPONSA (85.4% [n = 41/48] vs. 27.5% [n = 11/40])[1]

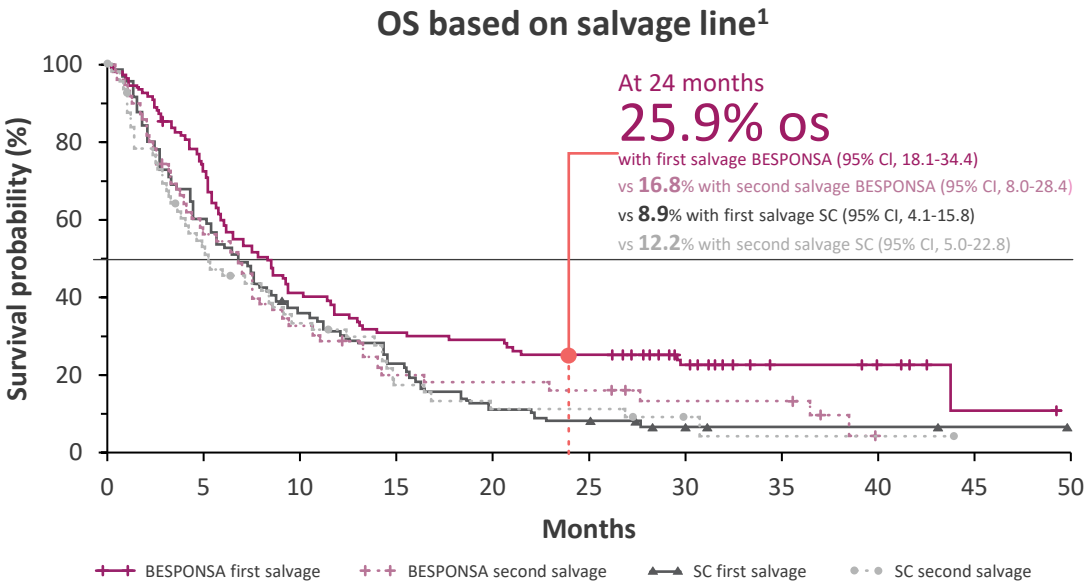
Note: The increased CR/CRi rates for SC in S2 vs S1 was not expected, and may be due to the limited sample size or differences in baseline charcteristics.[1]

[a] In S1, 40.5% (95% CI, 31.3-50.3) of BESPONSA-treated patients and 16.7% (95% CI, 10.0-25.3) of SC-treated patients achieved CR; 37.8% (95% CI, 28.8-47.5) and 11.8% (95% CI, 6.2-19.6) achieved CRi, respectively. In S2, 19.6% (95% CI, 9.8-33.1) of BESPONSA-treated patients and 15.3% (95% CI, 7.2-27.0) of SC-treated patients achieved CR and 45.1% (95% CI, 31.1-59.7) and 20.3% (95% CI, 11.0-32.8) achieved CRi, respectively. [b] Lighter-colored bar segments represent patients who achieved CR/CRi but did not achieve MRD-negativity. Salvage treatment line was according to the clinical report form.[1]

CI=confidence interval; CR=complete remission; CRi=complete remission with incomplete hematologic recovery of peripheral blood counts; MRD=minimal residual disease; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy.

BESPONSA™ inotuzumab ozogamicin INJECTION FOR IV INFUSION

Improvements in Long-term Survival Were More Pronounced in Patients Treated With BESPONSA in First Salvage



Note: Due to the small sample size, results should be interpreted with caution.

The primary endpoint of OS was not met in INO-VATE ALL.[2,4]

In this post hoc analysis, 24-month OS with BESPONSA was 25.9% in S1 vs. 16.8% in S2[1]

In the INO-VATE ALL trial, a higher post-HSCT non relapse mortality rate was observed in patients receiving BESPONSA compared to the Investigator's choice of chemotherapy arm, resulting in a higher Day 100 post-HSCT mortality rate.[3]

Monitor closely for toxicities post-HSCT, including signs and symptoms of infection and VOD.[3]

Hashmarks on Kaplan-Meier graphs correspond to patients censored.
Salvage treatment line by clinical report form; ITT population.[1]
ALL=acute lymphoblastic leukemia; CI=confidence interval; HSCT=hematopoietic stem cell transplantation; ITT=intent to treat; OS=overall survival; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; VOD=veno-occlusive disease.

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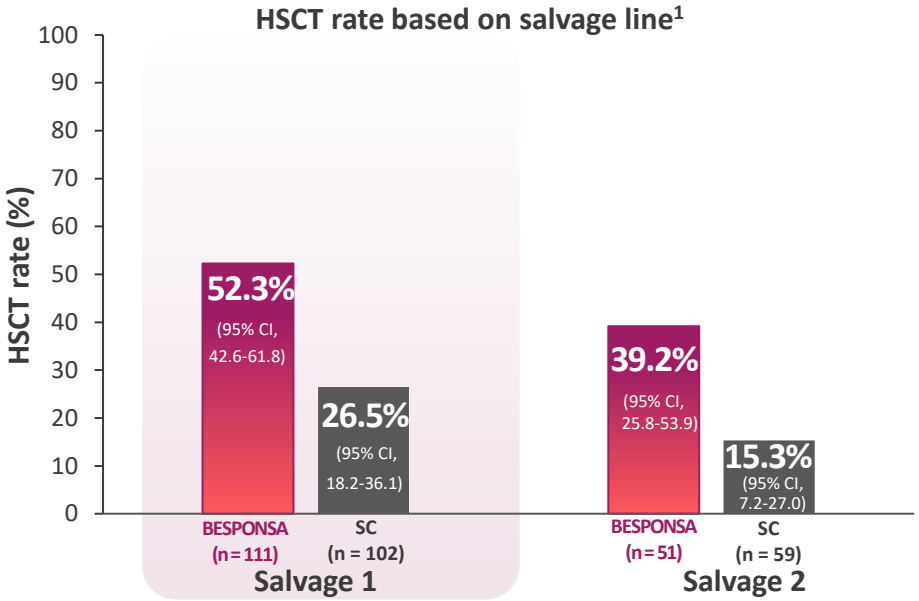
More Patients Proceeded to Transplant With BESPONSA When Treated in First Salvage

- **In this post hoc analysis, a greater proportion of patients proceeded to post-treatment HSCT with BESPONSA when treated in first salvage (52.3% in S1 vs. 39.2% in S2)[1,a]**

Higher frequency of early death post-HSCT: There was a higher frequency of early death post-HSCT (at Day 100) in the BESPONSA arm; however, there was evidence of a late survival benefit for BESPONSA. Monitor closely for toxicities post-HSCT, including signs and symptoms of infection and VOD[3]



[a] **There was an increased risk of VOD in BESPONSA-treated patients proceeding to HSCT in INO-VATE ALL.[3,4]**

ALL=acute lymphoblastic leukemia; CI=confidence interval; HSCT=hematopoietic stem cell transplantation; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; VOD=veno-occlusive disease.

BESPONSA™ inotuzumab ozogamicin

BESPONSA Safety Profile Compared With SC

All causality grade ≥ 3 TEAEs in ≥ 10% of patients in any arm by salvage line (safety population)[1]

	S1		S2	
MedDRA, System Organ Class, and Preferred Term, n (%)	BESPONSA (n = 111)	SC (n = 93)	BESPONSA (n = 51)	SC (n = 49)
Blood and lymphatic system disorders	90 (81.1)	81 (87.1)	39 (76.5)	42 (85.7)
Neutropenia	56 (50.5)	40 (43.0)	21 (41.2)	22 (44.9)
Thrombocytopenia	46 (41.4)	56 (60.2)	20 (39.2)	28 (57.1)
Anemia	25 (22.5)	37 (39.8)	12 (23.5)	26 (53.1)
Leukopenia	31 (27.9)	28 (30.1)	12 (23.5)	25 (51.0)
Febrile neutropenia	27 (24.3)	53 (57.0)	15 (29.4)	24 (49.0)
Lymphopenia	18 (16.2)	18 (19.4)	9 (17.6)	17 (34.7)
Hepatobiliary disorders	14 (12.6)	7 (7.5)	13 (25.5)	5 (10.2)
VOD	11 (9.9)	2 (2.2)	8 (15.7)	1 (2.0)
Metabolism and nutrition disorders	19 (17.1)	20 (21.5)	7 (13.7)	12 (24.5)
Hypokalemia	5 (4.5)	9 (9.7)	6 (11.8)	4 (8.2)
Infections and infestations	31 (27.9)	51 (54.8)	15 (29.4)	27 (55.1)
Bacteremia	5 (4.5)	4 (4.3)	1 (2.0)	6 (12.2)
Sepsis	4 (3.6)	7 (7.5)	1 (2.0)	5 (10.2)

VOD incidence with BESPONSA appeared greater in second salvage:[1]

- During study treatment/follow-up without HSCT **(1.8% [n = 2/111]) in S1 vs. 5.9% [n = 3/51] in S2)**
- Or following HSCT **(19.0% [n = 11/58] in S1 vs. 35.0% [n = 7/20] in S2)**

Note: Due to the small sample size, results should be interpreted with caution.

- Grade ≥ 3 TEAE incidence with BESPONSA and SC was 91.0% vs. 95.7% (S1) and 90.2% vs. 98.0% (S2), respectively[1]

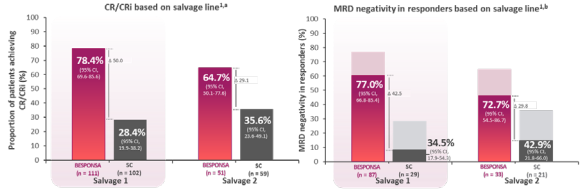
Salvage treatment line was according to the clinical report form.[1]

HSCT=hematopoietic stem cell transplantation; MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment emergent adverse event; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; VOD=veno-occlusive disease.

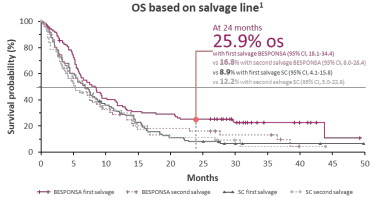
BESPONSA™ inotuzumab ozogamicin INJECTION FOR IV INFUSION

Conclusions

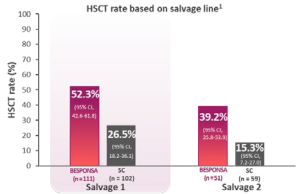
Rates of CR/CRi and MRD negativity in BESPONSA-treated patients were greater in first salvage[1]



Improvements in long-term survival were more pronounced in patients treated with BESPONSA in first salvage[1]

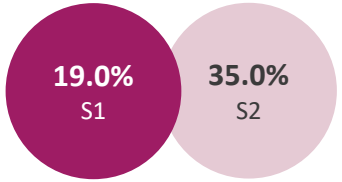


More patients proceeded to transplant with BESPONSA when treated in first salvage[1,c]



VOD incidence with BESPONSA appeared greater in second salvage[1]

Post-HSCT VOD:



Use of BESPONSA in first salvage may maximize the chance of a successful treatment outcome in R/R B-cell ALL[1]

The primary endpoint of OS was not met in INO-VATE ALL.[2,4]

[a] In S1, 40.5% (95% CI, 31.3-50.3) of BESPONSA-treated patients and 16.7% (95% CI, 10.0-25.3) of SC-treated patients achieved CR; 37.8% (95% CI, 28.8-47.5) and 11.8% (95% CI, 6.2-19.6) achieved CRi, respectively. In S2, 19.6% (95% CI, 9.8-33.1) of BESPONSA-treated patients and 15.3% (95% CI, 7.2-27.0) of SC-treated patients achieved CR and 45.1% (95% CI, 31.1-59.7) and 20.3% (95% CI, 11.0-32.8) achieved CRi, respectively. [b] Lighter-colored bar segments represent patients who achieved CR/CRi but did not achieve MRD-negativity. Salvage treatment line was according to the clinical report form.[1] [c] **There was an increased risk of VOD in BESPONSA-treated patients proceeding to HSCT in INO-VATE ALL.** [3,4]

ALL=acute lymphoblastic leukemia; CI=confidence interval; CR=complete remission; CRi=complete remission with incomplete hematologic recovery of peripheral blood counts; HSCT=hematopoietic stem cell transplantation; MRD=minimal residual disease; OS=overall survival; R/R=relapsed/refractory; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; VOD=veno-occlusive disease.

BESPONSA™ inotuzumab ozogamicin INJECTION FOR IV INFUSION

References

1. Jabbour E, et al. Impact of salvage treatment phase on inotuzumab ozogamicin treatment for relapsed/refractory acute lymphoblastic leukemia: an update from the INO-VATE final study database. *Leuk Lymphoma.* 2020;61(8):2012-2015 and supplement.
2. Kantarjian HM, et al. Inotuzumab ozogamicin versus standard care for acute lymphoblastic leukemia. *N Engl J Med.* 2016;375(8):740-753.
3. Besponsa summary of product characteristics, February 2022.
4. Kantarjian HM, et al. Inotuzumab ozogamicin versus standard of care in relapsed or refractory acute lymphoblastic leukemia: final report and long-term survival follow-up from the randomized, phase 3 INO-VATE study. *Cancer*. 2019;125(14):2474-2487.

Before prescribing Besponsa, please refer to the full Summary of Product Characteristics (SmPC).

Please refer to your local authorities concerning reimbursement status. Medicinal product subject to medical prescription.

BESPONSA™ inotuzumab ozogamicin

Fachkurzinformation

BESPONSA 1 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung

Qualitative und quantitative Zusammensetzung: Jede Durchstechflasche enthält 1mg Inotuzumab Ozogamicin. Nach der Rekonstitution enthält 1 ml Lösung 0,25 mg Inotuzumab Ozogamicin.

Liste der sonstigen Bestandteile: Sucrose, Polysorbat 80, Natriumchlorid, Tromethamin.

Anwendungsgebiete: BESPONSA ist indiziert als Monotherapie für die Behandlung von Erwachsenen mit rezidivierter oder refraktärer CD22-positiver B-Vorläufer-ALL (akuter lymphatischer Leukämie). Erwachsene Patienten mit Philadelphia-Chromosom-positiver (Ph+) rezidivierter oder refraktärer B-Vorläufer-ALL sollten eine vorhergehende erfolglose Behandlung mit mindestens 1 Tyrosinkinase-Inhibitor (TKI) aufweisen.

Gegenanzeigen: Überempfindlichkeit gegen den Wirkstoff oder einen der in Abschnitt 6.1 der Fachinformation genannten sonstigen Bestandteile. Patienten mit vorhergehender bestätigter schwerer oder bestehender venookklusiver Lebererkrankung/ sinusoidalem Obstruktionssyndrom (VOD/ SOS). Patienten mit schwerer bestehender Lebererkrankung (z. B. Leberzirrhose, nodulär regenerative Hyperplasie der Leber, aktive Hepatitis).

Pharmakotherapeutische Gruppe: Antineoplastische Mittel, andere antineoplastische Mittel, monoklonale Antikörper. ATC-Code: L01XC26.

Inhaber der Zulassung: Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Brüssel, Belgien.

Stand der Information: Februar 2022.

Rezeptpflicht/Apothekenpflicht: Rezept- und apothekenpflichtig, wiederholte Abgabe verboten. **Angaben zu besonderen Warnhinweisen und Vorsichtsmaßnahmen für die Anwendung, Wechselwirkungen mit anderen Arzneimitteln und sonstigen Wechselwirkungen, Fertilität, Schwangerschaft und Stillzeit und Nebenwirkungen entnehmen Sie bitte der veröffentlichten Fachinformation.**

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