

Rationale

CR/CRI & MRD

Survival

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References



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

[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.
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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 S2¹
MRD negativity: 77.0% in S1 vs. 72.7% in S2¹

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 months¹

More patients proceeded to HSCT with BESPONSA when treated in first salvage^a
52.3% in S1 vs. 39.2% in S2¹

VOD incidence with BESPONSA appeared greater in second salvage
Post-HSCT VOD: 19.0% in S1 vs. 35.0% in S2¹

▼ This medicinal product is subject to additional monitoring.
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

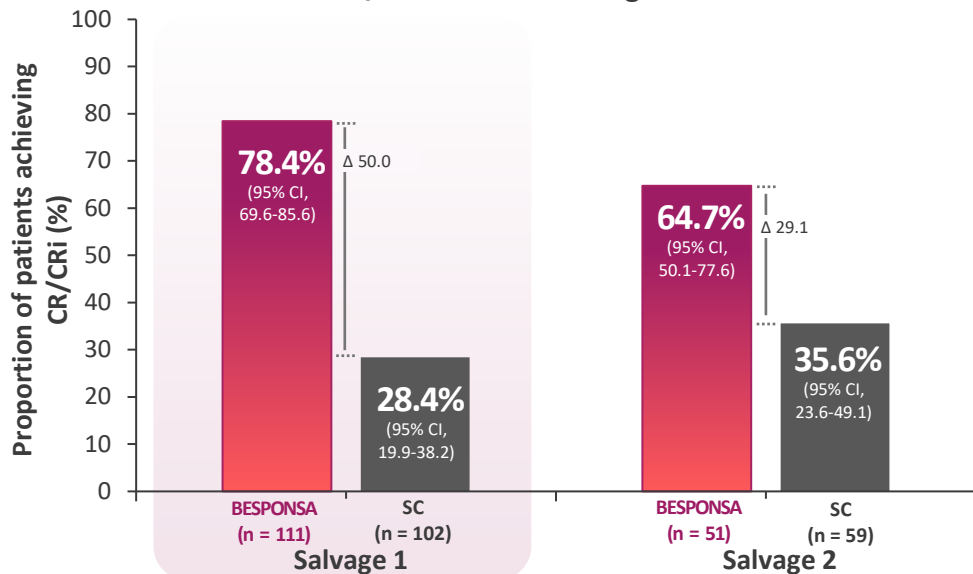
- The prognosis of adults with R/R B-cell ALL is poor; however, outcomes are generally improved among first salvage patients with a longer duration of first complete remission (CR1)¹
- INO-VATE ALL, the pivotal phase 3 registration study for BESPONSA, was an open-label, randomized trial in adults (N = 326) with R/R B-cell ALL^{1,2}
 - CR/CRi and OS were the two primary endpoints²
 - **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

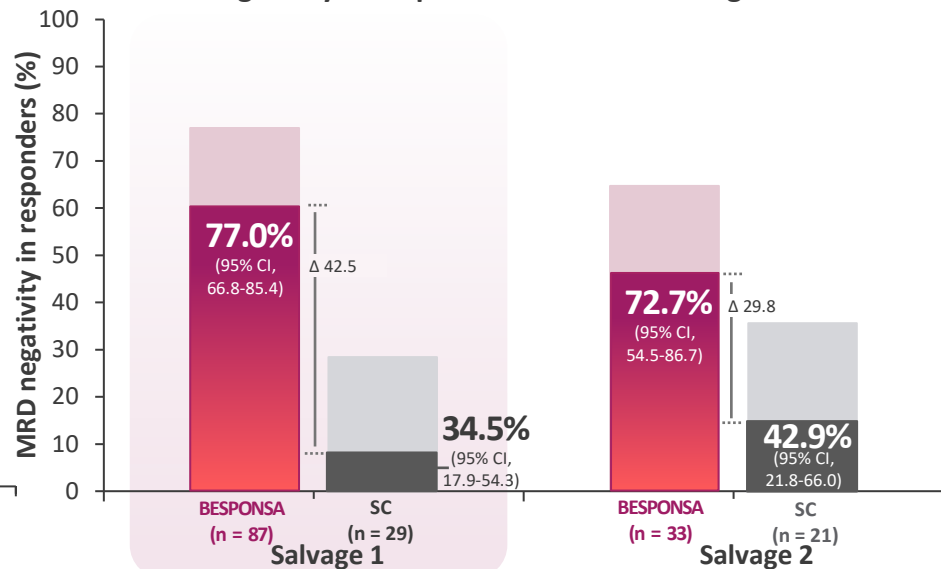
^aResults are from the phase 3 INO-VATE ALL study remission-analysis population, which included the first 218 patients who underwent randomization in the intention-to-treat population. ²
ALL=acute lymphoblastic leukemia; CR=complete remission; CRi=complete remission with incomplete hematologic recovery of peripheral blood counts; OS=overall survival;
R/R=relapsed/refractory; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy.

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

CR/CRi based on salvage line^{1,a}



MRD negativity in responders based on salvage line^{1,b}



- CR/CRi rates were also improved in S1 patients with a pre-study extended CR1 \geq 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 characteristics.¹

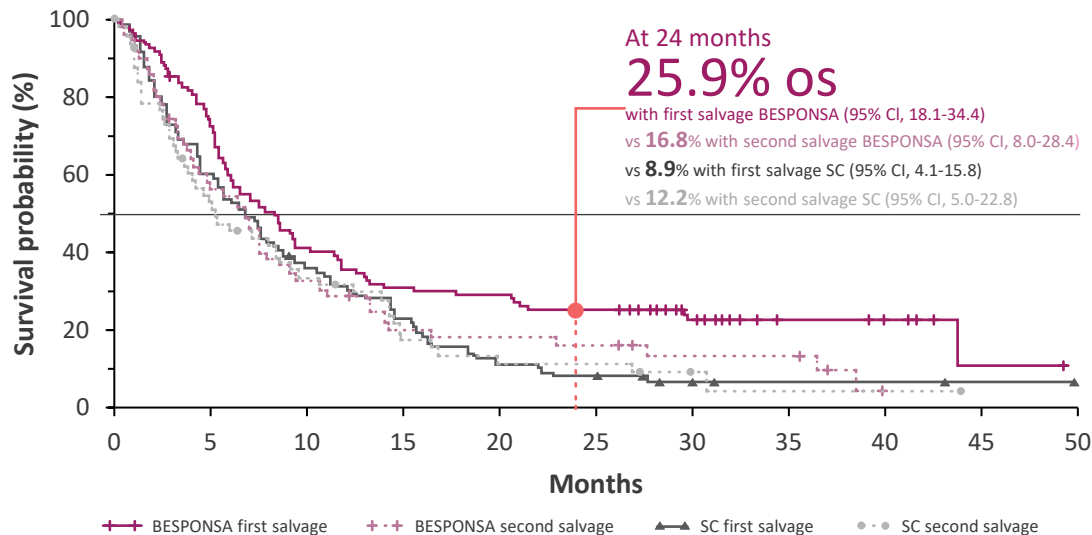
^a In S1, 40.5% (95% CI, 31.3-50.3) of BESPONSA-treated patients and 16.7% (95% CI, 10.0-25.3) of SC-treated patients achieved CR; 37.8% (95% CI, 28.8-47.5) and 11.8% (95% CI, 6.2-19.6) achieved CRi, respectively. In S2, 19.6% (95% CI, 9.8-33.1) of BESPONSA-treated patients and 15.3% (95% CI, 7.2-27.0) 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.

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

OS based on salvage line¹



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 S2¹

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 VOD³

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.

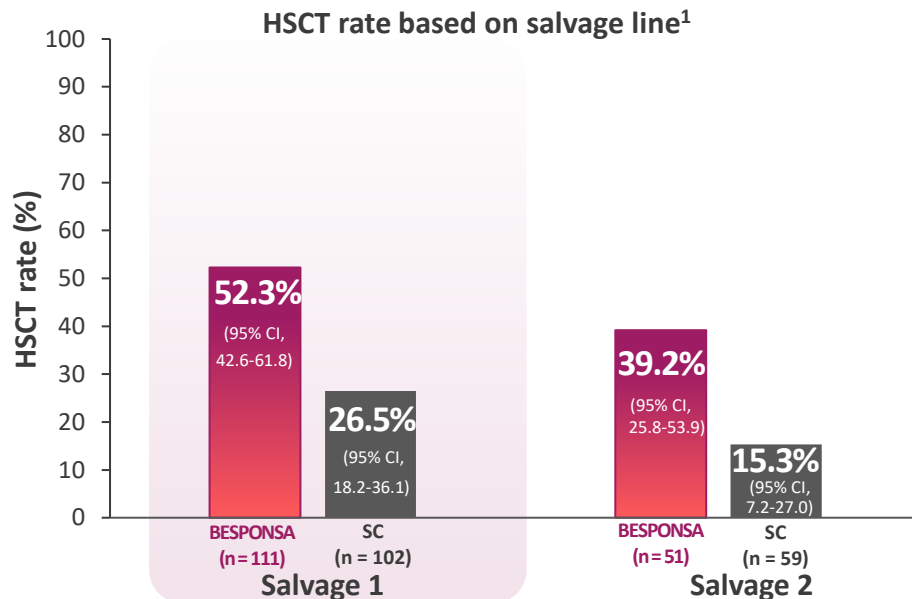
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More Patients Proceeded to Transplant With BESPONSA When Treated in First Salvage

- 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 VOD³



^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 Safety Profile Compared With SC

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

MedDRA, System Organ Class, and Preferred Term, n (%)	S1		S2	
	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), respectively¹

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

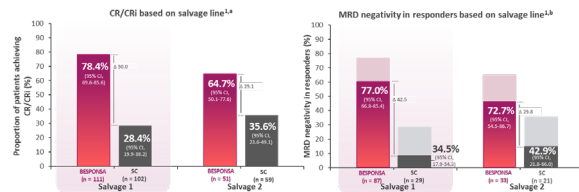
HSCT=hematopoietic stem cell transplantation; MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment emergent adverse event; S1=salvage 1; S2=salvage 2; SC=standard chemotherapy; VOD=veno-occlusive disease.

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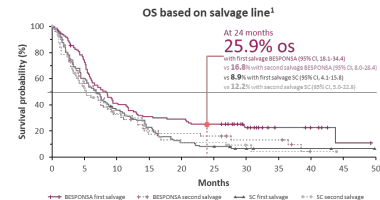


Conclusions

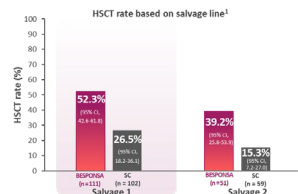
Rates of CR/CRi and MRD negativity in BESPONSA-treated patients were greater in first salvage¹



Improvements in long-term survival were more pronounced in patients treated with BESPONSA in first salvage¹



More patients proceeded to transplant with BESPONSA when treated in first salvage^{1,c}



VOD incidence with BESPONSA appeared greater in second salvage¹

Post-HSCT VOD:

19.0%
S1

35.0%
S2

Use of BESPONSA in first salvage may maximize the chance of a successful treatment outcome in R/R B-cell ALL¹

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.

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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.
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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.