# Outcomes in Patients With B-Cell Precursor Acute Lymphoblastic Leukemia Receiving Inotuzumab Ozogamicin Stratified by Body Mass Index

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## Objective

- To assess efficacy and safety of InO in adult patients with relapsed/refractory B-cell precursor acute lymphoblastic leukemia, stratified by baseline BMI.

## Conclusions

- This pooled analysis is the first to investigate the effect of BMI on efficacy of an antibody-drug conjugate in ALL.
- In patients treated with InO for R/R B-ALL, efficacy and safety outcomes were broadly consistent across BMI groups.
- A trend of lower PFS and OS rates was noted in patients with increasing BMI.
- Morbidly obese patients were observed to have the highest non-relapse mortality, consistent with previous reports.

## Background

- Inotuzumab ozogamicin (InO) is an antibody–drug conjugate composed of anti-CD22 monoclonal antibody conjugated to calicheamicin, a potent cytotoxic antitumor antibiotic.[1,2]
- InO is approved for the treatment of adults for relapsed/refractory B-cell precursor acute lymphoblastic leukemia (R/R B-ALL).[1,2]
- In previous studies, elevated body mass index (BMI) has been associated with worse outcomes in adult patients treated for ALL.[3-5]
- This analysis was conducted to assess the efficacy and safety of InO in adult patients with R/R B-ALL, stratified by BMI, across Pfizer sponsored clinical trials.

## Methods

- Data from 3 previous studies were pooled for analysis:
  - In study B1931010 (NCT01363297) participants received InO at 0.8–1.8 mg/m$^2$/cycle in the Phase 1 portion of the study, and 1.6–1.8 mg/m$^2$/cycle in the Phase 2 portion,[6]
  - In study B1931022 (NCT01564784) patients received InO at 1.5–1.8 mg/m$^2$/cycle,[7]
  - In study B1931030 (NCT03677596) patients received InO at 0.9–1.2 mg/m$^2$ or 1.5–1.8 mg/m$^2$/cycle.[8]
- Participants were grouped by formal BMI definitions of <25 kg/m$^2$ (healthy), 25–30 kg/m$^2$ (overweight) and >30 kg/m$^2$ (obese). Data presented as descriptive statistics only.

## Results

- Data from 338 participants were analyzed, with 155 participants in the <25 kg/m$^2$ group, 116 participants in the 25–30 kg/m$^2$ group and 67 participants in the >30 kg/m$^2$ group. Baseline characteristics were comparable across BMI groups (**Table 1**).

**Table 1: Demographics and baseline characteristics**

| | <25 kg/m$^2$ n=155 | 25 kg/m$^2$–30 kg/m$^2$ n=116 | >30 kg/m$^2$ n=67 | Total N=338 |
|---|---|---|---|---|
| Age, yrs | | | | |
| 18 to <45, n (%) | 93 (60.0) | 48 (41.4) | 31 (46.3) | 172 (50.9) |
| 45 to <65, n (%) | 43 (27.7) | 50 (43.1) | 25 (37.3) | 118 (34.9) |
| ≥65, n (%) | 19 (12.3) | 18 (15.5) | 11 (16.4) | 48 (14.2) |
| Mean (SD) | 41.19 (16.30) | 47.42 (16.19) | 46.12 (16.93) | 44.31 (16.59) |
| Median (min, max) | 39.00 (18, 79) | 49.00 (20, 78) | 47.00 (18, 76) | 44.00 (18, 79) |
| Gender, n (%) | | | | |
| Female | 70 (45.2) | 51 (44.0) | 19 (28.4) | 140 (41.4) |
| Race, n (%) | | | | |
| White | 106 (68.4) | 82 (70.7) | 55 (82.1) | 243 (71.9) |
| Black or African American | 4 (2.6) | 0 (0.0) | 2 (3.0) | 6 (1.8) |
| Asian | 36 (23.2) | 20 (17.2) | 3 (4.5) | 59 (17.5) |
| Native Hawaiian or Other Pacific Islander | 0 (0.0) | 0 (0.0) | 1 (1.5) | 1 (0.3) |
| Other | 7 (4.5) | 7 (6.0) | 1 (1.5) | 15 (4.4) |
| Unknown | 1 (0.6) | 2 (1.7) | 2 (3.0) | 5 (1.5) |
| Not reported | 1 (0.6) | 5 (4.3) | 3 (4.5) | 9 (2.7) |
| ECOG, n (%) | | | | |
| 0 | 53 (34.2) | 44 (37.9) | 25 (37.3) | 122 (36.1) |
| 1 | 78 (50.3) | 56 (48.3) | 34 (50.7) | 168 (49.7) |
| 2 | 22 (14.2) | 15 (12.9) | 8 (11.9) | 45 (13.3) |
| 3 | 2 (1.3) | 1 (0.9) | 0 (0.0) | 3 (0.9) |
| Salvage status, n (%) | | | | |
| Salvage 1 | 73 (47.1) | 60 (51.7) | 41 (61.2) | 174 (51.5) |
| Salvage ≥2 | 80 (51.6) | 56 (48.3) | 26 (38.8) | 162 (47.9) |
| Duration of first remission, n (%) | | | | |
| <6 months | 42 (27.1) | 30 (25.9) | 16 (23.9) | 88 (26.0) |
| ≥6–<12 months | 32 (20.6) | 15 (12.9) | 6 (9.0) | 53 (15.7) |
| ≥12–<24 months | 23 (14.8) | 21 (18.1) | 11 (16.4) | 55 (16.3) |
| ≥24 months | 19 (12.3) | 21 (18.1) | 13 (19.4) | 53 (15.7) |
| Missing | 39 (25.2) | 29 (25.0) | 21 (31.3) | 89 (26.3) |
| Prior stem cell transplant, n (%) | | | | |
| Yes | 43 (27.7) | 24 (20.7) | 9 (13.4) | 76 (22.5) |

ECOG=Eastern Cooperative Oncology Group performance status

### EFFICACY

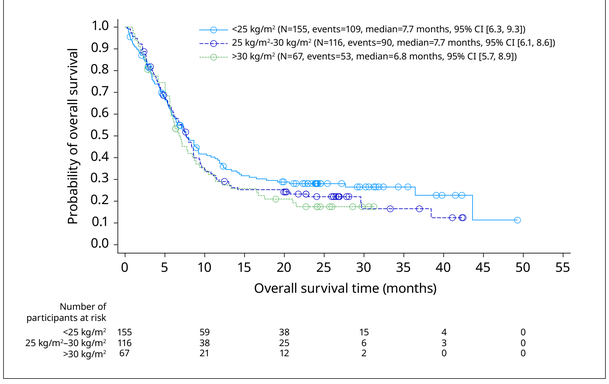
- Efficacy outcomes were broadly consistent across the 25 kg/m$^2$, 25–30 kg/m$^2$ and >30 kg/m$^2$ groups (**Table 2**); however, a trend of lower overall survival (**Figure 1**) and progression-free survival rates was observed with increasing BMI.
- A subgroup of morbidly obese (>40 kg/m$^2$) patients was also evaluated (**Table 2**). This group was observed to have the highest non-relapse mortality, consistent with previous reports.

**Table 2: Summary of outcomes**

| | <25 kg/m$^2$ n=155 | 25 kg/m$^2$–30 kg/m$^2$ n=116 | >30 kg/m$^2$ n=67 | >40 kg/m$^2$ n=13 |
|---|---|---|---|---|
| CR/CRi, n (%) | 108 (70) | 88 (76) | 46 (69) | 11 (85) |
| CR, n (%) | 51 (33) | 42 (36) | 27 (40) | 4 (31) |
| CRi, n (%) | 57 (37) | 46 (40) | 19 (28) | 7 (54) |
| MRD-negativity, n (%) | 87 (56) | 73 (63) | 35 (52) | 6 (46) |
| PFS,% at 24 months (95% CI) | 20 (13.2, 27.5) | 13 (7.2, 20.1) | 11 (4.2, 21.1) | 23 (5.6, 47.5) |
| OS,% at 24 months (95% CI) | 28 (21.0, 35.6) | 22 (14.8, 30.3) | 18 (9.2, 27.8) | 23 (5.6, 47.5) |
| Deaths, n (%) | 109 (70) | 90 (78) | 53 (79) | 10 (77) |
| Disease progression | 57 (37) | 46 (40) | 31 (46) | 2 (15) |
| Non-relapse mortality | 45 (29) | 41 (35) | 21 (31) | 8 (62) |

CI=confidence interval; CR=complete remission; CRi=complete remission with incomplete hematologic recovery; MRD=minimum residual disease; OS=overall survival; PFS=progression-free survival

**Figure 1: Kaplan-Meier plot of overall survival by BMI**




### SAFETY

- Most patients experienced treatment-emergent adverse events (TEAEs), with similar incidence between 97% and 99% observed across BMI groups.
- Common Grade ≥3 TEAEs were neutropenia, thrombocytopenia, anemia, leukopenia, pneumonia, sinusoidal obstruction syndrome (SOS) and gamma-glutamyl transferase increase (**Table 3**).
  - TEAEs in the morbidly obese subgroup were similar to other BMI groups.

**Table 3: All-causality TEAE Grades ≥3 reported in ≥5% patients**

| Adverse event, n (%) | <25 kg/m$^2$ n=155 | 25 kg/m$^2$–30 kg/m$^2$ n=116 | >30 kg/m$^2$ n=67 | Total N=338 |
|---|---|---|---|---|
| Any adverse event | 109 (70.3) | 83 (71.6) | 45 (67.2) | 237 (70.1) |
| Anemia | 30 (19.4) | 23 (19.8) | 11 (16.4) | 64 (18.9) |
| Febrile neutropenia | 37 (23.9) | 21 (18.1) | 22 (32.8) | 80 (23.7) |
| Leukopenia | 28 (18.1) | 20 (17.2) | 10 (14.9) | 58 (17.2) |
| Lymphopenia | 14 (9.0) | 9 (7.8) | 5 (7.5) | 28 (8.3) |
| Neutropenia | 56 (36.1) | 46 (39.7) | 20 (29.9) | 122 (36.1) |
| Thrombocytopenia | 55 (35.5) | 38 (32.8) | 25 (37.3) | 118 (34.9) |
| Disease progression | 7 (4.5) | 7 (6.0) | 5 (7.5) | 19 (5.6) |
| Sinusoidal obstruction syndrome | 15 (9.7) | 7 (6.0) | 6 (9.0) | 28 (8.3) |
| Pneumonia | 9 (5.8) | 8 (6.9) | 2 (3.0) | 19 (5.6) |
| Gamma-glutamyl transferase increase | 11 (7.1) | 6 (5.2) | 3 (4.5) | 20 (5.9) |

TEAE=treatment-related adverse events

### POST-HSCT OUTCOMES

- Overall, 143 participants (42%) proceeded to hematopoietic stem cell transplantation (HSCT) (**Table 4**).

**Table 4: Post-HSCT outcomes**

| | <25 kg/m$^2$ n=155 | 25 kg/m$^2$–30 kg/m$^2$ n=116 | >30 kg/m$^2$ n=67 | >40 kg/m$^2$ n=13 |
|---|---|---|---|---|
| Proceeded to HSCT, n (%) | 67 (43) | 49 (42) | 27 (40) | 7 (53) |
| Post-HSCT NRM,[a] % (95% CI) | 22.4 (12.6, 33.8) | 22.2 (11.4, 35.3) | 19.1 (5.7, 38.3) | 28.6 (3.1, 63.6) |
| Post-HSCT SOS, n (%) | 18 (27) | 7 (14) | 6 (22) | 2 (29) |
| Grade 3–4 SOS, n (%) | 10 (15) | 7 (14) | 5 (19) | 2 (29) |

[a] within 100 days
HSCT=hematopoietic stem cell transplantation; NRM=non-relapse mortality; SOS=sinusoidal obstruction syndrome

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