# NON-INTERVENTIONAL (NI) FINAL STUDY REPORT

## Study Information

| | |
|---|---|
| **Title** | A Non-Interventional Post-Authorization Safety Study (PASS) of Inotuzumab Ozogamicin to Characterize Complications Post-Hematopoietic Stem Cell Transplantation (HSCT) Following Inotuzumab Ozogamicin Treatment in Adult and Pediatric Patients with B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) |
| **Protocol number** | B1931028 |
| **Version identifier of the final study report** | 1.0 |
| **Date** | 18 February 2023 |
| **EU Post Authorization Study (PAS) register number** | EUPAS23056 |
| **Active substance** | Inotuzumab ozogamicin<br>ATC code L01FB01 |
| **Medicinal product** | Inotuzumab ozogamicin (Besponsa®) |
| **Research question and objectives** | Research question:<br>What are the toxicities after hematopoietic stem cell transplantation (HSCT) in adult and pediatric patients who receive inotuzumab ozogamicin?<br><br>Objectives:<br>Based on collected data obtained from the Center for International Blood and Marrow Transplant Research (CIBMTR) registry, the following will be evaluated in adult and pediatric patients with B-cell ALL who received inotuzumab ozogamicin and proceeded to HSCT: |

| | |
|---|---|
| | • Patient-, disease- and HSCT-related characteristics, including details of all prior anti-cancer therapies;<br>• Timing of inotuzumab ozogamicin treatment prior to HSCT;<br>• Transplant-related mortality (non-relapse mortality), non-transplant-related mortality, relapse, and overall survival (OS);<br>• Post HSCT adverse events of interest including hepatic veno-occlusive disease /sinusoidal obstruction syndrome (VOD/SOS); and<br>• Cause of death (COD). |
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# TABLE OF CONTENTS

## LIST OF IN-TEXT TABLES

## LIST OF FIGURES

**Annex 1. List of stand-alone documents**

## Appendix 6. SAMPLE STANDARD SUBJECT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT (ICD)

Not applicable.

## Appendix 7. LIST OF SUBJECT DATA LISTINGS

Not applicable.

## Appendix 8. ADDITIONAL DOCUMENTS

Statistical programming plan for additional analyses: Study B1931028 Version 1.1 dated 14 Sept. 2020

## 1. ABSTRACT (STAND-ALONE DOCUMENT)

## 2. LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---|---|
| ABT | antibody-based therapy |
| ADC | antibody-drug conjugate |
| AE | adverse event |
| ALL | acute lymphoblastic leukemia |
| alloHSCT | allogeneic hematopoietic cell transplantation |
| ANC | absolute neutrophil count |
| AST/ALT | ratio between aspartate transaminase and alanine transaminase |
| BM | bone marrow |
| BMI | Body Mass Index |
| BOOP | bronchiolitis obliterans organizing pneumonia |
| CD22 | cluster of differentiation 22 |
| CI | confidence interval |
| CIBMTR | Center for International Blood and Marrow Transplant Research |
| CMV | cytomegalovirus |
| CNS | central nervous system |
| COD | cause of death |
| COP/BOOP | cryptogenic organizing pneumonia/bronchiolitis obliterans organizing pneumonia |
| CR | complete remission |
| CR1, CR2…. | first complete remission, second complete remission…. |
| CRF | Comprehensive Report Form |
| Cri | complete remission with incomplete hematologic recovery |
| CSA | cyclosporine |
| CVAD | cyclophosphamide, vincristine, doxorubicin (Adriamycin), and dexamethasone |
| EU | European Union |
| FDA | Food and Drug Administration |
| Form 2000 | Recipient Baseline Data |
| Form 2011 | ALL Pre-HSCT Data |
| Form 2100 | Post-HSCT Data |
| Form 2111 | ALL Post-HSCT Data |
| Form 2400 | Pre-Transplant Essential Data |
| Form 2402 | Pre-Transplant Essential Data: Disease Classification |
| Form 2450 | Post-Transplant Essential Data |
| Form 2541 | Inotuzumab Ozogamicin Supplemental Data |
| Form 2553 | VOD/SOS Supplemental Data |
| Form 2900 | Recipient Death Data |
| GVHD | graft-versus-host disease |
| HCT-CI | Hematopoietic Cell Transplantation Comorbidity Index |
| HLA | human leukocyte antigen |

| Abbreviation | Definition |
|---|---|
| HRSA | Health Resources and Services Administration |
| HSCT | hematopoietic stem cell transplantation |
| HTN | hypertension |
| IPN | interstitial pneumonitis |
| IRB | Institutional Review Board |
| IV | intravenous |
| MAC | myeloablative conditioning |
| MCW | Medical College of Wisconsin |
| MMF | mycophenolate mofetil |
| MRD | minimal residual disease |
| MTX | methotrexate |
| N/A | not applicable |
| NE | not evaluable |
| NA | nonmyeloablative |
| NMDP | National Marrow Donor Program |
| NTRM | non-transplant-related mortality |
| OS | overall survival |
| PAS | post-authorization study |
| PASS | post-authorization safety study |
| PBSC | peripheral blood stem cells |
| PIF | primary induction failure |
| PMR | post-marketing requirement |
| PT-Cy | post-transplant cyclophosphamide |
| PTSD | post-traumatic stress disorder |
| REL1 | first relapse |
| R/R | relapsed or refractory |
| RIC | reduced-intensity conditioning |
| SAP | statistical analysis plan |
| SIRS | systemic inflammatory response syndrome |
| SOS | sinusoidal obstruction syndrome |
| Tac | tacrolimus |
| TBI | total body irradiation |
| TCD | T-cell depletion |
| TED | transplant essential data |
| TKI | tyrosine-kinase inhibitor (includes dasatinib, imatinib, nilotinib, ponatinib) |
| TMA | thrombotic microangiopathy |
| TRM | transplant-related mortality |
| UCB | umbilical cord blood |
| US | United States |
| VOD | veno-occlusive disease |
| WBC | white blood cell |

## 3. INVESTIGATORS

The names, affiliations, and contact information of the investigators at each study site are listed in Appendix 3.1.

### Principal Investigator(s) of the Protocol

| Name, degree(s) | Title | Affiliation |
|---|---|---|
| Kofi Asomaning, PhD | Epidemiology Lead | Pfizer Inc |
| Mary Horowitz, MD | Scientific Director Emeritus, CIBMTR; Deputy Cancer Center Director, MCW | Medical College of Wisconsin |
| Wael Saber, MD | Scientific Director | CIBMTR |
| Mei-Jie Zhang, PhD | Chief Statistical Director | CIBMTR |
| Manmeet Kaur, MPH | Biostatistician I | CIBMTR |

### Lead Country Investigator(s) of the Protocol

Not applicable.

## 4. OTHER RESPONSIBLE PARTIES

Not applicable.

## 5. MILESTONES

| Milestone | Planned date | Actual date | Comments |
|---|---|---|---|
| Draft protocol submission to the FDA | End November 2017 | 28 November 2017 | |
| Final protocol submission to the FDA | 28 February 2018 | 22 January 2018 | |
| Registration in EU PAS register | 28 March 2018 | 14 March 2018 | |
| Start of data collection | 18 August 2018 | 18 August 2018 | |
| Interim study report #1 (18 Aug 2017 - 17 Aug 2018) | 28 February 2019 | 20 February 2019 | |
| Interim report 2 (18 Aug 2017 - 17 Aug 2019) | 28 February 2020 | 20 February 2020 | |
| Interim report 3 (18 Aug 2017 - 17 Aug 2020) | 28 February 2021 | 23 February 2021 | |
| Interim report 4 (18 Aug 2017 - 17 Aug 2021) | 28 February 2022 | 23 February 2022 | |
| End of data collection | 17 August 2022 | 17 August 2022 | |
| Final study report (18 Aug 2017 - 17 Aug 2022) | 28 February 2023 | 18 February 2023 | |

## 6. RATIONALE AND BACKGROUND

Inotuzumab ozogamicin is an antibody-drug conjugate (ADC) composed of a cluster of differentiation 22 (CD22)-directed monoclonal antibody that is covalently linked to N-acetyl-gamma-calicheamicin dimethylhydrazide.

In the United States (US), inotuzumab ozogamicin was approved by the Food and Drug Administration (FDA), on 17 August 2017, for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

ALL is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs[1]. ALL represents approximately 20% of leukemias among adults and 80% of acute leukemias in children[1]. The age-adjusted incidence rate (2008-2012) of ALL in the US was 1.7 per 100,000 individuals per year, with males having a slightly higher overall rate than females (1.9/100,000 versus 1.5/100,000)[2]. The median age of diagnosis for ALL is 14 years, with approximately 58% of patients diagnosed before the age of 20 years. By contrast, approximately 26% of cases are diagnosed after 45 years of age, and approximately 11% of patients are diagnosed after 65 years of age[2]. The B-cell subtype accounts for approximately 75% of ALL cases in adults and approximately 88% in children[3,4]. B-cell ALL is a frequently fatal disease in adults. While the cure rates and survival outcomes for B-cell- ALL have improved during the last several decades, most of the improvements have occurred in younger patients, primarily among children[5].

Inotuzumab ozogamicin has been associated with severe, life-threatening, and sometimes fatal adverse events (AEs), including hepatotoxicity and hepatic veno-occlusive disease / sinusoidal obstruction syndrome (VOD/SOS). In Phase 3 Study B1931022, VOD/SOS occurred during inotuzumab treatment and, more frequently, after subsequent treatment with hematopoietic stem cell transplantation (HSCT). Inotuzumab ozogamicin showed a statistically significant improvement in complete remission/complete remission with incomplete hematologic recovery (CR/CRi) compared to treating physicians' choice of 3 chemotherapy regimens (80.7% vs 29.4%). While HSCT after treatment with inotuzumab ozogamicin appeared to be associated with improved long-term survival, post-HSCT toxicity, especially VOD/SOS and TRM (transplant-related mortality or non-relapse mortality), was higher in patients treated with inotuzumab ozogamicin than with treating physicians' choice of chemotherapy. Specifically, among the 79 patients in the study treated with inotuzumab ozogamicin who proceeded to a subsequent HSCT, 18/79 patients (23%) developed VOD/SOS post-HSCT compared to 3/34 patients (9%) in the treating physicians' choice of chemotherapy arm. In addition, the cumulative post-HSCT non-relapse mortality was 31/79 (39%) in the inotuzumab ozogamicin arm compared to 8/35 (23%) in the control arm.

The current non-interventional study was designated as a post-authorization safety study (PASS) and was a commitment to post-marketing requirement (PMR 3259-1) by the FDA. The PMR wording which was agreed upon with the FDA is as follows:

"Characterize toxicity after HSCT in adult and pediatric patients who receive inotuzumab ozogamicin. Include hepatic VOD, TRM (transplant-related mortality), and NTRM. Conduct an analysis of registry data (for example the CIBMTR registry) to evaluate safety at least through day 180 after transplantation. The number of available patients in the database will determine the sample size. Include details of all prior therapies. The minimum duration of the study is to be no less than 5 years."

## 7. RESEARCH QUESTION AND OBJECTIVES

### 7.1. Research question

What are the toxicities after HSCT in adult and pediatric patients who receive inotuzumab ozogamicin?

### 7.2. Objectives

Based on data obtained from the Center for International Blood and Marrow Transplant Research® (CIBMTR®) Research Database, the objectives were to evaluate the following in adult and pediatric patients with B-cell ALL who received inotuzumab ozogamicin and proceeded to HSCT:

- Patient-, disease- and HSCT-related characteristics, including details of all prior anti-cancer therapies;
- Timing of inotuzumab ozogamicin treatment prior to HSCT;
- TRM (transplant-related mortality), NTRM, relapse, and OS;
- Post-HSCT AEs of interest, including hepatic VOD/SOS;
- Cause of death (COD).

The term "adverse events" used in the study objectives and throughout this report generally refers to the safety events of interest in this study. Section 10.6 refers to the requirements of individual case reporting of AEs.

## 8. AMENDMENTS AND UPDATES

None.

# 9. RESEARCH METHODS

## 9.1. Study design

This secondary data collection non-interventional PASS used de-identified healthcare data from the CIBMTR database. This retrospective study evaluated safety outcomes post-HSCT in patients with B-cell precursor ALL who have been treated with inotuzumab ozogamicin prior to HSCT. The study utilized all relevant data available in the CIBMTR database from US transplant centers for a 5-year period following the approval of inotuzumab ozogamicin in the US (i.e., 18 August 2017 – 17 August 2022).

The protocol is included in Appendix 2.

## 9.2. Setting

The study population included all adult and pediatric patients in the US with B-cell ALL in the CIBMTR database at the CRF level of data collection treated with inotuzumab ozogamicin who proceeded to HSCT. Data in pediatric patients were included in accordance with the agreement reached during negotiation of the PMR with the FDA.

## 9.3. Subjects

### 9.3.1. Inclusion criteria

Patients met each of the following inclusion criteria:

- A record of B-cell precursor ALL diagnosis for adult and pediatric patients receiving dispensation/prescription of inotuzumab ozogamicin prior to or at the time of the dispensation/prescription
- At least 1 dose of inotuzumab ozogamicin prior to proceeding to HSCT
- Received HSCT from a US transplant center participating in the study

### 9.3.2. Exclusion criteria

Only data from patients who consented were used in the study. Patients were excluded from the study if they met 1 of the following criteria:

- Treated at a transplant center not participating in the study
- Treated at a transplant center embargoed from contributing to research studies because center did not meet the CIBMTR's data quality standards
- Had not given consent to participate in the CIBMTR Research Database

### 9.4. Variables

Definition of exposures, outcomes, and other variables including measured risk factors, comorbidities, co-medications, etc. with operational definitions and measurement; potential confounding variables and effect modifiers are included in the statistical analysis plan (SAP) (Appendix 4).

#### 9.4.1. Demographic

- Patient characteristics (including age, sex, race, weight, body mass index, body surface area, height)

#### 9.4.2. Baseline

- Comorbid conditions (i.e., Sorror Hematopoietic Cell Transplantation Comorbidity Index[6] [HCT-CI], and specific comorbidities like arrhythmia, cardiac, cerebrovascular disease, mild and moderate/severe hepatic disease)

- Pre-HSCT therapy (lines of therapy prior to transplant, lines of therapy prior to inotuzumab ozogamicin) are defined in the CIBMTR Forms Instruction Manual, question 28:[7]

    - "Induction [first line]: The first line(s) of therapy given following diagnosis. If the first line of therapy (induction) fails to produce a complete response (CR), the recipient may undergo another cycle or a different line of therapy (re-induction) in order to achieve their first CR. "First line" is reported as the purpose for all lines of therapy given to achieve the first CR.

    - Consolidation: Once a recipient has achieved a hematologic CR (first, second, third or greater), they may receive several additional lines of therapy as part of a protocol or to eliminate known minimal residual disease. In either case, "consolidation" is reported as the purpose for these lines of therapy.

    - Maintenance: Following induction and consolidation, a recipient may receive low-dose chemotherapy over an extended period of time to maintain a CR. Maintenance therapy is usually given as a single drug taken in the outpatient setting when the recipient has no known evidence of disease. "Maintenance" is reported as the purpose for these lines of therapy.

    - Treatment for disease relapse: Once the recipient has achieved their first CR, their disease may relapse and require further treatment to produce another CR (second or greater). The intent is the same as induction, but setting is different as the recipient has already achieved at least one prior CR. "Treatment for disease relapse" is reported as the purpose for all lines of therapy given to induce a CR following relapse."

- Baseline organ function of recipient prior to HSCT conditioning regimen (aspartate transaminase levels, total serum bilirubin levels)
- Baseline hematologic function prior to HSCT conditioning regimen (platelets, neutrophils, hemoglobin levels)
- Laboratory values at diagnosis of B-cell ALL (white blood cells, blasts in blood, blasts in bone marrow)
- Laboratory values prior to transplant (white blood cells, blasts in blood, blasts in bone marrow)
- Karnofsky/Lansky performance score prior to transplant
- Disease assessment at diagnosis
- HSCT data (prior autologous HSCT, time from diagnosis to HSCT)
- Graft-versus-host disease (GVHD) prophylaxis
- Pre-HSCT conditioning regimen (including use of dual alkylators, use of busulfan, use of thiotepa)
- Product type (bone marrow, peripheral blood stem cell, or cord blood for index HSCT)
- Donor type
- Number of treatment regimen(s) prior to receiving inotuzumab ozogamicin
- Pre-HSCT therapy (central nervous system prophylaxis, lines of therapy prior to transplant, purpose of therapy prior to inotuzumab ozogamicin, radiation therapy prior to inotuzumab ozogamicin, regimens for different purposes of therapy prior to inotuzumab ozogamicin)

### 9.4.3. Exposure

- Inotuzumab ozogamicin data (number of cycles, regimen containing inotuzumab ozogamicin, response to inotuzumab ozogamicin, minimal residual disease rate and methods of testing, time from last dose of inotuzumab ozogamicin to HSCT, inotuzumab ozogamicin doses)
- Treatments received at time of HSCT (liver toxicity prophylaxis, antibacterial infection prophylaxis, antiviral infection prophylaxis, antifungal infection prophylaxis, anti-pneumocystis infection prophylaxis)

- Post-HSCT therapies (systemic therapy given for reasons other than relapse, persistent or minimal residual disease; systemic therapy given for relapse, persistent or minimal residual disease; radiation therapy given for reasons other than relapse, persistent or minimal residual disease)

### 9.4.4. Outcomes

- Post-HSCT infections, up to day 100 (viral, bacterial, fungal)
- Systemic inflammatory response syndrome (SIRS) development, up to day 100
- Septic shock, up to day 100
- Acute GVHD, up to day 100 (maximum grade, time to date of acute GVHD)
- Chronic GVHD, up to 1 year (time to date of chronic GVHD)
- VOD/SOS data (time to VOD/SOS, grade of VOD/SOS, treatment for VOD/SOS, post-VOD/SOS survival)
- Secondary malignancy (time to secondary malignancy)
- Pulmonary AEs, within 100 days post-HSCT (IPN/idiopathic pneumonia syndrome, bronchiolitis obliterans, COP/BOOP, diffuse alveolar hemorrhage)
- Cardiovascular AEs, within 100 days post-HSCT (arrhythmia, congestive heart failure, coronary artery disease, myocardial infarction or unstable angina, hypertension requiring therapy, thrombotic microangiopathy [TMA])
- Acute renal failure requiring dialysis, within 100 days post-HSCT
- Avascular necrosis, within 100 days post-HSCT
- Endocrine dysfunction, within 100 days post-HSCT (diabetes or hyperglycemia requiring chronic treatment, growth hormone deficiency or short stature, hypothyroidism requiring replacement therapy, pancreatitis, depression requiring therapy, anxiety requiring therapy, CNS hemorrhage and stroke, post-traumatic stress disorder [PTSD] requiring therapy)
- Post-HSCT clinical status (best response to HSCT, granulopoiesis/neutrophil recovery, megakaryopoiesis/platelet recovery, engraftment syndrome within 100 days post-HSCT, time to engraftment syndrome within 100 days post-HSCT, recipient weight (most recent post-HSCT), recipient height (most recent post-HSCT), Karnofsky/ Lansky performance status (post-HSCT), total inpatient days in first 100 days post-HSCT, time from HSCT to date of last contact)

### 9.5. Data sources and measurement

This non-interventional PASS used data from the CIBMTR Research Database.

The CIBMTR® is a research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin. The CIBMTR facilitates critical research through medical, scientific, and statistical expertise; a network of more than 330 centers worldwide; a database with clinical data for more than 600,000 patients; and a biospecimen repository[8].

The CIBMTR holds the contract for the Stem Cell Therapeutic Outcomes Database (SCTOD), awarded by the Health Resources and Services Administration of the US Department of Health and Human Services. As the contract holder, the CIBMTR is charged with collecting data on all allogeneic (related and unrelated) HSCTs performed in the US. All US transplant centers are required to report data to the CIBMTR; participation of non-US centers is voluntary.

The CIBMTR receives data for approximately 24,000 new HSCT recipients annually as well as follow-up data on previously reported patients. In 2014-2016, a total of 2,506 (1984 adult [age ≥ 18 years] and 522 pediatric [age < 18 years at time of transplantation]) B-cell ALL patients in the US underwent their first allogeneic HSCT and who provided consent to CIBMTR for research.

The CIBMTR collects data on two levels, using a Transplant Essential Data (TED) form and a Comprehensive Report Form (CRF). CIBMTR collects TED data, an internationally accepted standard data set, on all patients receiving an allogeneic transplant within the US. Also, using a regularly reviewed, weighted algorithm, CIBMTR selects some patients for more detailed CRF data.

The algorithm randomly selects an epidemiologic sample of recipients for whom a CRF is to be requested. The algorithm includes, but is not limited to, type of HSCT, age of the recipient, disease, etc. It gives higher weights to patients receiving HSCT for rare indications, to very young and very old patients, and novel treatment approaches. It aims to provide representative, adequately sized subsets of patients for studies requiring detailed data. The algorithm is periodically reviewed to assess the burden of data submission for centers.

The CRF captures additional patient, disease and treatment-related data for a subset of patients. (i.e., the CRF does not include data from all patients in the registry). Approximately 75% of CIBMTR centers provide CRF data; this accounts for more than 25% of cases submitted to CIBMTR annually.

TED- and CRF-level data are collected pre-transplant, 100 days post-transplant, 6 months post-transplant, annually until year 6 post-transplant, and biannually thereafter until death or lost to follow-up.

Data (TED- and CRF-level) from all consenting US patients in the CIBMTR database treated with inotuzumab ozogamicin during the accrual period are included in the analysis. These patients were placed on the CRF data track, so data necessary for the study would be collected.

Data for the PASS regarding post-HSCT AEs of interest in patients treated with inotuzumab ozogamicin were collected from the CIBMTR database using the standard and supplemental forms shown in Appendix 5.

**Table 1. Data collection forms for post-HSCT adverse events of interest in patients with B-cell precursor ALL who received inotuzumab ozogamicin prior to HSCT**

| Variable | Data Source (CIBMTR form number and title) |
|---|---|
| **Infection up to day 100** | 2100 Post-HSCT Follow-up Data, |
| GVHD | 2450 Post-Transplant Essential Data |
| VOD up to day 100 | 2100 Post-HSCT Follow-up Data, |
| | 2450 Post-Transplant Essential Data, |
| | 2553 VOD/SOS Supplemental Data, |
| Secondary Malignancy | 2100 Post-HSCT Follow-up Data, |
| | 2450 Post-Transplant Essential Data |
| **Pulmonary adverse events** | |
| IPN/Idiopathic pneumonia syndrome | 2100 Post-HSCT Follow-up Data, |
| Bronchiolitis obliterans | 2450 Post-Transplant Essential Data |
| COP/BOOP | |
| Diffuse alveolar hemorrhage | |
| **Cardiovascular disease** | |
| Arrhythmia | 2100 Post-HSCT Follow-up Data, |
| Congestive heart failure | 2450 Post-Transplant Essential Data |
| Coronary artery disease | |
| Myocardial infarction/unstable angina | |
| Hypertension requiring therapy | |
| Thrombotic microangiopathy | |
| **Renal adverse events** | |
| Acute renal failure requiring dialysis | 2100 Post-HSCT Follow-up Data, |
| | 2450 Post-Transplant Essential Data |
| **Musculoskeletal dysfunction** | |
| Avascular necrosis | 2100 Post-HSCT Follow-up Data, |
| | 2450 Post-Transplant Essential Data |
| **Endocrine dysfunction** | |
| Diabetes/hyperglycemia requiring chronic treatment | 2100 Post-HSCT Follow-up Data, |
| Growth hormone deficiency/short stature | 2450 Post-Transplant Essential Data |
| Hypothyroidism requiring replacement therapy | |
| Pancreatitis | |
| **Neurologic/psychiatric** | |
| Depression requiring therapy | 2100 Post-HSCT Follow-up Data, |
| Anxiety requiring therapy | 2450 Post-Transplant Essential Data |
| Central nervous system hemorrhage and stroke | |
| PTSD requiring therapy | |

Note: Forms are available online; see Appendix 5: CIBMTR Data Collection Forms.

### 9.6. Bias

Selection bias was minimal as all patients who consent for research from participating US transplant centers are eligible for the study and the rate of non-consenting patients is low (10%). Selection bias is possible in any registry study; however, the CIBMTR Research Database was designed specifically to collect data prospectively on real-world effectiveness with long-term follow-up. CIBMTR tracks outcomes that treating physicians can measure objectively, rather than subjectively.

### 9.7. Study Size

The CIBMTR invited 203 US transplant centers to participate in this study. Patients were eligible if they consented for research and received inotuzumab ozogamicin prior to HSCT for B-cell ALL from a participating US center.

### 9.8. Data transformation

Detailed methodology for data transformations are documented in the SAP, which is dated, filed and maintained by the Sponsor (Appendix 4).

Data analyses in adult and pediatric patients with B-cell ALL who proceeded to HSCT:

- Patient-, disease- and HSCT-related characteristics, including details of all prior anti-cancer therapies;
- Timing of inotuzumab ozogamicin treatment prior to HSCT;
- TRM or transplant-related mortality; NTRM; relapse; and OS;
- Post-HSCT AEs of interest, including hepatic VOD/SOS;
- Causes of death.

Data are presented for adults, pediatric patients, and adults and pediatrics combined.

The study baseline time point is the date of the current HSCT. Pediatric patients were defined as patients who were < 18 years at the time of HSCT, regardless of whether they became > 18 years of age during the 5-year follow-up. There was no minimum age requirement for this study.

### 9.9. Statistical methods

#### 9.9.1. Main summary measures

The following are the main summary measures that were collected and presented for all study participants (Appendix 4). The definitions are provided below.

#### 9.9.1.1. Transplant-related mortality (TRM)

TRM (which can also be referred to as non-relapse mortality) is time from HSCT to death within the first 28 days post-HSCT, or death from any cause without prior relapse/progression post-HSCT. In the absence of confirmation of death, TRM was censored at the date that the patient was last known to be alive. The duration (in months) of TRM was calculated as follows: [date of event/ competing event/ last known to be alive − date of transplant + 1]/30.4375.

#### 9.9.1.2. Non-transplant-related mortality (NTRM)

NTRM is time from HSCT to death after the first 28 days from any cause with prior relapse/progression post-HSCT. In the absence of confirmation of death, NTRM was censored at the date that the patient was last known to be alive. The duration (in months) of NTRM was calculated as follows: [date of event/ competing event/ last known to be alive − date of transplant + 1]/30.4375.

#### 9.9.1.3. Post-transplant relapse

Post-transplant relapse of B-cell ALL is time from HSCT to first relapse post-HSCT without death post-relapse, or with death after the first 28 days post-HSCT. In the absence of confirmation of relapse/death, relapse was censored at the date that the patient was last known to be alive. The duration (in months) of relapse was calculated as follows: [date of event/ competing event/ last known to be alive − date of transplant + 1]/30.4375.

#### 9.9.1.4. Post-transplant overall survival (OS)

Post-transplant OS is the time from HSCT to death due to any cause. In the absence of confirmation of death, post-transplant OS was censored at the date that the patient was last known to be alive. The duration (months) of post-transplant OS was calculated as follows: [date of death/ last known to be alive − date of transplant + 1]/30.4375.

#### 9.9.1.5. Post-inotuzumab ozogamicin survival

Post-inotuzumab ozogamicin survival is the time from the first dose (i.e., cycle 1 day 1 [C1D1]) of inotuzumab ozogamicin to death due to any cause. In the absence of confirmation of death, post-inotuzumab ozogamicin survival was censored at the date that the patient was last known to be alive. The duration (months) of post-inotuzumab ozogamicin survival was calculated as follows: [date of death/ last known to be alive − date of C1D1 + 1]/30.4375.

#### 9.9.1.6. Post-HSCT follow-up

Post-HSCT follow-up is the time from HSCT to date of last contact. The duration (months) of post-HSCT follow-up was calculated as follows: [date of last contact − date of HSCT + 1]/30. 4375.

#### 9.9.1.7. Subgroups

Exploratory subgroup analysis was conducted separately for the following patient cohorts:

- Adult patients (≥18 years);
- Pediatric patients (<18 years);
- All patients who had relapsed or refractory B-cell ALL prior to HSCT;
    - Adult patients (≥18 years) who had relapsed or refractory B-cell ALL prior to HSCT;
    - Pediatric patients (<18 years) who had relapsed or refractory B-cell ALL prior to HSCT.
- All patients who were in first complete remission B-cell ALL prior to HSCT;
    - Adult patients (≥18 years);
    - Pediatric patients (<18 years).

#### 9.9.1.8. Lines of therapy

Lines of therapy given prior to inotuzumab ozogamicin treatment and prior to receiving the HSCT conditioning regimen were measured in the following categories:

- No therapy given prior to event
- One line of therapy given prior to event
- Two lines of therapy given prior to event
- Three lines of therapy given prior to event
- Four or more lines of therapy given prior to event

### 9.9.2. Main statistical methods

All analyses were based on descriptive statistics (i.e., no hypothesis testing was planned). Unadjusted P values were provided, but no definite conclusions were made based on P values, and no adjustments for multiple comparisons were applied.

#### 9.9.2.1. Time-to-event endpoints

Time-to-event endpoints (e.g., post-transplant OS and post-inotuzumab ozogamicin survival) were summarized using the Kaplan-Meier method. Median event times were summarized, with 95% confidence intervals (CI) calculated using the method described by Brookmeyer and Crowley[9].

#### 9.9.2.2. Competing-risks analyses

TRM, NTRM, and post-transplant relapse were summarized using competing-risks analyses. Competing-risks analyses evaluated the hazard of events in the presence of potentially competing events. For TRM, competing events are event for post-transplant relapse; and for NTRM, and post-transplant relapse, competing events are TRM. The cumulative incidence of events was summarized with the 95% CI calculated based on the cumulative incidence function using the SAS macro by Lin et al[10], which is based on the method described by Kalbfleisch JD and Prentice RL (1980)[11].

#### 9.9.2.3. Categorical variables

Categorical variables were summarized using counts and percentages.

#### 9.9.2.4. Continuous variables

Continuous variables were summarized using descriptive statistics (median, minimum, maximum and number of patients).

### 9.9.3. Missing values

Missing event dates (except for death dates) were handled by the following conventions for partial dates following Pfizer standard which was used for the submissions for the approval of inotuzumab ozogamicin:

- If the day of the month was missing for any date used in a calculation, the 1st of the month was used to replace the missing date unless the calculation resulted in a negative time duration (i.e., date of onset cannot be prior to day 1 date). In this case, the date resulting in 0 time duration was used;

- If the day of the month and the month was missing for any date used in a calculation, the 1st of January was used to replace the missing data;

Missing death dates were handled by the following conventions:

- If the entire date was missing, it was not imputed, and the time-to-event was censored at the date that the patient was last known to be alive;

- If the day of the month was missing, the maximum of the full (non-imputed) day after the date of last contact and the 1st of the month was used to replace the missing date;

- If the day of the month and the month were both missing, the maximum of the full (non-imputed) day after the date of last contact and the 1st of January was used to replace the missing date.

For time-to-event endpoints, patients who had not yet experienced the event of interest by the end of follow-up were censored.

There were no plans for imputation of missing values for other variables; all missing values were excluded from specific analyses.

### 9.9.4. Sensitivity analyses

None.

### 9.9.5. Amendments to the statistical analysis plan

The original SAP dated 15 January 2018 was amended three times (versions 2, 3 and 4).

Major changes from the original SAP to SAP version 2.0 (dated 06 July 2018) were:

- The definitions of TRM and NTRM were revised to allow deaths within the first 28 days post-transplant to be considered as an event for TRM (transplant-related mortality);
- An alternative method to estimate the cumulative incidence rate of NTRM, with its CI, was added.

Major changes from SAP version 2.0 to SAP version 3.0 (dated 30 October 2019) were:

- The full analysis set was used only for analyses of pre- and at-HSCT variables.
- The post-transplant evaluable set was introduced to allow the analyses of time-to-event endpoints and post-HSCT variables only being based on patients with post-transplant follow-up.
- The competing risk for TRM was changed from NTRM to post-transplant relapse.
- The definition of post-transplant relapse was revised to allow its competing risk to include any death within 28 days post-transplant.
- Subgroup analyses for patients by number of prior HSCTs ($0, \geq 1$) and for patients who underwent allogeneic HSCT were removed. Separate analyses were conducted for patients who underwent first, second, third (if applicable) allogeneic HSCT for B-cell ALL, and patients who underwent autologous HSCT for B-cell ALL (if applicable).
- The subgroup analysis for patients who had relapsed or refractory B-cell ALL prior to receiving inotuzumab ozogamicin was changed to patients who had relapsed or refractory B-cell ALL prior to HSCT.
- A subgroup analysis for patients who were in first complete remission of B-cell ALL prior to HSCT was added.

The major change from SAP version 3.0 to SAP version 4.0 (dated 21 July 2020) was the addition of Section 8.2.13 for Additional Exploratory Analyses.

### 9.10. Quality control

US centers reported to the CIBMTR longitudinal clinical outcomes data on all allogeneic transplants. CIBMTR ensured accuracy via monitoring for consecutive reporting, verification, validation, and computerized record checks. In addition, CIBMTR audited each transplant center every 4 years. These validations and verifications produced high-quality data.

### 9.11. Protection of human subjects

#### 9.11.1. Subject information and consent

CIBMTR complied with all laws that protect research participants and their personal data. Patients and/or legal guardian(s) provided informed consent for research participation.

Protected health information was collected and maintained in CIBMTR's capacity as a Public Health Authority under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

Only data from patients in CIBMTR's registry who had consented were used in this study.

CIBMTR did not include patient identifiers in reports, publications, or in any other disclosures.

#### 9.11.2. Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

The NMDP/Be The Match central IRB, which is fully accredited by the Association for the Accreditation of Human Research Protection Programs, reviews and approves all human subject research conducted by the CIBMTR.

CIBMTR rules requiring the registration of all consecutive HSCT recipients ensure the inclusion of women, minorities, and children, so the CIBMTR Research Database includes women and minorities in the same proportion as found in the general HSCT population. Children are included in most CIBMTR studies; their inclusion is dependent on the study focus.

#### 9.11.3. Ethical conduct of the study

The CIBMTR is committed to the ethical conduct of research. All Coordinating Center personnel maintain Collaborative IRB Training Initiative (CITI) certification.

The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in FDA Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting of Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data Sets, Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE), the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidance, and Pharmaceutical Research and Manufacturers Association (PhRMA) guidelines.

# 10. RESULTS

Note: The data presented in this final study report were obtained from the Coordinating Center of the CIBMTR. The analysis has not been reviewed or approved by the Statistical or Scientific Committees of the CIBMTR. The data may not be published without prior approval of the CIBMTR.

## 10.1. Participants

A total of 5,891 B-cell ALL patients underwent an allogeneic HSCT transplant in the US between 18 August 2017 and 17 August 2022 (Table 2). Out of those 5,891 patients, 577 patients were excluded from this study as they had not consented to research, 131 patients were excluded from embargoed centers, and 2,669 patients were excluded as they belonged to centers not participating in the study. Of the remaining 2,514 patients, 371 received at least one dose of inotuzumab ozogamicin.

**Table 2. Disposition of participants**

| Selection criteria | No. excluded | No. included |
|---|---|---|
| AlloHSCT for B-cell ALL in US between 18 Aug. 2017 – 17 Aug. 2022 | | 5891 |
| Patient consented for research | 577 | 5314 |
| Excluded patients from embargoed centers [a] | 131 | 5183 |
| Excluded patients from centers not participating in study | 2669 | 2514 |
| Patient indicated inotuzumab ozogamicin had been given | 2143 | 371 |

[a] Embargoed centers are those with data that do not meet CIBMTR's quality standards

Between 18 August 2017 and 17 August 2022, 371 patients (304 adult and 67 pediatric) were accrued and included in the study. The data lock date for this final report, when data collection forms were last evaluated, was 17 August 2022.

Of the 371 patients included in the study, 319 patients (261 adult and 58 pediatric) underwent their first allogeneic HSCT for B-cell ALL (Table 5); and 52 patients (43 adult and 9 pediatric) had received a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin.

Most patients whose B-cell ALL relapses post first allogeneic HSCT do not proceed to a second. Patients who proceed for a 2nd allogeneic HSCT are extremely carefully selected.

The 52 patients who had a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin are described separately since the underlying disease, patient-related factors, risk of relapse, and post-HSCT complications are different for patients with a prior HSCT than for patients who underwent their first allogeneic HSCT for B-cell ALL.

### 10.1.1. Patients who underwent their first allogeneic HSCT for B-cell ALL

In total, 319 patients (261 adults and 58 pediatric patients, with a median age of 32 years) underwent their first allogeneic HSCT for B-cell ALL after treatment with inotuzumab ozogamicin (Table 5). Among the 319 patients (261 adults and 58 pediatric patients) who

underwent first allogeneic HSCT for B-cell ALL, 137 patients (43%) had Sorror HCT-CI score ≥ 3 prior to HSCT.

Lines of therapy prior to transplant were:

- 9 (3%) patients had 1 line of therapy: 8 (3%) adult, 1 (2%) pediatric;
- 66 (21%) patients had 2 lines of therapy: 57 (22%) adult, 9 (16%) pediatric;
- 63 (20%) patients had 3 lines of therapy: 59 (23%) adult, 4 (7%) pediatric; and
- 144 (45%) patients had 4 or more lines of therapy: 114 (44%) adult, 30 (52%) pediatric.
- Data were not available for 37 patients (Table 5).

As of the data lock date, post-HSCT follow-up information was available for 296 / 319 (93%) patients: 244 (93%) adult, 52 (90%) pediatric (Table 13):

- 182 / 296 (61%) patients did not experience post-HSCT relapse: 151 (62%) adult, 31 (60%) pediatric; of these:
    - 56 / 182 (31%) patients (50 [33%] adult and 6 [19%] pediatric) died in remission within 18 months, with a median time from transplant to TRM of 2.23 months; primary causes of death were (Table 16):
        - VOD/SOS – 15 (27%) patients: 13 (26%) adult, 2 (33%) pediatric
        - GVHD – 12 (21%) patients: 11 (22%) adult, 1 (17%) pediatric
        - Organ failure – 11 (20%) patients: 10 (20%) adult, 1 (17%) pediatric
        - Hemorrhage – 3 (5%) patients: 3 (6%) adult, 0 pediatric
        - Interstitial pneumonitis – 4 (7%) patients: 4 (8%) adult, 0 pediatric
        - Infection – 6 (11%) patients: 5 (10%) adult, 1 (17%) pediatric
        - Septic shock – 2 (4%) patients: 2 (4%) adult, 0 pediatric
        - Thrombotic microangiopathy – 1 (2%) patient: 0 adult, 1 (17%) pediatric
        - Graft failure – 1 (2%) patient: 1 (2%) adult, 0 pediatric
        - Other – 1 (2%) patient: 1 (2%) adult, 0 pediatric

- 114 / 296 (39%) patients experienced post-HSCT relapse: 93 (38%) adult, 21 (40%) pediatric; of these:
    - 56 / 114 (49%) patients died after post-HSCT relapse of B-cell ALL within 18 months, with a median time from transplant to NTRM of 6.92 months: 49 (53%) adult, 7 (33%) pediatric (Table 17)
- 51 / 296 (17%) patients (35 (14%) adult, 16 (31%) pediatric) experienced post-transplant VOD/SOS (Table 19 and Table 36); of these:
    - 23 (45%) cases were mild: 15 (43%) adult, 8 (50%) pediatric
    - 28 (55%) cases were severe: 20 (57%) adult, 8 (50%) pediatric
    - 3 (6%) patients did not receive liver toxicity prophylaxis: 2 (6%) adult, 1 (6%) pediatric
    - 29 (57%) patients died after reporting VOD with a median follow-up of 1.34 months after VOD: 22 (63%) adult, 7 (44%) pediatric.
        - 16 out of the 29 (55%) patients had VOD as cause of death and had a median follow-up of 1.36 months after VOD: 14 (64%) adult, 2 (29%) pediatric.
            - 1 out of the 16 (6%) patients with reported VOD as cause of death had not received liver toxicity prophylaxis: 1 (7%) adult.
    - Other causes of death were:
        - Recurrence of B-cell ALL – 5 (17%) patients: 3 (14%) adult patients died 0.3, 2.9, and 7.2 months after VOD, 2 (29%) pediatric patients died 0.3 and 1.5 months after VOD,
        - GVHD – 3 (10%) patients: 2 (9%) adult patients died after 0.3 and 1.8 months after VOD, 1 pediatric (14%) died after 29.9 months,
        - Organ failure – 3 (10%) patients: 2 (9%) adult patients died after 1.1 and 1.3 months after VOD; 1 (14%) pediatric patient died 0.1 months after VOD,
        - Septic shock– 1 (3%) patient: 1 (5%) adult patient died 0.5 months after VOD,
        - Infection – 1 (3%) patient: 1 (14%) pediatric patient died 2.0 months after VOD.

- Liver toxicity prophylaxis:
    - 20 / 296 (7%) patients did not receive liver toxicity prophylaxis: 14 (6%) adult and 6 (12%) pediatric
    - 217 / 296 (73%) patients received liver toxicity prophylaxis with ursodiol alone: 198 (81%) adult and 19 (37%) pediatric
    - 42 / 296 (14%) patients received liver toxicity prophylaxis with ursodiol and defibrotide: 20 (8%) adult and 22 (42%) pediatric
    - 9 / 296 (3%) patients received liver toxicity prophylaxis with ursodiol and other drugs (not specified): 6 (2%) adult and 3 (6%) pediatric
    - 3 / 296 (1%) patients received liver toxicity prophylaxis with defibrotide alone: 2 (1%) adult and 1 (2%) pediatric
    - 5 / 296 (2%) patients did not have data reported for liver toxicity prophylaxis: 4 (2%) adult and 1 (2%) pediatric
- Transplant-related mortality:
    - Of the 296 patients with post-transplant follow-up information available, 112 patient deaths occurred within the first 18 months post-transplant, with TRM occurring in 56 patients.

In an adjusted analysis of 18-month outcomes of 204 adult patients with at least 12 months of follow-up, disease status, namely advanced disease stage, age and donor type were negative prognostic factors for 18 months overall survival. Karnofsky performance score and conditioning regimen intensity (dual alkylators) were negative prognostic factors for 18 months TRM. Only choice of conditioning regimen (dual alkylators), and not cumulative inotuzumab exposure, was a negative prognostic factor of day-100 VOD incidence.

### 10.1.2. Patients who underwent second, or greater, HSCT for B-cell ALL

As of the data lock date, post-HSCT follow-up information was available for all patients.

Among the 52 patients (43 adult, 9 pediatric) who had a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin, 27 patients (52%) had Sorror HCT-CI scores ≥ 3 prior to HSCT, and 16 patients (31%) had mild hepatic disease prior to HSCT. Fifty (50) patients (96%) underwent HSCT for relapsed or refractory disease and for another 2 patients (4%), disease status prior to transplant was not reported. Out of 52 patients, 9 patients (18%) had a history of proven invasive fungal infection.

Nine (9) of the 52 patients who had a prior allogeneic HSCT before receiving inotuzumab ozogamicin (17%) had received a bone marrow product, 7 patients (13%) received a cord blood

product, and the remaining 36 patients (69%) received peripheral blood stem cells. Thirty-four (34) patients (65%) received their product from an unrelated donor, 4 patients (8%) had an HLA-identical sibling donor, and the remaining 14 patients (27%) had another related donor (though not a human leukocyte antigen [HLA]-identical sibling). The median time from B-cell ALL diagnosis to transplant was 39 months, and the median time from B-cell ALL diagnosis to first dose of inotuzumab ozogamicin was 33 months.

Twelve (12) of the 52 patients for whom post-HSCT follow-up information was available with prior allogeneic HSCT (23%) experienced VOD/SOS after the second allogeneic HSCT. Seven (7) patients (58%) experienced severe VOD/SOS and 5 patients (42%) experienced mild VOD/SOS. Of the patients who had VOD/SOS, 7 (58%) patients (3 adult, 4 pediatric) died after reporting VOD/SOS at 0.1 months, 0.5 months, 0.5 months, 1.1 months, 2.8 months, 22.5 months, and 43.1 months after VOD.

Causes of death for the 7 patients included:

- 3 due to primary disease: 1 (33%) adult and 2 (50%) pediatric
- 4 due to VOD/SOS: 2 (67%) adult and 2 (50%) pediatric

Four (4) of the 9 pediatric patients (44%) experienced VOD/SOS after the second allogeneic HSCT. Three of the 4 patients (75%) experienced severe VOD/SOS and 1 patient (25%) experienced mild VOD/SOS. Four (4) pediatric patients (44%) died after reporting VOD/SOS at 0.1 months, 0.5 months, 1.1 months, and 22.5 months after VOD.

Eight (8) of the 43 adult patients (19%) experienced VOD/SOS after the second allogeneic HSCT. Four patients (50%) had mild VOD/SOS grade and 4 patients (50%) experienced severe VOD/SOS. Three (3) adult patients (37%) died after reporting VOD/SOS at 0.5 months, 2.8 months, and 43.1 months.

For the 52 patients, relapse status was:

- 7/52 (13%) patients experienced post-HSCT relapse: 4 (9 %) adult, 3 (33%) pediatric
- 43/52 (83%) patients did not experience post-HSCT relapse: 38 adult (88%), 5 pediatric (56%), of these:
    - 13/43 (30%) patients died in remission within 18 months: 11 (29 %) adult and 2 (40 %) pediatric
- 2/52 (4%) patients had relapse status not reported: 1 (2 %) adult, 1 (11 %) pediatric

## 10.2. Descriptive data

### 10.2.1. Subject evaluation groups

#### 10.2.1.1. Form completeness

The 319 patients who underwent their first allogeneic HSCT for B-cell ALL after inotuzumab ozogamicin treatment were requested to complete data collection forms necessary for the study. Table 3 below summarizes the descriptive data collected for these 319 patients.

**Table 3. Forms completed**

| Form | Pediatric patients No. (%) | Adult patients No. (%) | All patients No. (%) |
|---|---|---|---|
| **No. patients** | **58** | **261** | **319** |
| Form 2000 Recipient Baseline Data | 57 (98) | 253 (97) | 310 (97) |
| Form 2011 ALL Pre-HSCT Data | 53 (91) | 249 (95) | 302 (95) |
| Form 2541 Inotuzumab Ozogamicin Supplemental Data | 58 (100) | 257 (98) | 315 (99) |
| Follow-up reported [a] | 52 (90) | 244 (93) | 296 (93) |
| Form 2100 Post-HSCT Data | 51 (88) | 243 (93) | 294 (92) |
| Form 2111 ALL Post-HSCT Data | 52 (90) | 241 (92) | 293 (92) |
| Form 2450 Post-Transplant Essential Data [b] | 3 (5) | 11 (4) | 14 (4) |

[a] Since some patients completed multiple follow-up forms; therefore, the number of follow-up forms (forms 2100, 2111, 2450) does not add up to the number of patients who reported follow-up. A patient needed a complete Form 2100 or 2450 to be considered as having reported follow-up, as survival status and date of last contact are only reported on those follow-up forms.
[b] Patients enrolled in the study are moved to the CRF track, and the CRF follow-up forms (Forms 2100, 2111) are required. These CRF follow-up forms include the data collected on the TED follow-up form (Form 2450), plus additional data. However, any data submitted on the Form 2450 will still be assessed, when applicable.

#### 10.2.1.2. Completeness index

Table 4 summarizes the completeness of follow-up (completeness index) in patients who underwent their first allogeneic HSCT and whose centers submitted post-HSCT follow-up forms. This was measured to quantify the effect of losses to follow-up.

The completeness index was calculated as the ratio of observed time (entry time into study until study end or event [death]) to potential time. Follow-up was determined at last contact date on 1-month, 100-day, 6-month, and 12-month follow-up forms submitted by transplant centers.

**Table 4. Completeness index**

| Time | Pediatric patients | Adult patients | All patients |
|---|---|---|---|
| **No. patients with follow-up** | **52** | **244** | **296** |
| 1 month | 100% | 100% | 100% |
| 100 days | 100% | 100% | 100% |
| 6 months | 98% | 98% | 98% |
| 12 months | 92% | 93% | 93% |
| 18 months | 86% | 88% | 88% |

**Table 4. Completeness index**

| Time | Pediatric patients | Adult patients | All patients |
|---|---|---|---|
| Note: Completeness Index calculated per Clark et al.[12] | | | |

### 10.2.2. Demographic, baseline characteristics, and comorbid conditions

Table 5 summarizes the demographic characteristics and baseline characteristics among all patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| No. of centers | 20 | 55 | 60 |
| Age, years, no. (%) | | | |
| < 1 | 1 (2) | 0 | 1 (<1) |
| 1-9 | 26 (45) | 0 | 26 (8) |
| 10-17 | 31 (53) | 0 | 31 (10) |
| 18-29 | 0 | 88 (34) | 88 (28) |
| 30-39 | 0 | 48 (18) | 48 (15) |
| 40-49 | 0 | 48 (18) | 48 (15) |
| 50-59 | 0 | 33 (13) | 33 (10) |
| ≥ 60 | 0 | 44 (17) | 44 (14) |
| Median | 10 | 39 | 32 |
| Range | (<1-17) | (18-75) | (<1-75) |
| Mean | 9.7 | 40.7 | 35.1 |
| Standard deviation | 5.1 | 16 | 18.9 |
| Race, no. (%) | | | |
| White | 47 (81) | 202 (77) | 249 (78) |
| Black or African American | 1 (2) | 16 (6) | 17 (5) |
| Asian or Native Hawaiian and other Pacific Islander | 2 (3) | 15 (6) | 17 (5) |
| Others | 2 (3) | 4 (2) | 6 (2) |
| Not reported | 6 (10) | 24 (9) | 30 (9) |
| Weight, kg | | | |
| Number evaluable | 58 | 261 | 319 |
| Median | 36 | 88 | 82 |
| Range | (8-126) | (32-203) | (8-203) |
| Mean | 43 | 90 | 82 |
| Standard deviation | 26 | 27 | 32 |
| Body mass index, $kg/m^2$, no. (%) | | | |
| N/A; BMI does not apply to pediatric patients | 58 | 0 | 58 (18) |
| Underweight | 0 | 8 (3) | 8 (3) |
| Healthy weight | 0 | 48 (18) | 48 (15) |
| Overweight | 0 | 76 (29) | 76 (24) |
| Obese | 0 | 129 (49) | 129 (40) |
| Number evaluable | 58 | 261 | 319 |
| Median | 19.3 | 29.9 | 28.3 |
| Range | (14.6-46.3) | (12.2-62.5) | (12.2-62.5) |
| Mean | 21.2 | 30.7 | 29 |
| Standard deviation | 6.3 | 7.9 | 8.5 |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Body surface area, $m^2$ | | | |
| Number evaluable | 58 | 261 | 319 |
| Median | 1.2 | 2 | 2 |
| Range | (0.4-2.4) | (1.2-3.2) | (0.4-3.2) |
| Mean | 1.2 | 2.1 | 1.9 |
| Standard deviation | 0.5 | 0.3 | 0.5 |
| Height, cm | | | |
| Number evaluable | 58 | 261 | 319 |
| Median | 139.5 | 172 | 170 |
| Range | (67-176) | (130-191) | (67-191) |
| Mean | 134.3 | 170.7 | 164.1 |
| Standard deviation | 29.1 | 10 | 20.8 |
| Sex, no. (%) | | | |
| Male | 32 (55) | 152 (58) | 184 (58) |
| Female | 26 (45) | 109 (42) | 135 (42) |
| Sorror HCT-CI, no. (%) [a] | | | |
| 0 | 23 (40) | 36 (14) | 59 (18) |
| 1-2 | 19 (33) | 97 (37) | 116 (36) |
| 3-4 | 15 (26) | 86 (33) | 101 (32) |
| 5 | 1 (2) | 19 (7) | 20 (6) |
| 6 | 0 | 10 (4) | 10 (3) |
| 7 | 0 | 6 (2) | 6 (2) |
| Not reported | 0 | 7 (3) | 7 (2) |
| Arrhythmia, no. (%) [b] | | | |
| Yes | 1 (2) | 17 (7) | 18 (6) |
| No | 57 (98) | 237 (91) | 294 (92) |
| Not reported | 0 | 7 (3) | 7 (2) |
| Cardiac disease, no. (%) [c] | | | |
| Yes | 1 (2) | 11 (4) | 12 (4) |
| No | 57 (98) | 243 (93) | 300 (94) |
| Not reported | 0 | 7 (3) | 7 (2) |
| Cerebrovascular disease, no. (%) [d] | | | |
| Yes | 0 | 9 (3) | 9 (3) |
| No | 58 | 245 (94) | 303 (95) |
| Not reported | 0 | 7 (3) | 7 (2) |
| Hepatic disease, no. (%) | | | |
| Moderate/severe [e], not mild | 7 (12) | 9 (3) | 16 (5) |
| Mild [f], not moderate/severe | 13 (22) | 62 (24) | 75 (24) |
| No hepatic disease | 38 (66) | 183 (70) | 221 (69) |
| Not reported | 0 | 7 (3) | 7 (2) |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Lines of therapy prior to transplant, no. (%) [g] | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| First line | 1 (2) | 8 (3) | 9 (3) |
| Salvage 1 | 9 (16) | 57 (22) | 66 (21) |
| Salvage 2 | 4 (7) | 59 (23) | 63 (20) |
| Salvage > 2 | 30 (52) | 114 (44) | 144 (45) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (14) | 10 (4) | 18 (6) |
| Not reported | 1 (2) | 1 (<1) | 2 (1) |
| Number evaluable | 44 | 238 | 282 |
| Median | 4.5 | 3 | 4 |
| Range | (1-14) | (1-10) | (1-14) |
| Mean | 5.4 | 3.8 | 4 |
| Standard deviation | 3.3 | 1.8 | 2.2 |
| Lines of therapy prior to inotuzumab ozogamicin, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| No treatment given | 3 (5) | 28 (11) | 31 (10) |
| First line | 8 (14) | 71 (27) | 79 (25) |
| Salvage 1 | 4 (7) | 47 (18) | 51 (16) |
| Salvage 2 | 8 (14) | 44 (17) | 52 (16) |
| Salvage > 2 | 21 (36) | 42 (16) | 63 (20) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (14) | 10 (4) | 18 (6) |
| Not reported | 1 (2) | 7 (3) | 8 (3) |
| Number evaluable | 44 | 232 | 276 |
| Median | 3 | 2 | 2 |
| Range | (0-13) | (0-8) | (0-13) |
| Mean | 43.5 | 2.21 | 2.53 |
| Standard deviation | 33.2 | 1.7 | 2.1 |
| Aspartate transaminase (AST), prior to transplant, no. (%), units/L | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Normal | 23 (40) | 171 (66) | 194 (61) |
| Abnormal | 34 (59) | 81 (31) | 115 (36) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Number evaluable | 57 | 252 | 309 |
| Median | 1.2 | 0.8 | 0.9 |
| Range | (0.3-3.6) | (0.3-3.6) | (0.3-3.6) |
| Mean | 1.3 | 0.9 | 1 |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Standard deviation | 0.6 | 0.5 | 0.5 |
| Total serum bilirubin, prior to transplant, mg/dL, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Normal | 54 (93) | 232 (89) | 286 (90) |
| Abnormal | 3 (5) | 19 (7) | 22 (7) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Number evaluable | 57 | 251 | 308 |
| Median | 0.3 | 0.4 | 0.4 |
| Range | (0-1.1) | (0-4.4) | (0-4.4) |
| Mean | 0.4 | 0.5 | 0.5 |
| Standard deviation | 0.3 | 0.4 | 0.4 |
| Platelets, prior to transplant, $\times 10^9$/L | | | |
| N/A; CIBMTR Form 2000 not received | 1 (2) | 8 (3) | 9 (3) |
| Not reported | 1 (2) | 9 (3) | 10 (3) |
| Number evaluable | 56 | 244 | 300 |
| Median | 128 | 123.5 | 124 |
| Range | (9-386) | (11-414) | (9-414) |
| Mean | 135.2 | 129.8 | 130.8 |
| Standard deviation | 80.7 | 70.3 | 72.3 |
| Neutrophils, prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2000 nor Form 2402 revision 6 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Not reported | 3 (5) | 5 (2) | 8 (3) |
| Number evaluable | 54 | 248 | 302 |
| Median | 50.5 | 57 | 56 |
| Range | (6-86) | (4-100) | (4-100) |
| Mean | 50.1 | 55.3 | 54.4 |
| Standard deviation | 18.3 | 17 | 17.3 |
| Hemoglobin, prior to transplant, g/dL, no. (%) | | | |
| N/A; CIBMTR Form 2000 nor Form 2402 revision 6 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Number evaluable | 57 | 252 | 309 |
| Median | 11.8 | 12.2 | 12.2 |
| Range | (6.7-16.3) | (6.4-17.7) | (6.4-17.7) |
| Mean | 11.6 | 12.2 | 12.1 |
| Standard deviation | 1.8 | 2.1 | 2 |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| White blood cells at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| Not reported | 10 (17) | 28 (11) | 38 (12) |
| Number evaluable | 43 | 221 | 264 |
| Median | 10.4 | 13.3 | 12.8 |
| Range | (0.4-525) | (0.5-468.5) | (0.4-525) |
| Mean | 54.7 | 51.7 | 52.2 |
| Standard deviation | 102 | 83.5 | 86.6 |
| Blasts in blood, at diagnosis of B-cell ALL, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| < 1% | 2 (3) | 20 (8) | 22 (7) |
| ≥ 1% | 32 (55) | 187 (72) | 219 (69) |
| Not reported | 19 (33) | 42 (16) | 61 (19) |
| Number evaluable | 34 | 207 | 241 |
| Median | 54.5 | 62 | 61.5 |
| Range | (0-98) | (0-99) | (0-99) |
| Mean | 52.6 | 52 | 52.1 |
| Standard deviation | 34.2 | 33.6 | 33.6 |
| Blasts in bone marrow, at diagnosis of B-cell ALL, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| < 50% | 4 (7) | 19 (7) | 23 (7) |
| 50-89% | 13 (22) | 94 (36) | 107 (34) |
| ≥ 90% | 18 (31) | 95 (36) | 113 (35) |
| Not reported | 18 (31) | 41 (16) | 59 (18) |
| Number evaluable | 35 | 208 | 243 |
| Median | 90 | 88 | 88 |
| Range | (10-98) | (2-100) | (2-100) |
| Mean | 79.9 | 79.9 | 79.9 |
| Standard deviation | 24.4 | 20.9 | 21.4 |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| White blood cells, at last evaluation prior to transplant, × $10^9$/L, no. (%) | | | |
| N/A; CIBMTR Form 2011 nor Form 2000 revision 6 not yet received | 1 (2) | 7 (3) | 8 (3) |
| Number evaluable | 57 | 254 | 311 |
| Median | 3.4 | 3.7 | 3.7 |
| Range | (0.4-11.8) | (0-37) | (0-37) |
| Mean | 3.8 | 4.2 | 4.1 |
| Standard deviation | 2.4 | 3.1 | 3 |
| Blasts in blood prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| < 1% | 33 (57) | 196 (75) | 229 (72) |
| ≥ 1% | 1 (2) | 7 (3) | 8 (3) |
| Not reported | 19 (33) | 46 (18) | 65 (20) |
| Number evaluable | 34 | 203 | 237 |
| Median | 0 | 0 | 0 |
| Range | (0-4) | (0-3) | (0-4) |
| Mean | 0.12 | 0.05 | 0.06 |
| Standard deviation | 0.69 | 0.32 | 0.39 |
| Blasts in bone marrow prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| < 5% | 43 (74) | 222 (85) | 265 (83) |
| ≥ 5% | 1 (2) | 3 (1) | 4 (1) |
| Not reported | 9 (16) | 24 (9) | 33 (10) |
| Number evaluable | 44 | 225 | 269 |
| Median | 0 | 1 | 1 |
| Range | (0-94) | (0-7) | (0-94) |
| Mean | 2.7 | 1.32 | 1.54 |
| Standard deviation | 14.11 | 1.3 | 5.8 |
| Extramedullary disease, at diagnosis of B-cell ALL, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| Yes | 9 (16) | 34 (13) | 43 (13) |
| No | 24 (41) | 191 (73) | 215 (67) |
| Unknown | 2 (3) | 15 (6) | 17 (5) |
| Not reported | 18 (31) | 9 (3) | 27 (8) |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Extramedullary disease, at last evaluation prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| Yes | 1 (2) | 6 (2) | 7 (2) |
| No | 52 (90) | 238 (91) | 290 (91) |
| Unknown | 0 | 4 (2) | 4 (1) |
| Not reported | 0 | 1 (0) | 1 (0) |
| Performance score prior to transplant, no. (%) | | | |
| Karnofsky score | | | |
| 90-100 | 8 (14) | 140 (54) | 148 (46) |
| 10-80 | 1 (2) | 108 (41) | 109 (34) |
| Not reported | 0 | 13 (5) | 13 (4) |
| Lansky score | | | |
| 90-100 | 42 (72) | 0 | 42 (13) |
| 10-80 | 7 (12) | 0 | 7 (2) |
| Not reported | 0 | 0 | 0 |
| History of proven invasive fungal infection, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Yes | 8 (14) | 9 (3) | 17 (5) |
| No | 49 (84) | 243 (93) | 292 (92) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Disease status prior to transplant, no. (%) | | | |
| 1st complete remission | 10 (17) | 94 (36) | 104 (33) |
| 2nd complete remission | 23 (40) | 121 (46) | 144 (45) |
| ≥ 3rd complete remission | 25 (43) | 28 (11) | 53 (17) |
| 1st relapse | 0 | 10 (4) | 10 (3) |
| ≥ 3rd relapse | 0 | 3 (1) | 3 (1) |
| Primary induction failure | 0 | 4 (2) | 4 (1) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Prior autologous HSCT, no. (%) | | | |
| Yes | 0 | 7 (3) | 7 (2) |
| No | 58 | 254 (97) | 312 (98) |
| Time from diagnosis to HSCT, no. (%), months | | | |
| < 3 | 1 (2) | 1 (<1) | 2 (1) |
| 3-5 | 3 (5) | 40 (15) | 43 (13) |
| 6-11 | 12 (21) | 76 (29) | 88 (28) |
| ≥ 12 | 25 (43) | 94 (36) | 119 (37) |
| Outliers [h] | 17 (29) | 49 (19) | 66 (21) |
| Not reported | 0(0) | 1(<1) | 1(<1) |
| Number evaluable | 41 | 211 | 252 |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Median | 22.08 | 10.35 | 11.17 |
| Range | (2.89-47.57) | (2.96-47.64) | (2.89-47.64) |
| Mean | 21.92 | 15.83 | 16.82 |
| Standard deviation | 14.2 | 11.82 | 12.41 |
| Time from diagnosis to first dose of inotuzumab ozogamicin, no. (%), months | | | |
| < 3 | 4 (7) | 57 (22) | 61 (19) |
| 3-5 | 3 (5) | 31 (12) | 34 (11) |
| 6-11 | 10 (17) | 34 (13) | 44 (14) |
| ≥ 12 | 22 (38) | 79 (30) | 101 (32) |
| Outliers [h] | 14 (24) | 36 (14) | 50 (16) |
| Not reported | 5(9) | 24 (9) | 29(9) |
| Number evaluable | 39 | 201 | 240 |
| Median | 16.53 | 7.43 | 8.49 |
| Range | (0.3-46.09) | (0.1-44.35) | (0.1-46.09) |
| Mean | 19.14 | 12.38 | 13.48 |
| Standard deviation | 13.96 | 12.08 | 12.62 |
| GVHD prophylaxis, no. (%) | | | |
| Ex-vivo T-cell depletion | 9 (16) | 3 (1) | 12 (4) |
| CD34 selection | 0 | 1 (<1) | 1 (<1) |
| Cyclophosphamide ± others | 17 (29) | 106 (41) | 123 (39) |
| Tac + MMF ± others (not Cy) | 3 (5) | 30 (11) | 33 (10) |
| Tac + MTX ± others (not Cy, MMF) | 5 (9) | 93 (36) | 98 (31) |
| Tac ± others (not Cy, MMF, MTX) | 1 (2) | 8 (3) | 9 (3) |
| CsA + MMF ± others (not Cy, Tac) | 7 (12) | 6 (2) | 13 (4) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 13 (22) | 13 (5) | 26 (8) |
| CsA ± others (not Cy, Tac, MMF, MTX) | 1 (2) | 0 | 1 (<1) |
| Others (not Cy, Tac, CsA) | 0 | 1 (<1) | 1 (<1) |
| Not reported | 2 (2) | 0 | 2 (<1) |
| Conditioning regimen intensity, no. (%) [i] | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 8 (3) | 9 (3) |
| Myeloablative | 55 (95) | 135 (52) | 190 (60) |
| RIC/NMA | 2 (3) | 113 (43) | 115 (36) |
| Unknown [j] | 0 | 5 (2) | 5 (2) |
| Dual alkylators used in conditioning regimen, no. (%) [k] | | | |
| Yes | 15 (26) | 18 (7) | 33 (10) |
| No | 42 (72) | 235 (90) | 277 (87) |
| Not reported | 1 (2) | 8 (3) | 9 (3) |

**Table 5. Demographics, baseline characteristics, comorbidities and follow-up of participants**

| Characteristic | Pediatric patients (< 18 y) | Adult patients (≥ 18 y) | All patients |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Busulfan used in conditioning regimen, no. (%) | | | |
| Yes | 4 (7) | 30 (11) | 34 (11) |
| No | 53 (91) | 223 (85) | 276 (87) |
| Not reported | 1 (2) | 8 (3) | 9 (3) |
| Thiotepa used in conditioning regimen, no. (%) | | | |
| Yes | 17 (29) | 20 (8) | 37 (12) |
| No | 40 (69) | 233 (89) | 273 (86) |
| Not reported | 1 (2) | 8 (3) | 9 (3) |
| Product type, no. (%) | | | |
| Bone marrow | 33 (57) | 48 (18) | 81 (25) |
| Peripheral blood stem cells | 16 (28) | 195(75) | 211(67) |
| Umbilical cord blood | 9 (16) | 18 (7) | 27 (8) |
| Donor type, no. (%) | | | |
| HLA-identical sibling | 13 (22) | 70 (27) | 83 (26) |
| Other related | 16 (28) | 67 (26) | 83 (26) |
| Unrelated | 29 (50) | 124 (48) | 153 (48) |
| Follow-up, median (range), months | 15.2 (3.32-50.72) | 23.98 (2.43-50.86) | 23.62 (2.43-50.86) |

Note: Median and range values are calculated using only patients with complete data for that variable. For CIBMTR forms, see Appendix 3: CIBMTR Data Collection Forms.

[a] Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. Blood 2004; 104:961-8.

[b] History of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment

[c] History of coronary artery disease (one or more vessel-coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, OR ejection fraction ⩽ 50% on the most recent test

[d] History of transient ischemic attack, subarachnoid hemorrhage or cerebrovascular accident

[e] Liver cirrhosis, bilirubin > 1.5 × upper limit of normal, or AST/ALT > 2.5 × upper limit of normal

[f] Chronic hepatitis, bilirubin > upper limit of normal to 1.5 × upper limit of normal, or AST/ALT > upper limit of normal to 2.5 × upper limit of normal at the time of transplant OR any history of hepatitis B or hepatitis C infection

[g] The lines of therapy prior to a specified event are defined as follows. “No treatment given” means no lines of therapy given prior to specified event; “First line” means 1 line of therapy; “Salvage 1” means 2 lines of therapy; “Salvage 2” means 3 lines of therapy; “Salvage > 2” means 4 (or more) lines of therapy.

[h] Outliers are defined as patients who underwent HSCT in CR1 more than 12 months after disease diagnosis, or patients who underwent HSCT for all other disease statuses more than 48 months after disease diagnosis.

[i] Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009;15:1628-33.

[j] CIBMTR staff are querying the transplant center

[k] Dual alkylators were defined as the conditioning regimen including one of the following pairs of treatments: busulfan + cyclophosphamide; busulfan + melphalan; cyclophosphamide + melphalan; busulfan + thiotepa; or cyclophosphamide + thiotepa.

### 10.2.3. Treatments at time of HSCT

Table 6 summarizes treatments received at time of HSCT, except for drugs given for conditioning regimen, among patients who received inotuzumab ozogamicin.

**Table 6. Summary of treatments received at time of HSCT, except for drugs given for conditioning regimen, among patients who received inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| Liver toxicity prophylaxis | | | |
| N/A; CIBMTR Form 2450 or 2100 not yet received | 6 (10) | 17 (7) | 23 (7) |
| No specific therapy used to prevent liver toxicity | 6 (10) | 14 (5) | 20 (6) |
| Ursodiol | 19 (33) | 198 (76) | 217 (68) |
| Ursodiol + defibrotide | 11 (19) | 15 (6) | 26 (8) |
| Ursodiol + defibrotide + others | 11 (19) | 5 (2) | 16 (5) |
| Ursodiol + others | 3 (5) | 6 (2) | 9 (3) |
| Defibrotide | 1 (2) | 2 (1) | 3 (1) |
| Not reported | 1 (2) | 4 (2) | 5 (2) |
| Antibacterial infection prophylaxis | | | |
| N/A; CIBMTR Form 2100 not yet received | 7 (12) | 18 (7) | 25 (8) |
| None | 26 (45) | 63 (24) | 89 (28) |
| Levofloxacin (IV or oral) | 9 (16) | 119 (46) | 128 (40) |
| Ciprofloxacin (IV or oral) | 1 (2) | 19 (7) | 20 (6) |
| Vancomycin (IV) | 4 (7) | 13 (5) | 17 (5) |
| Levofloxacin (IV or oral) + others | 1 (2) | 7 (3) | 8 (3) |
| Ciprofloxacin (IV or oral) + others | 1 (2) | 5 (2) | 6 (2) |
| Ceftazidime | 2 (3) | 2 (1) | 4 (1) |
| Cefepime | 3 (5) | 2 (1) | 5 (2) |
| Cefdinir oral (Omnicef) | 0 | 1 (<1) | 1 (<1) |
| Cefpodoxime oral (Vantin) | 0 | 5 (2) | 5 (2) |
| Ceftaroline | 1 (2) | 0 | 1 (<1) |
| Ceftriaxone | 0 | 1 (<1) | 1 (<1) |
| Piperacillin tazobactam | 0 | 1 (<1) | 1 (<1) |
| Ampicillin | 1 (2) | 0 | 1 (<1) |
| Not reported | 0 | 5 (2) | 5 (2) |
| Other | 2 (3) | 0 | 2 (1) |
| Antiviral infection prophylaxis | | | |
| N/A; CIBMTR Form 2100 not yet received | 7 (12) | 18 (7) | 25 (8) |
| None | 4 (7) | 5 (2) | 9 (3) |
| Acyclovir | 33 (57) | 146 (56) | 179 (56) |
| Valacyclovir | 7 (12) | 66 (25) | 73 (23) |
| Ganciclovir | 1 (2) | 10 (4) | 11 (3) |
| Valganciclovir | 3 (5) | 5 (2) | 8 (3) |
| Letermovir | 0 | 6 (2) | 6 (2) |
| Cidofovir | 1 (2) | 0 | 1 (<1) |
| Foscarnet | 2 (3) | 3 (1) | 5 (2) |

**Table 6. Summary of treatments received at time of HSCT, except for drugs given for conditioning regimen, among patients who received inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| Acyclovir + valacyclovir + letermovir | 0 | 1 (<1) | 1 (<1) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Antifungal infection prophylaxis | | | |
| N/A; CIBMTR Form 2100 not yet received | 7 (12) | 18 (7) | 25 (8) |
| None | 0 | 6 (2) | 6 (2) |
| Fluconazole | 26 (45) | 99 (38) | 125 (39) |
| Posaconazole | 5 (9) | 43 (16) | 48 (15) |
| Micafungin | 10 (17) | 33 (13) | 43 (13) |
| Caspofungin | 1 (2) | 46 (18) | 47 (15) |
| Voriconazole | 7 (12) | 5 (2) | 12 (4) |
| Nystatin | 0 | 5 (2) | 5 (2) |
| Isavuconazole | 0 | 3 (1) | 3 (1) |
| Anidulafungin | 1 (2) | 2 (1) | 3 (1) |
| Not reported | 1 (2) | 1 (<1) | 2 (1) |
| Anti-pneumocystis infection prophylaxis | | | |
| N/A; CIBMTR Form 2100 not yet received | 7 (12) | 18 (7) | 25 (8) |
| None | 1 (2) | 28 (11) | 29 (9) |
| Trimethoprim/sulfamethoxazole | 28 (48) | 96 (37) | 124 (39) |
| Pentamidine inhaled | 4 (7) | 28 (11) | 32 (10) |
| Pentamidine IV | 16 (28) | 67 (26) | 83 (26) |
| Atovaquone | 2 (3) | 7 (3) | 9 (3) |
| Dapsone | 0 | 16 (6) | 16 (5) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| GVHD prophylaxis | | | |
| Ex-vivo T-cell depletion | 9 (16) | 3 (1) | 12 (4) |
| CD34 selection | 0 | 1 (<1) | 1 (<1) |
| Cyclophosphamide + others | 17 (29) | 106 (41) | 123 (39) |
| Tac + MMF + others | 3 (5) | 30 (11) | 33 (10) |
| Tac + MTX + others | 5 (9) | 93 (36) | 98 (31) |
| Tac + others | 1 (2) | 8 (3) | 9 (3) |
| CsA + MMF + others (not Cy, Tac) | 7 (12) | 6 (2) | 13 (4) |
| CsA + MTX + others (not Cy, Tac, MMF) | 13 (22) | 13 (5) | 26 (8) |
| CsA + others (not Cy, Tac, MMF, MTX) | 1 (2) | 0 | 1 (<1) |
| Others | 0 | 1 (<1) | 1 (<1) |
| Not reported | 2 (2) | 0 | 2 (<1) |

### 10.2.4. Post-HSCT therapies

Table 7 summarizes post-HSCT therapies following inotuzumab ozogamicin treatment in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Table 7. Post-HSCT therapies following inotuzumab ozogamicin treatment**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with follow-up** | **52** | **244** | **296** |
| Systemic therapy given for reasons other than relapse, persistent, or MRD | | | |
| None | 46 (88) | 217 (89) | 263 (89) |
| Blinatumomab | 2 (4) | 8 (3) | 10 (3) |
| Ponatinib | 1 (2) | 8 (3) | 9 (3) |
| Dasatinib | 1 (2) | 3 (1) | 4 (1) |
| Inotuzumab + chemotherapy | 0 | 1 (<1) | 1 (<1) |
| Nilotinib | 0 | 1 (<1) | 1 (<1) |
| Imatinib | 1 (2) | 2 (1) | 3 (1) |
| Rituximab | 0 | 1 (<1) | 1 (<1) |
| Ruxolitinib | 1 (2) | 1 (<1) | 2 (1) |
| Vidaza | 0 | 2 (1) | 2 (1) |
| Systemic therapy given for relapse, persistent or MRD | | | |
| None | 38 (73) | 187 (77) | 225 (76) |
| Inotuzumab | 2 (4) | 6 (2) | 8 (3) |
| Inotuzumab + chemotherapy | 1 (2) | 4 (2) | 5 (2) |
| Inotuzumab + blinatumomab | 0 | 1 (<1) | 1 (<1) |
| Inotuzumab + blinatumomab + Hyper-CVAD | 0 | 1 (<1) | 1 (<1) |
| Inotuzumab + blinatumomab + chemotherapy + vincristine | 0 | 1 (<1) | 1 (<1) |
| Inotuzumab + blinatumomab + chemotherapy + methotrexate + dexamethasone | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab | 0 | 3 (1) | 3 (1) |
| Blinatumomab + chemotherapy | 0 | 3 (1) | 3 (1) |
| Blinatumomab + vincristine | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab + ponatinib | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab + dexamethasone | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab + ponatinib + chemotherapy | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab + ponatinib + chemotherapy + dexamethasone | 0 | 1 (<1) | 1 (<1) |
| Blinatumomab + rituximab + chemotherapy | 0 | 1 (<1) | 1 (<1) |
| Chemotherapy | 10 (19) | 11 (5) | 21 (7) |
| Ponatinib | 0 | 1 (<1) | 1 (<1) |
| Ponatinib + chemotherapy | 0 | 2 (1) | 2 (1) |
| Cytarabine | 0 | 1 (<1) | 1 (<1) |
| Vincristine | 0 | 2 (1) | 2 (1) |
| Dexamethasone | 0 | 2 (1) | 2 (1) |
| Venetoclax + chemotherapy | 1 (2) | 1 (<1) | 2 (1) |
| Bosutinib | 0 | 1 (<1) | 1 (<1) |
| Pegaspargase + chemotherapy | 0 | 1 (<1) | 1 (<1) |
| Prednisone + chemotherapy | 0 | 1 (<1) | 1 (<1) |

**Table 7. Post-HSCT therapies following inotuzumab ozogamicin treatment**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| Dasatinib | 0 | 1 (<1) | 1 (<1) |
| Imatinib + Hydrea | 0 | 1 (<1) | 1 (<1) |
| Other [a] | 0 | 2 (1) | 2 (1) |
| Not reported | 0 | 4 (2) | 4 (2) |
| Radiation therapy given for reasons other than relapse, persistent, or MRD | | | |
| No | 52 | 243 (100) | 295 (100) |
| Yes | 0 | 1 (<1) | 1 (<1) |

[a] Ruxolitinib + prednisone + daunorubicin + vincristine (n = 1); cyclophosphamide + vincristine + venetoclax n = 1)

### 10.2.5. Summary of treatment

This section provides information on the summary of treatment.

#### 10.2.5.1. Therapies prior to inotuzumab ozogamicin

Table 8 summarizes the therapies patients received prior to inotuzumab ozogamicin treatment, including information on the number of lines of therapy prior to transplant and the purpose of therapy prior to patients receiving inotuzumab ozogamicin.

**Table 8. Summary of therapies received prior to inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| No. of treatment regimen(s) prior to receiving inotuzumab ozogamicin | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| 0 | 3 (5) | 28 (11) | 31 (10) |
| 1 | 8 (14) | 71 (27) | 79 (25) |
| 2 | 4 (7) | 47 (18) | 51 (16) |
| 3 | 8 (14) | 44 (17) | 52 (16) |
| 4 | 2 (3) | 19 (7) | 21 (7) |
| ≥ 5 | 19 (33) | 23 (9) | 42 (13) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (14) | 10 (4) | 18 (6) |
| Not reported | 1 (2) | 7 (3) | 8 (3) |
| No. of patients with ≥ 1 treatment prior to inotuzumab ozogamicin | 41 | 204 | 245 |
| Prior autologous HSCT | | | |
| Yes | 0 | 0 | 0 |
| No | 41 | 204 | 245 |
| CNS prophylaxis | | | |
| Yes | 28 (68) | 150 (74) | 178 (73) |
| No | 13 (32) | 54 (26) | 67 (27) |
| Lines of therapy prior to transplant | | | |
| 1 | 0 | 1 (<1) | 1 (<1) |
| 2 | 7 (17) | 39 (19) | 46 (19) |
| 3 | 4 (10) | 55 (27) | 59 (24) |
| 4 or more | 30 (73) | 109 (53) | 139 (57) |
| Purpose of therapy prior to inotuzumab ozogamicin | | | |
| First line | 7 (17) | 86 (42) | 93 (38) |
| Consolidation | 5 (12) | 20 (10) | 25 (10) |
| Maintenance | 12 (29) | 57 (28) | 69 (28) |
| Treatment for disease relapse a | 16 (39) | 36 (18) | 52 (21) |
| Not reported | 1 (2) | 5 (2) | 6 (2) |
| Radiation therapy prior to inotuzumab ozogamicin | | | |
| Yes | 37 (90) | 188 (92) | 225 (92) |
| No | 4 (10) | 12 (6) | 16 (7) |
| Not reported | 0 | 4 (2) | 4 (2) |

**Table 8. Summary of therapies received prior to inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| Blinatumomab given during lines of therapies, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| Yes | 16 (28) | 116 (44) | 132 (41) |
| No | 37 (64) | 133 (51) | 170 (53) |
| Regimens for first line of therapy, prior to inotuzumab ozogamicin | | | |
| None | 9 (22) | 17 (8) | 26 (11) |
| ABT | 0 | 7 (3) | 7 (3) |
| ABT / ABT | 0 | 2 (1) | 2 (1) |
| ABT / ABT / ABT / ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo | 19 (46) | 103 (50) | 122 (50) |
| Chemo + ABT | 0 | 31 (15) | 31 (13) |
| Chemo + ABT + TKI | 0 | 2 (1) | 2 (1) |
| Chemo + ABT / chemo + ABT | 0 | 2 (1) | 2 (1) |
| Chemo + ABT / chemo + ABT / ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo + ABT / chemo + ABT / chemo + ABT / chemo | 0 | 1 (<1) | 1 (<1) |
| Chemo + ABT / chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo + TKI | 1 (2) | 18 (9) | 19 (8) |
| Chemo + TKI / chemo | 0 | 1 (<1) | 1 (<1) |
| Chemo + TKI / chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo + TKI / chemo + TKI / chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo + TKI / chemo + TKI / chemo + TKI / TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo / ABT | 2 (5) | 4 (2) | 6 (2) |
| Chemo / chemo | 6 (15) | 5 (2) | 11 (4) |
| Chemo / chemo + ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo / chemo / ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo / chemo / chemo | 4 (10) | 0 | 4 (2) |
| Chemo / chemo / chemo / chemo / chemo | 0 | 1 (<1) | 1 (<1) |
| TKI | 0 | 1 (<1) | 1 (<1) |
| TKI / chemo | 0 | 1 (<1) | 1 (<1) |
| Regimens for consolidation therapy, prior to inotuzumab ozogamicin | | | |
| None | 14 (34) | 134 (66) | 148 (60) |
| Chemo | 18 (44) | 35 (17) | 53 (22) |
| Chemo + ABT | 0 | 13 (6) | 13 (5) |
| Chemo + TKI | 0 | 8 (4) | 8 (3) |
| Chemo + TKI / chemo + TKI / chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo / ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo / ABT / chemo | 0 | 1 (<1) | 1 (<1) |
| Chemo / chemo | 4 (10) | 7 (3) | 11 (4) |
| Chemo / chemo / chemo | 2 (5) | 2 (1) | 4 (2) |
| Chemo / chemo / chemo / chemo | 2 (5) | 0 | 2 (1) |
| Chemo / chemo / chemo / chemo / chemo / chemo | 1 (2) | 0 | 1 (<1) |
| TKI | 0 | 1 (<1) | 1 (<1) |
| TKI / ABT | 0 | 1 (<1) | 1 (<1) |

**Table 8. Summary of therapies received prior to inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| Regimens for maintenance therapy, prior to inotuzumab ozogamicin | | | |
| None | 18 (44) | 132 (65) | 150 (61) |
| ABT | 0 | 3 (1) | 3 (1) |
| Chemo | 15 (37) | 47 (23) | 62 (25) |
| Chemo + ABT | 1 (2) | 3 (1) | 4 (2) |
| Chemo + TKI | 0 | 9 (4) | 9 (4) |
| Chemo / chemo | 2 (5) | 4 (2) | 6 (2) |
| Chemo / chemo / chemo | 3 (7) | 2 (1) | 5 (2) |
| Chemo / chemo / chemo / chemo | 2 (5) | 1 (<1) | 3 (1) |
| TKI | 0 | 1 (<1) | 1 (<1) |
| TKI / ABT | 0 | 1 (<1) | 1 (<1) |
| TKI / chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Regimens for therapy, prior to inotuzumab ozogamicin | | | |
| None | 24 (59) | 165 (81) | 189 (77) |
| ABT | 1 (2) | 7 (3) | 8 (3) |
| ABT + TKI | 0 | 2 (1) | 2 (1) |
| ABT / chemo | 0 | 1 (<1) | 1 (<1) |
| ABT / chemo / chemo | 0 | 1 (<1) | 1 (<1) |
| Chemo | 10 (24) | 12 (6) | 22 (9) |
| Chemo + ABT | 1 (2) | 4 (2) | 5 (2) |
| Chemo + ABT / chemo | 0 | 2 (1) | 2 (1) |
| Chemo + TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo + TKI / TKI / chemo / TKI | 0 | 1 (<1) | 1 (<1) |
| Chemo / ABT | 0 | 1 (<1) | 1 (<1) |
| Chemo / chemo | 3 (7) | 4 (2) | 7 (3) |
| Chemo / chemo / ABT / chemo | 1 (2) | 0 | 1 (<1) |
| Chemo / chemo / chemo | 1 (2) | 1 (<1) | 2 (1) |
| TKI | 0 | 1 (<1) | 1 (<1) |
| TKI / chemo + TKI | 0 | 1 (<1) | 1 (<1) |

Note: Pluses (+) denote the same line of therapy, while forward slash lines ("/") denote separate lines of therapy. For example, "Chemotherapy + ABT" means that chemo and ABT were given in the same line of therapy. "Chemotherapy / ABT" means that chemo was given in the first line, then ABT was given in a subsequent line of therapy.

[a] Of the n=56 patients who had received therapy to treat disease relapse in the line prior to inotuzumab ozogamicin, the following number of patient(s) received these numbers of lines of therapy prior to inotuzumab ozogamicin: n=6 patients received 1 line, n=10 patients received 2 lines, n=10 patients received 3 lines, n=9 patients received 4 lines, n=8 patients received 5 lines, n=8 patients received 6 lines, and n=5 patients received 7 or more lines prior to inotuzumab ozogamicin.

### 10.2.5.2. Inotuzumab ozogamicin treatment prior to HSCT

Table 9 summarizes inotuzumab ozogamicin treatment received prior to HSCT.

**Table 9. Summary of inotuzumab ozogamicin treatment prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| Number of treatment regimen(s) prior to inotuzumab ozogamicin | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| 0 | 3 (5) | 28 (11) | 31 (10) |
| 1 | 8 (14) | 71 (27) | 79 (25) |
| 2 | 4 (7) | 47 (18) | 51 (16) |
| 3 | 8 (14) | 44 (17) | 52 (16) |
| 4 | 2 (3) | 19 (7) | 21 (7) |
| ≥ 5 | 19 (33) | 23 (9) | 42 (13) |
| Outliers | 8 (14) | 10 (4) | 18 (6) |
| Not reported | 1 (2) | 7 (3) | 8 (3) |
| Number of cycles of inotuzumab ozogamicin | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| 1 | 31 (53) | 83 (32) | 114 (36) |
| 2 | 24 (41) | 122 (47) | 146 (46) |
| 3 | 2 (3) | 37 (14) | 39 (12) |
| 4 | 1 (2) | 13 (5) | 14 (4) |
| 5 | 0 | 1(<1) | 1 (<1) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Regimen containing inotuzumab ozogamicin | | | |
| N/A; CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| Single agent | 25 (43) | 120 (46) | 145 (45) |
| Combined with other chemotherapy/systemic therapy | 19 (33) | 112 (43) | 131 (41) |
| Outliers | 8 (14) | 10 (4) | 18 (6) |
| Not reported | 1 (2) | 7 (3) | 8 (3) |
| Response to inotuzumab ozogamicin | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| CR | 43 (74) | 159 (61) | 202 (63) |
| CRi [a] | 10 (17) | 50 (19) | 60 (19) |
| No CR | 5 (9) | 47 (18) | 52 (16) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| MRD rate, among responders | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| Positive | 12 (21) | 56 (21) | 68 (21) |
| Negative | 41 (71) | 167 (64) | 208 (65) |
| MRD evaluation not done | 4 (7) | 34 (13) | 38 (12) |
| Not reported | 1 (2) | 0 | 1 (<1) |

**Table 9. Summary of inotuzumab ozogamicin treatment prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No (%) |
|---|---|---|---|
| **Number of patients** | **58** | **261** | **319** |
| MRD method of testing | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| Flow cytometry | 40 (69) | 184 (70) | 224 (70) |
| Next generation sequencing | 8 (14) | 7 (3) | 15 (5) |
| Polymerase chain reaction | 2 (3) | 9 (3) | 11 (3) |
| Not collected | 7(12) | 57 (22) | 64 (20) |
| Not reported | 1 (2) | 0 | 1 (<1) |
| MRD testing method and results in responders | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| Flow cytometry | | | |
| Positive | 2 (3) | 20 (8) | 22 (7) |
| Negative | 38 (66) | 164 (63) | 202 (63) |
| Next generation sequencing | | | |
| Positive | 5 (9) | 6 (2) | 11 (3) |
| Negative | 3 (5) | 1 (0) | 4 (1) |
| Polymerase chain reaction | | | |
| Positive | 2 (3) | 7 (3) | 9 (3) |
| Negative | 0 | 2 (1) | 2 (1) |
| Not collected | | | |
| Positive | 3 (5) | 23 (9) | 26 (8) |
| MRD evaluation not done | 4 (7) | 34 (13) | 38 (12) |
| Not reported | | | |
| Not reported | 1 (2) | 0 | 1 (0) |
| Time from last dose of inotuzumab ozogamicin to HSCT, months | | | |
| N/A; CIBMTR Form 2541 not yet received | 0 | 4 (2) | 4 (1) |
| < 1 | 7 (12) | 22 (8) | 29 (9) |
| 1-1.6 | 27 (47) | 57 (22) | 84 (26) |
| 1.7-3 | 13 (22) | 71 (27) | 84 (26) |
| > 3 | 8 (14) | 97 (37) | 105 (33) |
| Not reported | 3 (5) | 10 (4) | 13 (4) |
| Number evaluable | 55 | 247 | 302 |
| Median | 1.4 | 2.4 | 2.1 |
| Range | (0.6-12.5) | (0.6-26.2) | (0.6-26.2) |
| Mean | 2 | 3.3 | 3.1 |
| Standard deviation | 1.8 | 3.4 | 3.2 |

[a] CRi defined as < 5% blasts in bone marrow and the absence of peripheral blood leukemic blasts, incomplete recovery of peripheral blood counts (platelets < $100 \times 10^9$/L and/or ANC < $1 \times 10^9$/L) and resolution of any extramedullary disease

Table 10 summarizes inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included only inotuzumab ozogamicin.

**Table 10. Summary of inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included only inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **No. patients who received inotuzumab ozogamicin without other agent(s)** | **25** | **120** | **145** |
| No. patients who received 1 cycle of inotuzumab ozogamicin | 14 | 43 | 57 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 1.8 | 6 (43) | 9 (21) | 15 (26) |
| 1.8 | 8 (57) | 30 (70) | 38 (67) |
| > 1.8 | 0 | 2 (5) | 2 (4) |
| Not reported | 0 | 2 (5) | 2 (4) |
| Number evaluable | 14 | 41 | 55 |
| Median | 1.8 | 1.8 | 1.8 |
| Range [a] | (0.5-1.8) | (0.8-3.6) | (0.5-3.6) |
| Mean | 1.5 | 1.7 | 1.7 |
| Standard deviation | 0.4 | 0.4 | 0.4 |
| No. patients who received 2 cycles of inotuzumab ozogamicin | 10 | 54 | 64 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 3.0 | 2 (20) | 3 (6) | 5 (8) |
| 3.0-3.2 | 1 (10) | 11 (20) | 12 (19) |
| 3.3-3.6 | 6 (60) | 34 (63) | 40 (63) |
| > 3.6 | 1 (10) | 1 (2) | 2 (3) |
| Not reported | 0 | 5 (9) | 5 (8) |
| Number evaluable | 10 | 49 | 59 |
| Median | 3.4 | 3.3 | 3.3 |
| Range | (2.4-3.8) | (1.2-5.8) | (1.2-5.8) |
| Mean | 3.3 | 3.3 | 3.3 |
| Standard deviation | 0.4 | 0.5 | 0.5 |
| No. patients who received 3 or more cycles of inotuzumab ozogamicin | 1 | 22 | 23 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 2.8 | 0 | 1 (5) | 1 (4) |
| 2.8 - 4.8 | 1 | 9 (41) | 10 (43) |
| 4.9-5.3 | 0 | 4 (18) | 4 (17) |
| > 5.3 | 0 | 3 (14) | 3 (13) |
| Not reported | 0 | 5 (23) | 5 (22) |
| Number evaluable | 1 | 17 | 18 |
| Median | 4.8 | 4.8 | 4.8 |
| Range | NE | (2.7-5.4) | (2.7-5.4) |
| Mean | 4.8 | 4.8 | 4.8 |
| Standard deviation | NE | 0.6 | 0.6 |

Note: Outcomes are not evaluable (NE) if sample size is < 20.
[a] CIBMTR has confirmed with centers that the maximum numbers were correct

Table 11 summarizes inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included other agents.

**Table 11. Summary of inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included other agents**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients who received inotuzumab ozogamicin with other agent(s)** | **19** | **112** | **131** |
| No. patients who received 1 cycle of inotuzumab ozogamicin | 10 | 30 | 40 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 1.8 | 3 (30) | 20 (67) | 23 (58) |
| 1.8 | 6 (60) | 8 (27) | 14 (35) |
| Not reported | 1 (10) | 2 (7) | 3 (8) |
| Number evaluable | 9 | 28 | 37 |
| Median | 1.8 | 1.2 | 1.3 |
| Range | (0.5-1.8) | (0.3-1.8) | (0.3-1.8) |
| Mean | 1.5 | 1.2 | 1.3 |
| Standard deviation | 0.5 | 0.5 | 0.5 |
| No. patients who received 2 cycles of inotuzumab ozogamicin | 9 | 45 | 54 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 3.0 | 3 (43) | 40 (70) | 43 (67) |
| 3.0-3.2 | 1 (14) | 2 (4) | 3 (5) |
| 3.3-3.6 | 3 (43) | 11 (19) | 14 (22) |
| > 3.6 | 0 | 1 (2) | 1 (2) |
| Not reported | 0 | 3 (5) | 3 (5) |
| Number evaluable | 7 | 54 | 61 |
| Median | 3.2 | 1.8 | 2 |
| Range | (1.5-3.6) | (0.9-4.9) | (0.9-4.9) |
| Mean | 2.9 | 2.1 | 2.2 |
| Standard deviation | 0.7 | 0.9 | 0.9 |
| No. patients who received 3 or more cycles of inotuzumab ozogamicin | 2 | 25 | 27 |
| Inotuzumab ozogamicin cumulative dose, mg/m² | | | |
| < 2.8 | 2 | 11 (44) | 13 (48) |
| 2.8-4.8 | 0 | 11 (44) | 11 (41) |
| 4.9-5.3 | 0 | 1 (4) | 1 (4) |
| > 5.3 | 0 | 1 (4) | 1 (4) |
| Not reported | 0 | 1 (4) | 1 (4) |
| Number evaluable | 2 | 24 | 26 |
| Median | NE | 3 | 2.6 |
| Range | (2.1-2.2) | (1.5-5.4) | (1.5-5.4) |
| Mean | 2.2 | 3 | 2.9 |
| Standard deviation | 0.1 | 1.1 | 1.1 |

Note: Outcomes are not evaluable (NE) if sample size is < 20.

### 10.2.5.3. Post-inotuzumab intervening therapies for all patients

Table 12 summarizes post-inotuzumab intervening therapies for patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL.

**Table 12. Post-inotuzumab intervening therapies for patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **58** | **261** | **319** |
| Inotuzumab given in last line of therapy, no. (%) | | | |
| N/A: CIBMTR Form 2011 not yet received | 5 (9) | 12 (5) | 17 (5) |
| No | 6 (10) | 76 (29) | 82 (26) |
| Yes | 38 (66) | 156 (60) | 194 (61) |
| Outliers for lines of therapies | 8 (14) | 10 (4) | 18 (6) |
| Lines of therapies not reported | 1 (2) | 7 (3) | 8 (3) |
| Systemic therapies given post inotuzumab, no. (%) | | | |
| ABT | 0 | 16 (21) | 16 (20) |
| ABT + ABT | 0 | 1 (1) | 1 (1) |
| ABT + TKI | 1 (17) | 6 (8) | 7 (9) |
| ABT/ chemo + TKI | 0 | 1 (1) | 1 (1) |
| Chemo | 4 (67) | 11 (14) | 15 (18) |
| Chemo + ABT | 0 | 6 (8) | 6 (7) |
| Chemo + ABT + TKI/ chemo + TKI/ ABT + TKI/ chemo | 0 | 1 (1) | 1 (1) |
| Chemo + ABT/ ABT | 0 | 1 (1) | 1 (1) |
| Chemo + ABT/ chemo | 0 | 1 (1) | 1 (1) |
| Chemo + ABT/ chemo + ABT | 0 | 1 (1) | 1 (1) |
| Chemo + ABT/ chemo/ chemo | 0 | 1 (1) | 1 (1) |
| Chemo + TKI | 0 | 4 (5) | 4 (5) |
| Chemo + TKI/ chemo + TKI | 0 | 1 (1) | 1 (1) |
| Chemo + TKI/ chemo + TKI/ TKI | 0 | 1 (1) | 1 (1) |
| Chemo/ ABT | 0 | 2 (3) | 2 (2) |
| Chemo/ ABT/ chemo | 0 | 1 (1) | 1 (1) |
| Chemo/ ABT/ chemo/ ABT | 0 | 1 (1) | 1 (1) |
| Chemo/ chemo | 0 | 4 (5) | 4 (5) |
| Chemo/ TKI/ ABT | 0 | 1 (1) | 1 (1) |
| None | 1 (17) | 10 (13) | 11 (13) |
| TKI | 0 | 1 (1) | 1 (1) |
| TKI/ chemo | 0 | 1 (1) | 1 (1) |
| TKI/ chemo + TKI | 0 | 1 (1) | 1 (1) |
| TKI/ chemo + TKI/ TKI | 0 | 1 (1) | 1 (1) |
| TKI/ chemo/ chemo | 0 | 1 (1) | 1 (1) |
| Radiation therapy given post inotuzumab, no. (%) | | | |
| No | 6 | 69 (91) | 75 (91) |
| Yes | 0 | 7 (9) | 7 (9) |

## 10.3. Outcome data

### 10.3.1. Post-transplant overall survival

Table 13 summarizes post-transplant OS within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

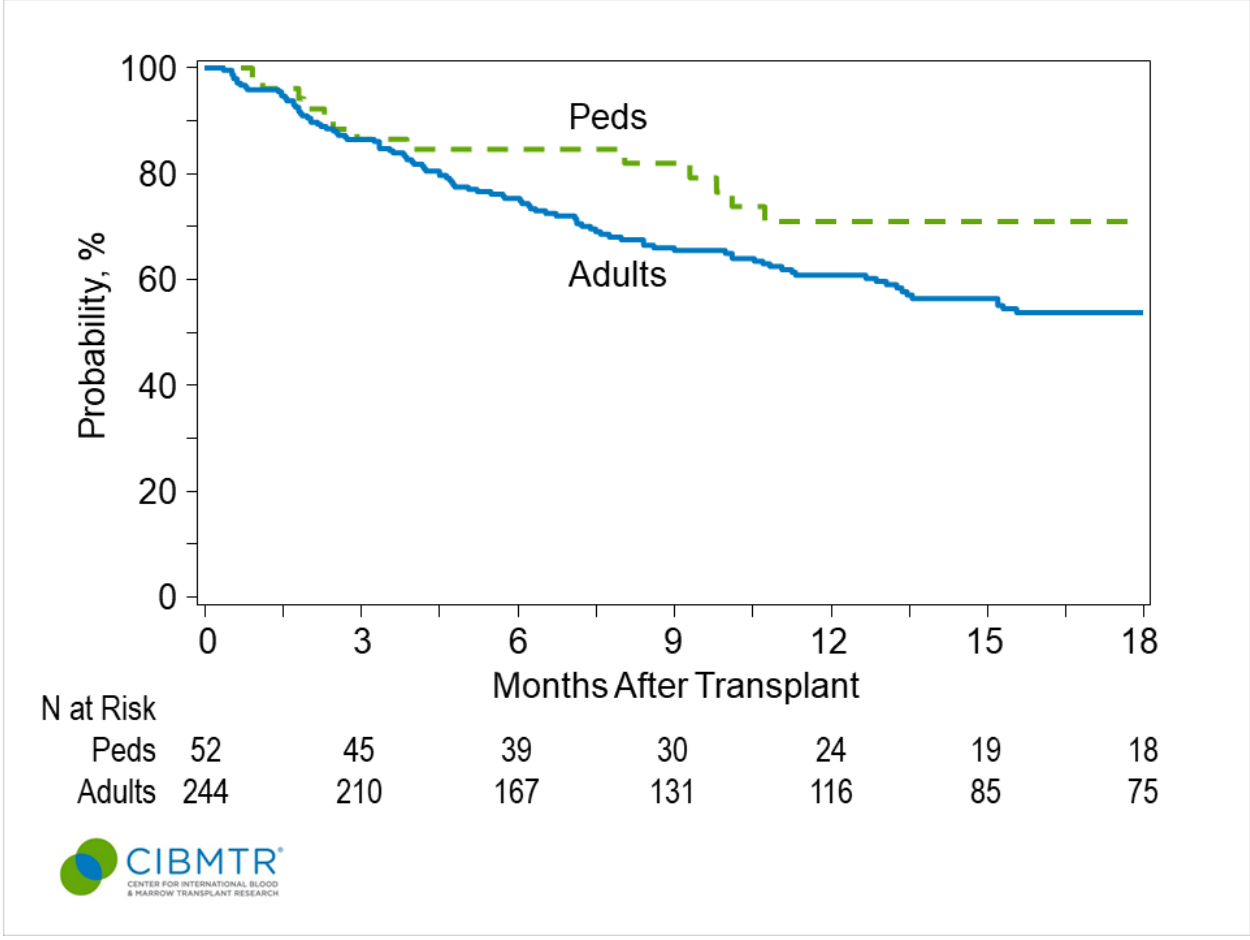
**Table 13. Post-transplant overall survival within 18 months**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| Post-transplant overall survival (95% CI) | | | |
| 6 months | 85 (74-93)% | 75 (70-81)% | 77 (72-82)% |
| 12 months | 71 (56-83)% | 61 (54-67)% | 63 (57-68)% |
| 18 months | NE | 54 (47-61)% | 57 (50-63)% |
| Number of deaths within 18 months | 13 | 99 | 112 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 7 (54) | 33 (33) | 40 (36) |
| New malignancy | 0 | 1 (1) | 1 (1) |
| GVHD | 1 (8) | 16 (16) | 17 (15) |
| VOD/SOS | 2 (15) | 15 (15) | 17 (15) |
| Interstitial pneumonitis | 0 | 6 (6) | 6 (5) |
| Infection | 1 (8) | 9 (9) | 10 (9) |
| Septic shock | 0 | 2 (2) | 2 (2) |
| Thrombotic microangiopathy (TMA) | 1 (8) | 0 | 1 (1) |
| Hemorrhage | 0 | 4 (4) | 4 (4) |
| Organ failure | 1 (8) | 11 (11) | 12 (11) |
| Graft failure | 0 | 1 (1) | 1 (1) |
| Other | 0 | 1 (1) | 1 (1) |
| Time from transplant to death, no. (%) months | | | |
| < 3 | 7 (54) | 33 (33) | 40 (36) |
| 3-5 | 1 (8) | 26 (26) | 27 (24) |
| 6-11 | 5 (38) | 29 (29) | 34 (30) |
| 12-18 | 0 | 11 (11) | 11 (10) |
| Median (95% CI) | 2.92 (1.81 - 9.82) | 4.63 (3.81 - 6.05) | 4.50 (3.61 - 5.74) |
| Range | (0.92-10.74) | (0.36-15.57) | (0.36-15.57) |
| Mean | 5.03 | 5.65 | 5.58 |
| Standard deviation | 3.88 | 4.16 | 4.12 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-transplant overall survival is time from HSCT to death from any cause. Patients were censored at the last date that the patient was known to be alive. There are no competing risks.

Figure 1 shows post-transplant OS within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 1 Post-transplant overall survival within 18 months**



### 10.3.2. Post-transplant overall mortality

Table 14 summarizes post-transplant overall mortality within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

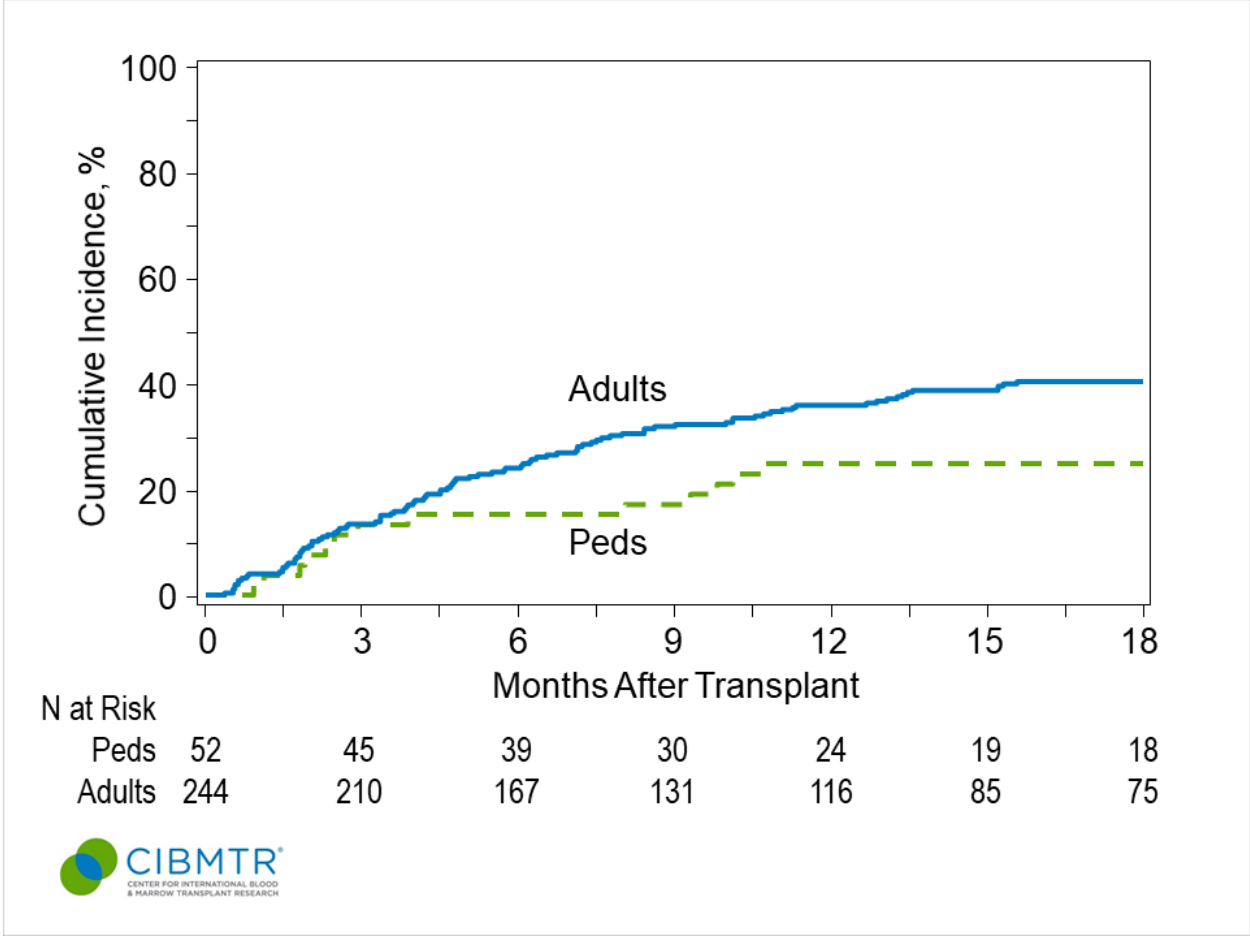
**Table 14. Post-transplant overall mortality within 18 months**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| Post-transplant overall mortality (95% CI) | | | |
| 6 months | 15 (7-26)% | 25 (19-30)% | 23 (18-28)% |
| 12 months | 29 (17-44)% | 39 (33-46)% | 37 (32-43)% |
| 18 months | NE | 46 (39-53)% | 43 (37-50)% |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-transplant overall mortality is time from HSCT to death from any cause. Patients were censored at the last date that the patient was known to be alive. There are no competing risks.

Figure 2 shows cumulative incidence of post-transplant overall mortality within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 2 Post-transplant overall mortality within 18 months**




Note: Overall mortality = 1 – overall survival

### 10.3.3. Post-inotuzumab overall survival

Table 15 summarizes OS within 18 months of first dose of inotuzumab ozogamicin in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

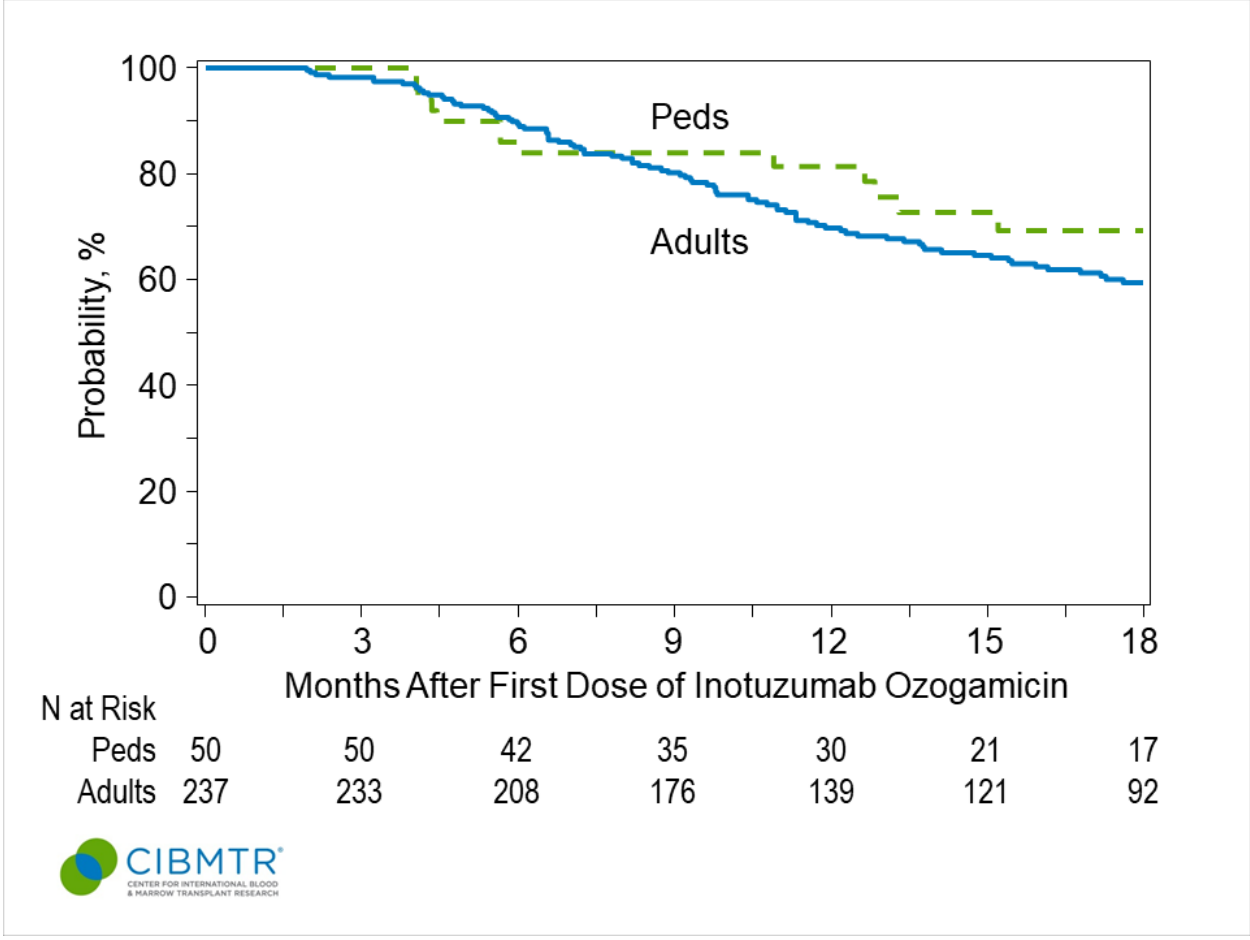
**Table 15. Overall survival within 18 months of first dose of inotuzumab ozogamicin**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with follow-up and CIBMTR Form 2541 and date of first dose of inotuzumab ozogamicin provided** | **50** | **237** | **287** |
| Post-inotuzumab ozogamicin overall survival (95% CI) | | | |
| 6 months | 84 (73-93)% | 89 (85-93)% | 88 (84-92)% |
| 12 months | 81 (69-91)% | 70 (64-76)% | 72 (66-77)% |
| 18 months | NE | 59 (53-66)% | 61 (55-67)% |
| Number of deaths within 18 months | 13 | 87 | 100 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 7 (54) | 29 (33) | 36 (36) |
| GVHD | 1 (8) | 15 (17) | 16 (16) |
| VOD/SOS | 2 (15) | 14 (16) | 16 (16) |
| Interstitial pneumonitis | 0 | 3 (3) | 3 (3) |
| Infection | 1 (8) | 9 (10) | 10 (10) |
| Septic shock | 0 | 2 (2) | 2 (2) |
| Thrombotic microangiopathy | 1 (8) | 0 | 1 (1) |
| Hemorrhage | 0 | 3 (3) | 3 (3) |
| Organ failure | 1 (8) | 10 (11) | 11 (11) |
| Graft failure | 0 | 1 (1) | 1 (1) |
| Other | 0 | 1 (1) | 1 (1) |
| Time from first dose of inotuzumab ozogamicin to death, no. (%), months | | | |
| < 3 | 0 | 4 (5) | 4 (4) |
| 3-5 | 8 (62) | 21 (24) | 29 (29) |
| 6-11 | 1 (8) | 43 (49) | 44 (44) |
| 12-18 | 4 (31) | 19 (22) | 23 (23) |
| Median (95% CI) | 5.65 (4.07 - 12.85) | 8.51 (7.06 - 9.79) | 8.24 (6.76-9.79) |
| Range | (4.04-15.21) | (1.94-17.61) | (1.94-17.61) |
| Mean | 7.93 | 8.88 | 8.76 |
| Standard deviation | 4.3 | 4.05 | 4.07 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-inotuzumab ozogamicin survival is time from first dose of inotuzumab ozogamicin to death from any cause. Patients were censored at the last date that the patient was known to be alive. There are no competing risks.

Figure 3 shows OS within 18 months of first dose of inotuzumab ozogamicin in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 3 Overall survival within 18 months of first dose of inotuzumab ozogamicin**



### 10.3.4. Transplant-related mortality (post-transplant non-relapse mortality)

Table 16 summarizes TRM within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

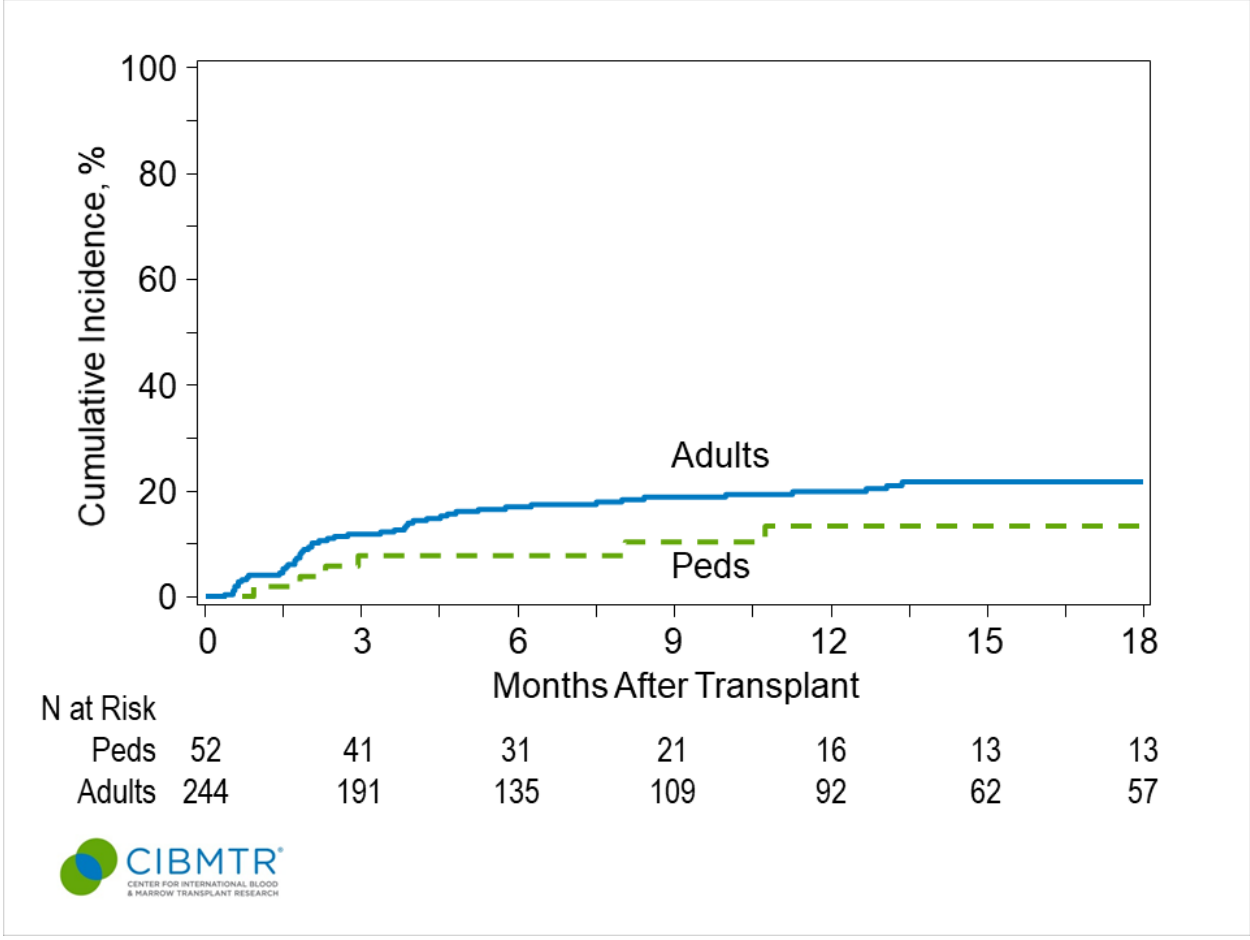
**Table 16. Transplant-related mortality within 18 months**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **52** | **244** | **296** |
| Transplant-related mortality (95% CI) | | | |
| 6 months | 8 (2-17)% | 17 (13-22)% | 15 (12-20)% |
| 12 months | NE | 20 (15-25)% | 19 (14-24)% |
| 18 months | NE | 22 (17-27)% | 20 (16-25)% |
| No. patients with TRM within 18 months | 6 | 50 | 56 |
| No. patients with competing risk (post-transplant relapse) | 19 | 87 | 106 |
| Primary cause of death, among patients with TRM, no. (%) | | | |
| GVHD | 1 (17) | 11 (22) | 12 (21) |
| VOD/SOS | 2 (33) | 13 (26) | 15 (27) |
| Interstitial pneumonitis | 0 | 4 (8) | 4 (7) |
| Infection | 1 (17) | 5 (10) | 6 (11) |
| Septic shock | 0 | 2 (4) | 2 (4) |
| Thrombotic microangiopathy (TMA) | 1 (17) | 0 | 1 (2) |
| Hemorrhage | 0 | 3 (6) | 3 (5) |
| Organ failure | 1 (17) | 10 (20) | 11 (20) |
| Graft failure | 0 | 1 (2) | 1 (2) |
| Other | 0 | 1 (2) | 1 (2) |
| Time from transplant to TRM, no. (%), months | | | |
| < 3 | 4 (67) | 29 (58) | 33 (59) |
| 3-5 | 0 | 12 (24) | 12 (21) |
| 6-11 | 2 (33) | 6 (12) | 8 (14) |
| 12-18 | 0 | 3 (6) | 3 (5) |
| Median (95% CI) | 2.61 (0.92 - 10.74) | 2.1 (1.81 - 3.84) | 2.23 (1.81 - 3.81) |
| Range | (0.92-10.74) | (0.36-13.37) | (0.36-13.37) |
| Mean | 4.46 | 3.68 | 3.76 |
| Standard deviation | 3.97 | 3.47 | 3.5 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Transplant-related mortality (post-transplant non-relapse mortality) is time from HSCT to death within the first 28 days post-HSCT, or death from any cause without prior relapse/progression post-HSCT.

Figure 4 shows cumulative incidence of TRM within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 4 Transplant-related mortality within 18 months**



### 10.3.5. Non-transplant-related mortality

Table 17 summarizes NTRM within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

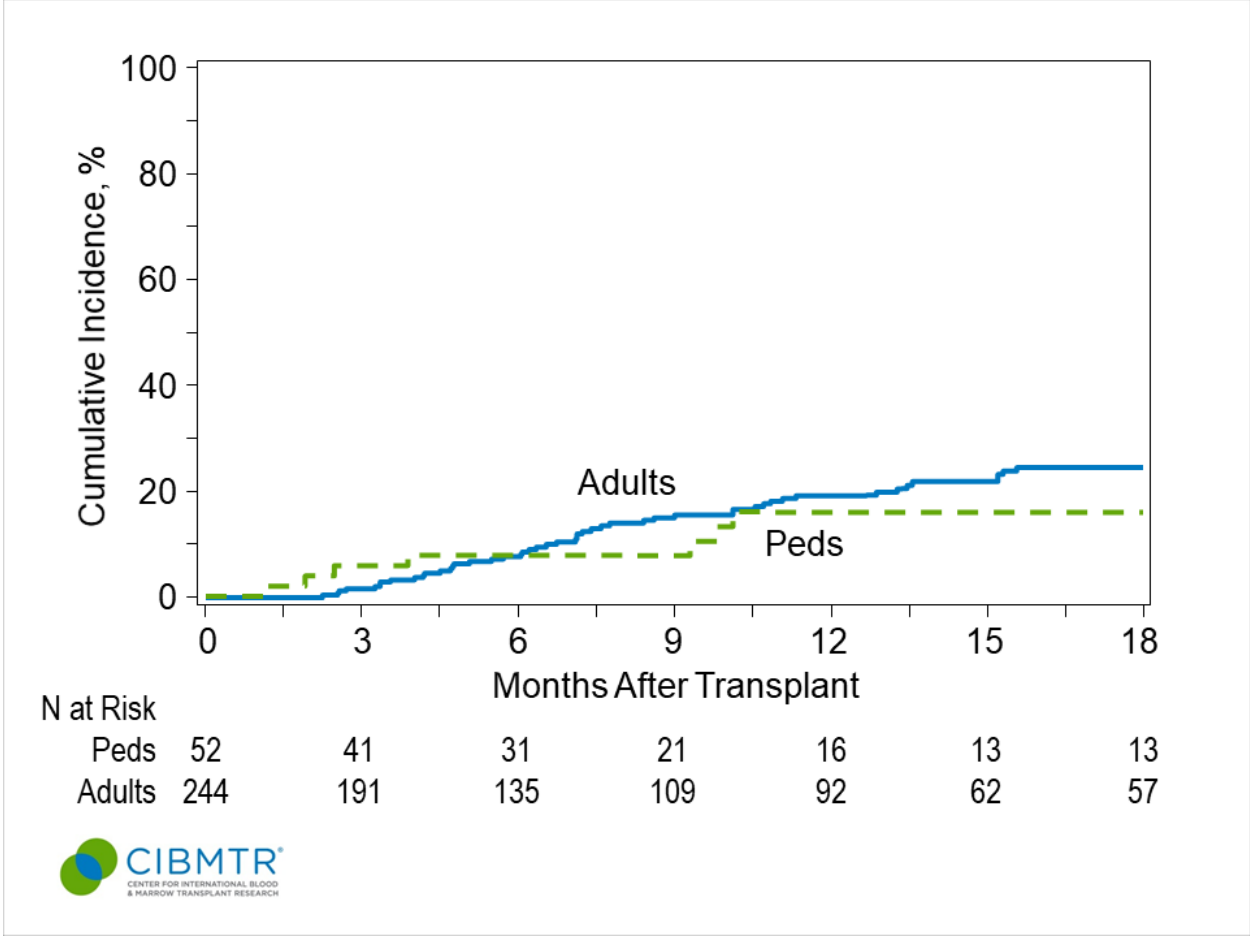
**Table 17. Non-transplant-related mortality within 18 months**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **52** | **244** | **296** |
| Non-transplant-related mortality (95% CI) | | | |
| 6 months | 8 (3-17)% | 8 (5-11)% | 8 (5-11)% |
| 12 months | NE | 19 (14-25)% | 19 (14-24)% |
| 18 months | NE | 24 (19-31)% | 23 (18-29)% |
| No. patients with NTRM within 18 months | 7 | 49 | 56 |
| No. patients with competing risk (transplant-related mortality) | 6 | 50 | 56 |
| Time from transplant to NTRM, no. (%), months | | | |
| < 3 | 3 (43) | 4 (8) | 7 (13) |
| 3-5 | 1 (14) | 14 (29) | 15 (27) |
| 6-11 | 3 (43) | 23 (47) | 26 (46) |
| 12-18 | 0 | 8 (16) | 8 (14) |
| Median (95% CI) | 3.88 (1.12 - 10.12) | 7.1 (5.72 - 8.41) | 6.92 (5.48 – 8.41) |
| Range | (1.12-10.12) | (2.23-15.57) | (1.12-15.57) |
| Mean | 5.51 | 7.66 | 7.39 |
| Standard deviation | 4.05 | 3.85 | 3.9 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Non-transplant-related mortality is time from HSCT to death after the first 28 days post-HSCT from any cause after prior relapse/progression post-HSCT.

Figure 5 shows cumulative incidence of NTRM within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 5 Non-transplant-related mortality within 18 months**



### 10.3.6. Post-transplant relapse

Table 18 summarizes post-transplant relapse within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

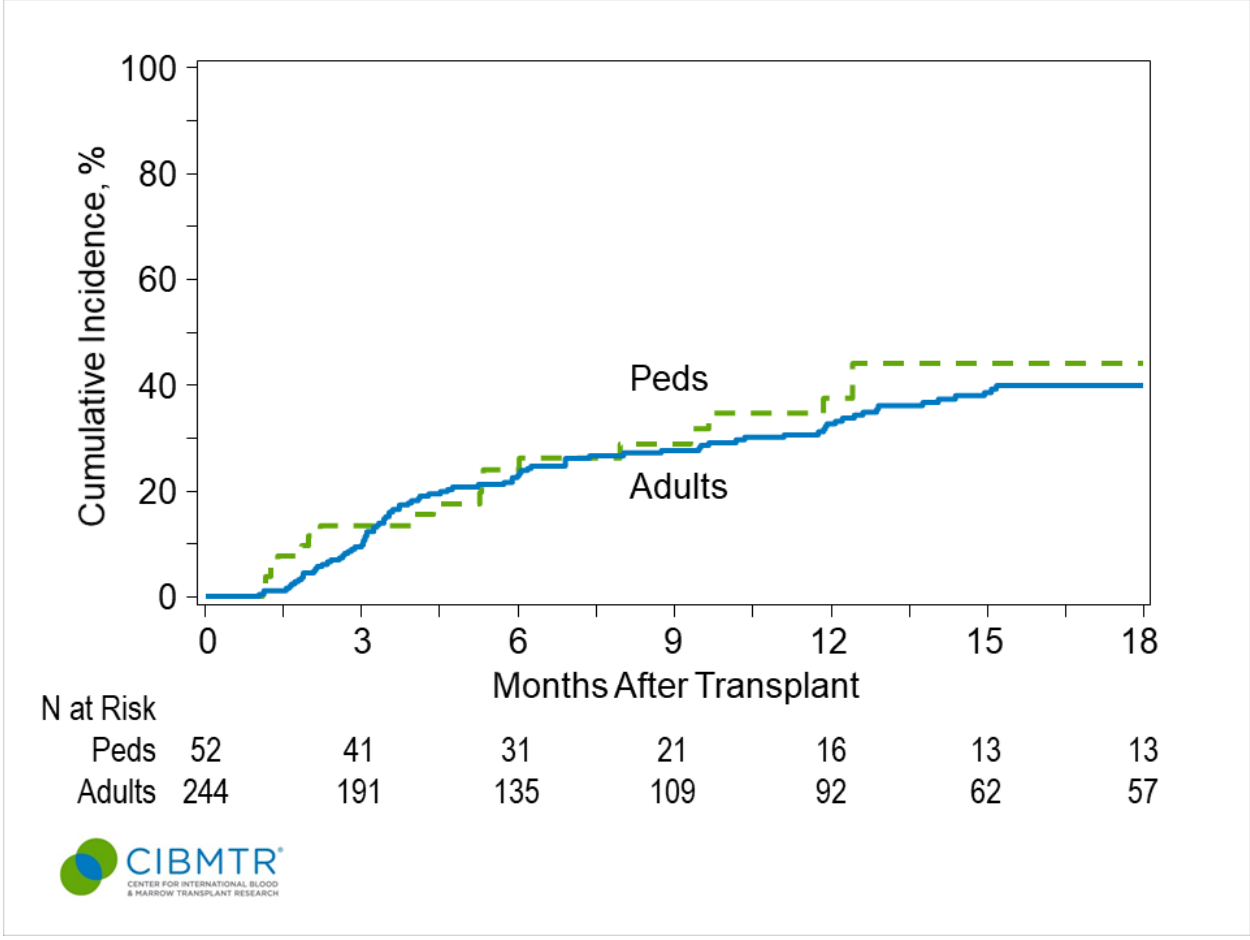
**Table 18. Post-transplant relapse within 18 months**

| | **Pediatric patients (< 18 y)** | **Adults (≥ 18 y)** | **All patients** |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **52** | **244** | **296** |
| Post-transplant relapse (95% CI) | | | |
| 6 months | 24 (13-37)% | 23 (18-29)% | 23 (18-28)% |
| 12 months | NE | 33 (27-39)% | 33 (28-39)% |
| 18 months | NE | 40 (33-47)% | 41 (34-47)% |
| No. patients with post-transplant relapse within 18 months | 19 | 87 | 106 |
| No. patients with competing risk (transplant-related mortality) | 6 | 50 | 56 |
| Time from transplant to post-transplant relapse, no. (%), months | | | |
| < 3 | 7 (37) | 24 (28) | 31 (29) |
| 3-5 | 5 (26) | 31 (36) | 36 (34) |
| 6-11 | 5 (26) | 20 (23) | 25 (24) |
| 12-18 | 2 (11) | 12 (14) | 14 (13) |
| Median (95% CI) | 5.26 (1.97 - 9.3) | 3.94 (3.42 - 5.88) | 4.09 (3.41-5.71) |
| Range | (1.08-12.42) | (1.02-15.18) | (1.02-15.18) |
| Mean | 5.51 | 5.88 | 5.81 |
| Standard deviation | 4 | 4.16 | 4.11 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-transplant relapse is time from HSCT to first relapse post-HSCT without death post-relapse, or with death after the first 28 days post-HSCT.

Figure 6 shows cumulative incidence of post-transplant relapse within 18 months in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 6 Post-transplant relapse within 18 months**



### 10.3.7. 100-day post-HSCT adverse events of interest, including hepatic VOD/SOS

Table 19 summarizes 100-day post-HSCT AEs of interest in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Table 19. 100-day post-HSCT adverse events of interest**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| Viral infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 20 (38) | 107 (44) | 127 (43) |
| No | 24 (46) | 129 (53) | 153 (52) |
| Not reported | 7 (13) | 7 (3) | 14 (5) |
| Bacterial infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 14 (27) | 125 (51) | 139 (47) |
| No | 30 (58) | 111 (45) | 141 (48) |
| Not reported | 7 (13) | 7 (3) | 14 (5) |
| Fungal infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 4 (8) | 22 (9) | 26 (9) |
| No | 40 (77) | 214 (88) | 254 (86) |
| Not reported | 7 (13) | 7 (3) | 14 (5) |
| SIRS development, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 4 (8) | 9 (4) | 13 (4) |
| No | 47 (90) | 233 (95) | 280 (95) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Septic shock, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 6 (12) | 34 (14) | 40 (14) |
| No | 45 (87) | 208 (85) | 253 (85) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Maximum grade of acute GVHD, up to day 100 [a] | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| None | 30 (58) | 111 (45) | 141 (48) |
| I | 4 (8) | 26 (11) | 30 (10) |
| II | 9 (17) | 72 (30) | 81 (27) |
| III | 4 (8) | 17 (7) | 21 (7) |
| IV | 4 (8) | 16 (7) | 20 (7) |
| Not reported | 0 | 1 (<1) | 1 (<1) |
| Time from HSCT to date of maximum acute GVHD, months | | | |
| Number evaluable | 21 | 129 | 150 |
| Median | 1 | 1.3 | 1.3 |
| Range | (0.4-2.9) | (0.4-3.2) | (0.4-3.2) |
| Mean | 1.1 | 1.4 | 1.4 |

**Table 19. 100-day post-HSCT adverse events of interest**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| Standard deviation | 0.6 | 0.6 | 0.6 |
| Chronic GVHD, up to 1 year post-transplant | | | |
| Yes | 6 (12) | 66 (27) | 72 (24) |
| No | 45 (87) | 172 (70) | 217 (73) |
| Not reported | 1 (2) | 6 (2) | 7 (2) |
| Time from HSCT to chronic GVHD, months | | | |
| Number evaluable | 6 | 66 | 72 |
| Median | 5.3 | 7.3 | 7.2 |
| Range | (3.3-12.4) | (2-30.6) | (2-30.6) |
| Mean | 6.2 | 8.4 | 8.2 |
| Standard deviation | 3.4 | 4.9 | 4.8 |
| VOD/SOS within 100 days post-transplant | | | |
| Yes | 16 (31) | 35 (14) | 51 (17) |
| No | 36 (69) | 207 (85) | 243 (82) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Time from HSCT to VOD/SOS, months | | | |
| Number evaluable | 16 | 35 | 51 |
| Median | 0.3 | 0.5 | 0.4 |
| Range | (0.2-0.8) | (0.2-3) | (0.2-3) |
| Mean | 0.4 | 0.7 | 0.6 |
| Standard deviation | 0.2 | 0.7 | 0.6 |
| Secondary malignancy | | | |
| Yes [b] | 0 | 6 (2) | 6 (2) |
| No | 45 (87) | 231 (95) | 276 (93) |
| Not reported | 7 (13) | 7 (3) | 14 (5) |
| Time from HSCT to secondary malignancy, months | | | |
| Number evaluable | NE | 6 | 6 |
| Median | NE | 5 | 5 |
| Range | NE | (2-21) | (2-21) |
| Mean | NE | 8 | 8 |
| Standard deviation | NE | 7 | 7 |
| **Pulmonary AEs within 100 days post-transplant** | | | |
| IPN / Idiopathic pneumonia syndrome | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 5 (10) | 15 (6) | 20 (7) |
| No | 46 (88) | 226 (93) | 272 (92) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Bronchiolitis obliterans | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 1 (<1) | 1 (<1) |
| No | 51 (98) | 242 (99) | 293 (99) |

**Table 19. 100-day post-HSCT adverse events of interest**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| COP/BOOP | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |
| Diffuse alveolar hemorrhage | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 5 (2) | 5 (2) |
| No | 51 (98) | 238 (98) | 289 (98) |
| **Cardiovascular AEs within 100 days post-transplant** | | | |
| Arrhythmia | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 8 (3) | 8 (3) |
| No | 51 (98) | 233 (95) | 284 (96) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Congestive heart failure | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 1 (<1) | 1 (<1) |
| No | 51 (98) | 242 (99) | 293 (99) |
| Coronary artery disease | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |
| Myocardial infarction or unstable angina | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 1 (<1) | 1 (<1) |
| No | 51 (98) | 242 (99) | 293 (99) |
| Hypertension (HTN) requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 6 (12) | 13 (5) | 19 (6) |
| No | 44 (85) | 229 (94) | 273 (92) |
| Not reported | 1 (2) | 1 (<1) | 2 (1) |
| TMA | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 2 (4) | 8 (3) | 10 (3) |
| No | 49 (94) | 235 (96) | 284 (96) |
| **Renal AEs within 100 days post-transplant** | | | |
| Acute renal failure requiring dialysis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 5 (10) | 21 (9) | 26 (9) |
| No | 46 (88) | 222 (91) | 268 (91) |

**Table 19. 100-day post-HSCT adverse events of interest**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |
| **Musculoskeletal AEs within 100 days post-transplant** | | | |
| Avascular necrosis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 1 (<1) | 1 (<1) |
| No | 51 (98) | 242 (99) | 293 (99) |
| **Endocrine dysfunction within 100 days post-transplant** | | | |
| Diabetes or hyperglycemia requiring chronic treatment | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 2 (4) | 9 (4) | 11 (4) |
| No | 49 (94) | 234 (96) | 283 (96) |
| Growth hormone deficiency or short stature | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |
| Hypothyroidism requiring replacement therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |
| Pancreatitis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |
| Depression requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 1 (2) | 2 (1) | 3 (1) |
| No | 49 (94) | 240 (98) | 289 (98) |
| Not reported | 1 (2) | 1 (<1) | 2 (1) |
| Anxiety requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 3 (6) | 4 (2) | 7 (2) |
| No | 48 (92) | 237 (97) | 285 (96) |
| Not reported | 0 | 2 (1) | 2 (1) |
| CNS hemorrhage and stroke | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 1 (2) | 3 (1) | 4 (1) |
| No | 50 (96) | 240 (98) | 290 (98) |
| PTSD requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 51 (98) | 243 (100) | 294 (99) |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table.
All events were evaluated up to 100 days post-transplant unless noted otherwise.

**Table 19. 100-day post-HSCT adverse events of interest**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **52** | **244** | **296** |

[a] Acute GVHD grading follows the Consensus criteria (Przepiorka D, Weisdorf D, Martin P, et al. [1995] 1994 Consensus Conference on Acute GVHD Grading. Bone Marrow Transplant 15:825–828.) Acute GVHD was evaluated up to 100 days post-transplant; 2 patients were reported with acute GVHD more than 100 days post-HSCT. These patients were reported as not having acute GVHD in this table.

[b] Secondary malignancies reported for n=6 patients were squamous cell cancer of the skin, acute myeloid leukemia, non-Hodgkin lymphoma, myelodysplastic syndrome, lung cancer, and genitourinary malignancy.

### 10.3.8. Outcomes by line of therapy

**Table 20. Outcomes by lines of therapy prior to transplant for adult and pediatric patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | First line (N = 9) | | Salvage 1 (N = 62) | | Salvage 2 (N = 61) | | Salvage > 2 (N = 140) | |
|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Overall survival | 9 | | 62 | | 61 | | 140 | |
| 6 months | | NE | | 77 (65-87)% | | 73 (61-83)% | | 78 (70-84)% |
| 1 year | | NE | | 66 (53-78)% | | 59 (46-72)% | | 64 (55-72)% |
| 18 months | | NE | | 63 (50-76)% | | NE | | 55 (46-64)% |
| Overall mortality | 9 | | 62 | | 61 | | 140 | |
| 6 months | | NE | | 23 (13-35)% | | 27 (17-39)% | | 22 (16-30)% |
| 1 year | | NE | | 34 (22-47)% | | 41 (28-54)% | | 36 (28-45)% |
| 18 months | | NE | | 37 (24-50)% | | NE | | 45 (36-54)% |
| Overall survival post first dose of inotuzumab | 9 | | 60 | | 57 | | 138 | |
| 6 months | | NE | | 87 (77-94)% | | 91 (82-97)% | | 87 (81-92)% |
| 1 year | | NE | | 74 (61-84)% | | 64 (51-77)% | | 75 (67-82)% |
| 18 months | | NE | | 66 (53-78)% | | NE | | 61 (52-70)% |
| Transplant-related mortality | 9 | | 62 | | 61 | | 140 | |
| 6 months | | NE | | 23 (13-34)% | | 13 (6-23)% | | 14 (8-20)% |
| 1 year | | NE | | 25 (15-37)% | | 16 (7-27)% | | 15 (10-22)% |
| 18 months | | NE | | NE | | NE | | 17 (11-24)% |
| Non-transplant-related mortality | 9 | | 62 | | 61 | | 140 | |
| 6 months | | NE | | 0 (0-1)% | | 14 (7-24)% | | 9 (5-14)% |
| 1 year | | NE | | 9 (3-19)% | | NE | | 21 (15-29)% |
| 18 months | | NE | | NE | | NE | | 28 (20-36)% |
| Relapse | 9 | | 62 | | 61 | | 140 | |
| 6 months | | NE | | 21 (12-32)% | | 26 (16-38)% | | 23 (17-31)% |
| 1 year | | NE | | 23 (13-35)% | | 35 (23-49)% | | 37 (29-45)% |
| 18 months | | NE | | NE | | NE | | 45 (36-53)% |
| Post-HSCT VOD/SOS | 9 | | 61 | | 61 | | 139 | |
| 100-day | | NE | | 11 (5-21)% | | 20 (11-31)% | | 18 (12-25)% |

**Table 21. Outcomes by lines of therapy prior to transplant for adult patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | First line (N = 8) | | Salvage 1 (N = 54) | | Salvage 2 (N = 57) | | Salvage > 2 (N = 111) | |
|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Overall survival | 8 | | 54 | | 57 | | 111 | |
| 6 months | | NE | | 75 (63-86)% | | 71 (58-82)% | | 77 (69-85)% |
| 1 year | | NE | | 62 (48-76)% | | 57 (43-71)% | | 63 (53-72)% |
| 18 months | | NE | | NE | | NE | | 53 (42-63)% |
| Overall mortality | 8 | | 54 | | 57 | | 111 | |
| 6 months | | NE | | 25 (14-37)% | | 29 (18-42)% | | 23 (15-31)% |
| 1 year | | NE | | 38 (24-52)% | | 43 (29-57)% | | 37 (28-47)% |
| 18 months | | NE | | NE | | NE | | 47 (37-58)% |
| Overall survival post first dose of inotuzumab | 8 | | 52 | | 55 | | 109 | |
| Overall survival | | NE | | 86 (76-94)% | | 91 (82-97)% | | 89 (82-94)% |
| 6 months | | NE | | 71 (58-83)% | | 63 (50-76)% | | 73 (64-81)% |
| 1 year | | NE | | NE | | NE | | 60 (50-70)% |
| Transplant-related mortality | 8 | | 54 | | 57 | | 111 | |
| 6 months | | NE | | 25 (14-37)% | | 14 (6-25)% | | 15 (9-23)% |
| 1 year | | NE | | 27 (16-40)% | | NE | | 17 (11-25)% |
| 18 months | | NE | | NE | | NE | | 20 (13-28)% |
| Non-transplant-related mortality | 8 | | 54 | | 57 | | 111 | |
| 6 months | | NE | | 0 (0-2)% | | 15 (7-25)% | | 7 (3-13)% |
| 1 year | | NE | | NE | | NE | | 20 (13-28)% |
| 18 months | | NE | | NE | | NE | | 28 (19-37)% |
| Relapse | 8 | | 54 | | 57 | | 111 | |
| 6 months | | NE | | 17 (8-28)% | | 28 (17-41)% | | 22 (15-30)% |
| 1 year | | NE | | 19 (10-31)% | | NE | | 34 (25-43)% |
| 18 months | | NE | | NE | | NE | | 41 (32-51)% |
| Post-HSCT VOD/SOS | 8 | | 53 | | 57 | | 110 | |
| 100-day | | NE | | 6 (1-13)% | | 19 (10-31)% | | 16 (10-24)% |

### 10.3.9. Veno-occlusive disease

Table 22 describes characteristics of adults who received inotuzumab ozogamicin, by severity of VOD.

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| No. of centers | 51 | 11 | 9 | 52 |
| Age, years, no. (%) | | | | |
| 18-29 | 64 (31) | 6 (40) | 10 (50) | 80 (33) |
| 30-39 | 39 (19) | 5 (33) | 1 (5) | 45 (18) |
| 40-49 | 40 (19) | 2 (13) | 5 (25) | 47 (19) |
| 50-59 | 28 (13) | 1 (7) | 1 (5) | 30 (12) |
| ≥ 60 | 38 (18) | 1 (7) | 3 (15) | 42 (17) |
| Median | 40 | 33 | 29.5 | 39 |
| Range | (18-75) | (19-73) | (18-66) | (18-75) |
| Mean | 41.8 | 35.2 | 36 | 40.9 |
| Standard deviation | 16 | 14.6 | 16 | 16 |
| Race, no. (%) | | | | |
| White | 163 (78) | 12 (80) | 17 (85) | 192 (79) |
| Black or African American | 15 (7) | 0 | 1 (5) | 16 (7) |
| Asian or Native Hawaiian and other Pacific Islander | 12 (6) | 0 | 1 (5) | 13 (5) |
| Others | 2 (1) | 1 (7) | 0 | 3 (1) |
| Not reported | 17 (8) | 2 (13) | 1 (5) | 20 (8) |
| Body mass index, $kg/m^2$, no. (%) | | | | |
| Underweight | 4 (2) | 0 | 3 (15) | 7 (3) |
| Healthy weight | 38 (18) | 3 (20) | 4 (20) | 45 (18) |
| Overweight | 61 (29) | 4 (27) | 4 (20) | 69 (28) |
| Obese | 106 (51) | 8 (53) | 9 (45) | 123 (50) |
| Number evaluable | 209 | 15 | 20 | 244 |
| Median | 30.4 | 30 | 29.1 | 30 |
| Range | (12.2-60.1) | (20.6-54.3) | (17.1-62.5) | (12.2-62.5) |
| Mean | 30.9 | 30.7 | 30.5 | 30.8 |
| Standard deviation | 7.6 | 8.4 | 11.2 | 8 |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Sex, no. (%) | | | | |
| Male | 117 (56) | 11 (73) | 13 (65) | 141 (58) |
| Female | 92 (44) | 4 (27) | 7 (35) | 103 (42) |
| Sorror HCT-CI, no. (%) [a] | | | | |
| 0 | 29 (14) | 3 (20) | 3 (15) | 35 (14) |
| 1-2 | 73 (35) | 9 (60) | 5 (25) | 87 (36) |
| 3-4 | 70 (33) | 2 (13) | 11 (55) | 83 (34) |
| 5 | 18 (9) | 1 (7) | 0 | 19 (8) |
| 6 | 8 (4) | 0 | 0 | 8 (3) |
| 7 | 5 (2) | 0 | 1 (5) | 6 (2) |
| Not reported | 6 (3) | 0 | 0 | 6 (2) |
| Arrhythmia, no. (%) [b] | | | | |
| Yes | 12 (6) | 0 | 3 (15) | 15 (6) |
| No | 191 (91) | 15 | 17 (85) | 223 (91) |
| Not reported | 6 (3) | 0 | 0 | 6 (2) |
| Cardiac, no. (%) [c] | | | | |
| Yes | 10 (5) | 0 | 1 (5) | 11 (5) |
| No | 193 (92) | 15 | 19 (95) | 227 (93) |
| Not reported | 6 (3) | 0 | 0 | 6 (2) |
| Cerebrovascular disease, no. (%) [d] | | | | |
| Yes | 6 (3) | 1 (7) | 1 (5) | 8 (3) |
| No | 197 (94) | 14 (93) | 19 (95) | 230 (94) |
| Not reported | 6 (3) | 0 | 0 | 6 (2) |
| Hepatic disease, no. (%) | | | | |
| Moderate/severe [e], not mild | 8 (4) | 0 | 1 (5) | 9 (4) |
| Mild [f], not moderate/severe | 49 (23) | 4 (27) | 5 (25) | 58 (24) |
| No hepatic disease | 146 (70) | 11 (73) | 14 (70) | 171 (70) |
| Not reported | 6 (3) | 0 | 0 | 6 (2) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Lines of therapy prior to transplant, no. (%) [g] | | | | |
| N/A, CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| First line | 7 (3) | 1 (7) | 0 | 8 (3) |
| Salvage 1 | 51 (24) | 1 (7) | 2 (10) | 54 (22) |
| Salvage 2 | 46 (22) | 2 (13) | 9 (45) | 57 (23) |
| Salvage > 2 | 93 (44) | 10 (67) | 8 (40) | 111 (45) |
| Outliers | 8 (4) | 1 (7) | 0 | 9 (4) |
| Number evaluable | 197 | 14 | 19 | 230 |
| Median | 3 | 4 | 3 | 3 |
| Range | (1-10) | (1-7) | (2-8) | (1-10) |
| Mean | 3.7 | 4.3 | 3.9 | 3.8 |
| Standard deviation | 1.8 | 1.7 | 1.6 | 1.8 |
| Lines of therapy prior to inotuzumab ozogamicin, no. (%) | | | | |
| N/A, CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| No treatment given | 23 (11) | 2 (13) | 2 (10) | 27 (11) |
| First line | 63 (30) | 2 (13) | 4 (20) | 69 (28) |
| Salvage 1 | 37 (18) | 2 (13) | 6 (30) | 45 (18) |
| Salvage 2 | 36 (17) | 3 (20) | 4 (20) | 43 (18) |
| Salvage > 2 | 34 (16) | 5 (33) | 3 (15) | 42 (17) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (4) | 1 (7) | 0 | 9 (4) |
| Not reported | 4 (2) | 0 | 0 | 4 (2) |
| Number evaluable | 193 | 14 | 19 | 226 |
| Median | 2 | 3 | 2 | 2 |
| Range | (0-8) | (0-6) | (0-5) | (0-8) |
| Mean | 2.2 | 2.8 | 2.2 | 2.2 |
| Standard deviation | 1.7 | 1.9 | 1.4 | 1.7 |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Aspartate transaminase (AST), prior to transplant, no. (%), units/L | | | | |
| N/A, CIBMTR Form 2000 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Normal | 143 (68) | 9 (60) | 13 (65) | 165 (68) |
| Abnormal | 65 (31) | 6 (40) | 6 (30) | 77 (32) |
| Not reported | 0 | 0 | 1 (5) | 1 (0) |
| Number evaluable | 208 | 15 | 19 | 242 |
| Median | 0.8 | 0.9 | 0.8 | 0.8 |
| Range | (0.3-3.6) | (0.4-1.6) | (0.4-3.3) | (0.3-3.6) |
| Mean | 0.9 | 0.9 | 0.9 | 0.9 |
| Standard deviation | 0.5 | 0.4 | 0.6 | 0.5 |
| Total serum bilirubin, prior to transplant, mg/dL, no. (%) | | | | |
| N/A, CIBMTR Form 2000 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Normal | 191 (91) | 14 (93) | 17 (85) | 222 (91) |
| Abnormal | 16 (8) | 1 (7) | 2 (10) | 19 (8) |
| Not reported | 1 (0) | 0 | 1 (5) | 2 (1) |
| Number evaluable | 207 | 15 | 19 | 241 |
| Median | 0.4 | 0.5 | 0.5 | 0.4 |
| Range | (0.2-1.8) | (0-1.4) | (0.2-4.4) | (0-4.4) |
| Mean | 0.5 | 0.5 | 0.8 | 0.5 |
| Standard deviation | 0.3 | 0.3 | 1.2 | 0.5 |
| Platelets, $\times 10^9$/L, prior to transplant, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Not reported | 7 (3) | 1 (7) | 1 (5) | 9 (4) |
| Number evaluable | 201 | 14 | 19 | 234 |
| Median | 127 | 89.5 | 116 | 122.5 |
| Range | (11-414) | (25-303) | (11-283) | (11-414) |
| Mean | 131.8 | 109.4 | 125.4 | 130 |
| Standard deviation | 70.6 | 75.4 | 71.5 | 70.8 |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Neutrophils, prior to transplant, × $10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received nor Form 2402 revision 6 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Not reported | 4 (2) | 0 | 1 (5) | 5 (2) |
| Number evaluable | 204 | 15 | 19 | 238 |
| Median | 57 | 57 | 59 | 57 |
| Range | (4-95) | (31-100) | (7-84) | (4-100) |
| Mean | 55.2 | 60.3 | 53.7 | 55.4 |
| Standard deviation | 16.7 | 17 | 21.4 | 17.1 |
| Hemoglobin, prior to transplant, g/dL, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received nor Form 2402 revision 6 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Number evaluable | 207 | 15 | 20 | 242 |
| Median | 12.2 | 12 | 12.5 | 12.2 |
| Range | (6.4-17.7) | (8.2-15.3) | (7.3-16.8) | (6.4-17.7) |
| Mean | 12.1 | 12.1 | 12.5 | 12.1 |
| Standard deviation | 2.1 | 1.8 | 2.3 | 2.1 |
| White blood cells at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| Not reported | 22 (11) | 0 | 5 (25) | 27 (11) |
| Number evaluable | 183 | 15 | 14 | 212 |
| Median | 12.9 | 22.2 | 15.4 | 13.8 |
| Range | (0.5-468.5) | (0.7-80.3) | (1.1-148.6) | (0.5-468.5) |
| Mean | 57.2 | 24.1 | 33.2 | 53.3 |
| Standard deviation | 89.6 | 21.2 | 44.9 | 84.8 |
| Blasts in blood, at diagnosis of B-cell ALL, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| < 1% | 17 (8) | 1 (7) | 1 (5) | 19 (8) |
| ≥ 1% | 155 (74) | 14 (93) | 10 (50) | 179 (73) |
| Not reported | 33 (16) | 0 | 8 (40) | 41 (17) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Number evaluable | 172 | 15 | 11 | 198 |
| Median | 59.5 | 70 | 67 | 63 |
| Range | (0-99) | (0-96) | (0-92) | (0-99) |
| Mean | 51.5 | 64.5 | 55.7 | 52.7 |
| Standard deviation | 34.1 | 30.3 | 32.2 | 33.8 |
| Blasts in bone marrow, at diagnosis of ALL, no. (%) | | | | |
| N/A, CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| < 50% | 16 (8) | 2 (13) | 1 (5) | 19 (8) |
| 50-89%% | 75 (36) | 7 (47) | 6 (30) | 88 (36) |
| ≥ 90% | 82 (39) | 5 (33) | 5 (25) | 92 (38) |
| Not reported | 32 (15) | 1 (7) | 7 (35) | 40 (16) |
| Number evaluable | 173 | 14 | 12 | 199 |
| Median | 89 | 84 | 81.5 | 88 |
| Range | (5-100) | (7-97) | (2-95) | (2-100) |
| Mean | 80.5 | 75.4 | 76.5 | 79.9 |
| Standard deviation | 20.6 | 26.6 | 25.1 | 21.3 |
| White blood cells, at last evaluation prior to transplant, $\times 10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2011 or Form 2000 revision 6 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Number evaluable | 208 | 15 | 20 | 243 |
| Median | 3.7 | 3.7 | 4 | 3.7 |
| Range | (0.4-37) | (0-5.8) | (0.3-8.4) | (0-37) |
| Mean | 4.2 | 3.4 | 4.1 | 4.1 |
| Standard deviation | 3.3 | 1.5 | 2.5 | 3.2 |
| Blasts in blood prior to transplant, no. (%) | | | | |
| N/A, CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| < 1% | 163 (78) | 12 (80) | 14 (70) | 189 (77) |
| ≥ 1% | 7 (3) | 0 | 0 | 7 (3) |
| Not reported | 35 (17) | 3 (20) | 5 (25) | 43 (18) |
| Number evaluable | 170 | 12 | 14 | 196 |
| Median | 0 | 0 | 0 | 0 |
| Range | (0-3) | (0-0) | (0-0) | (0-3) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Mean | 0.06 | 0 | 0 | 0.06 |
| Standard deviation | 0.35 | 0 | 0 | 0.32 |
| Blasts in bone marrow, prior to transplant, no. (%) | | | | |
| N/A, CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| < 5% | 184 (88) | 12 (80) | 16 (80) | 212 (87) |
| ≥ 5% | 1 (0) | 2 (13) | 0 | 3 (1) |
| Not reported | 20 (10) | 1 (7) | 3 (15) | 24 (10) |
| Number evaluable | 185 | 14 | 16 | 215 |
| Median | 1 | 1 | 1 | 1 |
| Range | (0-7) | (0-5) | (0-3) | (0-7) |
| Mean | 1.31 | 1.36 | 1.38 | 1.32 |
| Standard deviation | 1.3 | 1.74 | 1.02 | 1.31 |
| Extramedullary disease, at diagnosis of B-cell ALL, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| Yes | 27 (13) | 3 (20) | 3 (15) | 33 (14) |
| No | 161 (77) | 11 (73) | 11 (55) | 183 (75) |
| Unknown | 12 (6) | 1 (7) | 2 (10) | 15 (6) |
| Not reported | 5 (2) | 0 | 3 (15) | 8 (3) |
| Extramedullary disease, at last evaluation prior to transplant, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (2) | 0 | 1 (5) | 5 (2) |
| Yes | 6 (3) | 0 | 0 | 6 (2) |
| No | 195 (93) | 15 | 18 (90) | 228 (93) |
| Unknown | 3 (1) | 0 | 1 (5) | 4 (2) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Performance score prior to transplant, no. (%) | | | | |
| Karnofsky score 90-100 | 115 (55) | 5 (33) | 10 (50) | 130 (53) |
| Karnofsky score 10-80 | 84 (40) | 10 (67) | 7 (35) | 101 (41) |
| Karnofsky score Not reported | 10 (5) | 0 | 3 (15) | 13 (5) |
| History of proven invasive fungal infection, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (0) | 0 | 0 | 1 (0) |
| Yes | 7 (3) | 0 | 2 (10) | 9 (4) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| No | 201 (96) | 15 | 17 (85) | 233 (95) |
| Not reported | 0 | 0 | 1 (5) | 1 (0) |
| Disease status prior to transplant, no. (%) | | | | |
| 1st complete remission | 79 (38) | 6 (40) | 2 (10) | 87 (36) |
| 2nd complete remission | 94 (45) | 8 (53) | 12 (60) | 114 (47) |
| ≥ 3rd complete remission | 20 (10) | 0 | 6 (30) | 26 (11) |
| 1st relapse | 9 (4) | 1 (7) | 0 | 10 (4) |
| ≥ 3rd relapse | 3 (1) | 0 | 0 | 3 (1) |
| Primary induction failure | 3 (1) | 0 | 0 | 3 (1) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Prior autologous HCT, no. (%) | | | | |
| Yes | 7 (3) | 0 | 0 | 7 (3) |
| No | 202 (97) | 15 | 20 | 237 (97) |
| Time from diagnosis to HSCT, months, no. (%) | | | | |
| < 3 | 0 | 0 | 0 | 0 |
| 3-5 | 31 (15) | 3 (20) | 2 (10) | 36 (15) |
| 6-11 | 66 (32) | 5 (33) | 1 (5) | 72 (30) |
| ≥ 12 | 73 (35) | 5 (33) | 12 (60) | 90 (37) |
| Outliers [h] | 38 (18) | 2 (13) | 5 (25) | 45 (18) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Number evaluable | 170 | 13 | 15 | 198 |
| Median | 10.2 | 9.56 | 26.05 | 10.73 |
| Range | (3.35-47.64) | (3.52-42.38) | (3.48-42.68) | (3.35-47.64) |
| Mean | 15.53 | 13.96 | 24.25 | 16.09 |
| Standard deviation | 11.65 | 11.35 | 12.05 | 11.84 |
| Time from diagnosis to first dose of inotuzumab ozogamicin, months, no. (%) | | | | |
| < 3 | 50 (24) | 2 (13) | 2 (10) | 54 (22) |
| 3-5 | 25 (12) | 4 (27) | 0 | 29 (12) |
| 6-11 | 31 (15) | 2 (13) | 1 (5) | 34 (14) |
| ≥ 12 | 59 (28) | 4 (27) | 12 (60) | 75 (31) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Outliers [h] | 30 (14) | 1 (7) | 3 (15) | 34 (14) |
| Not reported | 14 (7) | 2 (13) | 2 (10) | 18 (7) |
| Number evaluable | 165 | 12 | 15 | 192 |
| Median | 7.2 | 6.24 | 23.03 | 7.43 |
| Range | (0.1-44.35) | (0.16-39.59) | (2.04-40.61) | (0.1-44.35) |
| Mean | 11.64 | 11.31 | 21.41 | 12.38 |
| Standard deviation | 11.84 | 11.89 | 12 | 12.08 |
| GVHD prophylaxis, no. (%) | | | | |
| Ex-vivo T-cell depletion | 3 (1) | 0 | 0 | 3 (1) |
| CD34 selection | 1 (0) | 0 | 0 | 1 (0) |
| Cyclophosphamide ± others | 82 (39) | 4 (27) | 11 (55) | 97 (40) |
| Tac + MMF ± others (not Cy) | 25 (12) | 4 (27) | 0 | 29 (12) |
| Tac + MTX ± others (not Cy, MMF) | 76 (36) | 6 (40) | 6 (30) | 88 (36) |
| Tac ± others (not Cy, MMF, MTX) | 7 (3) | 0 | 0 | 7 (3) |
| CsA + MMF ± others (not Cy, Tac) | 5 (2) | 0 | 1 (5) | 6 (2) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 9 (4) | 1 (7) | 2 (10) | 12 (5) |
| Others (not Cy, Tac, CsA) | 1 (0) | 0 | 0 | 1 (0) |
| Conditioning regimen intensity, no. (%) [i] | | | | |
| N/A; CIBMTR Form 2000 not completed | 1 (0) | 0 | 0 | 1 (0) |
| Myeloablative | 102 (49) | 12 (80) | 13 (65) | 127 (52) |
| RIC/NMA | 101 (48) | 3 (20) | 7 (35) | 111 (45) |
| Not reported | 5 (2) | 0 | 0 | 5 (2) |
| Unknown [j] | 0 | 0 | 0 | 0 |
| Dual alkylators used in conditioning regimen, no. (%) [k] | | | | |
| Yes | 11 (5) | 2 (13) | 5 (25) | 18 (7) |
| No | 197 (94) | 13 (87) | 15 (75) | 225 (92) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Busulfan used in conditioning regimen, no. (%) | | | | |
| Yes | 24 (11) | 2 (13) | 3 (15) | 29 (12) |
| No | 184 (88) | 13 (87) | 17 (85) | 214 (88) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |
| Thiotepa used in conditioning regimen, no. (%) | | | | |
| Yes | 13 (6) | 2 (13) | 5 (25) | 20 (8) |
| No | 195 (93) | 13 (87) | 15 (75) | 223 (91) |
| Not reported | 1 (0) | 0 | 0 | 1 (0) |
| Product type, no. (%) | | | | |
| Bone marrow | 35 (17) | 4 (27) | 8 (40) | 47 (19) |
| Peripheral blood stem cells | 158 (75) | 10 (67) | 12 (60) | 180 (73) |
| Umbilical cord blood | 16 (8) | 1 (7) | 0 | 17 (7) |
| Donor type, no. (%) | | | | |
| HLA-identical sibling | 56 (27) | 3 (20) | 5 (25) | 64 (26) |
| Other related | 52 (25) | 3 (20) | 9 (45) | 64 (26) |
| Unrelated | 101 (48) | 9 (60) | 6 (30) | 116 (48) |
| Follow-up, median (range), months | 23.98 (2.43-48.26) | 23.95 (6.34-50.79) | 18.69 (3.29-29.31) | 23.95 (2.43-50.79) |

Note: Median and range values are calculated using only patients with complete data for that variable. For CIBMTR forms, see Appendix 3: CIBMTR Data Collection Forms.

[a] Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. Blood 2004; 104:961-8.

[b] History of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment

[c] History of coronary artery disease (one or more vessel-coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, OR ejection fraction $\leqslant$ 50% on the most recent test

[d] History of transient ischemic attack, subarachnoid hemorrhage or cerebrovascular accident

[e] Liver cirrhosis, bilirubin > 1.5 × upper limit of normal, or AST/ALT > 2.5 × upper limit of normal

[f] Chronic hepatitis, bilirubin > upper limit of normal to 1.5 × upper limit of normal, or AST/ALT > upper limit of normal to 2.5 × upper limit of normal at the time of transplant OR any history of hepatitis B or hepatitis C infection

[g] The lines of therapy prior to a specified event are defined as follows. “No treatment given” means no lines of therapy given prior to specified event; “First line” means 1 line of therapy; “Salvage 1” means 2 lines of therapy; “Salvage 2” means 3 lines of therapy; “Salvage > 2” means 4 (or more) lines of therapy.

[h] Outliers are defined as patients who underwent HSCT in CR1 more than 12 months after disease diagnosis, or patients who underwent HSCT for all other disease statuses more than 48 months after disease diagnosis.

[i] Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009;15:1628-33.

[j] CIBMTR staff are querying the transplant center

**Table 22. Characteristics of adult patients who received inotuzumab ozogamicin prior to first alloHSCT for B-cell ALL and have complete follow-up data, by severity of VOD**

| Characteristic | N/A, no VOD | Mild | Severe | Total |
|---|---|---|---|---|
| **Number of patients** | **209** | **15** | **20** | **244** |

[k] Dual alkylators were defined as the conditioning regimen including one of the following pairs of treatments: busulfan + cyclophosphamide; busulfan + melphalan; cyclophosphamide + melphalan; busulfan + thiotepa; or cyclophosphamide + thiotepa.

Table 23 shows a summary of VOD/SOS in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

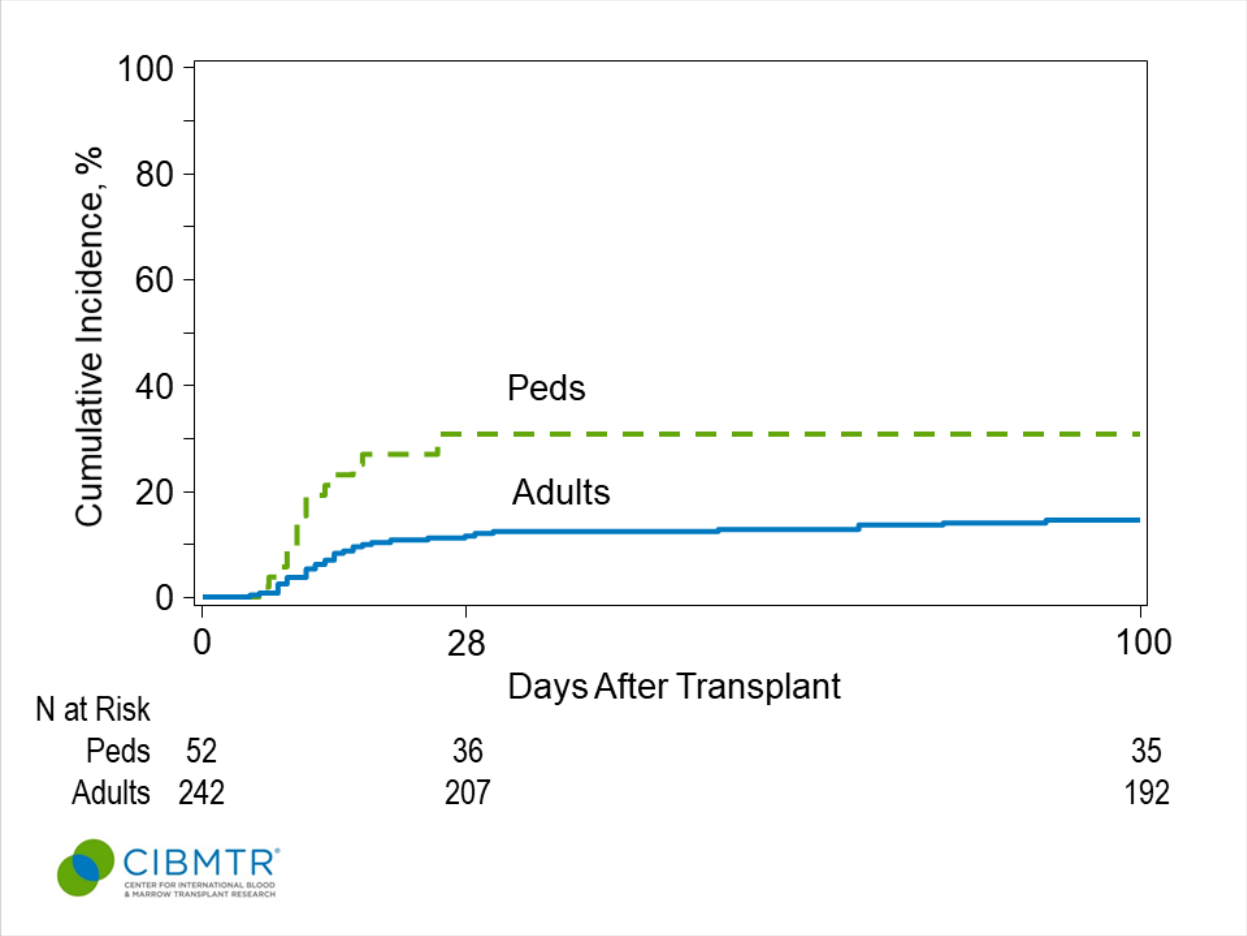
**Table 23. Veno-occlusive disease within 100 days**

| | **Pediatric patients (< 18 y)** | **Adults (≥ 18 y)** | **All patients** |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **52** | **244** | **296** |
| Veno-occlusive disease | | | |
| 100 days (95% CI) | 31 (19-44)% | 14 (10-19)% | 17 (13-22)% |
| No. patients with veno-occlusive disease | 16 | 35 | 51 |
| No. patients with competing risk (death without VOD) | 1 | 14 | 15 |
| Time from transplant to veno-occlusive disease, no. (%), months | | | |
| < 3 | 16 | 35 | 51 |
| Median (95% CI) | 0.34 (0.3 - 0.53) | 0.46 (0.36 - 0.56) | 0.42 (0.36-0.49) |
| Range | (0.2-0.82) | (0.16-2.96) | (0.16-2.96) |
| Mean | 0.41 | 0.74 | 0.63 |
| Standard deviation | 0.19 | 0.73 | 0.63 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table.
VOD is the occurrence of veno-occlusive disease/sinusoidal obstruction syndrome reported on the CIBMTR Form 2100. VOD is only considered within the first 100 days post-HSCT. Death without VOD is the competing risk.

Figure 7 shows cumulative incidence of veno-occlusive disease within 100 days in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Figure 7 Veno-occlusive disease within 100 days**




Note: Table 23 included 296 adults, but 2 patients did not have the applicable post-transplant data VOD data reported, so they were excluded from Figure 7.

**Table 24. VOD by lines of therapy prior to transplant, for adult and pediatric patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Post-HSCT VOD | First line | Salvage 1 | Salvage 2 | Salvage > 2 | Total |
|---|---|---|---|---|---|
| Yes | 1 (11) | 7 (11) | 12 (20) | 25 (18) | 45 (16) |
| No | 8 (89) | 54 (87) | 49 (80) | 114 (81) | 225 (83) |
| Not reported | 0 | 1 (2) | 0 | 1 (1) | 2 (1) |

**Table 25. VOD by lines of therapy prior to transplant, for adult patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Post-HSCT VOD | First line | Salvage 1 | Salvage 2 | Salvage > 2 | Total |
|---|---|---|---|---|---|
| Yes | 7 (88) | 50 (93) | 46 (81) | 92 (83) | 195 (85) |
| No | 1 (13) | 3 (6) | 11 (19) | 18 (16) | 33 (14) |
| Not reported | 0 | 1 (2) | 0 (0) | 1 (1) | 2 (1) |

Note: Among adults, 35 patients had VOD. Lines of therapy information is available for 33 only.

**Table 26. VOD by number of inotuzumab cycles, for adult and pediatric patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | 1 Cycle | | 2 Cycles | | ≥ 3 Cycles | |
|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 105 | | 136 | | 52 | |
| 100-day | | 21 (14-29)% | | 13 (8-19)% | | 21 (11-33)% |

**Table 27. VOD by number of inotuzumab cycles, for only adult patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | 1 Cycle | | 2 Cycles | | ≥ 3 Cycles | |
|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 78 | | 114 | | 49 | |
| 100-day | | 17 (9-26)% | | 11 (6-18)% | | 18 (9-30)% |

**Table 28. VOD by cumulative inotuzumab dose, for patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | Dose of inotuzumab ozogamicin | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | < 1.8 mg/m² | | 1.8-2.7 mg/m² | | 2.8-3.2 mg/m² | | ≥ 3.3 mg/m² | |
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 70 | | 87 | | 29 | | 85 | |
| 100-day | | 20 (11-30)% | | 17 (10-26)% | | 10 (2-24)% | | 16 (9-25)% |

**Table 29. VOD by cumulative inotuzumab dose, for patients with B-cell ALL who received inotuzumab as single agent prior to first alloHSCT**

| | Dose of inotuzumab ozogamicin | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | < 1.8 mg/m² | | 1.8-2.7 mg/m² | | 2.8-3.2 mg/m² | | ≥ 3.3 mg/m² | |
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 16 | | 41 | | 14 | | 56 | |
| 100-day | | NE | | 22 (11-36)% | | NE | | 16 (8-27)% |

Note: Outcomes are not evaluable (NE) if sample size is < 20.

**Table 30. VOD by cumulative inotuzumab dose, for patients with B-cell ALL who received inotuzumab with other agents prior to first alloHSCT**

| | Dose of inotuzumab ozogamicin | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | < 1.8 mg/m² | | 1.8-2.7 mg/m² | | 2.8-3.2 mg/m² | | ≥ 3.3 mg/m² | |
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 51 | | 33 | | 12 | | 24 | |
| 100-day | | 18 (8-29)% | | 9 (2-21)% | | NE | | NE |

Note: Outcomes are not evaluable (NE) if sample size is < 20.

**Table 31. VOD by lines of therapy prior to inotuzumab for patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Post-HSCT VOD | First line | Salvage 1 | Salvage 2 | Salvage > 2 | Total |
|---|---|---|---|---|---|
| Yes | 10 (13) | 9 (19) | 9 (18) | 13 (21) | 41 (17) |
| No | 66 (86) | 39 (80) | 42 (82) | 49 (79) | 196 (82) |
| Not reported | 0 | 1 (1) | 0 | 0 | 1 (1) |

**Table 32. VOD rates by remission type for patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | CR1 (N = 96) | | CR2 (N = 135) | | Advanced (N = 64) | |
|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 96 | | 133 | | 64 | |
| 100-day | | 11 (6-19)% | | 20 (14-28)% | | 20 (11-31)% |

**Table 33. VOD grade by disease stage at inotuzumab administration for patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Post-HSCT VOD | First line | Salvage 1 | Salvage 2 | Salvage > 2 | Total |
|---|---|---|---|---|---|
| Mild | 4 (5) | 3 (6) | 3 (6) | 6 (10) | 16 (7) |
| Severe | 6 (8) | 6 (13) | 6 (12) | 7 (11) | 25 (10) |
| N/A, no VOD | 66 (87) | 40 (81) | 42 (82) | 49 (79) | 197 (83) |

**Table 34. VOD rates by time from last inotuzumab dose to first alloHSCT, months for patients with B-cell ALL**

| | <1 Months (N = 26) | | 1-1.6 Months (N = 78) | | 1.7-3 Months (N = 78) | | >3 Months (N = 103) | |
|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 26 | | 77 | | 77 | | 103 | |
| 100-day | | 15 (4-32)% | | 25 (16-35)% | | 17 (9-26)% | | 14 (8-21)% |

**Table 35. VOD rates by study year for patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| | Aug 2017-Aug 2018 | | Aug 2018-Aug 2019 | | Aug 2019-Aug 2020 | | Aug 2020-Aug 2021 | | Aug 2021-Aug 2022 | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 53 | | 77 | | 62 | | 60 | | 42 | |
| 100-day | | 15 (7-26)% | | 21 (12-31)% | | 15 (7-24)% | | 17 (8-27)% | | 19 (9-32)% |

### 10.3.10. VOD with and without defibrotide prophylaxis

Table 36 shows a summary of VOD characteristics up to 100 days post-transplant, with and without defibrotide used as liver toxicity prophylaxis in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Table 36. VOD characteristics up to 100 days post-transplant, with and without defibrotide used as liver toxicity prophylaxis**

| | Pediatric patients (< 18 years) No. (%) | | Adult patients (≥ 18 years) No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | **Defibrotide** | **No defibrotide** | **Defibrotide** | **No defibrotide** | **Defibrotide** | **No defibrotide** |
| **Number of patients with post-transplant follow-up** | **23** | **29** | **22** | **222** | **45** | **251** |
| **Number of patients with post-transplant VOD/SOS** | **7** | **9** | **8** | **27** | **15** | **36** |
| Time to post-transplant VOD/SOS, days | | | | | | |
| Median | 10 | 13 | 23 | 13 | 11 | 13 |
| Range | (8-17) | (6-25) | (6-90) | (5-79) | (6-90) | (5-79) |
| Mean | 11 | 14 | 32 | 19 | 22 | 18 |
| Standard deviation | 3 | 7 | 31 | 18 | 25 | 16 |
| Grade of VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 16 (70) | 20 (69) | 14 (64) | 195 (88) | 30 (67) | 215 (86) |
| Mild VOD/SOS (no other organs involved within 60 days of VOD/SOS diagnosis) | 5 (22) | 3 (10) | 4 (18) | 11 (5) | 9 (20) | 14 (6) |
| Severe VOD/SOS (multiple organ dysfunction within 60 days of VOD/SOS diagnosis) | 2 (9) | 6 (21) | 4 (18) | 16 (7) | 6 (13) | 22 (9) |
| Liver toxicity prophylaxis | | | | | | |
| None (or no additional) | 0 | 6 (21) | 0 | 14 (6) | 0 | 20 (8) |
| Ursodiol | 0 | 19 (66) | 0 | 198 (89) | 0 | 217 (86) |
| Ursodiol + defibrotide | 11 (48) | 0 | 15 (68) | 0 | 26 (58) | 0 |
| Ursodiol + defibrotide + others | 11 (48) | 0 | 5 (23) | 0 | 16 (36) | 0 |
| Ursodiol + others | 0 | 3 (10) | 0 | 6 (3) | 0 | 9 (4) |
| Defibrotide | 1 (4) | 0 | 2 (9) | 0 | 3 (7) | 0 |
| Not reported | 0 | 1 (3) | 0 | 4 (2) | 0 | 5 (2) |

**Table 36. VOD characteristics up to 100 days post-transplant, with and without defibrotide used as liver toxicity prophylaxis**

| | Pediatric patients (< 18 years) No. (%) | | Adult patients (≥ 18 years) No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | **Defibrotide** | **No defibrotide** | **Defibrotide** | **No defibrotide** | **Defibrotide** | **No defibrotide** |
| **Number of patients with post-transplant follow-up** | **23** | **29** | **22** | **222** | **45** | **251** |
| Treatment for VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 16 (70) | 20 (69) | 14 (64) | 195 (88) | 30 (67) | 215 (86) |
| None | 0 | 0 | 2 (9) | 2 (1) | 2 (4) | 2 (1) |
| Defibrotide | 0 | 1 (3) | 1 (5) | 2 (1) | 1 (2) | 3 (1) |
| Defibrotide + ursodiol | 1 (4) | 0 | 0 | 0 | 1 (2) | 0 |
| Defibrotide + ursodiol + diuretics | 1 (4) | 2 (7) | 0 | 5 (2) | 1 (2) | 7 (3) |
| Diuretics | 0 | 0 | 0 | 1 (<1) | 0 | 1 (<1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics + heparin | 1 (4) | 1 (3) | 0 | 2 (1) | 1 (2) | 3 (1) |
| Defibrotide + ursodiol + methylprednisolone + N-acetylcysteine + rifaximin/lactulose | 0 | 0 | 0 | 1 (<1) | 0 | 1 (<1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics | 0 | 0 | 0 | 1 (<1) | 0 | 1 (<1) |
| Defibrotide + diuretics | 0 | 0 | 0 | 1 (<1) | 0 | 1 (<1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics + N-acetylcysteine + tissue plasminogen activator | 0 | 0 | 0 | 1 (<1) | 0 | 1 (<1) |
| Not reported | 4 (17) | 5 (17) | 5 (23) | 11 (5) | 9 (20) | 16 (6) |
| Post-VOD/SOS survival | | | | | | |
| N/A; no VOD/SOS | 16 (70) | 20 (69) | 14 (64) | 195 (88) | 30 (67) | 215 (86) |
| Alive | 4 (17) | 5 (17) | 3 (14) | 10 (5) | 7 (16) | 15 (6) |
| Dead | 3 (13) | 4 (14) | 5 (23) | 17 (8) | 8 (18) | 21 (8) |

**Table 37. Descriptive characteristics of pediatric patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Characteristic | Defibrotide | No defibrotide | Total |
|---|---|---|---|
| **Number of patients** | **23** | **29** | **52** |
| No. of centers | 11 | 14 | 19 |
| Age, years, no. (%) | | | |
| < 1 | 0 | 1 (3) | 1 (2) |
| 1-9 | 11 (48) | 15 (52) | 26 (50) |
| 10-17 | 12 (52) | 13 (45) | 25 (48) |
| Number evaluable | 23 | 29 | 52 |
| Median | 10 | 9 | 9 |
| Range | (1-17) | (0-17) | (0-17) |
| Mean | 10 | 9 | 9.4 |
| Standard deviation | 5.7 | 4.9 | 5.2 |
| Race, no. (%) | | | |
| White | 22 (96) | 20 (69) | 42 (81) |
| Asian or Native Hawaiian and other Pacific Islander | 0 | 2 (7) | 2 (4) |
| Others | 0 | 2 (7) | 2 (4) |
| Not reported | 1 (4) | 5 (17) | 6 (12) |
| Sex, no. (%) | | | |
| Male | 11 (48) | 17 (59) | 28 (54) |
| Female | 12 (52) | 12 (41) | 24 (46) |
| Sorror HCT-CI, no. (%) | | | |
| 0 | 9 (39) | 12 (41) | 21 (40) |
| 1-2 | 10 (43) | 9 (31) | 19 (37) |
| 3-4 | 3 (13) | 8 (28) | 11 (21) |
| 5 | 1 (4) | 0 | 1 (2) |
| Hepatic disease, no. (%) | | | |
| Severe | 2 (9) | 4 (14) | 6 (12) |
| Mild | 6 (26) | 6 (21) | 12 (23) |
| No hepatic disease | 15 (65) | 19 (66) | 34 (65) |
| Total serum bilirubin, prior to transplant, no. (%), units/L | | | |
| Normal | 22 (96) | 28 (97) | 50 (96) |
| Abnormal | 1 (4) | 1 (3) | 2 (4) |
| Number evaluable | 23 | 29 | 52 |
| Median | 0.3 | 0.3 | 0.3 |
| Range | (0-1) | (0-1.1) | (0-1.1) |
| Mean | 0.3 | 0.4 | 0.4 |
| Standard deviation | 0.2 | 0.3 | 0.3 |
| Performance score prior to transplant, no. (%) | | | |
| Karnofsky score | | | |
| 90-100 | 5 (22) | 2 (7) | 7 (13) |
| 10-80 | 1 (4) | 0 | 1 (2) |
| Lansky | | | |
| 90-100 | 15 (65) | 23 (79) | 38 (73) |
| 10-80 | 2 (9) | 4 (14) | 6 (12) |
| Disease status prior to transplant, no. (%) | | | |
| CR1 | 4 (17) | 5 (17) | 9 (17) |
| CR2 | 14 (61) | 7 (24) | 21 (40) |
| CR3+ | 5 (22) | 17 (59) | 22 (42) |

**Table 37. Descriptive characteristics of pediatric patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Characteristic | Defibrotide | No defibrotide | Total |
|---|---|---|---|
| **Number of patients** | **23** | **29** | **52** |
| Prior autologous HCT, no. (%) | | | |
| No | 23 | 29 | 52 |
| GVHD prophylaxis, no. (%) | | | |
| Ex-vivo T-cell depletion | 1 (4) | 8 (28) | 9 (17) |
| Cyclophosphamide ± others | 7 (30) | 6 (21) | 13 (25) |
| Tac + MMF ± others (not Cy) | 1 (4) | 2 (7) | 3 (6) |
| Tac + MTX ± others (not Cy, MMF) | 1 (4) | 4 (14) | 5 (10) |
| Tac ± others (not Cy, MMF, MTX) | 1 (4) | 0 | 1 (2) |
| CsA + MMF ± others (not Cy, Tac) | 4 (17) | 3 (10) | 7 (13) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 7 (30) | 4 (14) | 11 (21) |
| CsA ± others (not Cy, Tac, MMF, MTX) | 0 | 1 (3) | 1 (2) |
| Not reported | 1 (4) | 1 (3) | 2 (4) |
| Conditioning regimen intensity, no. (%) | | | |
| Myeloablative | 22 (96) | 28 (97) | 50 (96) |
| RIC/NMA | 1 (4) | 1 (3) | 2 (4) |
| Dual alkylators used in conditioning regimen, no. (%) | | | |
| Yes | 5 (22) | 10 (34) | 15 (29) |
| No | 18 (78) | 19 (66) | 37 (71) |
| Product type, no. (%) | | | |
| BM | 16 (70) | 13 (45) | 29 (56) |
| PBSC | 3 (13) | 11 (38) | 14 (27) |
| UCB | 4 (17) | 5 (17) | 9 (17) |
| Donor type, no. (%) | | | |
| HLA-identical sibling | 4 (17) | 8 (28) | 12 (23) |
| Other related | 5 (22) | 9 (31) | 14 (27) |
| Unrelated | 14 (61) | 12 (41) | 26 (50) |

**Table 38. Descriptive characteristics of adult patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Characteristic | Defibrotide | No defibrotide | Total |
|---|---|---|---|
| **Number of patients** | **22** | **222** | **244** |
| No. of centers | 15 | 48 | 52 |
| Age, years, no. (%) | | | |
| 18-29 | 12 (55) | 68 (31) | 80 (33) |
| 30-39 | 3 (14) | 42 (19) | 45 (18) |
| 40-49 | 4 (18) | 43 (19) | 47 (19) |
| 50-59 | 2 (9) | 28 (13) | 30 (12) |
| 60+ | 1 (5) | 41 (18) | 42 (17) |
| Median | 25.5 | 40 | 39 |
| Range | (18-73) | (18-75) | (18-75) |
| Mean | 33 | 41.7 | 40.9 |
| Standard deviation | 14.4 | 16 | 16 |
| Race, no. (%) | | | |
| White | 17 (77) | 175 (79) | 192 (79) |
| Black or African American | 0 | 16 (7) | 16 (7) |
| Asian or Native Hawaiian and other Pacific Islander | 2 (9) | 11 (5) | 13 (5) |
| Others | 1 (5) | 2 (1) | 3 (1) |
| Not reported | 2 (9) | 18 (8) | 20 (8) |
| Sex, no. (%) | | | |
| Male | 10 (45) | 131 (59) | 141 (58) |
| Female | 12 (55) | 91 (41) | 103 (42) |
| Sorror HCT-CI, no. (%) | | | |
| 0 | 5 (23) | 30 (14) | 35 (14) |
| 1-2 | 8 (36) | 79 (36) | 87 (36) |
| 3-4 | 8 (36) | 75 (34) | 83 (34) |
| 5 | 0 | 19 (9) | 19 (8) |
| 6 | 1 (5) | 7 (3) | 8 (3) |
| 7 | 0 | 6 (3) | 6 (2) |
| Not reported | 0 | 6 (3) | 6 (2) |
| Hepatic disease, no. (%) | | | |
| Severe | 1 (5) | 8 (4) | 9 (4) |
| Mild | 8 (36) | 50 (23) | 58 (24) |
| No hepatic disease | 13 (59) | 158 (71) | 171 (70) |
| Not reported | 0 | 6 (3) | 6 (2) |
| Total serum bilirubin, prior to transplant, mg/dL, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 0 | 1 (0) | 1 (0) |
| Normal | 21 (95) | 201 (91) | 222 (91) |
| Abnormal | 1 (5) | 18 (8) | 19 (8) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Number evaluable | 22 | 219 | 241 |
| Median | 0.5 | 0.4 | 0.4 |
| Range | (0.2-1.4) | (0-4.4) | (0-4.4) |
| Mean | 0.6 | 0.5 | 0.5 |
| Standard deviation | 0.3 | 0.5 | 0.5 |
| Karnofsky Performance score prior to transplant, no. (%) | | | |
| 90-100 | 16 (73) | 114 (51) | 130 (53) |
| 10-80 | 6 (27) | 95 (43) | 101 (41) |
| Not reported | 0 | 13 (6) | 13 (5) |

**Table 38. Descriptive characteristics of adult patients with B-cell ALL who received inotuzumab prior to first alloHSCT**

| Characteristic | Defibrotide | No defibrotide | Total |
|---|---|---|---|
| **Number of patients** | **22** | **222** | **244** |
| Disease status prior to transplant, no. (%) | | | |
| CR1 | 5 (23) | 82 (37) | 87 (36) |
| CR2 | 15 (68) | 99 (45) | 114 (47) |
| CR3+ | 2 (9) | 24 (11) | 26 (11) |
| REL1 | 0 | 10 (5) | 10 (4) |
| REL3+ | 0 | 3 (1) | 3 (1) |
| PIF | 0 | 3 (1) | 3 (1) |
| Not reported | 0 | 1 (0) | 1 (0) |
| Prior autologous HCT, no. (%) | | | |
| Yes | 0 | 7 (3) | 7 (3) |
| No | 22 | 215 (97) | 237 (97) |
| GVHD prophylaxis, no. (%) | | | |
| Ex-vivo T-cell depletion | 0 | 3 (1) | 3 (1) |
| CD34 selection | 1 (5) | 0 | 1 (0) |
| Cyclophosphamide ± others | 8 (36) | 89 (40) | 97 (40) |
| Tac + MMF ± others (not Cy) | 2 (9) | 27 (12) | 29 (12) |
| Tac + MTX ± others (not Cy, MMF) | 5 (23) | 83 (37) | 88 (36) |
| Tac ± others (not Cy, MMF, MTX) | 0 | 7 (3) | 7 (3) |
| CsA + MMF ± others (not Cy, Tac) | 1 (5) | 5 (2) | 6 (2) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 4 (18) | 8 (4) | 12 (5) |
| Others (not Cy, Tac, CsA) | 1 (5) | 0 | 1 (0) |
| Conditioning regimen intensity, no. (%) | | | |
| N/A, Form 2000 not completed | 0 | 1 (0) | 1 (0) |
| Myeloablative | 17 (77) | 110 (50) | 127 (52) |
| RIC/NMA | 5 (23) | 106 (48) | 111 (45) |
| Not reported | 0 | 5 (2) | 5 (2) |
| Dual alkylators used in conditioning regimen, no. (%) | | | |
| Yes | 3 (14) | 15 (7) | 18 (7) |
| No | 19 (86) | 206 (93) | 225 (92) |
| Not reported | 0 | 1 (0) | 1 (0) |
| Product type, no. (%) | | | |
| BM | 8 (36) | 39 (18) | 47 (19) |
| PBSC | 12 (55) | 167 (75) | 179 (73) |
| UCB | 2 (9) | 15 (7) | 17 (7) |
| Not reported | 0 | 1 (0) | 1 (0) |
| Donor type, no. (%) | | | |
| HLA-identical sibling | 7 (32) | 57 (26) | 64 (26) |
| Other related | 5 (23) | 59 (27) | 64 (26) |
| Unrelated | 10 (45) | 106 (48) | 116 (48) |

### 10.3.11. Post-HSCT clinical status

Table 39 shows a summary of post-HSCT clinical status following inotuzumab ozogamicin treatment in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for B-cell ALL.

**Table 39. Post-HSCT clinical status**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with follow-up** | **52** | **244** | **296** |
| Best response to HSCT | | | |
| Continued complete remission (CR)[a] | 51 (98) | 226 (93) | 277 (94) |
| CR | 0 | 11 (5) | 11 (4) |
| Not in CR | 1 (2) | 4 (2) | 5 (2) |
| Not reported | 0 | 3 (1) | 3 (1) |
| Granulopoiesis / neutrophil recovery[b] | | | |
| Yes | 51 (98) | 230 (94) | 281 (95) |
| No | 0 | 8 (3) | 8 (3) |
| Not reported | 1 (2) | 6 (2) | 7 (2) |
| Time from HSCT to granulopoiesis/neutrophil recovery, days | | | |
| Number evaluable | 51 | 230 | 281 |
| Median | 18 | 17 | 17 |
| Range | (5-31) | (9-52) | (5-52) |
| Mean | 19 | 18 | 18 |
| Standard deviation | 6 | 6 | 6 |
| Megakaryopoiesis / platelet recovery[c] | | | |
| Yes | 44 (85) | 200 (82) | 244 (82) |
| No | 7 (13) | 36 (15) | 43 (15) |
| Not reported | 1 (2) | 8 (3) | 9 (3) |
| Time from HSCT to megakaryopoiesis/platelet recovery, days | | | |
| Number evaluable | 44 | 200 | 244 |
| Median | 33 | 28 | 28 |
| Range | (13-89) | (12-97) | (12-97) |
| Mean | 36 | 31 | 32 |
| Standard deviation | 17 | 16 | 16 |
| Engraftment syndrome within 100 days post-transplant | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Yes | 11 (21) | 18 (7) | 29 (10) |
| No | 40 (77) | 223 (91) | 263 (89) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Time from HSCT to engraftment syndrome, days | | | |
| Number evaluable | 11 | 18 | 29 |
| Median | 12 | 14 | 13 |
| Range | (9-23) | (2-42) | (2-42) |
| Mean | 14 | 15 | 15 |
| Standard deviation | 5 | 8 | 7 |

## Table 39. Post-HSCT clinical status

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with follow-up** | **52** | **244** | **296** |
| Weight, most recent post-HSCT, kg | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Not reported | 0 | 4 (2) | 4 (1) |
| Number evaluable | 51 | 239 | 290 |
| Median | 40 | 79 | 75 |
| Range | (8-104) | (24-199) | (8-199) |
| Mean | 43 | 84 | 77 |
| Standard deviation | 22 | 25 | 29 |
| Height, most recent post-HSCT, cm | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Not reported | 16 (31) | 242 (99) | 258 (87) |
| Number evaluable | 35 | 1 | 36 |
| Median | 138 | 173 | 140 |
| Range | (87-173) | NE | (87-173) |
| Mean | 134 | 173 | 135 |
| Standard deviation | 25 | NE | 26 |
| Performance scale and status, post-HSCT | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| Karnofsky | | | |
| 90-100 | 1 (2) | 90 (37) | 91 (31) |
| 10-80 | 6 (12) | 84 (34) | 90 (30) |
| Not reported | 44 (85) | 69 (28) | 113 (38) |
| Total inpatient days in first 100 days post-HSCT [d] | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (<1) | 2 (1) |
| < 30 | 12 (23) | 119 (49) | 131 (44) |
| 30-59 | 26 (50) | 60 (25) | 86 (29) |
| 60-100 | 6 (12) | 31 (13) | 37 (13) |
| Not reported | 7 (13) | 33 (14) | 40 (14) |
| Number evaluable | 44 | 210 | 254 |
| Median | 38 | 26 | 29 |
| Range | (21-93) | (6-94) | (6-94) |
| Mean | 42 | 34 | 35 |
| Standard deviation | 17 | 21 | 20 |
| Time from HSCT to date of last contact, months | | | |
| < 3 | 7 (13) | 34 (14) | 41 (14) |
| 3-5 | 6 (12) | 43 (18) | 49 (17) |
| 6-11 | 15 (29) | 51 (21) | 66 (22) |
| ≥ 12 | 24 (46) | 116 (48) | 140 (47) |
| Number evaluable | 52 | 244 | 296 |
| Median | 10.43 | 10.63 | 10.63 |
| Range | (0.92-50.66) | (0.36-54.08) | (0.36-54.08) |
| Mean | 14.98 | 14.02 | 14.19 |
| Standard deviation | 12.55 | 11.88 | 11.98 |

Note: Outcomes are not evaluable (NE) if sample size is < 20.

**Table 39. Post-HSCT clinical status**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with follow-up** | **52** | **244** | **296** |

[a] Continued complete remission is defined as a patient who underwent transplant during complete remission, and the complete remission is sustained post-transplant. Complete remission is defined as all the following: < 5% blasts in bone marrow, no blasts with Auer rods, no extramedullary disease and no disease progression for at least 4 weeks.
[b] Absolute neutrophil count (ANC) > 500/$mm^3$ sustained for 3 lab values; evaluated ≤ 100 days post-transplant.
[c] Initial platelet count > 20 × $10^9$/L achieved; evaluated ≤ 100 days post-transplant.
[d] The form asks for the number of inpatient days in the first 100 days (day 0 to day 100) post-HSCT.

## 10.4. Main results

These results are provided in Sections 10.1, 10.2 and 10.3 above.

## 10.5. Other analyses

### 10.5.1. Outcome analysis

***Patients who underwent their first allogeneic HSCT for B-cell ALL***

Post-transplant follow-up information was available for 296/319 (93%) patients who underwent their first allogeneic HSCT for B-cell ALL. Of these 296 patients, post-transplant VOD/SOS occurred in 51 patients (17%; 35 adult, 16 pediatric). One hundred twelve (112) deaths occurred within the first 18 months post-transplant with TRM occurring in 56 patients within the first 18 months.

Twenty-nine (57%; 22 adult, 7 pediatric) of the 51 patients (35 adult, 16 pediatric) who developed post-transplant VOD/SOS died within 18 months post-transplant; 13 patients (45%) had a primary COD that was not VOD/SOS (n=5 recurrence of B-cell ALL, n=3 acute GVHD, n=3 organ failure, n=1 septic shock, n=1 infection).

Table 40 shows the incidence and mortality of VOD/SOS, as well as OS, TRM, and relapse, in adult patients without a prior HSCT.

**Table 40. Patients without a prior HSCT: Summary of VOD/SOS incidence, post-transplant VOD/SOS mortality, overall survival, transplant-related mortality and relapse, up to 18 months**

| | Day 100 incidence of VOD/SOS[a] | Post-transplant VOD/SOS mortality[b] | 6-mo OS[c] | 12-mo OS[c] | 18-mo OS | 6-mo TRM[d] | 12-mo TRM[d] | 18-mo TRM | 6-mo relapse[e] | 12-mo relapse[e] | 18-mo relapse[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| All adult patients n=261[f] | 14% | 36% | 75% | 61% | 54% | 17% | 20% | 22% | 23% | 33% | 40% |
| Adult R/R n= 166[g] | 18% | 40% | 70% | 56% | 50% | 20% | 23% | 25% | 23% | 34% | 40% |
| All pediatric patients n = 52[h] | 31% | 63% | 85% | 71% | NE | 8% | NE | NE | 24% | NE | NE |
| Pediatric R/R n = 43[i] | 30% | 54% | 81% | 68% | NE | 9% | NE | NE | 21% | NE | NE |

[a] VOD/SOS cumulative incidence estimate at 100 days following HSCT. Death without VOD/SOS was treated as a competing risk. Surviving patients without VOD/SOS were censored on the date of last follow-up, if applicable.

[b] Mortality cumulative incidence estimate at 18 months following post-transplant VOD/SOS. Caution must be exercised in assessing unadjusted mortality rates. There were n=35 adults who experienced post-transplant VOD/SOS and n=27 adults with R/R B-cell ALL who experienced post-transplant VOD/SOS.

[c] OS Kaplan-Meier estimate at 6 months, 12 months, and 18 months following HSCT. Surviving patients were censored on the date of last follow-up.

[d] TRM cumulative incidence estimate at 6 months, 12 months, and 18 months following HSCT. Post-HSCT relapse was treated as a competing risk. Surviving patients without post-HSCT relapse were censored on the date of last follow-up, if applicable.
[e] Relapse cumulative incidence estimate at 6 months, 12 months, and 18 months following HSCT. TRM was treated as a competing risk. Surviving patients without post-HSCT relapse were censored on the date of last follow-up, if applicable.
[f] Follow-up information available for 244 / 261 adult patients.
[g] Follow-up information available for 156 / 166 adult R/R patients.
[h] Follow-up information available for 52 / 58 pediatric patients.
[i] Follow-up information available for 43 / 48 pediatric R/R patients.

***Patients who underwent second, or greater HSCT for B-cell ALL***

As of the data lock date, post-HSCT follow-up information was available for all patients (43 adult, 9 pediatric). Table 41 below includes adult patients only, as sample size for pediatric population was too small for evaluation.

**Table 41. Adults with a prior HSCT: Summary of VOD/SOS incidence, post-transplant VOD/SOS mortality, overall survival, transplant-related mortality and relapse, up to 18 months**

| | Day 100 incidence VOD/SOS[a] | Post-HSCT VOD/SOS mortality[b] | 6-mo OS[c] | 12-mo OS[c] | 18-mo OS | 6-mo TRM[d] | 12-mo TRM[d] | 18-mo TRM | 6-mo relapse[e] | 12-mo relapse[e] | 18-mo relapse[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| All adult patients n=43 | 21% | 75% | 73% | NE | NE | 20% | 27% | NE | 5% | 8% | NE |
| Adult R/R n= 41 | 22% | 75% | 74% | NE | NE | 21% | 28% | NE | 3% | 3% | NE |

[a] VOD/SOS cumulative incidence estimate at 100 days following HSCT. Death without VOD/SOS was treated as a competing risk. Surviving patients without VOD/SOS were censored on the date of last follow-up, if applicable.
[b] Mortality cumulative incidence estimate at 18 months following post-transplant VOD/SOS. Caution must be exercised in assessing unadjusted mortality rates. There were n=35 adults who experienced post-transplant VOD/SOS and n=27 adults with R/R B-cell ALL who experienced post-transplant VOD/SOS.
[c] OS Kaplan-Meier estimate at 6 months, 12 months, and 18 months following HSCT. Surviving patients were censored on the date of last follow-up.
[d] TRM cumulative incidence estimate at 6 months, 12 months, and 18 months following HSCT. Post-HSCT relapse was treated as a competing risk. Surviving patients without post-HSCT relapse were censored on the date of last follow-up, if applicable.
[e] Relapse cumulative incidence estimate at 6 months, 12 months, and 18 months following HSCT. TRM was treated as a competing risk. Surviving patients without post-HSCT relapse were censored on the date of last follow-up, if applicable.

### 10.5.2. Subset analysis: adults who underwent first alloHSCT with sufficient follow-up

The following is a final subset analysis to provide a further evaluation of the outcomes of interest in a subset of the patients included in the broader study population. This subset population includes adults who underwent first allogeneic HSCT and who were either:

- Alive at the date of last contact and reported at least 1 year of follow-up, or
- Died at any time following their first allogeneic HSCT.

By selecting these patients who either experienced mortality or at least 1 year of follow-up, outcomes could be evaluated at 1-year post-HSCT.

The selection of this subset of patients to be evaluated in this final analysis are described in Table 42, while their baseline characteristics are described in Table 43. The correlation between number of inotuzumab ozogamicin cycles and disease status at transplant are described in Table 44. Each outcome of interest is evaluated in a univariate analysis and a multivariable analysis. The outcomes were OS (Table 45 and Table 46), transplant-related mortality (Table 47 and Table 48), and VOD/SOS (Table 49 and Table 50).

**Table 42. Disposition of adult patients who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Selection criteria | No. patients excluded | No. patients remaining in the study cohort |
|---|---|---|
| AlloHSCT for B-cell ALL in US during 18 Aug. 2017 – 17 Aug. 2022 | | 5891 |
| Patient consented for research | 577 | 5314 |
| Excluded patients from embargoed centers | 131 | 5183 |
| Excluded patients from centers not participating in study | 2669 | 2514 |
| Patient received inotuzumab ozogamicin prior to alloHSCT | 2143 | 371 |
| Patient underwent first allogeneic HSCT (patients who received inotuzumab ozogamicin prior to a subsequent alloHSCT) | 52 | 319 |
| Adult patient (≥ 18 years old at HSCT) | 58 | 261 |
| Exclude patients who were alive at date of last contact and have < 12 months of follow-up | 57 | 204 |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Characteristic | No. (%) |
|---|---|
| **No. of patients** | **204** |
| Age, no. (%) | |
| Median (range), years | 40 (18-75) |
| 18-29 | 67 (33) |
| 30-39 | 35 (17) |
| 40-49 | 41 (20) |
| 50-59 | 22 (11) |
| ≥ 60 | 39 (19) |
| Performance score prior to transplant, no. (%) | |
| 90-100 | 113 (55) |
| < 90 | 82 (40) |
| Not reported | 9 (4) |
| Sorror HCT-CI, no. (%) | |
| 0 | 28 (14) |
| 1 | 38 (19) |
| 2 | 29 (14) |
| 3 | 47 (23) |
| 4 | 31 (15) |
| 5 | 17 (8) |
| 6 | 5 (2) |
| 7 | 5 (2) |
| 8 | 1 (0) |
| 9 | 1 (0) |
| Not reported | 2 (1) |
| History of hepatitis B or C, no. (%) | |
| Yes | 8 (4) |
| No | 196 (96) |
| Liver disease/hepatitis B or C, no. (%) | |
| Yes | 59 (29) |
| No | 141 (69) |
| Not reported | 4 (2) |
| Line of therapy prior to HSCT, no. (%) | |
| First line | 7 (3) |
| Relapsed/refractory to therapy | 184 (90) |
| Outliers | 8 (4) |
| N/A, Form 2011 not received | 5 (2) |
| Lines of salvage therapy prior to inotuzumab ozogamicin, no. (%) | |
| No treatment given | 19 (9) |
| First line | 54 (26) |
| Salvage 1 | 38 (19) |
| Salvage ≥ 2 | 76 (37) |
| Outliers | 8 (4) |
| N/A: CIBMTR Form 2011 not yet received | 5 (2) |
| Not reported | 4 (2) |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| **Characteristic** | **No. (%)** |
|---|---|
| **No. of patients** | **204** |
| Number of cycles of inotuzumab ozogamicin, no. (%) | |
| 1 | 66 (32) |
| 2 | 98 (48) |
| 3 | 28 (14) |
| 4 | 10 (5) |
| Not reported | 2 (1) |
| Inotuzumab ozogamicin cumulative dose, mg/m² no. (%) | |
| 1 | |
| *Median (range)* | *1.8 (0.3-4.6)* |
| < 1.8 | 24 (36) |
| 1.8 | 34 (52) |
| > 1.8 | 4 (6) |
| Not reported | 4 (6) |
| 2 | |
| *Median (range)* | *3.1 (0.9-6.9)* |
| <.3.0 | 36 (37) |
| 3.0-3.2 | 10 (10) |
| 3.3-3.6 | 42 (43) |
| > 3.6 | 2 (2) |
| Not reported | 8 (8) |
| 3 | |
| *Median (range)* | *3.8 (1.8-5.4)* |
| < 2.8 | 6 (21) |
| 2.8-4.8 | 10 (36) |
| 4.9-5.3 | 4 (14) |
| > 5.3 | 4 (14) |
| Not reported | 4 (14) |
| 4 | |
| *Median (range)* | *4.8 (3.0-5.4)* |
| 2.8-4.8 | 6 (60) |
| 4.9-5.3 | 1 (10) |
| > 5.3 | 1 (10) |
| Not reported | 2 (20) |
| Not reported | 2 (1) |
| Inotuzumab ozogamicin cumulative dose, median (range) | 2.2 (0.3-6.9) |
| Time from last dose of inotuzumab ozogamicin to HSCT, months, no. (%) | |
| Median (range) | 2 (<1-26) |
| < 1 | 18 (9) |
| 1-1.6 | 45 (22) |
| 1.7-3 | 28) |
| > 3 | 74 (36) |
| Not reported | 9 (4) |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Characteristic | No. (%) |
|---|---|
| **No. of patients** | **204** |
| Regimen containing inotuzumab ozogamicin, no. (%) | |
| N/A; CIBMTR Form 2011 not yet received | 5 (2) |
| Single agent | 101 (50) |
| Combined with other chemotherapy/systemic therapy | 86 (42) |
| Outliers | 8 (4) |
| Not reported | 4 (2) |
| Disease status prior to HSCT, no. (%) | |
| CR1 | 67 (33) |
| CR2 | 98 (48) |
| Advanced | 38 (19) |
| CR3+ | 23 |
| REL1 | 10 |
| REL3+ | 3 |
| PIF | 2 |
| Not reported | 1 (0) |
| Time from diagnosis to 1st CR/CRi, months, no. (%) | |
| Median (range), months | 3 (<1-217) |
| < 3 | 85 (42) |
| 3-5 | 25 (12) |
| 6-11 | 29 (14) |
| ≥ 12 | 14 (7) |
| N/A, CIBMTR Form 2011 not yet received | 5 (2) |
| N/A, not in CR prior to HSCT | 20 (10) |
| Not reported | 26 (13) |
| Time from 1st CR/CRi to HSCT, months, no. (%) | |
| Median (range), months | 11 (<1-226) |
| < 6 | 57 (28) |
| 6-11 | 23 (11) |
| 12-17 | 19 (9) |
| 18-23 | 12 (6) |
| ≥ 24 | 42 (21) |
| N/A, CIBMTR Form 2011 not yet received | 5 (2) |
| Not in CR prior to HSCT | 20 (10) |
| Not reported | 26 (13) |
| MRD status prior to HSCT, no. (%) | |
| Positive | 47 (23) |
| Negative | 136 (67) |
| N/A, patient not in CR at HSCT | 16 (8) |
| Not reported | 5 (2) |
| Donor type, no. (%) | |
| HLA-identical sibling | 53 (26) |
| Other related | 53 (26) |
| Unrelated | 98 (48) |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Characteristic | No. (%) |
|---|---|
| **No. of patients** | **204** |
| Last platelet count, prior to HSCT, no. (%) | |
| ≥ 100 | 83 (41) |
| <100 | 114 (56) |
| Not reported | 7 (3) |
| Conditioning regimen intensity, no. (%) | |
| Myeloablative | 111 (54) |
| RIC/NMA | 90 (44) |
| Not reported | 2 (1) |
| N/A, Form 2000 not yet received | 1 (0) |
| Busulfan used in conditioning regimen, no. (%) | |
| Yes | 23 (11) |
| Busulfan dose guided by pharmacokinetics | 11 |
| No | 180 (88) |
| N/A, Form 2000 not received | 1 (0) |
| Thiotepa used in conditioning regimen, no. (%) | |
| Yes | 16 (8) |
| No | 187 (92) |
| N/A, Form 2000 not received | 1 (0) |
| Dual alkylating agents or one alkylating agent, no. (%) | |
| Two alkylating agents | 14 (7) |
| One alkylating agent | 138 (68) |
| No alkylating agents | 50 (25) |
| N/A, CIBMTR Form 2000 not yet received | 1 (0) |
| Not reported | 1 (0) |
| Combination of alkylating agent(s) with TBI (≥ 12 Gy), no. (%) | |
| Yes | 43 (21) |
| No | 159 (78) |
| N/A, Form 2000 not received | 1 (0) |
| Not reported | 1 (0) |
| Defibrotide use for liver toxicity prophylaxis, no. (%) | |
| Yes | 19 (9) |
| No | 185 (91) |
| Ursodiol use for liver toxicity prophylaxis, no. (%) | |
| Yes | 185 (91) |
| No | 19 (9) |
| Graft type, no. (%) | |
| BM/PBSC | 190 (93) |
| UCB | 14 (7) |
| Total serum bilirubin, prior to transplant, no. (%) | |
| Normal | 188 (92) |
| Abnormal | 14 (7) |
| N/A, CIBMTR Form 2000 not yet received | 1 (0) |
| Not reported | 1 (0) |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Characteristic | No. (%) |
|---|---|
| **No. of patients** | **204** |
| Donor/recipient sex match, no. (%) | |
| M-M | 68 (33) |
| M-F | 55 (27) |
| F-M | 44 (22) |
| F-F | 37 (18) |
| Donor/recipient CMV match, no. (%) | |
| +/+ | 81 (40) |
| +/- | 15 (7) |
| -/+ | 52 (25) |
| -/- | 41 (20) |
| UCB[a] | 14 (7) |
| Not reported | 1 (0) |
| GVHD prophylaxis, no. (%) | |
| PT-Cy-based | 80 (39) |
| Tac-based | 103 (50) |
| CsA-based | 16 (8) |
| Ex-vivo T-cell depletion / CD34 selection | 4 (2) |
| Not reported | 1 (0) |
| Sirolimus used in GVHD prophylaxis, no. (%) | |
| Yes | 16 (8) |
| No | 188 (92) |
| In vivo T-cell depletion, no. (%) | |
| Yes | 35 (17) |
| No | 163 (80) |
| Not reported | 6 (3) |
| Antifungal infection prophylaxis, no. (%) | |
| N/A, Form 2100 not yet received | 1 (0) |
| None | 4 (2) |
| Fluconazole | 89 (44) |
| Posaconazole | 35 (17) |
| Micafungin | 29 (14) |
| Caspofungin | 33 (16) |
| Voriconazole | 4 (2) |
| Nystatin | 5 (2) |
| Isavuconazole | 1 (0) |
| Anidulafungin | 2 (1) |
| Not reported | 1 (0) |
| Year of transplant, no. (%) | |
| 2017 | 8 (4) |
| 2018 | 52 (25) |
| 2019 | 66 (32) |
| 2020 | 49 (24) |
| 2021 | 25 (12) |
| 2022 | 4 (2) |
| Follow-up, median (range), months | 24.51 (12.02-50.79) |

**Table 43. Baseline characteristics and follow-up of adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Characteristic | No. (%) |
|---|---|
| **No. of patients** | **204** |

[a] Of the UCB donors, n = 11 recipients were CMV-positive, and n = 3 recipients were CMV-negative.

**Table 44. Correlation between number of inotuzumab ozogamicin cycles and disease status at transplant, among n = 204 patients eligible for subset analysis**

| Characteristic | CR1 | CR2 | Advanced |
|---|---|---|---|
| **No. of patients** | **67** | **98** | **38** |
| 1 | 23 (34) | 29 (30) | 13 (34) |
| 2 | 33 (49) | 50 (51) | 15 (40) |
| ≥ 3 | 11 (17) | 19 (19) | 8 (21) |
| Not reported | 0 | 0 | 2 (5) |

**Table 45. Univariate analysis of overall survival at 18 months in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| No. of patients (N=204) | No. patients in each group | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Patient age at transplant, years | Continuous | 1.022 (1.01 - 1.034) | 0.0002 |
| Karnofsky performance score prior to transplant (10-80 vs 90-100) | 82 vs 113 | 1.523 (1.036 - 2.238) | 0.0323 |
| Sorror HCT-CI score | Continuous | 0.989 (0.964 - 1.015) | 0.4060 |
| History of hepatitis B or C (yes vs no) | 8 vs 196 | 0.175 (0.024 - 1.254) | 0.0828 |
| Liver disease / hepatitis B or C (yes vs no) | 59 vs 141 | 1.009 (0.665 - 1.531) | 0.9665 |
| Line of therapy prior to HSCT (first line vs relapsed/refractory to therapy) | 7 vs 184 | 1.553 (0.68 - 3.544) | 0.2957 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (no treatment given vs salvage ≥ 2) | 19 vs 76 | 1.502 (0.82 - 2.751) | 0.1880 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (first line vs salvage ≥ 2) | 54 vs 76 | 0.718 (0.429 - 1.203) | 0.2085 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (salvage 1 vs salvage ≥ 2) | 38 vs 76 | 1.322 (0.794 - 2.198) | 0.2830 |
| Number of cycles of inotuzumab ozogamicin | Continuous | 1.016 (1.001 - 1.03) | 0.0307 |
| Time from last dose of inotuzumab ozogamicin to HSCT | Continuous | 1.029 (0.963 - 1.099) | 0.3997 |
| Total dose of inotuzumab ozogamicin | Continuous | 1.254 (1.073 - 1.465) | 0.0045 |
| Regimen containing inotuzumab ozogamicin (combined with other agents vs single agent) | 86 vs 101 | 0.916 (0.618 - 1.357) | 0.6617 |
| Disease status prior to HSCT (advanced vs CR1) | 38 vs 67 | 2.145 (1.285 - 3.581) | 0.0035 |
| Disease status prior to HSCT (CR2 vs CR1) | 98 vs 67 | 1.209 (0.772 - 1.892) | 0.4072 |
| Time from diagnosis to CR1, months | Continuous | 0.993 (0.977 - 1.008) | 0.3509 |
| Time from CR1 to HSCT, months | Continuous | 0.993 (0.985 - 1.002) | 0.1416 |
| MRD status prior to HSCT (N/A not in CR at HSCT vs negative) | 16 vs 136 | 2.099 (1.157 - 3.807) | 0.0147 |
| MRD status prior to HSCT (positive vs negative) | 47 vs 136 | 0.951 (0.597 - 1.513) | 0.8309 |
| Donor type (other related vs HLA-identical sibling) | 53 vs 53 | 2.274 (1.377 - 3.754) | 0.0013 |
| Donor type (unrelated vs HLA-identical sibling) | 98 vs 53 | 0.966 (0.592 - 1.575) | 0.8893 |
| Platelet count, $\times 10^9$/L, last evaluation prior to HSCT (< 100 vs ≥ 100) | 114 vs 83 | 0.654 (0.446 - 0.959) | 0.0298 |
| Conditioning regimen intensity (RIC/NMA vs MAC) | 90 vs 111 | 1.433 (0.984 - 2.088) | 0.0608 |
| Busulfan used in conditioning regimen (yes vs no) | 23 vs 180 | 1.663 (0.978 - 2.828) | 0.0606 |
| Thiotepa used in conditioning regimen (yes vs no) | 16 vs 187 | 1.12 (0.566 - 2.216) | 0.7450 |
| Dual alkylating agents used in conditioning regimen (no alkylating agent vs one alkylating agent) | 50 vs 138 | 1.082 (0.691 - 1.695) | 0.7298 |
| Dual alkylating agents used in conditioning regimen (2 alkylating agents vs one alkylating agent) | 14 vs 138 | 1.907 (0.983 - 3.698) | 0.0562 |
| Combination of alkylating agent(s) with TBI ≥ 12 Gy (yes vs no) | 43 vs 159 | 0.508 (0.294 - 0.876) | 0.0148 |
| Defibrotide used in prophylaxis for VOD (yes vs no) | 19 vs 185 | 0.745 (0.363 - 1.529) | 0.4218 |
| Ursodiol used in prophylaxis for VOD (yes vs no) | 185 vs 19 | 0.648 (0.37 - 1.136) | 0.1298 |
| Graft source (UCB vs BM/PBSC) | 14 vs 190 | 0.574 (0.234 - 1.409) | 0.2260 |
| Bilirubin, last evaluation prior to HSCT (abnormal vs normal) | 14 vs 188 | 3.056 (1.631 - 5.728) | 0.0005 |
| Donor-recipient sex match (N/A UCB vs not matched) | 14 vs 88 | 0.453 (0.181 - 1.131) | 0.0898 |
| Donor-recipient sex match (matched vs not matched) | 102 vs 88 | 0.635 (0.433 - 0.932) | 0.0204 |

| | | | |
|---|---|---|---|
| Donor-recipient CMV match (N/A UCB vs not matched) | 14 vs 67 | 0.637 (0.25 - 1.625) | 0.3455 |
| Donor-recipient CMV match (matched vs not matched) | 122 vs 67 | 1.163 (0.777 - 1.743) | 0.4629 |
| GVHD prophylaxis (CsA-based vs Tac-based) | 16 vs 103 | 0.866 (0.392 - 1.91) | 0.7213 |
| GVHD prophylaxis (Ex-vivo TCD/CD34 selection vs Tac-based) | 4 vs 103 | 0.42 (0.058 - 3.034) | 0.3896 |
| GVHD prophylaxis (PT-Cy-based vs Tac-based) | 80 vs 103 | 1.679 (1.138 - 2.478) | 0.0090 |
| Sirolimus used in GVHD prophylaxis (yes vs no) | 16 vs 188 | 0.895 (0.452 - 1.771) | 0.7497 |
| In vivo T-cell depletion (yes vs no) | 35 vs 163 | 0.857 (0.51 - 1.439) | 0.5591 |
| Antifungal infection prophylaxis (azoles vs no-azoles) | 129 vs 69 | 0.935 (0.627 - 1.395) | 0.7432 |
| Year of transplant | Continuous | 1.017 (0.85 - 1.216) | 0.8536 |

Note: Due to small sample size, center effect cannot be included in univariate analysis.

**Table 46. Multivariable analysis of overall survival at 18 months in adults who underwent first allogeneic HSCT and were eligible for final analysis**

| Covariate | No. evaluable | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Age | | | 0.0121 [a] |
| 30-59 vs 18-29 | 98 vs 67 | 1.31 (0.81-2.13) | 0.2736 |
| ≥ 60 vs 18-29 | 38 vs 67 | 2.36 (1.32-4.20) | 0.0036 |
| ≥ 60 vs 30-59 | 38 vs 98 | 1.80 (1.08-3.00) | 0.0245 |
| Donor | | | 0.0002 [a] |
| Other related vs HLA-identical siblings | 53 vs 53 | 2.33 (1.37-3.99) | 0.0019 |
| Unrelated vs HLA-identical siblings | 97 vs 53 | 0.97 (0.57-4.66) | 0.9166 |
| Unrelated vs other related | 97 vs 53 | 0.42 (0.26-0.66) | 0.0002 |
| Disease status | | | 0.0024 [a] |
| CR2 vs CR1 | 98 vs 67 | 1.29 (0.77-2.14) | 0.3294 |
| Advanced vs CR1 | 38 vs 67 | 2.53 (1.45-4.43) | 0.0011 |
| Advanced vs CR2 | 38 vs 98 | 1.97 (1.21 vs 3.19) | 0.0060 |

Notes: Due to small sample size, center effect cannot be included in univariable analysis. The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who were alive at date of last contact and reported less than 1 year of post-HSCT follow-up were not included in this analysis.

Overall mortality is time from HSCT to death from any cause post-HSCT. A Cox proportional hazards model has been used to evaluate overall mortality. Data were censored at 1-year post-HSCT. There was n=1 patient who was excluded from this analysis due to missing disease status information.

The following 9 variables were evaluated in the multivariable analysis: patient age (18-29 vs 30-59 vs ≥ 60), patient sex (male vs female), Sorror HCT-CI (0 vs 1-2 vs ≥ 3), Karnofsky performance score prior to transplant (90-100 vs 10-80), Sirolimus use as GVHD prophylaxis given (yes vs no), disease status prior to HSCT (CR1 vs CR2 vs advanced), conditioning regiment intensity and dual alkylators (MAC/dual alkylators vs MAC/no dual alkylators vs RIC/non-MAC), donor type (HLA-identical sibling vs other related vs unrelated), number of cycles of inotuzumab ozogamicin treatment prior to HSCT.

[a] Wald test with 2 degrees of freedom

**Table 47. Univariate analysis of transplant-related mortality at 18 months in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| No. of patients (N=204) | No. patients in each group | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Patient age at transplant, years | Continuous | 1.032 (1.015 - 1.048) | 0.0001 |
| Karnofsky performance score prior to transplant (10-80 vs 90-100) | 82 vs 113 | 1.892 (1.077 - 3.323) | 0.0264 |
| Sorror HCT-CI score | Continuous | 0.989 (0.951 - 1.027) | 0.5596 |
| History of hepatitis B or C (yes vs no) | 8 vs 196 | 0.329 (0.045 - 2.381) | 0.2709 |
| Liver disease / hepatitis B or C (yes vs no) | 59 vs 141 | 0.895 (0.486 - 1.649) | 0.7231 |
| Line of therapy prior to HSCT (first line vs relapsed/refractory to therapy) | 7 vs 184 | 1.002 (0.243 - 4.122) | 0.9980 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (no treatment given vs salvage ≥ 2) | 19 vs 76 | 1.562 (0.619 - 3.939) | 0.3446 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (first line vs salvage ≥ 2)) | 54 vs 76 | 1.262 (0.643 - 2.475) | 0.4988 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (salvage 1 vs salvage ≥ 2)) | 38 vs 76 | 1.367 (0.611 - 3.054) | 0.4465 |
| Number of cycles of inotuzumab ozogamicin | Continuous | 1.013 (0.994 - 1.033) | 0.1760 |
| Time from last dose of inotuzumab ozogamicin to HSCT | Continuous | 1.065 (0.996 - 1.139) | 0.0657 |
| Total dose of inotuzumab ozogamicin | Continuous | 1.28 (1.029 - 1.592) | 0.0265 |
| Regimen containing inotuzumab ozogamicin (combined with other agents vs single agent) | 86 vs 101 | 0.97 (0.553 - 1.701) | 0.9150 |
| Disease status prior to HSCT (advanced vs CR1) | 38 vs 67 | 1.909 (0.907 - 4.02) | 0.0888 |
| Disease status prior to HSCT (CR2 vs CR1) | 98 vs 67 | 1.233 (0.653 - 2.328) | 0.5184 |
| Time from diagnosis to CR1, months | Continuous | 0.997 (0.983 - 1.012) | 0.7358 |
| Time from CR1 to HSCT, months | Continuous | 0.993 (0.981 - 1.006) | 0.2946 |
| MRD status prior to HSCT (N/A not in CR at HSCT vs negative) | 16 vs 136 | 1.162 (0.414 - 3.263) | 0.7749 |
| MRD status prior to HSCT (positive vs negative) | 47 vs 136 | 0.693 (0.336 - 1.431) | 0.3214 |
| Donor type (other related vs HLA-identical sibling) | 53 vs 53 | 2.337 (1.147 - 4.762) | 0.0194 |
| Donor type (unrelated vs HLA-identical sibling) | 98 vs 53 | 1.001 (0.495 - 2.023) | 0.9978 |
| Platelet count, $\times 10^9$/L, last evaluation prior to HSCT (< 100 vs ≥ 100) | 114 vs 83 | 0.719 (0.419 - 1.234) | 0.2309 |
| Conditioning regimen intensity (RIC/NMA vs MAC) | 90 vs 111 | 1.803 (1.051 - 3.094) | 0.0323 |
| Busulfan used in conditioning regimen (yes vs no) | 23 vs 180 | 1.958 (0.984 - 3.896) | 0.0555 |
| Thiotepa used in conditioning regimen (yes vs no) | 16 vs 187 | 1.517 (0.649 - 3.549) | 0.3364 |
| Dual alkylating agents used in conditioning regimen (no alkylating agent vs one alkylating agent) | 50 vs 138 | 1.232 (0.647 - 2.348) | 0.5259 |
| Dual alkylating agents used in conditioning regimen (2 alkylating agents vs one alkylating agent) | 14 vs 138 | 2.896 (1.333 - 6.294) | 0.0073 |
| Combination of alkylating agent(s) with TBI ≥ 12 Gy (yes vs no) | 43 vs 159 | 0.254 (0.092 - 0.703) | 0.0084 |
| Defibrotide used in prophylaxis for VOD (yes vs no) | 19 vs 185 | 0.713 (0.258 - 1.975) | 0.5157 |
| Ursodiol used in prophylaxis for VOD (yes vs no) | 185 vs 19 | 0.564 (0.266 - 1.193) | 0.1342 |
| Graft source (UCB vs BM/PBSC) | 14 vs 190 | 0.244 (0.034 - 1.768) | 0.1628 |
| Bilirubin, last evaluation prior to HSCT (abnormal vs normal) | 14 vs 188 | 4.413 (2.144 - 9.084) | <.0001 |
| Donor-recipient sex match (N/A UCB vs not matched) | 14 vs 88 | 0.187 (0.025 - 1.37) | 0.0988 |
| Donor-recipient sex match (matched vs not matched) | 102 vs 88 | 0.588 (0.343 - 1.007) | 0.0531 |

**Table 47. Univariate analysis of transplant-related mortality at 18 months in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| No. of patients (N=204) | No. patients in each group | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Donor-recipient CMV match (N/A UCB vs not matched) | 14 vs 67 | 0.278 (0.037 - 2.089) | 0.2137 |
| Donor-recipient CMV match (matched vs not matched) | 122 vs 67 | 1.195 (0.676 - 2.111) | 0.5401 |
| GVHD prophylaxis (CsA-based vs Tac-based) | 16 vs 103 | 1.083 (0.374 - 3.131) | 0.8833 |
| GVHD prophylaxis (Ex-vivo TCD/CD34 selection vs Tac-based) | 4 vs 103 | NE | NE |
| GVHD prophylaxis (PT-Cy-based vs Tac-based) | 80 vs 103 | 2.004 (1.151 - 3.489) | 0.0140 |
| Sirolimus used in GVHD prophylaxis (yes vs no) | 16 vs 188 | 1.042 (0.376 - 2.883) | 0.9372 |
| In vivo T-cell depletion (yes vs no) | 35 vs 163 | 0.905 (0.441 - 1.858) | 0.7861 |
| Antifungal infection prophylaxis (azoles vs no-azoles) | 129 vs 69 | 1.17 (0.659 - 2.078) | 0.5923 |
| Year of transplant | Continuous | 1.265 (0.989 - 1.618) | 0.0614 |

**Table 48. Multivariable analysis of transplant-related mortality at 18 months in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Covariate | N evaluable | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Karnofsky score | | | <0.0001 [a] |
| < 90 vs 90-100 | 81 vs 111 | 3.00 (1.56-5.79) | 0.0010 |
| Unknown vs 90-100 | 9 vs 111 | 7.55 (2.88-19.76) | <0.0001 |
| Conditioning regimen intensity and dual alkylators | | | 0.0002 [a] |
| MAC/No dual alkylators vs MAC/dual alkylators | 97 vs 14 | 0.15 (0.06-0.37) | <0.0001 |
| RIC/Non-MAC vs MAC/Dual alkylators | 90 vs 14 | 0.26 (0.11-0.62) | 0.0027 |
| RIC/Non-MAC vs MAC/No dual alkylators | 90 vs 97 | 1.73 (0.90-3.32) | 0.0972 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who were alive at date of last contact and reported less than 1 year of post-HSCT follow-up were not included in this analysis.

Transplant-related mortality (post-transplant non-relapse mortality) is time from HSCT to death within the first 28 days post-HSCT, or death from any cause without prior relapse/progression post-HSCT. A Fine and Gray's sub-distribution hazards model was used to account for the competing risk event (post-HSCT relapse). There were n=3 patients who were excluded from this analysis due to missing conditioning regiment intensity and dual alkylators information.

The following 9 variables were evaluated in the multivariable analysis: patient age (18-29 vs 30-59 vs ≥ 60), patient sex (male vs female), Sorror HCT-CI (0 vs 1-2 vs ≥ 3), Karnofsky performance score prior to transplant (90-100 vs 10-80), sirolimus use as GVHD prophylaxis given (yes vs no), disease status prior to HSCT (CR1 vs CR2 vs advanced), conditioning regiment intensity and dual alkylators (MAC/dual alkylators vs MAC/no dual alkylators vs RIC/non-MAC), donor type (HLA-identical sibling vs other related vs unrelated), number of cycles of inotuzumab ozogamicin treatment prior to HSCT.

[a] Wald test with 2 degrees of freedom

**Table 49. Univariate analysis of VOD/SOS at 100 days in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| No. of patients (N=204) | No. patients per group | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Patient age at transplant, years | Continuous | 0.983 (0.96 - 1.006) | 0.1520 |
| Karnofsky performance score prior to transplant (10-80 vs 90-100) | 82 vs 113 | 1.669 (0.794 - 3.508) | 0.1768 |
| Sorror HCT-CI score | Continuous | 0.966 (0.845 - 1.104) | 0.6079 |
| History of hepatitis B or C (yes vs no) | 8 vs 196 | 2.885 (0.876 - 9.494) | 0.0813 |
| Liver disease / hepatitis B or C (yes vs no) | 59 vs 141 | 1.116 (0.526 - 2.37) | 0.7748 |
| Line of therapy prior to HSCT (first line vs relapsed/refractory to therapy) | 7 vs 184 | 0.838 (0.114 - 6.161) | 0.8623 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (no treatment given vs salvage ≥ 2) | 19 vs 76 | 0.626 (0.238 - 1.646) | 0.3421 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (first line vs salvage ≥ 2) | 54 vs 76 | 0.908 (0.259 - 3.186) | 0.8799 |
| Lines of salvage therapy prior to inotuzumab ozogamicin (salvage 1 vs salvage ≥ 2) | 38 vs 76 | 1.117 (0.445 - 2.799) | 0.8141 |
| Number of cycles of inotuzumab ozogamicin | Continuous | 0.983 (0.91 - 1.063) | 0.6723 |
| Time from last dose of inotuzumab ozogamicin to HSCT | Continuous | 0.992 (0.878 - 1.121) | 0.8957 |
| Total dose of inotuzumab ozogamicin | Continuous | 0.992 (0.73 - 1.349) | 0.9614 |
| Regimen containing inotuzumab ozogamicin (combined with other agents vs single agent) | 86 vs 101 | 0.781 (0.373 - 1.635) | 0.5115 |
| Disease status prior to HSCT (advanced vs CR1) | 38 vs 67 | 1.4 (0.486 - 4.035) | 0.5333 |
| Disease status prior to HSCT (CR2 vs CR1) | 98 vs 67 | 1.593 (0.687 - 3.692) | 0.2775 |
| Time from diagnosis to CR1, months | Continuous | 0.999 (0.979 - 1.02) | 0.9565 |
| Time from CR1 to HSCT, months | Continuous | 1.005 (0.994 - 1.015) | 0.3918 |
| MRD status prior to HSCT (N/A not in CR at HSCT vs negative) | 16 vs 136 | 0.464 (0.062 - 3.477) | 0.4552 |
| MRD status prior to HSCT (positive vs negative) | 47 vs 136 | 1.732 (0.799 - 3.751) | 0.1640 |
| Donor type (other related vs HLA-identical sibling) | 53 vs 53 | 1.912 (0.707 - 5.172) | 0.2017 |
| Donor type (unrelated vs HLA-identical sibling) | 98 vs 53 | 1.336 (0.513 - 3.476) | 0.5530 |
| Platelet count, $\times 10^9$/L, last evaluation prior to HSCT (< 100 vs ≥ 100) | 114 vs 83 | 0.837 (0.409 - 1.716) | 0.6279 |
| Conditioning regimen intensity (RIC/NMA vs MAC) | 90 vs 111 | 0.492 (0.226 - 1.068) | 0.0727 |
| Busulfan used in conditioning regimen (yes vs no) | 23 vs 180 | 1.123 (0.393 - 3.209) | 0.8290 |
| Thiotepa used in conditioning regimen (yes vs no) | 16 vs 187 | 3.151 (1.292 - 7.687) | 0.0116 |
| Dual alkylating agents used in conditioning regimen (no alkylating agent vs one alkylating agent) | 50 vs 138 | 1.366 (0.589 - 3.165) | 0.4673 |
| Dual alkylating agents used in conditioning regimen (2 alkylating agents vs one alkylating agent) | 14 vs 138 | 4.189 (1.646 - 10.666) | 0.0027 |
| Combination of alkylating agent(s) with TBI ≥ 12 Gy (yes vs no) | 43 vs 159 | 1.088 (0.469 - 2.526) | 0.8440 |
| Defibrotide used in prophylaxis for VOD (yes vs no) | 19 vs 185 | 3.033 (1.307 - 7.042) | 0.0098 |
| Ursodiol used in prophylaxis for VOD (yes vs no) | 185 vs 19 | 0.699 (0.245 - 1.998) | 0.5040 |
| Graft source (UCB vs BM/PBSC) | 14 vs 190 | NE | NE |
| Bilirubin, last evaluation prior to HSCT (abnormal vs normal) | 14 vs 188 | 1.745 (0.529 - 5.757) | 0.3609 |
| Donor-recipient sex match (N/A UCB vs not matched) | 14 vs 88 | NE | NE |
| Donor-recipient sex match (matched vs not matched) | 102 vs 88 | 1.01 (0.498 - 2.049) | 0.9785 |

| No. of patients (N=204) | No. patients per group | Hazard ratio (95% CI) | P value |
|---|---|---|---|
| Donor-recipient CMV match (N/A UCB vs not matched) | 14 vs 67 | NE | NE |
| Donor-recipient CMV match (matched vs not matched) | 122 vs 67 | 2.398 (0.983 - 5.847) | 0.0545 |
| GVHD prophylaxis (CsA-based vs Tac-based) | 16 vs 103 | 1.542 (0.443 - 5.366) | 0.4963 |
| GVHD prophylaxis (Ex-vivo TCD/CD34 selection vs Tac-based) | 4 vs 103 | NE | NE |
| GVHD prophylaxis (PT-Cy-based vs Tac-based) | 80 vs 103 | 1.309 (0.624 - 2.746) | 0.4764 |
| Sirolimus used in GVHD prophylaxis (yes vs no) | 16 vs 188 | 1.339 (0.407 - 4.405) | 0.6304 |
| In vivo T-cell depletion (yes vs no) | 35 vs 163 | 0.892 (0.342 - 2.323) | 0.8149 |
| **Antifungal infection prophylaxis (azoles vs no-azoles)** | 129 vs 69 | 0.496 (0.239 - 1.027) | 0.0590 |
| Year of transplant | Continuous | 1.098 (0.802 - 1.503) | 0.5598 |

Note: Includes only patients with completed Form 2000 and/or Form 2011.
NE: There were no events reported for this category.

**Table 50. Multivariable analysis of VOD/SOS at 100 days in adults who underwent first allogeneic HSCT and were eligible for final subset analysis**

| Covariate | N evaluable | Odds ratio (95% CI) | P value |
|---|---|---|---|
| Conditioning regimen intensity and dual alkylators | | | 0.0131 [a] |
| MAC/No Dual alkylators vs MAC/Dual alkylators | 97 vs 14 | 0.26 (0.08-0.86) | 0.0275 |
| RIC/Non-MAC vs MAC/Dual alkylators | 89 vs 14 | 0.15 (0.04-0.53) | 0.0032 |
| RIC/Non-MAC vs MAC/No Dual alkylators | 89 vs 97 | 0.57 (0.24-.36) | 0.2064 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who were alive at date of last contact and reported less than 1 year of post-HSCT follow-up were not included in this analysis.

VOD is the occurrence of veno-occlusive disease/sinusoidal obstruction syndrome reported on the CIBMTR Form 2100. VOD is only considered within the first 100 days post-HSCT.

Logistic regression was used in this analysis to evaluate VOD within 100 days post-HSCT. There were n=2 patients who were excluded from this analysis due to missing VOD information. There were n=2 patients who were excluded from this analysis due to missing conditioning regiment intensity and dual alkylators.

The following 9 variables were evaluated in the multivariable analysis: patient age (18-29 vs 30-59 vs ≥ 60), patient sex (male vs female), HCT-CI (0 vs 1-2 vs ≥ 3), Karnofsky performance score prior to transplant (90-100 vs 10-80), Sirolimus use as GVHD prophylaxis given (yes vs no), disease status prior to HSCT (CR1 vs CR2 vs advanced), conditioning regiment intensity and dual alkylators (MAC/dual alkylators vs MAC/no dual alkylators vs RIC/non-MAC), donor type (HLA-identical sibling vs other related vs unrelated), number of cycles of inotuzumab ozogamicin treatment prior to HSCT.

[a] Wald test with 1 degree of freedom

### 10.6. Adverse events / adverse reactions

The CIBMTR Research Database supports non-interventional observational studies and utilizes a calendar-driven reporting of events but is not designed to be a means for detecting and reporting AEs in an expedited manner. As this non-interventional post-authorization safety study (PASS) utilizes a secondary data collection database, the CIBMTR has neither the jurisdiction nor the responsibility of expedited reporting of AEs to any regulatory authority. Expedited reporting of suspected adverse drug reactions was done by the physician responsible for the treatment of the patient, in accordance with standard routines used at the clinic as specified by regulatory agency.

This study includes unstructured data (e.g., narrative fields in the database) that were converted to structured (i.e., coded) data solely by a computer using automated/algorithmic methods and/or data that already existed as structured data in an electronic database. In these data sources, it is not possible to link (i.e., identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an AE (i.e., identifiable patient, identifiable reporter, a suspect product, and event) are not available and AEs are not reportable as individual AE reports.

## 11. DISCUSSION

### 11.1. Key results

A total of 5,891 B-cell ALL patients underwent an allogeneic HSCT transplant in the US between 18 August 2017 and 17 August 2022 (Table 2). Out of those 5,891 patients, 577 patients were excluded from this study as they had not consented to research, 131 patients were excluded from embargoed centers, and 2,669 patients were excluded as they belonged to centers not participating in the study. Of the remaining 2,514 patients, 371 received at least one dose of inotuzumab ozogamicin.

Therefore, between 18 August 2017 and 17 August 2022, 371 patients (304 adult and 67 pediatric) were accrued and included in the study. The data lock date for this final report, when data collection forms were last evaluated, was 17 August 2022.

Of the 371 patients included in the study, 319 patients (261 adult and 58 pediatric) underwent their first allogeneic HSCT for B-cell ALL (Table 5); and 52 patients (43 adult and 9 pediatric) had received a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin.

Most patients whose B-cell ALL relapses post first allogeneic HSCT do not proceed to a second. Patients who proceed for a 2$^{nd}$ allogeneic HSCT are extremely carefully selected.

The 52 patients who had a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin are described separately since the underlying disease, patient-related factors, risk of relapse, and post-HSCT complications are different for patients with a prior HSCT than for patients who underwent their first allogeneic HSCT for B-cell ALL.

### 11.1.1. Patients who underwent their first allogeneic HSCT for B-cell ALL

In total, 319 patients (261 adults and 58 pediatric patients, with a median age of 32 years) underwent their first allogeneic HSCT for B-cell ALL after treatment with inotuzumab ozogamicin (Table 5). Among the 319 patients (261 adults and 58 pediatric patients) who underwent first allogeneic HSCT for B-cell ALL, 137 patients (43%) had Sorror HCT-CI score ≥ 3 prior to HSCT.

Lines of therapy prior to transplant were:

- 9 (3%) patients had 1 line of therapy: 8 (3%) adult, 1 (2%) pediatric;
- 66 (21%) patients had 2 lines of therapy: 57 (22%) adult, 9 (16%) pediatric;
- 63 (20%) patients had 3 lines of therapy: 59 (23%) adult, 4 (7%) pediatric; and
- 144 (45%) patients had 4 or more lines of therapy: 114 (44%) adult, 30 (52%) pediatric.
- Data were not available for 37 patients (Table 5).

As of the data lock date, post-HSCT follow-up information was available for 296 / 319 (93%) patients: 244 (93%) adult, 52 (90%) pediatric (Table 13):

- 182 / 296 (61%) patients did not experience post-HSCT relapse: 151 (62%) adult, 31 (60%) pediatric; of these:
    - 56 / 182 (31%) patients (50 [33%] adult and 6 [19%] pediatric) died in remission within 18 months, with a median time from transplant to TRM of 2.23 months; primary causes of death were (Table 16):
        - VOD/SOS – 15 (27%) patients: 13 (26%) adult, 2 (33%) pediatric
        - GVHD – 12 (21%) patients: 11 (22%) adult, 1 (17%) pediatric
        - Organ failure – 11 (20%) patients: 10 (20%) adult, 1 (17%) pediatric
        - Hemorrhage – 3 (5%) patients: 3 (6%) adult, 0 pediatric
        - Interstitial pneumonitis – 4 (7%) patients: 4 (8%) adult, 0 pediatric
        - Infection – 6 (11%) patients: 5 (10%) adult, 1 (17%) pediatric
        - Septic shock – 2 (4%) patients: 2 (4%) adult, 0 pediatric
        - Thrombotic microangiopathy – 1 (2%) patient: 0 adult, 1 (17%) pediatric
        - Graft failure – 1 (2%) patient: 1 (2%) adult, 0 pediatric

        - Other – 1 (2%) patient: 1 (2%) adult, 0 pediatric

- 114 / 296 (39%) patients experienced post-HSCT relapse: 93 (38%) adult, 21 (40%) pediatric; of these:
    - 56 / 114 (49%) patients died after post-HSCT relapse of B-cell ALL within 18 months, with a median time from transplant to NTRM of 6.92 months: 49 (53%) adult, 7 (33%) pediatric (Table 17)
- 51 / 296 (17%) patients (35 (14%) adult, 16 (31%) pediatric) experienced post-transplant VOD/SOS (Table 19 and Table 36); of these:
    - 23 (45%) cases were mild: 15 (43%) adult, 8 (50%) pediatric
    - 28 (55%) cases were severe: 20 (57%) adult, 8 (50%) pediatric
    - 3 (6%) patients did not receive liver toxicity prophylaxis: 2 (6%) adult, 1 (6%) pediatric
    - 29 (57%) patients died after reporting VOD with a median follow-up of 1.34 months after VOD: 22 (63%) adult, 7 (44%) pediatric.
        - 16 out of the 29 (55%) patients had VOD as cause of death and had a median follow-up of 1.36 months after VOD: 14 (64%) adult, 2 (29%) pediatric.
            - 1 out of the 16 (6%) patients with reported VOD as cause of death had not received liver toxicity prophylaxis: 1 (7%) adult.
    - Other causes of death were:
        - Recurrence of B-cell ALL – 5 (17%) patients: 3 (14%) adult patients died 0.3, 2.9, and 7.2 months after VOD, 2 (29%) pediatric patients died 0.3 and 1.5 months after VOD,
        - GVHD – 3 (10%) patients: 2 (9%) adult patients died after 0.3 and 1.8 months after VOD, 1 pediatric (14%) died after 29.9 months,
        - Organ failure – 3 (10%) patients: 2 (9%) adult patients died after 1.1 and 1.3 months after VOD; 1 (14%) pediatric patient died 0.1 months after VOD,
        - Septic shock– 1 (3%) patient: 1 (5%) adult patient died 0.5 months after VOD,
        - Infection – 1 (3%) patient: 1 (14%) pediatric patient died 2.0 months after VOD.

- Liver toxicity prophylaxis:
    - 20 / 296 (7%) patients did not receive liver toxicity prophylaxis: 14 (6%) adult and 6 (12%) pediatric
    - 217 / 296 (73%) patients received liver toxicity prophylaxis with ursodiol alone: 198 (81%) adult and 19 (37%) pediatric
    - 42 / 296 (14%) patients received liver toxicity prophylaxis with ursodiol and defibrotide: 20 (8%) adult and 22 (42%) pediatric
    - 9 / 296 (3%) patients received liver toxicity prophylaxis with ursodiol and other drugs (not specified): 6 (2%) adult and 3 (6%) pediatric
    - 3 / 296 (1%) patients received liver toxicity prophylaxis with defibrotide alone: 2 (1%) adult and 1 (2%) pediatric
    - 5 / 296 (2%) patients did not have data reported for liver toxicity prophylaxis: 4 (2%) adult and 1 (2%) pediatric
- Transplant-related mortality:
    - Of the 296 patients with post-transplant follow-up information available, 112 patient deaths occurred within the first 18 months post-transplant, with TRM occurring in 56 patients.

In an adjusted analysis of 18-month outcomes of 204 adult patients with at least 12 months of follow-up, disease status, namely advanced disease stage, age and donor type were negative prognostic factors for 18 months overall survival. Karnofsky performance score and conditioning regimen intensity (dual alkylators) were negative prognostic factors for 18 months TRM. Only choice of conditioning regimen (dual alkylators), and not cumulative inotuzumab exposure, was a negative prognostic factor of day-100 VOD incidence.

### 11.1.2. Patients who underwent second, or greater, HSCT for B-cell ALL

As of the data lock date, post-HSCT follow-up information was available for all patients.

Among the 52 patients (43 adult, 9 pediatric) who had a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin, 27 patients (52%) had Sorror HCT-CI scores ≥ 3 prior to HSCT, and 16 patients (31%) had mild hepatic disease prior to HSCT. Fifty (50) patients (96%) underwent HSCT for relapsed or refractory disease and for another 2 patients (4%), disease status prior to transplant was not reported. Out of 52 patients, 9 patients (18%) had a history of proven invasive fungal infection.

Nine (9) of the 52 patients who had a prior allogeneic HSCT before receiving inotuzumab ozogamicin (17%) had received a bone marrow product, 7 patients (13%) received a cord blood

product, and the remaining 36 patients (69%) received peripheral blood stem cells. Thirty-four (34) patients (65%) received their product from an unrelated donor, 4 patients (8%) had an HLA-identical sibling donor, and the remaining 14 patients (27%) had another related donor (though not a human leukocyte antigen [HLA]-identical sibling). The median time from B-cell ALL diagnosis to transplant was 39 months, and the median time from B-cell ALL diagnosis to first dose of inotuzumab ozogamicin was 33 months.

Twelve (12) of the 52 patients for whom post-HSCT follow-up information was available with prior allogeneic HSCT (23%) experienced VOD/SOS after the second allogeneic HSCT. Seven (7) patients (58%) experienced severe VOD/SOS and 5 patients (42%) experienced mild VOD/SOS. Of the patients who had VOD/SOS, 7 (58%) patients (3 adult, 4 pediatric) died after reporting VOD/SOS at 0.1 months, 0.5 months, 0.5 months, 1.1 months, 2.8 months, 22.5 months, and 43.1 months after VOD.

Causes of death for the 7 patients included:

- 3 due to primary disease: 1 (33%) adult and 2 (50%) pediatric
- 4 due to VOD/SOS: 2 (67%) adult and 2 (50%) pediatric

Four (4) of the 9 pediatric patients (44%) experienced VOD/SOS after the second allogeneic HSCT. Three of the 4 patients (75%) experienced severe VOD/SOS and 1 patient (25%) experienced mild VOD/SOS. Four (4) pediatric patients (44%) died after reporting VOD/SOS at 0.1 months, 0.5 months, 1.1 months, and 22.5 months after VOD.

Eight (8) of the 43 adult patients (19%) experienced VOD/SOS after the second allogeneic HSCT. Four patients (50%) had mild VOD/SOS grade and 4 patients (50%) experienced severe VOD/SOS. Three (3) adult patients (37%) died after reporting VOD/SOS at 0.5 months, 2.8 months, and 43.1 months.

For the 52 patients, relapse status was:

- 7/52 (13%) patients experienced post-HSCT relapse: 4 (9 %) adult, 3 (33%) pediatric
- 43/52 (83%) patients did not experience post-HSCT relapse: 38 adult (88%), 5 pediatric (56%), of these:
    - 13/43 (30%) patients died in remission within 18 months: 11 (29 %) adult and 2 (40 %) pediatric
- 2/52 (4%) patients had relapse status not reported: 1 (2 %) adult, 1 (11 %) pediatric

**11.2. Limitations**

CIBMTR is mandated by the US HRSA to collect data from all patients undergoing allogeneic HSCT in the US, and only data included in the CIBMTR database was analyzed. Approximately

75% of CIBMTR centers provided additional patient data (CRF-level data); this accounts for > 25% of cases submitted to CIBMTR annually.

Due to the design of the study (i.e., no comparison group) only descriptive information were provided.

### 11.3. Interpretation

Overall, data collected between August 2017 and August 2022 in the CIBMTR Research Database appear to be consistent with the results observed in completed Phase 3 Study B1931022.

In Phase 3 Study B1931022, the safety and efficacy of inotuzumab ozogamicin was examined in adult patients with relapsed or refractory B-cell ALL who received either 1 or 2 lines of therapy prior to inotuzumab ozogamicin. In this study, the VOD incidence was 18% among adult patients who underwent a first HSCT for relapsed or refractory B-cell ALL (Table 67). Based on data collected between August 2017 and August 2022 in the CIBMTR Research Database, the VOD incidence rate was 18% (95% CI, 12-24) in adult patients with relapsed or refractory B-cell ALL who received a median of 4 lines of therapy prior to HSCT. Although there are only data from n=52 pediatric patients who underwent a first transplant collected between August 2017 and August 2022 in the CIBMTR Research Database with post-HSCT follow-up information available, the incidence of 100-day VOD post-HSCT appears to be higher than in adult patients at 30% (95% CI, 17-45; Table 67).

Among patients who underwent first alloHSCT for B-cell ALL and have follow-up (n=296), 17% had VOD/SOS (69% adults and 31% pediatrics). VOD incidence of relapsed/refractory adult patients at 100 days is 18%. For patients who underwent second, or greater HSCT for B-cell ALL (n = 52), 23% developed VOD/SOS (66% adults and 33% pediatrics). Incidence of VOD for relapsed/refractory adult patients after their second or greater HSCT is 22%.

Among patients who underwent first alloHSCT for B-cell ALL and developed VOD (51 patients), median follow-up was 2.92 months (adult, 6.57 months, pediatric, 1.83 months) after VOD with survival of 13 adults and 9 pediatrics out of total 35 adults and 16 pediatrics.

Among patients who underwent second, or greater HSCT for B-cell ALL and developed VOD (12 patients), median follow-up was 4.07 months (adult,13.60 months, pediatric, 0.85 months) after VOD. All 4 pediatric patients and 3 out of 8 adult patients died.

In adult patients (n=244), the 18-month OS was 54% (95% CI, 47-61; Table 13) and 18-month TRM was 22% (95% CI, 17-27; Table 16). This TRM rate compares favorably to published data. Pfizer had TRM data from both the INOVATE trial and pooled analyses[13].

In the INOVATE trial, 12-month TRM was 37% (95% CI, 26-47); and 18-month TRM was 38% (95% CI, 27-49). In pooled analyses, 12-month TRM was 38% (95% CI, 28-47); and 24-month TRM was 39% (95% CI, 30-50); 24-month TRM was 34.5% for those patients who proceeded to first HSCT.

Given the relatively small number of pediatric patients accrued for this final report, these time-to-event endpoints were not calculated.

The multivariable analysis confirms the adverse impact of conditioning regimens that contain dual alkylators on day-100 VOD as well as on 1-year TRM. Patients receiving these regimens should be considered for clinical trials testing novel prophylactic interventions for post-HSCT endothelial dysfunction syndromes, such as VOD.

### 11.4. Generalizability

This study is generalizable to post-HSCT B-cell precursor B-cell ALL patients following treatment with inotuzumab ozogamicin in the US. Because supportive treatment for B-cell ALL and post-HSCT AEs differ from country to country based on country-specific treatment guidelines, the findings from this study may not be generalizable to patients with B-cell ALL outside of the US. Since HSCT also results in AEs, the findings of this study may not be generalizable to patients with B-cell ALL who are treated with inotuzumab ozogamicin but who do not proceed to HSCT.

## 12. OTHER INFORMATION

Not applicable.

## 13. CONCLUSIONS

In conclusion, data collected between August 2017 and August 2022 in the CIBMTR Research Database suggest that the safety data obtained from the use of inotuzumab ozogamicin in the real-world post-transplant setting appear to be consistent with the data observed in Phase 3 Study B1931022. Among pre-HSCT inotuzumab recipients, in an analysis of a subset of patients, the cumulative exposure did not increase the day 100 VOD risk. The analysis confirms the negative prognostic impact of the use of dual alkylating agents in the conditioning regimen on the risk of VOD among patients who received inotuzumab ozogamicin prior to HSCT, which was shown previously by Kantarjian et al.[14]

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## 15. LIST OF SOURCE TABLES AND FIGURES

Not Applicable.

# 16. SUPPLEMENTARY ANALYSES

## 16.1. Relapsed/refractory subset and remission subset

### 16.1.1. R/R subset demographic, baseline characteristics, and comorbid conditions

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| No. of centers | 20 | 48 | 54 |
| Age, years, no. (%) | | | |
| < 1 | 1 (2) | 0 | 1 (0) |
| 1-9 | 24 (50) | 0 | 24 (11) |
| 10-17 | 23 (48) | 0 | 23 (11) |
| 18-29 | 0 | 62 (37) | 62 (29) |
| 30-39 | 0 | 31 (19) | 31 (14) |
| 40-49 | 0 | 33 (20) | 33 (15) |
| 50-59 | 0 | 19 (11) | 19 (9) |
| ≥ 60 | 0 | 21 (13) | 21 (10) |
| Number evaluable | 48 | 166 | 214 |
| Median | 9 | 36 | 28.5 |
| Range | (0-17) | (18-75) | (0-75) |
| Mean | 9.3 | 38.7 | 32.1 |
| Standard deviation | 5.2 | 15.2 | 18.4 |
| Race, no. (%) | | | |
| White | 38 (79) | 125 (75) | 163 (76) |
| Black or African American | 1 (2) | 13 (8) | 14 (7) |
| Asian/Native Hawaiian and other Pacific Islander | 1 (2) | 12 (7) | 13 (6) |
| Others | 2 (4) | 1 (1) | 3 (1) |
| Not reported | 6 (13) | 15 (9) | 21 (10) |
| Weight, kg | | | |
| Number evaluable | 48 | 166 | 214 |
| Median | 33 | 83 | 78 |
| Range | (8-126) | (32-203) | (8-203) |
| Mean | 41 | 89 | 78 |
| Standard deviation | 27 | 29 | 35 |
| Body mass index, $kg/m^2$, no. (%) | | | |
| N/A; BMI does not apply to pediatric patients | 48 | 0 | 48 (22) |
| Underweight | 0 | 8 (5) | 8 (4) |
| Healthy weight | 0 | 32 (19) | 32 (15) |
| Overweight | 0 | 48 (29) | 48 (22) |
| Obese | 0 | 78 (47) | 78 (36) |
| Number evaluable | 48 | 166 | 214 |
| Median | 19.1 | 29.6 | 27.6 |
| Range | (14.6-46.3) | (12.2-62.5) | (12.2-62.5) |
| Mean | 21 | 30.6 | 28.5 |
| Standard deviation | 6.2 | 8.6 | 9.1 |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Body surface area, $m^2$ | | | |
| Number evaluable | 48 | 166 | 214 |
| Median | 1.1 | 2 | 1.9 |
| Range | (0.4-2.4) | (1.2-3.2) | (0.4-3.2) |
| Mean | 1.2 | 2 | 1.8 |
| Standard deviation | 0.5 | 0.4 | 0.5 |
| Height, cm | | | |
| Number evaluable | 48 | 166 | 214 |
| Median | 135.5 | 170 | 167.8 |
| Range | (67-176) | (130-191) | (67-191) |
| Mean | 131.8 | 169.7 | 161.2 |
| Standard deviation | 30.3 | 9.9 | 23 |
| Sex, no. (%) | | | |
| Male | 27 (56) | 86 (52) | 113 (53) |
| Female | 21 (44) | 80 (48) | 101 (47) |
| Sorror HCT-CI, no. (%) [a] | | | |
| 0 | 18 (38) | 23 (14) | 41 (19) |
| 1-2 | 19 (40) | 57 (34) | 76 (36) |
| 3-4 | 10 (21) | 59 (36) | 69 (32) |
| 5 | 1 (2) | 13 (8) | 14 (7) |
| 6 | 0 | 5 (3) | 5 (2) |
| 7 | 0 | 3 (2) | 3 (1) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Arrhythmia, no. (%) [b] | | | |
| Yes | 1 (2) | 10 (6) | 11 (5) |
| No | 47 (98) | 150 (90) | 197 (92) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Cardiac disease, no. (%) [c] | | | |
| Yes | 1 (2) | 8 (5) | 9 (4) |
| No | 47 (98) | 152 (92) | 199 (93) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Cerebrovascular disease, no. (%) [d] | | | |
| Yes | 0 | 6 (4) | 6 (3) |
| No | 48 | 154 (93) | 202 (94) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Hepatic disease, no. (%) | | | |
| Moderate/severe [e] | 5 (10) | 9 (5) | 14 (7) |
| Mild [f] | 13 (27) | 37 (22) | 50 (23) |
| No hepatic disease | 30 (63) | 114 (69) | 144 (67) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Lines of salvage therapy prior to transplant, no. (%) [g] | | | |
| N/A: CIBMTR Form 2011 not yet received | 4 (8) | 8 (5) | 12 (6) |
| Salvage 1 | 6 (13) | 19 (11) | 25 (12) |
| Salvage 2 | 2 (4) | 39 (23) | 41 (19) |
| Salvage > 2 | 28 (58) | 89 (54) | 117 (55) |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Outliers | 8 (17) | 10 (6) | 18 (8) |
| Not reported | 0 | 1 (1) | 1 (0) |
| Number evaluable | 36 | 147 | 183 |
| Median | 6 | 4 | 4 |
| Range | (2-14) | (2-10) | (2-14) |
| Mean | 6 | 4.3 | 4.6 |
| Standard deviation | 3.3 | 1.8 | 2.3 |
| Lines of salvage therapy prior to inotuzumab ozogamicin, no. (%) | | | |
| N/A: CIBMTR Form 2011 not yet received | 4 (8) | 8 (5) | 12 (6) |
| No treatment given [h] | 1 (2) | 6 (4) | 7 (3) |
| First line | 5 (10) | 26 (16) | 31 (14) |
| Salvage 1 | 2 (4) | 39 (23) | 41 (19) |
| Salvage 2 | 8 (17) | 39 (23) | 47 (22) |
| Salvage > 2 | 20 (42) | 33 (20) | 53 (25) |
| Outliers | 8 (17) | 10 (6) | 18 (8) |
| Not reported | 0 | 5 (3) | 5 (2) |
| Number evaluable | 36 | 143 | 179 |
| Median | 4.5 | 3 | 3 |
| Range | (0-13) | (0-8) | (0-13) |
| Mean | 4.6 | 2.7 | 3.1 |
| Standard deviation | 3 | 1.6 | 2.1 |
| Aspartate transaminase (AST), prior to transplant, no. (%) | | | |
| N/A: necessary form not yet received | 1 (2) | 5 (3) | 6 (3) |
| Normal | 17 (35) | 107 (64) | 124 (58) |
| Abnormal | 30 (63) | 53 (32) | 83 (39) |
| Not reported | 0 | 1 (1) | 1 (0) |
| Number evaluable | 47 | 160 | 207 |
| Median | 1.2 | 0.9 | 0.9 |
| Range | (0.3-3.6) | (0.3-3.3) | (0.3-3.6) |
| Mean | 1.3 | 1 | 1 |
| Standard deviation | 0.7 | 0.5 | 0.5 |
| Total serum bilirubin, prior to transplant, no. (%) | | | |
| N/A: necessary form not yet received | 1 (2) | 5 (3) | 6 (3) |
| Normal | 44 (92) | 142 (86) | 186 (87) |
| Abnormal | 3 (6) | 17 (10) | 20 (9) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Number evaluable | 47 | 159 | 206 |
| Median | 0.3 | 0.4 | 0.4 |
| Range | (0-1.1) | (0.2-4.4) | (0-4.4) |
| Mean | 0.4 | 0.6 | 0.5 |
| Standard deviation | 0.3 | 0.5 | 0.5 |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Platelets, × $10^9$/L, prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 5 (3) | 6 (3) |
| Not reported | 1 (2) | 7 (4) | 8 (4) |
| Number evaluable | 46 | 154 | 200 |
| Median | 125 | 109.5 | 115 |
| Range | (9-310) | (11-316) | (9-316) |
| Mean | 127 | 120.1 | 121.6 |
| Standard deviation | 74.5 | 67.3 | 68.9 |
| Neutrophils, prior to transplant, × $10^9$/L, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 5 (3) | 6 (3) |
| Not reported | 2 (4) | 4 (2) | 6 (3) |
| Number evaluable | 45 | 157 | 202 |
| Median | 46 | 57 | 56 |
| Range | (6-86) | (4-95) | (4-95) |
| Mean | 48.3 | 55.5 | 53.9 |
| Standard deviation | 19.2 | 16.7 | 17.5 |
| Hemoglobin, prior to transplant, g/dL, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 5 (3) | 6 (3) |
| Number evaluable | 47 | 161 | 208 |
| Median | 11.6 | 12.2 | 12.1 |
| Range | (6.7-16.3) | (6.4-17.7) | (6.4-17.7) |
| Mean | 11.5 | 12.1 | 11.9 |
| Standard deviation | 1.8 | 2.2 | 2.1 |
| White blood cell (WBC) count at diagnosis, × $10^9$/L, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (8) | 8 (5) | 12 (6) |
| Not reported | 9 (19) | 22 (13) | 31 (14) |
| Number evaluable | 35 | 136 | 171 |
| Median | 10 | 14.5 | 13.3 |
| Range | (0.4-525) | (0.5-368) | (0.4-525) |
| Mean | 49 | 54.3 | 53.2 |
| Standard deviation | 104.6 | 82.2 | 86.9 |
| Blasts in blood, at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | |
| N/A: Form 2011 form not yet received | 4 (8) | 8 (5) | 12 (6) |
| < 1% | 1 (2) | 12 (7) | 13 (6) |
| ≥ 1% | 27 (56) | 114 (69) | 141 (66) |
| Not reported | 16 (33) | 32 (19) | 48 (22) |
| Number evaluable | 28 | 126 | 154 |
| Median | 51 | 58 | 56 |
| Range | (0-98) | (0-99) | (0-99) |
| Mean | 51.5 | 50.8 | 50.9 |
| Standard deviation | 32.6 | 34.3 | 33.9 |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Blasts in bone marrow, at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | |
| N/A: Form 2011 form not yet received | 4 (8) | 8 (5) | 12 (6) |
| < 50% | 4 (8) | 10 (6) | 14 (7) |
| 50-89% | 9 (19) | 54 (33) | 63 (29) |
| ≥ 90% | 15 (31) | 60 (36) | 75 (35) |
| Not reported | 16 (33) | 34 (20) | 50 (23) |
| Number evaluable | 28 | 124 | 152 |
| Median | 90 | 89 | 89 |
| Range | (10-98) | (2-100) | (2-100) |
| Mean | 78 | 80.3 | 79.9 |
| Standard deviation | 26.8 | 21.6 | 22.6 |
| White blood cell (WBC) count prior to transplant, × $10^9$/L, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 1 (2) | 4 (2) | 5 (2) |
| Number evaluable | 47 | 162 | 209 |
| Median | 3.4 | 3.4 | 3.4 |
| Range | (0.4-11.8) | (0.3-9.6) | (0.3-11.8) |
| Mean | 3.9 | 3.7 | 3.8 |
| Standard deviation | 2.5 | 2.1 | 2.2 |
| Blasts in blood prior to transplant, × $10^9$/L, no. (%) | | | |
| N/A: Form 2011 form not yet received | 4 (8) | 8 (5) | 12 (6) |
| < 1% | 28 (58) | 120 (72) | 148 (69) |
| ≥ 1% | 1 (2) | 5 (3) | 6 (3) |
| Not reported | 15 (31) | 33 (20) | 48 (22) |
| Number evaluable | 29 | 125 | 154 |
| Median | 0 | 0 | 0 |
| Range | (0-4) | (0-2) | (0-4) |
| Mean | 0.14 | 0.06 | 0.07 |
| Standard deviation | 0.74 | 0.29 | 0.41 |
| Blasts in bone marrow, prior to transplant, × $10^9$/L, no. (%) | | | |
| N/A: Form 2011 form not yet received | 4 (8) | 8 (5) | 12 (6) |
| < 5% | 35 (73) | 136 (82) | 171 (80) |
| ≥ 5% | 1 (2) | 2 (1) | 3 (1) |
| Not reported | 8 (17) | 20 (12) | 28 (13) |
| Number evaluable | 36 | 138 | 174 |
| Median | 0 | 1 | 1 |
| Range | (0-94) | (0-7) | (0-94) |
| Mean | 3.14 | 1.28 | 1.67 |
| Standard deviation | 15.6 | 1.36 | 7.16 |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Extramedullary disease, at diagnosis of B-cell ALL, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (8) | 8 (5) | 12 (6) |
| Yes | 6 (13) | 19 (11) | 25 (12) |
| No | 19 (40) | 121 (73) | 140 (65) |
| Unknown | 2 (4) | 10 (6) | 12 (6) |
| Not reported | 17 (35) | 8 (5) | 25 (12) |
| Extramedullary disease, at last evaluation prior to transplant, no. (%) | | | |
| N/A; CIBMTR Form 2011 not yet received | 4 (8) | 8 (5) | 12 (6) |
| Yes | 1 (2) | 6 (4) | 7 (3) |
| No | 43 (90) | 147 (89) | 190 (89) |
| Unknown | 0 | 4 (2) | 4 (2) |
| Not reported | 0 | 1 (1) | 1 (0) |
| Performance score prior to transplant, no. (%) | | | |
| Karnofsky, 90-100 | 7 (15) | 90 (54) | 97 (45) |
| Karnofsky, 10-80 | 0 | 70 (42) | 70 (33) |
| Karnofsky, Not reported | 0 | 6 (4) | 6 (3) |
| Lansky, 90-100 | 36 (75) | 0 | 36 (17) |
| Lansky, 10-80 | 5 (10) | 0 | 5 (2) |
| History of proven invasive fungal infection, no. (%) | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (2) | 5 (3) | 6 (3) |
| Yes | 8 (17) | 6 (4) | 14 (7) |
| No | 39 (81) | 154 (93) | 193 (90) |
| Not reported | 0 | 1 (1) | 1 (0) |
| Disease status prior to transplant, no. (%) | | | |
| CR2 | 23 (48) | 121 (73) | 144 (67) |
| CR3+ | 25 (52) | 28 (17) | 53 (25) |
| REL1 | 0 | 10 (6) | 10 (5) |
| REL3+ | 0 | 3 (2) | 3 (1) |
| PIF | 0 | 4 (2) | 4 (2) |
| Prior autologous HSCT, no. (%) | | | |
| Yes | 0 | 1 (1) | 1 (0) |
| No | 48 | 165 (99) | 213 (100) |
| Time from diagnosis to HSCT, months, no. (%) | | | |
| < 3 | 1 (2) | 1 (1) | 2 (1) |
| 3-5 | 0 | 1 (1) | 1 (0) |
| 6-11 | 5 (10) | 30 (18) | 35 (16) |
| ≥12 | 25 (52) | 94 (57) | 119 (56) |
| Outliers[i] | 17 (35) | 40 (24) | 57 (27) |
| Number evaluable | 31 | 126 | 157 |
| Median | 24.64 | 19.45 | 20.9 |
| Range | (2.89-47.57) | (2.96-47.64) | (2.89-47.64) |
| Mean | 26.61 | 21.99 | 22.9 |
| Standard deviation | 13.19 | 11.69 | 12.1 |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Time from diagnosis to first dose of inotuzumab ozogamicin, months, no. (%) | | | |
| < 3 | 1 (2) | 5 (3) | 6 (3) |
| 3-5 | 0 | 12 (7) | 12 (6) |
| 6-11 | 7 (15) | 24 (14) | 31 (14) |
| ≥12 | 22 (46) | 79 (48) | 101 (47) |
| Outliers[i] | 14 (29) | 33 (20) | 47 (22) |
| Not reported | 4 (8) | 13 (8) | 17 (8) |
| Number evaluable | 30 | 120 | 150 |
| Median | 21.11 | 16.2 | 17.38 |
| Range | (0.3-46.09) | (1.28-44.35) | (0.3-46.09) |
| Mean | 23.43 | 18.78 | 19.71 |
| Standard deviation | 13.07 | 11.81 | 12.17 |
| GVHD prophylaxis, no. (%) | | | |
| Ex-vivo T-cell depletion | 7 (15) | 3 (2) | 10 (5) |
| CD34 selection | 0 | 1 (1) | 1 (0) |
| Cyclophosphamide ± others | 17 (35) | 71 (43) | 88 (41) |
| Tac + MMF ± others (not Cy) | 3 (6) | 22 (13) | 25 (12) |
| Tac + MTX ± others (not Cy, MMF) | 4 (8) | 49 (30) | 53 (25) |
| Tac ± others (not Cy, MMF, MTX) | 0 | 4 (2) | 4 (2) |
| CsA + MMF ± others (not Cy, Tac) | 6 (13) | 4 (2) | 10 (5) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 8 (17) | 11 (7) | 19 (9) |
| CsA ± others (not Cy, Tac, MMF, MTX) | 1 (2) | 0 | 1 (0) |
| Others (not Cy, Tac, CsA) | 0 | 1 (1) | 1 (0) |
| Not reported | 2 (4) | 0 | 2 (0) |
| Conditioning regimen intensity, no. (%) [j] | | | |
| N/A necessary form (F2000) not completed | 1 (2) | 5 (3) | 6 (3) |
| Myeloablative | 45 (94) | 88 (53) | 133 (62) |
| RIC/NMA | 2 (4) | 70 (42) | 72 (34) |
| Not reported [k] | 0 | 3 (2) | 3 (1) |
| Dual alkylators used in conditioning regimen, no. (%)[l] | | | |
| Yes | 13 (27) | 14 (8) | 27 (13) |
| No | 34 (71) | 147 (89) | 181 (85) |
| Not reported | 1 (2) | 5 (3) | 6 (3) |
| Busulfan used in conditioning regimen, no. (%) | | | |
| Yes | 4 (8) | 20 (12) | 24 (11) |
| No | 43 (90) | 141 (85) | 184 (86) |
| Not reported | 1 (2) | 5 (3) | 6 (3) |
| Thiotepa used in conditioning regimen, no. (%) | | | |
| Yes | 13 (27) | 16 (10) | 29 (14) |
| No | 34 (71) | 145 (87) | 179 (84) |
| Not reported | 1 (2) | 5 (3) | 6 (3) |

**Table 51. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **48** | **166** | **214** |
| Product type, no. (%) | | | |
| BM | 26 (54) | 31 (19) | 57 (27) |
| PBSC | 14 (29) | 121 (73) | 135 (63) |
| UCB | 8 (17) | 14 (8) | 22 (10) |
| Donor type, no. (%) | | | |
| HLA-identical sibling | 9 (19) | 42 (25) | 51 (24) |
| Other related | 16 (33) | 50 (30) | 66 (31) |
| Unrelated | 23 (48) | 74 (45) | 97 (45) |
| Inotuzumab given in last line of therapy, no. (%) | | | |
| N/A, Form 2011 not complete or this item queried or therapies not reported | 12 (25) | 23 (14) | 35 (16) |
| No | 2 (4) | 47 (28) | 49 (23) |
| Yes | 34 (71) | 96 (58) | 130 (61) |
| Follow-up, median (range), months | 19.02 (3.32-50.66) | 24.21 (3.29-50.79) | 24.05 (3.29-50.79) |

Note: Median and range values are calculated using only patients with complete data for that variable.
[a] Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. Blood 2004; 104:961-8.
[b] History of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment.
[c] History of coronary artery disease (one or more vessel-coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, OR ejection fraction ≤ 50% on the most recent test.
[d] History of transient ischemic attack, subarachnoid hemorrhage or cerebrovascular accident.
[e] Liver cirrhosis, bilirubin > 1.5 × upper limit of normal, or AST/ALT > 2.5 × upper limit of normal.
[f] Chronic hepatitis, bilirubin > upper limit of normal to 1.5 × upper limit of normal, or AST/ALT > upper limit of normal to 2.5 × upper limit of normal at the time of transplant OR any history of hepatitis B or hepatitis C infection.
[g] The lines of therapy prior to a specified event are defined as follows. “No treatment given” means no lines of therapy given prior to specified event; “First line” means 1 line of therapy; “Salvage 1” means 2 lines of therapy; “Salvage 2” means 3 lines of therapy; “Salvage > 2” means 4 (or more) lines of therapy.
[h] No treatment given” indicates patients who received inotuzumab in first line of therapy, followed by disease relapse and more lines of therapies prior to HSCT.
[i] Outliers are defined as patients who underwent HSCT in CR1 more than 12 months after disease diagnosis, or patients who underwent HSCT for all other disease statuses more than 48 months after disease diagnosis.
[j] Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009;15:1628-33.
[k] CIBMTR staff are querying the transplant center.
[l] Dual alkylators were defined as the conditioning regimen including one of the following pairs of treatments: busulfan + cyclophosphamide; busulfan + melphalan; cyclophosphamide + melphalan; busulfan + thiotepa; or cyclophosphamide + thiotepa.

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| No. of centers | 46 | 6 | 8 | 46 |
| Age, years, no. (%) | | | | |
| 18-29 | 44 (34) | 5 (56) | 8 (44) | 57 (37) |
| 30-39 | 25 (19) | 3 (33) | 1 (6) | 29 (19) |
| 40-49 | 26 (20) | 1 (11) | 5 (28) | 32 (21) |
| 50-59 | 16 (12) | 0 | 1 (6) | 17 (11) |
| ≥ 60 | 18 (14) | 0 | 3 (17) | 21 (13) |
| Number evaluable | 129 | 9 | 18 | 156 |
| Median | 38 | 28 | 36 | 36 |
| Range | (18-75) | (20-42) | (20-66) | (18-75) |
| Mean | 39.9 | 29.2 | 37.6 | 39 |
| Standard deviation | 15.5 | 8 | 16 | 15.4 |
| Race, no. (%) | | | | |
| White | 97 (75) | 7 (78) | 16 (89) | 120 (77) |
| Black or African American | 12 (9) | 0 | 1 (6) | 13 (8) |
| Asian/Native Hawaiian and other Pacific Islander | 10 (8) | 0 | 1 (6) | 11 (7) |
| Others | 10 (8) | 2 (22) | 0 | 12 (8) |
| Not reported | 97 (75) | 7 (78) | 16 (89) | 120 (77) |
| Body mass index, $kg/m^2$, no. (%) | | | | |
| Underweight | 4 (3) | 0 | 3 (17) | 7 (4) |
| Healthy weight | 23 (18) | 2 (22) | 4 (22) | 29 (19) |
| Overweight | 39 (30) | 2 (22) | 3 (17) | 44 (28) |
| Obese | 63 (49) | 5 (56) | 8 (44) | 76 (49) |
| Number evaluable | 129 | 9 | 18 | 156 |
| Median | 29.9 | 30 | 29.1 | 29.9 |
| Range | (12.2-60.1) | (20.6-54.3) | (17.1-62.5) | (12.2-62.5) |
| Mean | 30.9 | 30.8 | 30.3 | 30.8 |
| Standard deviation | 8.2 | 10 | 11.8 | 8.7 |
| Sex, no. (%) | | | | |
| Male | 64 (50) | 6 (67) | 11 (61) | 81 (52) |
| Female | 65 (50) | 3 (33) | 7 (39) | 75 (48) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Sorror HCT-CI, no. (%) [a] | | | | |
| 0 | 19 (15) | 1 (11) | 3 (17) | 23 (15) |
| 1-2 | 41 (32) | 6 (67) | 5 (28) | 52 (33) |
| 3-4 | 46 (36) | 1 (11) | 9 (50) | 56 (36) |
| 5 | 12 (9) | 1 (11) | 0 | 13 (8) |
| 6 | 4 (3) | 0 | 0 | 4 (3) |
| 7 | 2 (2) | 0 | 1 (6) | 3 (2) |
| Not reported | 5 (4) | 0 | 0 | 5 (3) |
| Arrhythmia, no. (%) [b] | | | | |
| Yes | 6 (5) | 0 | 3 (17) | 9 (6) |
| No | 118 (91) | 9 | 15 (83) | 142 (91) |
| Not reported | 5 (4) | 0 | 0 | 5 (3) |
| Cardiac disease, no. (%) [c] | | | | |
| Yes | 7 (5) | 0 | 1 (6) | 8 (5) |
| No | 117 (91) | 9 | 17 (94) | 143 (92) |
| Not reported | 5 (4) | 0 | 0 | 5 (3) |
| Cerebrovascular disease, no. (%) [d] | | | | |
| Yes | 4 (3) | 1 (11) | 1 (6) | 6 (4) |
| No | 120 (93) | 8 (89) | 17 (94) | 145 (93) |
| Not reported | 5 (4) | 0 | 0 | 5 (3) |
| Hepatic disease, no. (%) | | | | |
| Moderate/severe [e] | 8 (6) | 0 | 1 (6) | 9 (6) |
| Mild [f] | 27 (21) | 3 (33) | 4 (22) | 34 (22) |
| No hepatic disease | 89 (69) | 6 (67) | 13 (72) | 108 (69) |
| Not reported | 5 (4) | 0 | 0 | 5 (3) |
| Lines of salvage therapy prior to transplant, no. (%) [g] | | | | |
| N/A: CIBMTR Form 2011 not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| Salvage 1 | 17 (13) | 0 | 2 (11) | 19 (12) |
| Salvage 2 | 28 (22) | 2 (22) | 7 (39) | 37 (24) |
| Salvage > 2 | 73 (57) | 6 (67) | 8 (44) | 87 (56) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (6) | 1 (11) | 0 | 9 (6) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Number evaluable | 118 | 8 | 17 | 143 |
| Median | 4 | 4 | 3 | 4 |
| Range | (2-10) | (3-6) | (2-8) | (2-10) |
| Mean | 4.4 | 4.3 | 4.1 | 4.3 |
| Standard deviation | 1.9 | 1 | 1.7 | 1.8 |
| Lines of salvage therapy prior to inotuzumab ozogamicin, no. (%) | | | | |
| N/A: CIBMTR Form 2011 not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| No treatment given [h] | 3 (2) | 1 (11) | 2 (11) | 6 (4) |
| First line | 22 (17) | 1 (11) | 3 (17) | 26 (17) |
| Salvage 1 | 30 (23) | 2 (22) | 5 (28) | 37 (24) |
| Salvage 2 | 32 (25) | 2 (22) | 4 (22) | 38 (24) |
| Salvage > 2 | 28 (22) | 2 (22) | 3 (17) | 33 (21) |
| Outliers (inconsistency between disease status and total lines of therapies) | 8 (6) | 1 (11) | 0 | 9 (6) |
| Not reported | 3 (2) | 0 | 0 | 3 (2) |
| Number evaluable | 115 | 8 | 17 | 140 |
| Median | 3 | 2.5 | 2 | 3 |
| Range | (0-8) | (0-4) | (0-5) | (0-8) |
| Mean | 2.8 | 2.4 | 2.3 | 2.7 |
| Standard deviation | 1.6 | 1.4 | 1.5 | 1.6 |
| Aspartate transaminase (AST), prior to transplant, no. (%) | | | | |
| N/A: necessary form not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Normal | 87 (67) | 6 (67) | 11 (61) | 104 (67) |
| Abnormal | 41 (32) | 3 (33) | 6 (33) | 50 (32) |
| Not reported | 0 | 0 | 1 (6) | 1 (1) |
| Number evaluable | 128 | 9 | 17 | 154 |
| Median | 0.9 | 0.9 | 0.8 | 0.9 |
| Range | (0.3-2.9) | (0.4-1.6) | (0.4-3.3) | (0.3-3.3) |
| Mean | 1 | 0.9 | 0.9 | 0.9 |
| Standard deviation | 0.4 | 0.4 | 0.7 | 0.5 |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Total serum bilirubin, prior to transplant, no. (%) | | | | |
| N/A: necessary form not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Normal | 113 (88) | 8 (89) | 15 (83) | 136 (87) |
| Abnormal | 14 (11) | 1 (11) | 2 (11) | 17 (11) |
| Not reported | 1 (1) | 0 | 1 (6) | 2 (1) |
| Number evaluable | 127 | 9 | 17 | 153 |
| Median | 0.4 | 0.5 | 0.4 | 0.4 |
| Range | (0.2-1.8) | (0.2-1.4) | (0.2-4.4) | (0.2-4.4) |
| Mean | 0.5 | 0.6 | 0.8 | 0.6 |
| Standard deviation | 0.4 | 0.4 | 1.2 | 0.5 |
| Platelets, $\times 10^9$/L, prior to transplant, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Not reported | 5 (4) | 1 (11) | 1 (6) | 7 (4) |
| Number evaluable | 123 | 8 | 17 | 148 |
| Median | 114 | 89.5 | 110 | 109.5 |
| Range | (11-316) | (60-303) | (11-283) | (11-316) |
| Mean | 119.1 | 133.5 | 119.8 | 119.9 |
| Standard deviation | 65.3 | 89.7 | 71.8 | 67 |
| Neutrophils, prior to transplant, $\times 10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Not reported | 3 (2) | 0 | 1 (6) | 4 (3) |
| Number evaluable | 125 | 9 | 17 | 151 |
| Median | 57 | 59 | 53 | 57 |
| Range | (4-95) | (31-84) | (7-84) | (4-95) |
| Mean | 55.7 | 59.2 | 51.8 | 55.5 |
| Standard deviation | 16.2 | 16.5 | 21.8 | 16.9 |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Hemoglobin, prior to transplant, g/dL, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Number evaluable | 128 | 9 | 18 | 155 |
| Median | 12.1 | 12.6 | 12.5 | 12.2 |
| Range | (6.4-17.7) | (10.3-15.3) | (7.3-16.8) | (6.4-17.7) |
| Mean | 11.9 | 12.8 | 12.4 | 12 |
| Standard deviation | 2.2 | 1.5 | 2.3 | 2.2 |
| White blood cell (WBC) count at diagnosis, $\times 10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| Not reported | 16 (12) | 0 | 5 (28) | 21 (13) |
| Number evaluable | 110 | 9 | 12 | 131 |
| Median | 14.5 | 13.6 | 15.4 | 14.6 |
| Range | (0.5-368) | (0.7-25.2) | (1.1-148.6) | (0.5-368) |
| Mean | 61.2 | 14.2 | 35.3 | 55.6 |
| Standard deviation | 88.4 | 8.8 | 48.1 | 83.2 |
| Blasts in blood, at diagnosis of B-cell ALL, $\times 10^9$/L, no. (%) | | | | |
| N/A: Form 2011 form not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| < 1% | 9 (7) | 1 (11) | 1 (6) | 11 (7) |
| ≥ 1% | 94 (73) | 8 (89) | 8 (44) | 110 (71) |
| Not reported | 23 (18) | 0 | 8 (44) | 31 (20) |
| Number evaluable | 103 | 9 | 9 | 121 |
| Median | 57 | 74 | 70 | 61 |
| Range | (0-99) | (0-96) | (0-92) | (0-99) |
| Mean | 50.4 | 61.8 | 59.4 | 51.9 |
| Standard deviation | 34.3 | 34.2 | 33.7 | 34.2 |
| Blasts in bone marrow, at diagnosis of B-cell ALL, $\times 10^9$/L, no. (%) | | | | |
| N/A: Form 2011 form not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| < 50% | 7 (5) | 2 (22) | 1 (6) | 10 (6) |
| 50-89% | 42 (33) | 3 (33) | 4 (28) | 50 (32) |
| ≥ 90% | 51(40) | 4 (44) | 4 (22) | 59 (38) |
| Not reported | 26 (20) | 0 | 7 (39) | 33 (21) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Number evaluable | 100 | 9 | 10 | 119 |
| Median | 90 | 83 | 81.5 | 89 |
| Range | (5-100) | (7-97) | (2-95) | (2-100) |
| Mean | 81.8 | 71.1 | 75.8 | 80.5 |
| Standard deviation | 20.2 | 32.4 | 27.3 | 22 |
| White blood cell (WBC) count prior to transplant, × $10^9$/L, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Number evaluable | 128 | 9 | 18 | 155 |
| Median | 3.3 | 3.7 | 3.8 | 3.3 |
| Range | (0.4-9.6) | (1.9-5.8) | (0.3-8.4) | (0.3-9.6) |
| Mean | 3.6 | 3.6 | 4 | 3.7 |
| Standard deviation | 2 | 1.5 | 2.6 | 2 |
| Blasts in blood prior to transplant, × $10^9$/L, no. (%) | | | | |
| N/A: Form 2011 form not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| < 1% | 96 (74) | 8 (89) | 12 (67) | 116 (74) |
| ≥ 1% | 5 (4) | 0 | 0 | 5 (3) |
| Not reported | 25 (19) | 1 (11) | 5 (28) | 31 (20) |
| Number evaluable | 101 | 8 | 12 | 121 |
| Median | 0 | 0 | 0 | 0 |
| Range | (0-2) | (0-0) | (0-0) | (0-2) |
| Mean | 0.07 | 0 | 0 | 0.06 |
| Standard deviation | 0.32 | 0 | 0 | 0.3 |
| Blasts in bone marrow, prior to transplant, × $10^9$/L, no. (%) | | | | |
| N/A: Form 2011 form not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| < 5% | 108 (84) | 8 (89) | 14 (78) | 130 (83) |
| ≥ 5% | 1 (1) | 1 (11) | 0 | 2 (1) |
| Not reported | 17 (13) | 0 | 3 (17) | 20 (13) |
| Number evaluable | 109 | 9 | 14 | 132 |
| Median | 1 | 1 | 1 | 1 |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Range | (0-7) | (0-5) | (0-3) | (0-7) |
| Mean | 1.28 | 1.22 | 1.43 | 1.3 |
| Standard deviation | 1.39 | 1.64 | 1.09 | 1.37 |
| Extramedullary disease, at diagnosis of B-cell ALL, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| Yes | 15 (12) | 2 (22) | 2 (11) | 19 (12) |
| No | 99 (77) | 7 (78) | 10 (56) | 116 (74) |
| Unknown | 8 (6) | 0 | 2 (11) | 10 (6) |
| Not reported | 4 (3) | 0 | 3 (17) | 7 (4) |
| Extramedullary disease, at last evaluation prior to transplant, no. (%) | | | | |
| N/A; CIBMTR Form 2011 not yet received | 3 (2) | 0 | 1 (6) | 4 (3) |
| Yes | 6 (5) | 0 | 0 | 6 (4) |
| No | 116 (90) | 9 | 16 (89) | 141 (90) |
| Unknown | 3 (2) | 0 | 1 (6) | 4 (3) |
| Not reported | 1 (1) | 0 | 0 | 1 (1) |
| Performance score prior to transplant, no. (%) | | | | |
| Karnofsky, 90-100 | 72 (56) | 3 (33) | 10 (56) | 85 (54) |
| Karnofsky, 10-80 | 53 (41) | 6 (67) | 6 (33) | 65 (42) |
| Karnofsky, Not reported | 4 (3) | 0 | 2 (11) | 6 (4) |
| History of proven invasive fungal infection, no. (%) | | | | |
| N/A; CIBMTR Form 2000 not yet received | 1 (1) | 0 | 0 | 1 (1) |
| Yes | 4 (3) | 0 | 2 (11) | 6 (4) |
| No | 124 (96) | 9 | 15 (83) | 148 (95) |
| Not reported | 0 | 0 | 1 (6) | 1 (1) |
| Disease status prior to transplant, no. (%) | | | | |
| CR2 | 94 (73) | 8 (89) | 12 (67) | 114 (73) |
| CR3+ | 20 (16) | 0 | 6 (33) | 26 (17) |
| REL1 | 9 (7) | 1 (11) | 0 | 10 (6) |
| REL3+ | 3 (2) | 0 | 0 | 3 (2) |
| PIF | 3 (2) | 0 | 0 | 3 (2) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Prior autologous HSCT, no. (%) | | | | |
| Yes | 1 (1) | 0 | 0 | 1 (1) |
| No | 128 (99) | 9 | 18 | 155 (99) |
| Time from diagnosis to HSCT, months, no. (%) | | | | |
| 6-11 | 26 (20) | 2 (22) | 1 (6) | 29 (19) |
| ≥12 | 73 (57) | 5 (56) | 12 (67) | 90 (58) |
| Outliers[i] | 30 (23) | 2 (22) | 5 (28) | 37 (24) |
| Number evaluable | 99 | 7 | 13 | 119 |
| Median | 19.09 | 15.08 | 28.45 | 19.58 |
| Range | (6.21-47.64) | (8.77-42.38) | (10.18-42.68) | (6.21-47.64) |
| Mean | 21.75 | 20.44 | 27.32 | 22.28 |
| Standard deviation | 11.72 | 12.12 | 9.62 | 11.58 |
| Time from diagnosis to first dose of inotuzumab ozogamicin, months, no. (%) | | | | |
| < 3 | 5 (4) | 0 | 0 | 5 (3) |
| 3-5 | 10 (8) | 1 (11) | 0 | 11 (7) |
| 6-11 | 22 (17) | 1 (11) | 1 (6) | 24 (15) |
| ≥12 | 59 (46) | 4 (44) | 12 (67) | 75 (48) |
| Outliers[i] | 27 (21) | 1 (11) | 3 (17) | 31 (20) |
| Not reported | 6 (5) | 2 (22) | 2 (11) | 10 (6) |
| Number evaluable | 96 | 6 | 13 | 115 |
| Median | 15.08 | 16.18 | 24.67 | 16 |
| Range | (1.28-44.35) | (3.02-39.59) | (7.62-40.61) | (1.28-44.35) |
| Mean | 17.96 | 18.85 | 24.34 | 18.73 |
| Standard deviation | 11.91 | 12.99 | 9.91 | 11.83 |
| GVHD prophylaxis, no. (%) | | | | |
| Ex-vivo T-cell depletion | 3 (2) | 0 | 0 | 3 (2) |
| CD34 selection | 1 (1) | 0 | 0 | 1 (1) |
| Cyclophosphamide ± others | 54 (42) | 1 (11) | 9 (50) | 64 (41) |
| Tac + MMF ± others (not Cy) | 19 (15) | 3 (33) | 0 | 22 (14) |
| Tac + MTX ± others (not Cy, MMF) | 38 (29) | 4 (44) | 6 (33) | 48 (31) |
| Tac ± others (not Cy, MMF, MTX) | 3 (2) | 0 | 0 | 3 (2) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| CsA + MMF ± others (not Cy, Tac) | 3 (2) | 0 | 1 (6) | 4 (3) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 7 (5) | 1 (11) | 2 (11) | 10 (6) |
| Others (not Cy, Tac, CsA) | 1 (1) | 0 | 0 | 1 (1) |
| Conditioning regimen intensity, no. (%) [j] | | | | |
| N/A necessary form (F2000) not completed | 1 (1) | 0 | 0 | 1 (1) |
| Myeloablative | 64 (50) | 8 (89) | 11 (61) | 83 (53) |
| RIC/NMA | 61 (47) | 1 (11) | 7 (39) | 69 (44) |
| Not reported [k] | 3 (2) | 0 | 0 | 3 (2) |
| Dual alkylators used in conditioning regimen, no. (%)[l] | | | | |
| Yes | 7 (5) | 2 (22) | 5 (28) | 14 (9) |
| No | 121 (94) | 7 (78) | 13 (72) | 141 (90) |
| Not reported | 1 (1) | 0 | 0 | 1 (1) |
| Busulfan used in conditioning regimen, no. (%) | | | | |
| Yes | 15 (12) | 2 (22) | 3 (17) | 20 (13) |
| No | 113 (88) | 7 (78) | 15 (83) | 135 (87) |
| Not reported | 1 (1) | 0 | 0 | 1 (1) |
| Thiotepa used in conditioning regimen, no. (%) | | | | |
| Yes | 9 (7) | 2 (22) | 5 (28) | 16 (10) |
| No | 119 (92) | 7 (78) | 13 (72) | 139 (89) |
| Not reported | 1 (1) | 0 | 0 | 1 (1) |
| Product type, no. (%) | | | | |
| BM | 19 (15) | 4 (44) | 7 (39) | 30 (19) |
| PBSC | 97 (75) | 4 (44) | 11 (61) | 112 (72) |
| UCB | 13 (10) | 1 (11) | 0 | 14 (9) |
| Donor type, no. (%) | | | | |
| HLA-identical sibling | 32 (25) | 3 (33) | 5 (28) | 40 (26) |
| Other related | 39 (30) | 1 (11) | 7 (39) | 47 (30) |
| Unrelated | 58 (45) | 5 (56) | 6 (33) | 69 (44) |

**Table 52. Characteristics of adult relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and have complete follow-up data, by VOD**

| Characteristic | No VOD | Mild VOD | Severe VOD | Total |
|---|---|---|---|---|
| **No. of patients** | **129** | **9** | **18** | **156** |
| Inotuzumab given in last line of therapy, no. (%) | | | | |
| N/A, Form 2011 not complete or this item queried or therapies not reported | 14 (11) | 1 (11) | 1 (6) | 16 (10) |
| No | 38 (29) | 3 (33) | 6 (33) | 47 (30) |
| Yes | 77 (60) | 5 (56) | 11 (61) | 93 (60) |
| Follow-up, median (range), months | 24.21 (3.61-48.26) | 24.16 (6.34-50.79) | 18.69 (3.29-29.31) | 24.21 (3.29-50.79) |

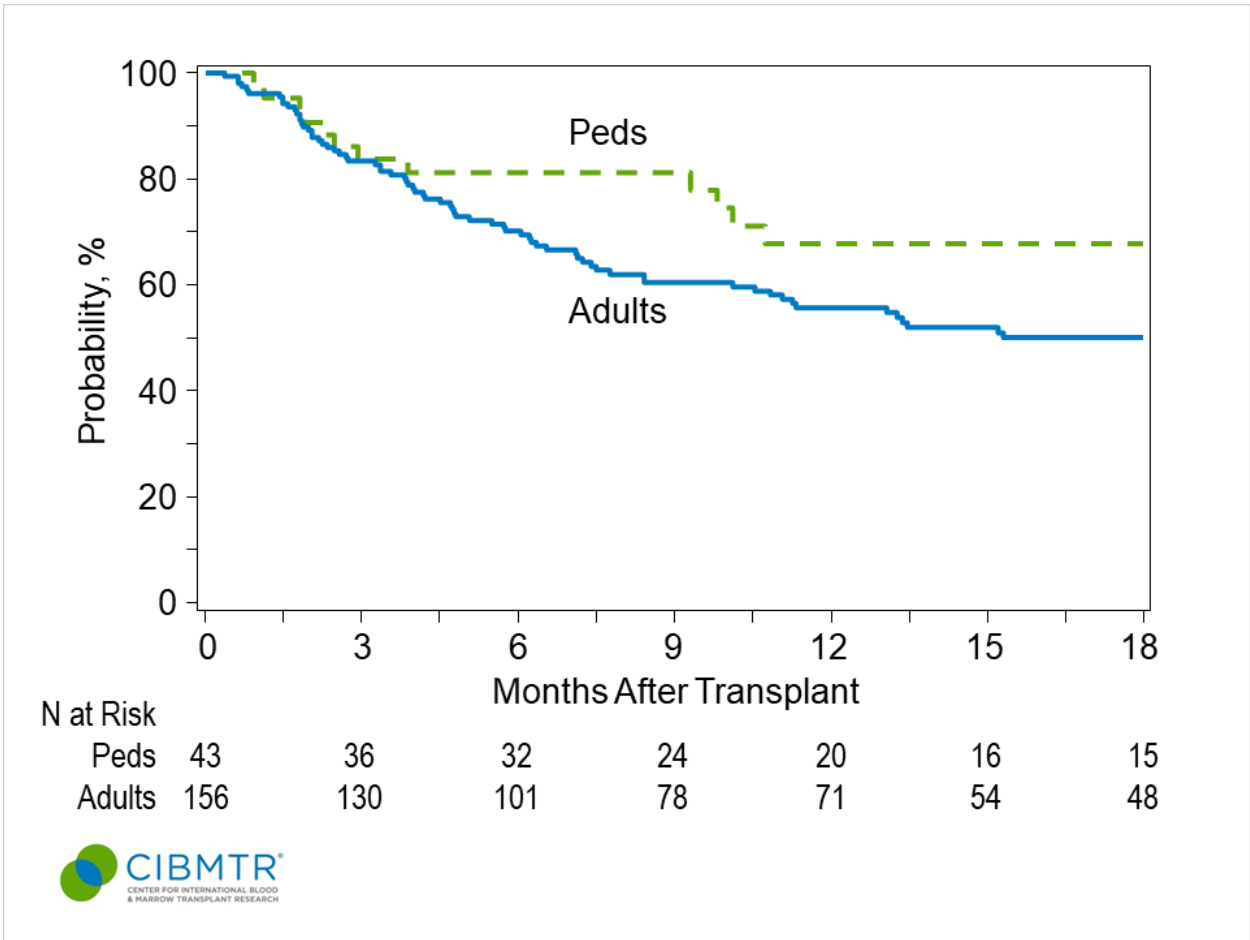
Note: Median and range values are calculated using only patients with complete data for that variable.
[a] Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. Blood 2004; 104:961-8.
[b] History of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment.
[c] History of coronary artery disease (one or more vessel-coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, OR ejection fraction ≤ 50% on the most recent test.
[d] History of transient ischemic attack, subarachnoid hemorrhage or cerebrovascular accident.
[e] Liver cirrhosis, bilirubin > 1.5 × upper limit of normal, or AST/ALT > 2.5 × upper limit of normal.
[f] Chronic hepatitis, bilirubin > upper limit of normal to 1.5 × upper limit of normal, or AST/ALT > upper limit of normal to 2.5 × upper limit of normal at the time of transplant OR any history of hepatitis B or hepatitis C infection.
[g] The lines of therapy prior to a specified event are defined as follows. “No treatment given” means no lines of therapy given prior to specified event; “First line” means 1 line of therapy; “Salvage 1” means 2 lines of therapy; “Salvage 2” means 3 lines of therapy; “Salvage > 2” means 4 (or more) lines of therapy.
[h] No treatment given” indicates patients who received inotuzumab in first line of therapy, followed by disease relapse and more lines of therapies prior to HSCT.
[i] Outliers are defined as patients who underwent HSCT in CR1 more than 12 months after disease diagnosis, or patients who underwent HSCT for all other disease statuses more than 48 months after disease diagnosis.
[j] Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009;15:1628-33.
[k] CIBMTR staff are querying the transplant center.
[l] Dual alkylators were defined as the conditioning regimen including one of the following pairs of treatments: busulfan + cyclophosphamide; busulfan + melphalan; cyclophosphamide + melphalan; busulfan + thiotepa; or cyclophosphamide + thiotepa.

### 16.1.2. R/R subset post-transplant overall survival

**Table 53. Post-transplant overall survival within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Post-transplant overall survival (95% CI) | | | |
| 6 months | 81 (68-91)% | 70 (63-77)% | 72 (66-78)% |
| 12 months | 68 (51-82)% | 56 (47-64)% | 59 (51-66)% |
| 18 months | NE | 50 (41-58)% | 54 (46-61)% |
| Number of deaths within 18 months | 12 | 71 | 83 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 7 (58) | 26 (37) | 33 (40) |
| GVHD | 1 (8) | 9 (13) | 10 (12) |
| VOD/SOS | 2 (17) | 10 (14) | 12 (14) |
| Interstitial pneumonitis | 0 | 4 (6) | 4 (5) |
| Infection | 1 (8) | 6 (8) | 7 (8) |
| Septic shock | 0 | 2 (3) | 2 (2) |
| Hemorrhage | 0 | 4 (6) | 4 (5) |
| Organ failure | 1 (8) | 8 (11) | 9 (11) |
| Graft failure | 0 | 1 (1) | 1 (1) |
| Other | 0 | 1 (1) | 1 (1) |
| Time from transplant to death, no. (%) months | | | |
| < 3 | 7 (58) | 26 (37) | 33 (40) |
| 3-5 | 1 (8) | 20 (28) | 21 (25) |
| 6-11 | 4 (33) | 19 (27) | 23 (28) |
| 12-18 | 0 | 6 (8) | 6 (7) |
| Median (95% CI) | 2.69 (1.81-9.82) | 4.17 (3.35-5.72) | 3.97 (2.92 – 5.06) |
| Range | (0.92-10.74) | (0.36-15.31) | (0.36-15.31) |
| Mean | 4.77 | 5.24 | 5.17 |
| Standard deviation | 3.94 | 3.91 | 3.9 |

**Figure 8 Post-transplant overall survival within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

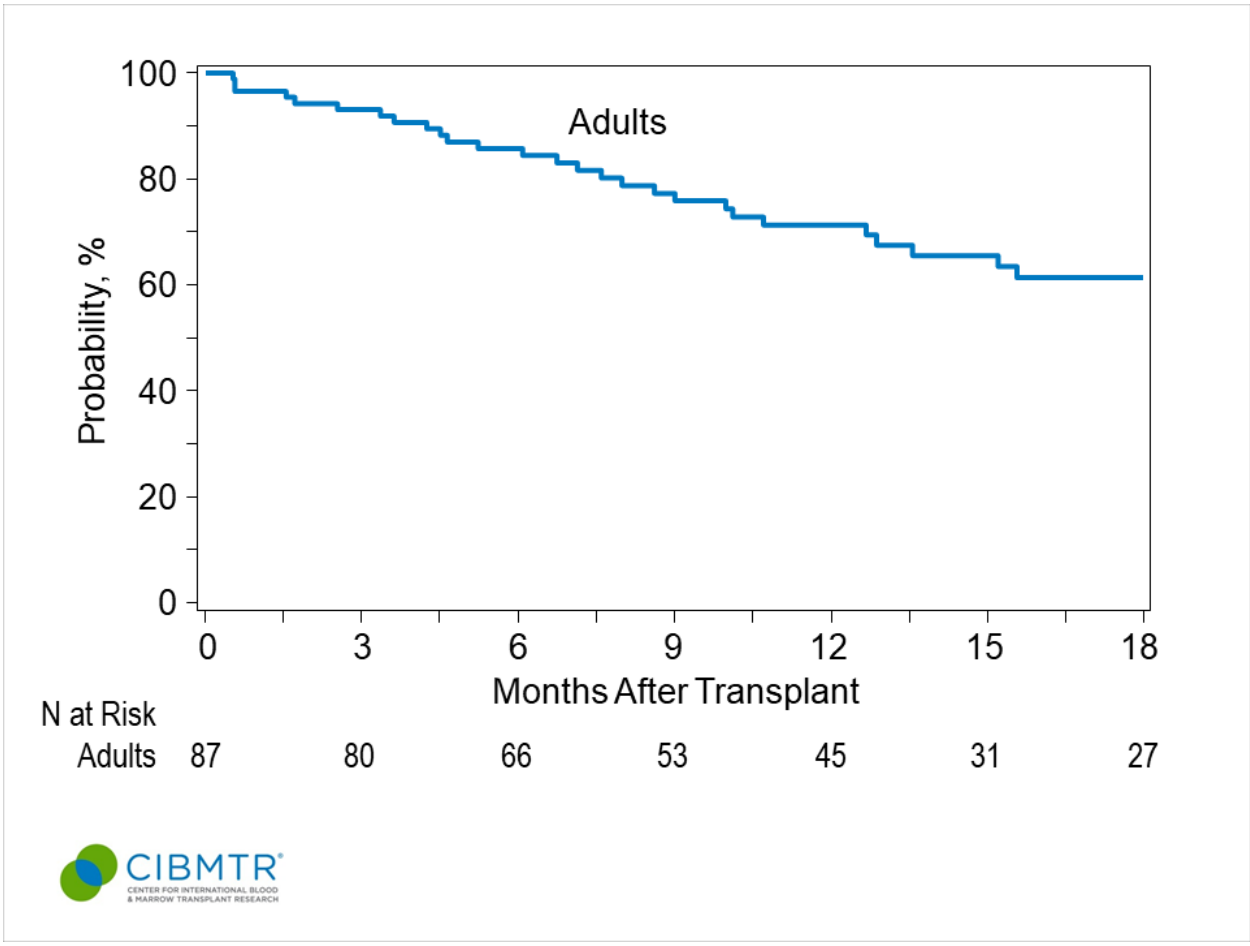


### 16.1.3. Remission subset post-transplant overall survival

**Table 54. Post-transplant overall survival within 18 months in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Post-transplant overall survival (95% CI) | | | |
| 6 months | NE | 86 (77-92)% | 87 (79-93)% |
| 12 months | NE | 71 (60-81)% | 72 (62-82)% |
| 18 months | NE | 61 (49-73)% | 63 (51-74)% |
| Number of deaths within 18 months | 1 | 27 | 28 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 0 | 7 (26) | 7 (25) |
| New malignancy | 0 | 1 (4) | 1 (4) |
| GVHD | 0 | 7 (26) | 7 (25) |
| VOD/SOS | 0 | 5 (19) | 5 (18) |
| Interstitial pneumonitis | 0 | 2 (7) | 2 (7) |
| Infection | 0 | 3 (11) | 3 (11) |
| Thrombotic microangiopathy (TMA) | 1 | 0 | 1 (4) |
| Organ Failure | 0 | 2 (7) | 2 (7) |
| Time from transplant to death, no. (%), months | | | |
| < 3 | 0 | 6 (22) | 6 (21) |
| 3-5 | 0 | 6 (22) | 6 (21) |
| 6-11 | 1 | 10 (37) | 11 (39) |
| 12-18 | 0 | 5 (19) | 5 (18) |
| Median (95% CI) | 8.05 (NE) | 6.74 (4.24 - 9.99) | 6.93 (4.23 - 9.00) |
| Range | NE | (0.53-15.57) | (0.53-15.57) |
| Mean | 8.05 | 6.92 | 6.96 |
| Standard deviation | NE | 4.57 | 4.49 |

**Figure 9 Post-transplant overall survival within 18 months in adult patients in first complete remission prior to HSCT**



### 16.1.4. R/R subset post-transplant overall mortality

**Table 55. Post-transplant overall mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Post-transplant overall mortality (95% CI) | | | |
| 6 months | 19 (9-32)% | 30 (23-37)% | 28 (22-34)% |
| 12 months | 32 (18-49)% | 44 (36-53)% | 41 (34-49)% |
| 18 months | NE | 50 (41-59)% | 46 (39-54)% |

**Figure 10 Post-transplant overall mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

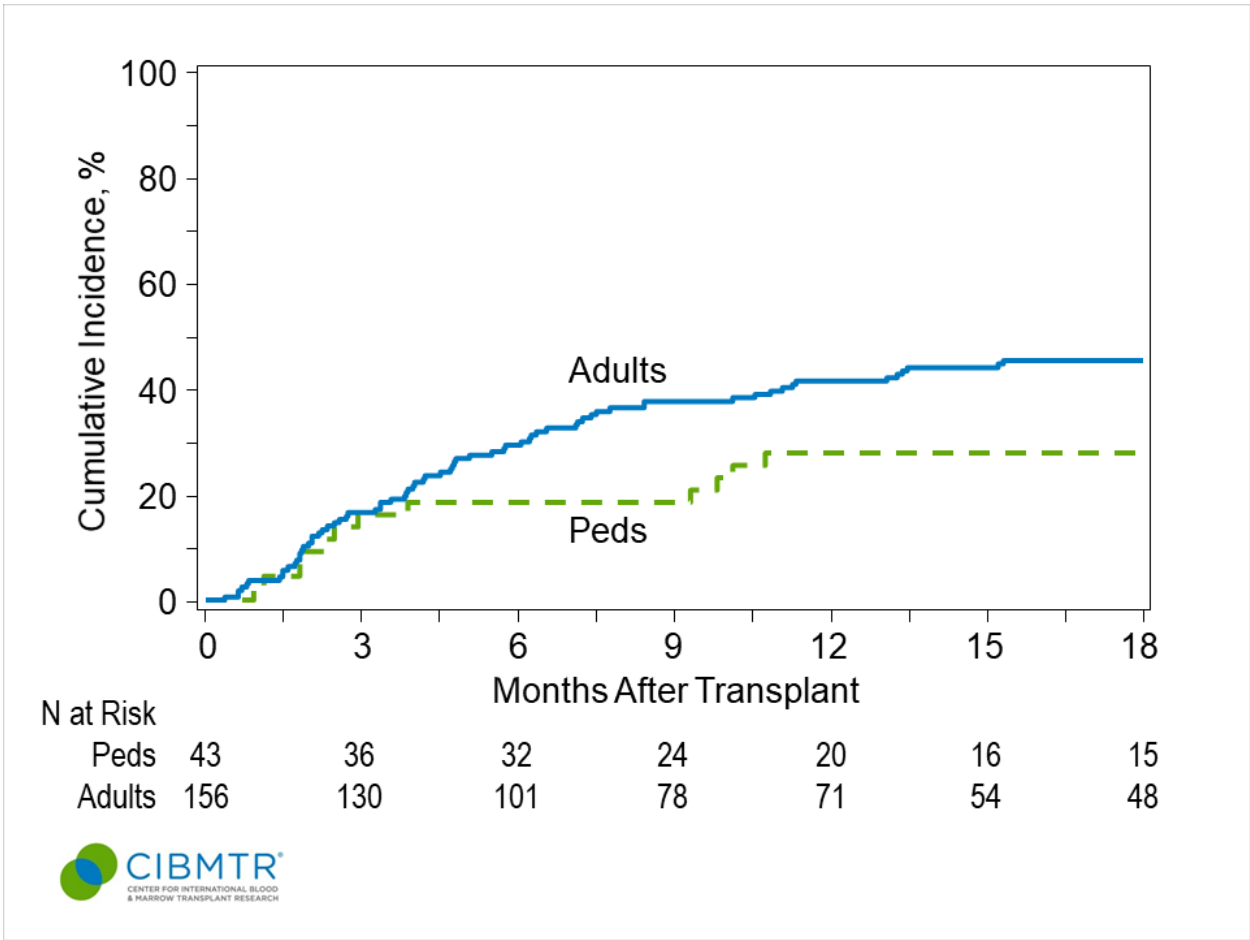
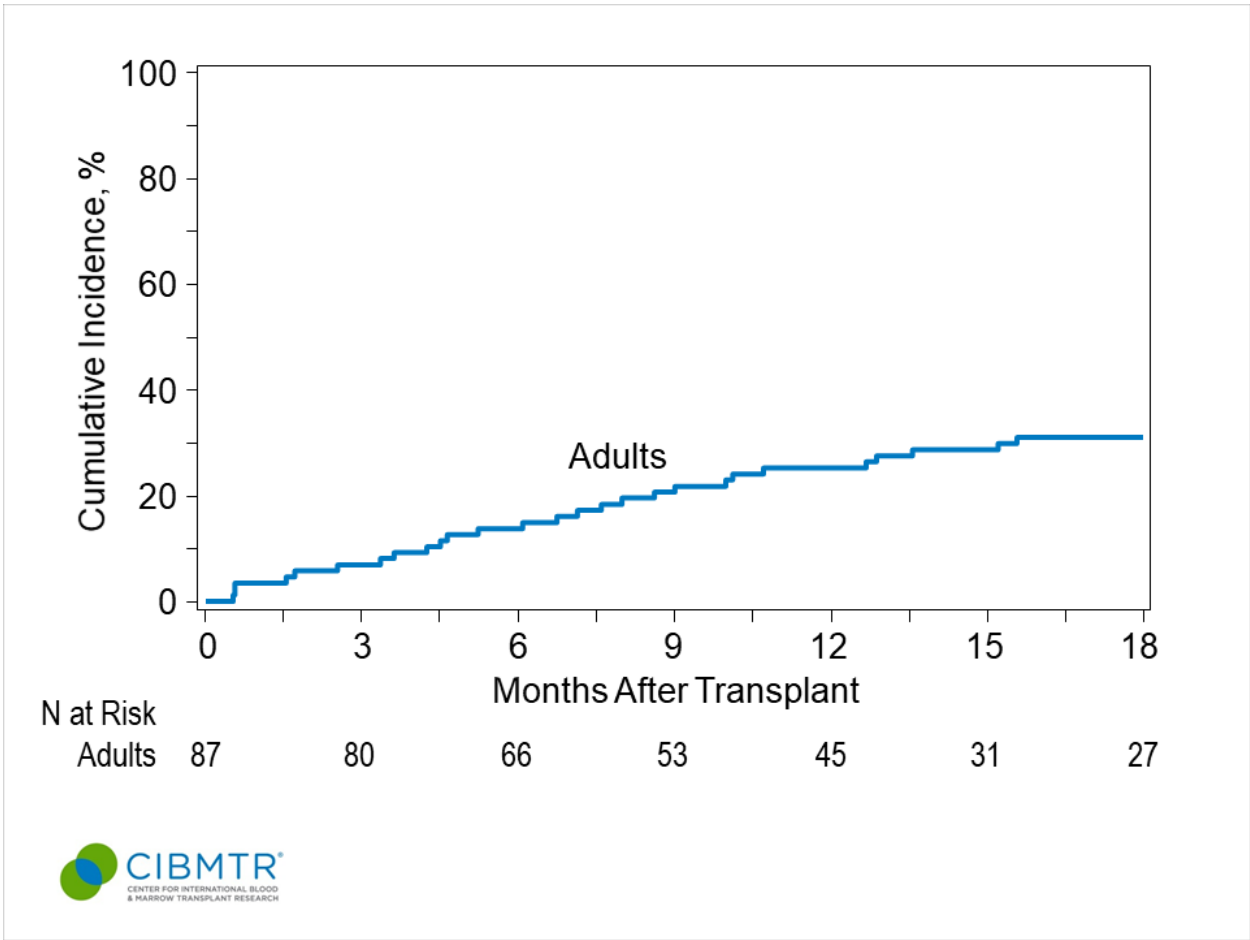


**Table 56. Post-transplant overall mortality within 18 months in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Post-transplant overall mortality (95% CI) | | | |
| 6 months | NE | 14 (8-23)% | 13 (7-21)% |
| 12 months | NE | 29 (19-40)% | 28 (18-38)% |
| 18 months | NE | 39 (27-51)% | 37 (26-49)% |

**Figure 11 Post-transplant overall mortality within 18 months in adult patients in first complete remission prior to HSCT**

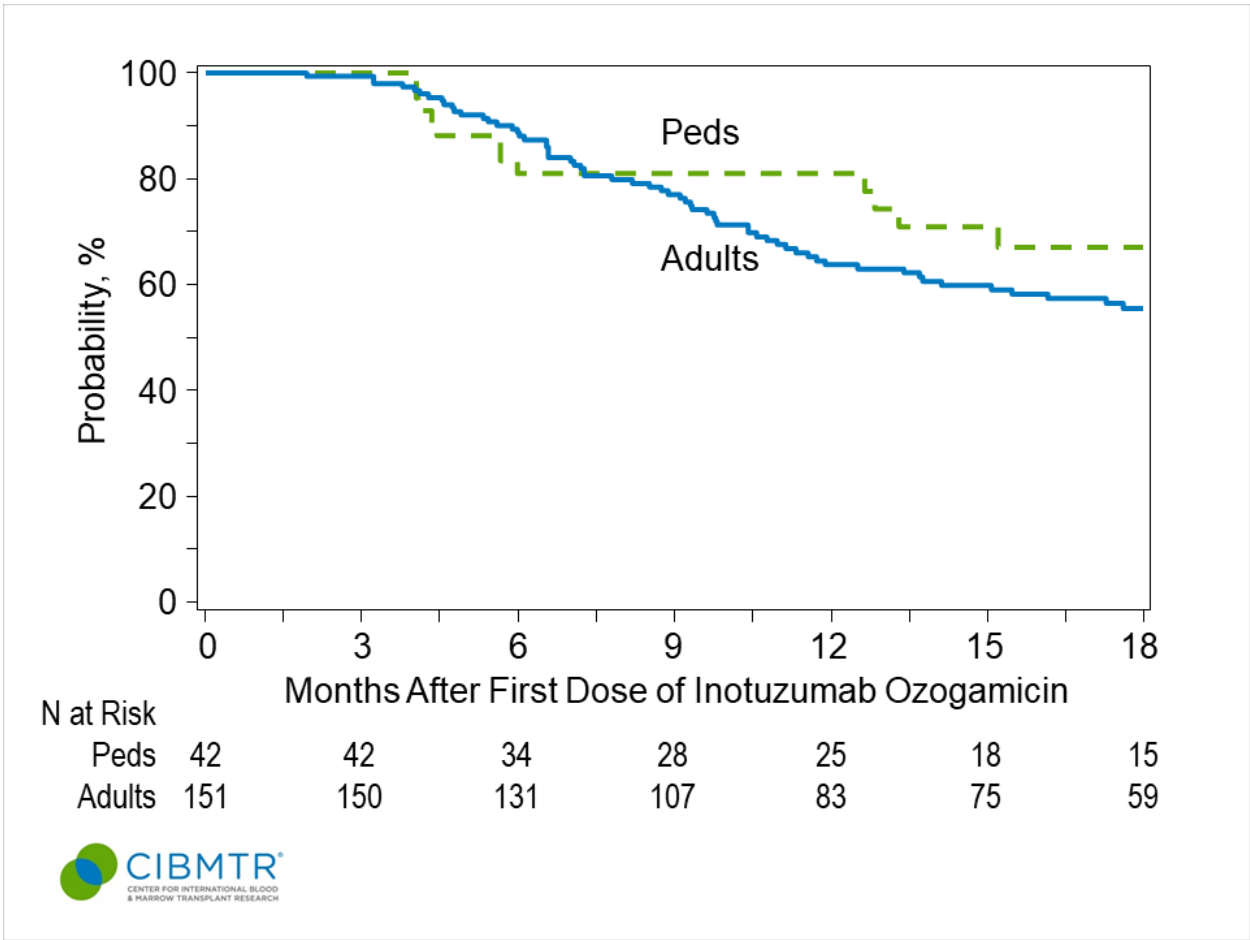


### 16.1.5. R/R subset post-inotuzumab overall survival

**Table 57. Overall survival within 18 months of first dose of inotuzumab ozogamicin in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT, with post-transplant follow-up and CIBMTR Form 2541 and date of first dose of inotuzumab ozogamicin provided** | **42** | **151** | **193** |
| Post-inotuzumab ozogamicin overall survival (95% CI) | | | |
| 6 months | 81 (68-91)% | 89 (83-93)% | 87 (82-91)% |
| 12 months | 81 (68-91)% | 64 (56-72)% | 67 (60-74)% |
| 18 months | NE | 55 (47-64)% | 58 (50-65)% |
| Number of deaths within 18 months | 12 | 62 | 74 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 7 (58) | 22 (35) | 29 (39) |
| GVHD | 1 (8) | 9 (15) | 10 (14) |
| VOD/SOS | 2 (17) | 9 (15) | 11 (15) |
| Interstitial pneumonitis | 0 | 2 (3) | 2 (3) |
| Infection | 1 (8) | 6 (10) | 7 (9) |
| Septic shock | 0 | 2 (3) | 2 (3) |
| Hemorrhage | 0 | 3 (5) | 3 (4) |
| Organ failure | 1 (8) | 7 (11) | 8 (11) |
| Graft failure | 0 | 1 (2) | 1 (1) |
| Other | 0 | 1 (2) | 1 (1) |
| Time from first dose of inotuzumab ozogamicin to death, no. (%), months | | | |
| < 3 | 0 | 1 (2) | 1 (1) |
| 3-5 | 8 (67) | 16 (26) | 24 (32) |
| 6-11 | 0 | 35 (56) | 35 (47) |
| 12-18 | 4 (33) | 10 (16) | 14 (19) |
| Median (95% CI) | 5.65 (4.07 - 12.85) | 8.34 (6.57 - 9.76) | 7.52 (6.54-9.33) |
| Range | (4.04-15.21) | (1.94-17.61) | (1.94-17.61) |
| Mean | 7.69 | 8.63 | 8.47 |
| Standard deviation | 4.39 | 3.73 | 3.82 |

**Figure 12 Post-inotuzumab ozogamicin overall survival within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

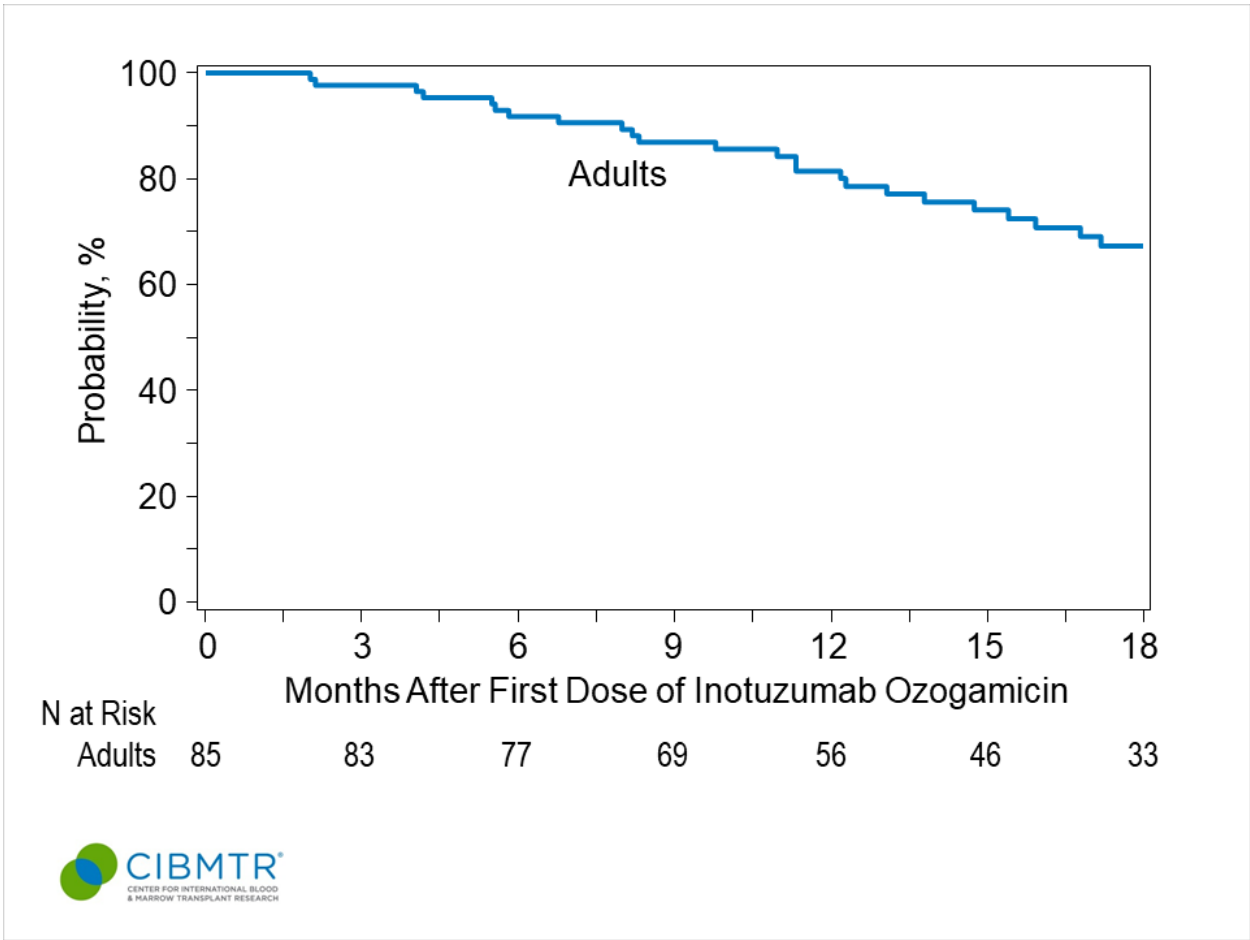


### 16.1.6. Remission subset post-inotuzumab overall survival

**Table 58. Survival within 18 months of first dose of inotuzumab ozogamicin in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT, with post-transplant follow-up and CIBMTR Form 2541 and date of first dose of inotuzumab ozogamicin provided** | **8** | **85** | **93** |
| Post-inotuzumab ozogamicin overall survival (95% CI) | | | |
| 6 months | NE | 92 (85-97)% | 92 (86-97)% |
| 12 months | NE | 81 (72-89)% | 82 (73-89)% |
| 18 months | NE | 67 (56-78)% | 68 (57-78)% |
| Number of deaths within 18 months | 1 | 24 | 25 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 0 | 7 (29) | 7 (28) |
| GVHD | 0 | 6 (25) | 6 (24) |
| VOD/SOS | 0 | 5 (21) | 5 (20) |
| Interstitial pneumonitis | 0 | 1 (4) | 1 (4) |
| Infection | 0 | 3 (13) | 3 (12) |
| Thrombotic microangiopathy (TMA) | 1 | 0 | 1 (4) |
| Organ failure | 0 | 2 (8) | 2 (8) |
| Time from first dose of inotuzumab ozogamicin to death, no. (%), months | | | |
| < 3 | 0 | 2 (8) | 2 (8) |
| 3-5 | 0 | 5 (21) | 5 (20) |
| 6-11 | 1 | 8 (33) | 9 (36) |
| 12-18 | 0 | 9 (38) | 9 (36) |
| Median (95% CI) | 10.91 (NE) | 10.38 (6.77 - 13.08) | 10.91 (6.77-12.29) |
| Range | NE | (2-17.18) | (2-17.18) |
| Mean | 10.91 | 9.8 | 9.85 |
| Standard deviation | NE | 4.65 | 4.55 |

**Figure 13 Post-inotuzumab ozogamicin overall survival within 18 months in adult patients in first complete remission prior to HSCT**

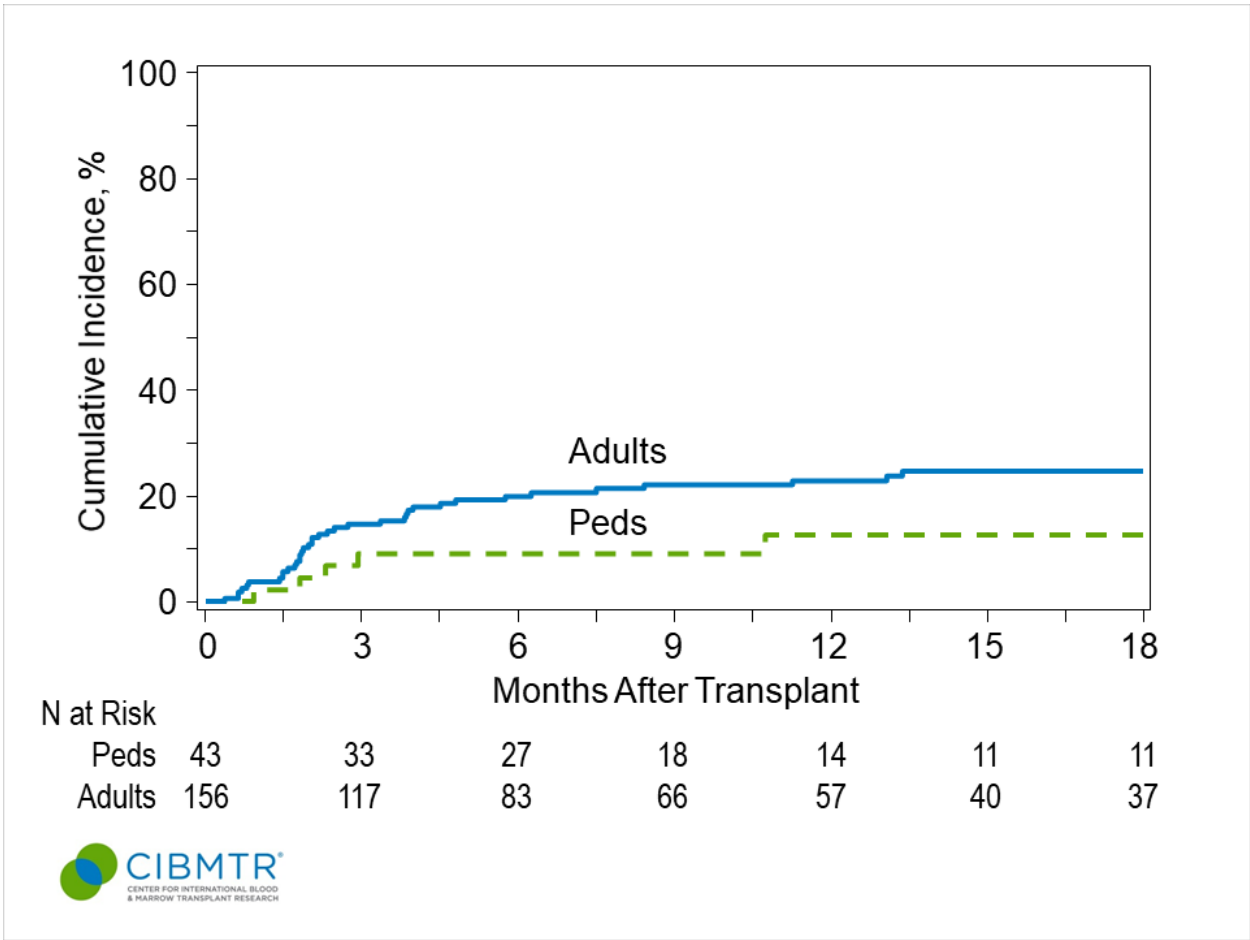


### 16.1.7. R/R subset transplant-related mortality

**Table 59. Transplant-related mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Transplant-related mortality (95% CI) | | | |
| 6 months | 9 (2-20)% | 20 (14-27)% | 20 (14-26)% |
| 12 months | NE | 23 (17-30)% | 29 (22-37)% |
| 18 months | NE | 25 (18-32)% | 32 (24-40)% |
| No. patients with TRM within 18 months | 5 | 37 | 42 |
| No. patients with competing risk (post-transplant relapse) | 16 | 57 | 73 |
| Primary cause of death, among patients with TRM, no. (%) | | | |
| GVHD | 1 (20) | 7 (19) | 8 (19) |
| VOD/SOS | 2 (40) | 9 (24) | 11 (26) |
| Interstitial pneumonitis | 0 | 4 (11) | 4 (10) |
| Infection | 1 (20) | 3 (8) | 4 (10) |
| Septic shock | 0 | 2 (5) | 2 (5) |
| Hemorrhage | 0 | 3 (8) | 3 (7) |
| Organ failure | 1 (20) | 7 (19) | 8 (19) |
| Graft failure | 0 | 1 (3) | 1 (2) |
| Other | 0 | 1 (3) | 1 (2) |
| Time from transplant to TRM, no. (%), months | | | |
| < 3 | 4 (80) | 23 (62) | 27 (64) |
| 3-5 | 0 | 8 (22) | 8 (19) |
| 6-11 | 1 (20) | 4 (11) | 5 (12) |
| 12-18 | 0 | 2 (5) | 2 (5) |
| Median (95% CI) | 2.3 (0.92-10.74) | 2.04 (1.81-3.81) | 2.10 (1.81-3.35) |
| Range | (0.92-10.74) | (0.36-13.37) | (0.36-13.37) |
| Mean | 3.74 | 3.52 | 3.54 |
| Standard deviation | 3.98 | 3.33 | 3.36 |

**Figure 14 Transplant-related mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

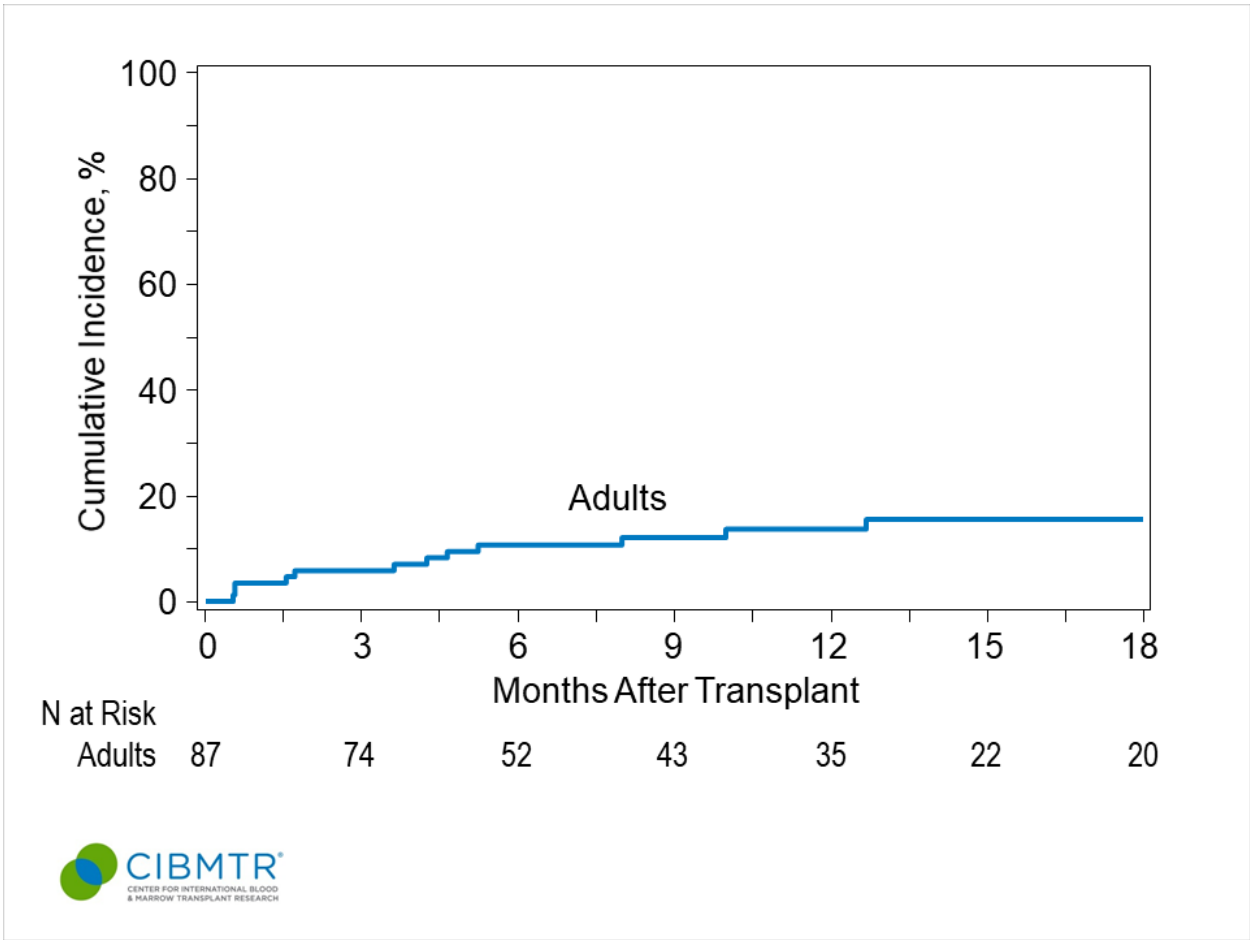


### 16.1.8. Remission subset transplant-related mortality

**Table 60. Transplant-related mortality within 18 months in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Transplant-related mortality (95% CI) | | | |
| 6 months | NE | 11 (5-18)% | 10 (5-17)% |
| 12 months | NE | 14 (7-22)% | 14 (7-22)% |
| 18 months | NE | 15 (8-25)% | 15 (8-24)% |
| No. patients with TRM within 18 months | 1 | 12 | 13 |
| No. patients with competing risk (post-transplant relapse) | 3 | 30 | 33 |
| Primary cause of death, among patients with TRM, no. (%) | | | |
| GVHD | 0 | 4 (33) | 4 (31) |
| VOD/SOS | 0 | 4 (33) | 4 (31) |
| Infection | 0 | 2 (17) | 2 (15) |
| Thrombotic microangiopathy (TMA) | 1 | 0 | 1 (8) |
| Organ failure | 0 | 2 (17) | 2 (15) |
| Time from transplant to TRM, no. (%), months | | | |
| < 3 | 0 | 5 (42) | 5 (38) |
| 3-5 | 0 | 4 (33) | 4 (31) |
| 6-11 | 1 | 2 (17) | 3 (23) |
| 12-18 | 0 | 1 (8) | 1 (8) |
| Median (95% CI) | 8.05 (NE) | 3.93 (0.56 - 7.98) | 4.24 (0.56-8.05) |
| Range | NE | (0.53-12.68) | (0.53-12.68) |
| Mean | 8.05 | 4.44 | 4.72 |
| Standard deviation | NE | 3.98 | 3.94 |

**Figure 15 Transplant-related mortality within 18 months in adult patients in first complete remission prior to HSCT**

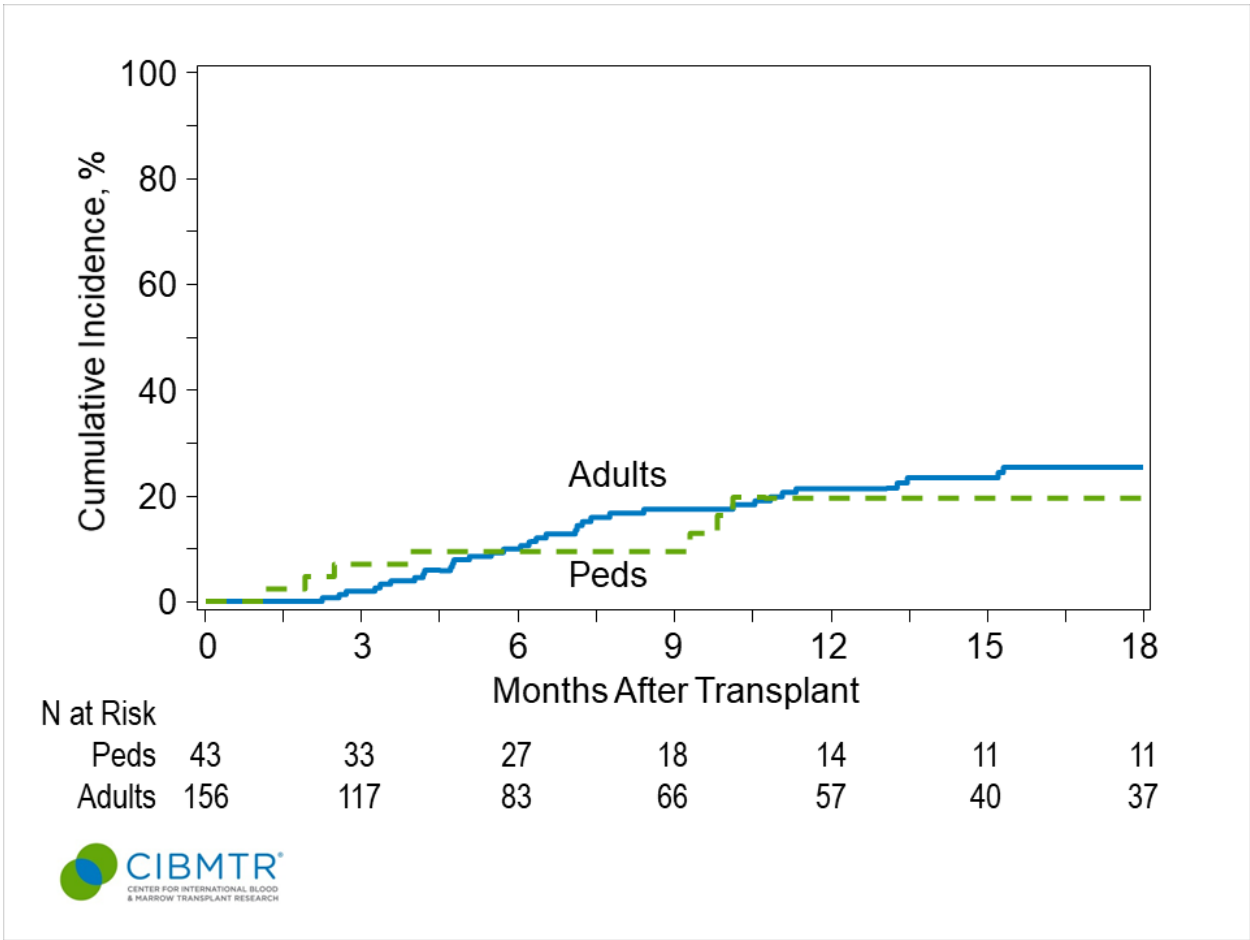


### 16.1.9. R/R subset non-transplant-related mortality

**Table 61. Non-transplant-related mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Non-transplant-related mortality (95% CI) | | | |
| 6 months | 9 (3-20)% | 10 (6-15)% | 10 (6-14)% |
| 12 months | NE | 21 (15-28)% | 21 (15-27)% |
| 18 months | NE | 25 (18-33)% | 24 (18-31)% |
| No. patients with NTRM within 18 months | 7 | 34 | 41 |
| No. patients with competing risk (transplant-related mortality) | 5 | 37 | 42 |
| Time from transplant to NTRM, no. (%), months | | | |
| < 3 | 3 (43) | 3 (9) | 6 (15) |
| 3-5 | 1 (14) | 12 (35) | 13 (32) |
| 6-11 | 3 (43) | 15 (44) | 18 (44) |
| 12-18 | 0 | 4 (12) | 4 (10) |
| Median (95% CI) | 3.88 (1.12-10.12) | 6.28 (4.76-7.75) | 6.21 (4.73-7.75) |
| Range | (1.12-10.12) | (2.23-15.31) | (1.12-15.31) |
| Mean | 5.51 | 7.11 | 6.84 |
| Standard deviation | 4.05 | 3.66 | 3.73 |

**Figure 16 Non-transplant-related mortality within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

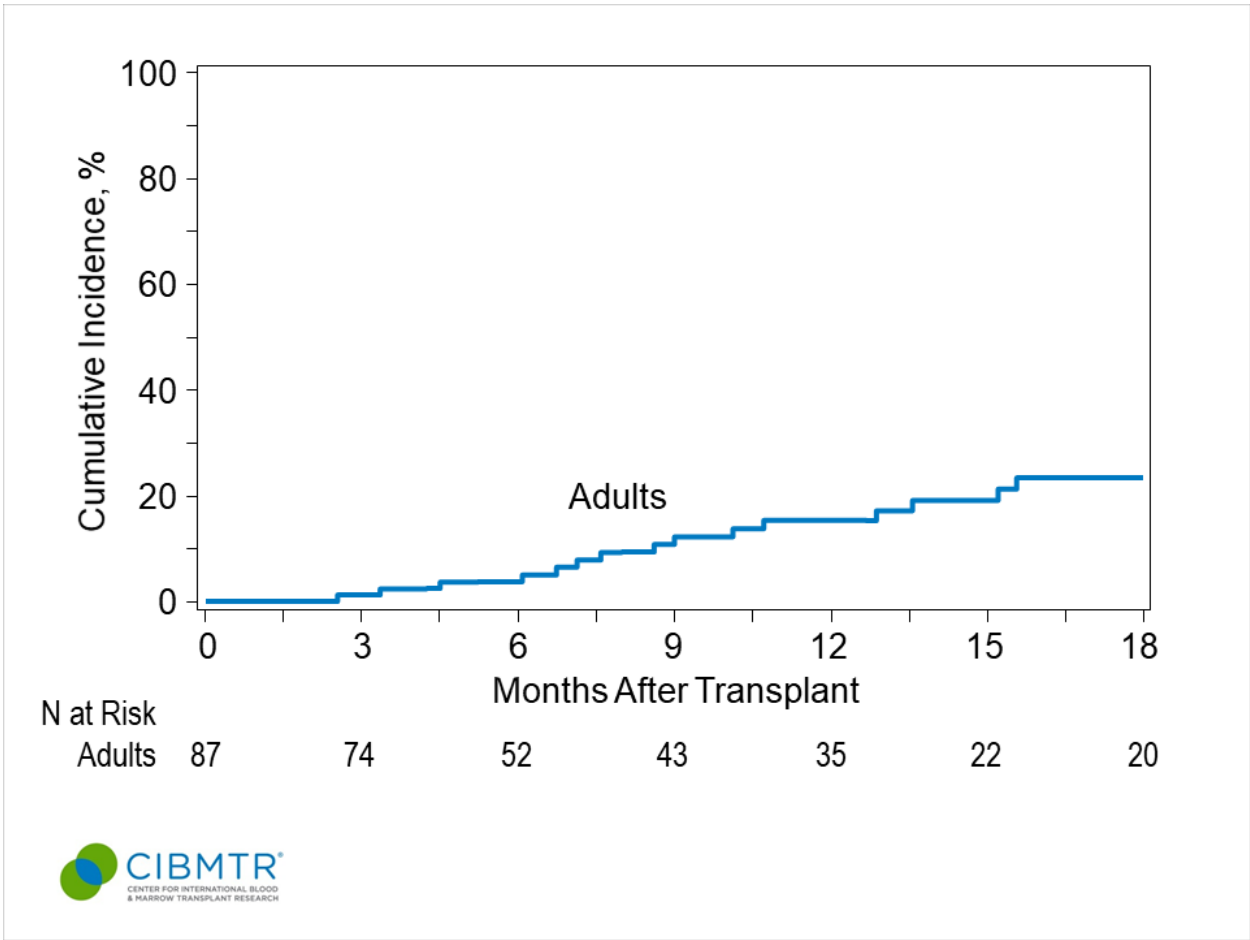


### 16.1.10. Remission subset non-transplant-related mortality

**Table 62. Non-transplant-related mortality within 18 months in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Non-transplant-related mortality (95% CI) | | | |
| 6 months | NE | 4 (1-9)% | 3 (1-8)% |
| 12 months | NE | 15 (8-24)% | 14 (7-22)% |
| 18 months | NE | 23 (14-34)% | 21 (13-32)% |
| No. patients with NTRM within 18 months | 0 | 15 | 15 |
| No. patients with competing risk (transplant-related mortality) | 1 | 11 | 12 |
| Time from transplant to NTRM, no. (%), months | | | |
| < 3 | NE | 1 (9) | 1 (9) |
| 3-5 | NE | 2 (18) | 2 (18) |
| 6-11 | NE | 8 (73) | 8 (73) |
| 12-18 | NE | 0 | 0 |
| Median (95% CI) | NE | 7.13 (4.5-10.12) | 8.61 (6.08 - 12.88) |
| Range | NE | (2.53-10.71) | (2.53-10.71) |
| Mean | NE | 6.94 | 6.94 |
| Standard deviation | NE | 2.66 | 2.66 |

**Figure 17 Non-transplant-related mortality within 18 months in adults in first complete remission prior to HSCT**

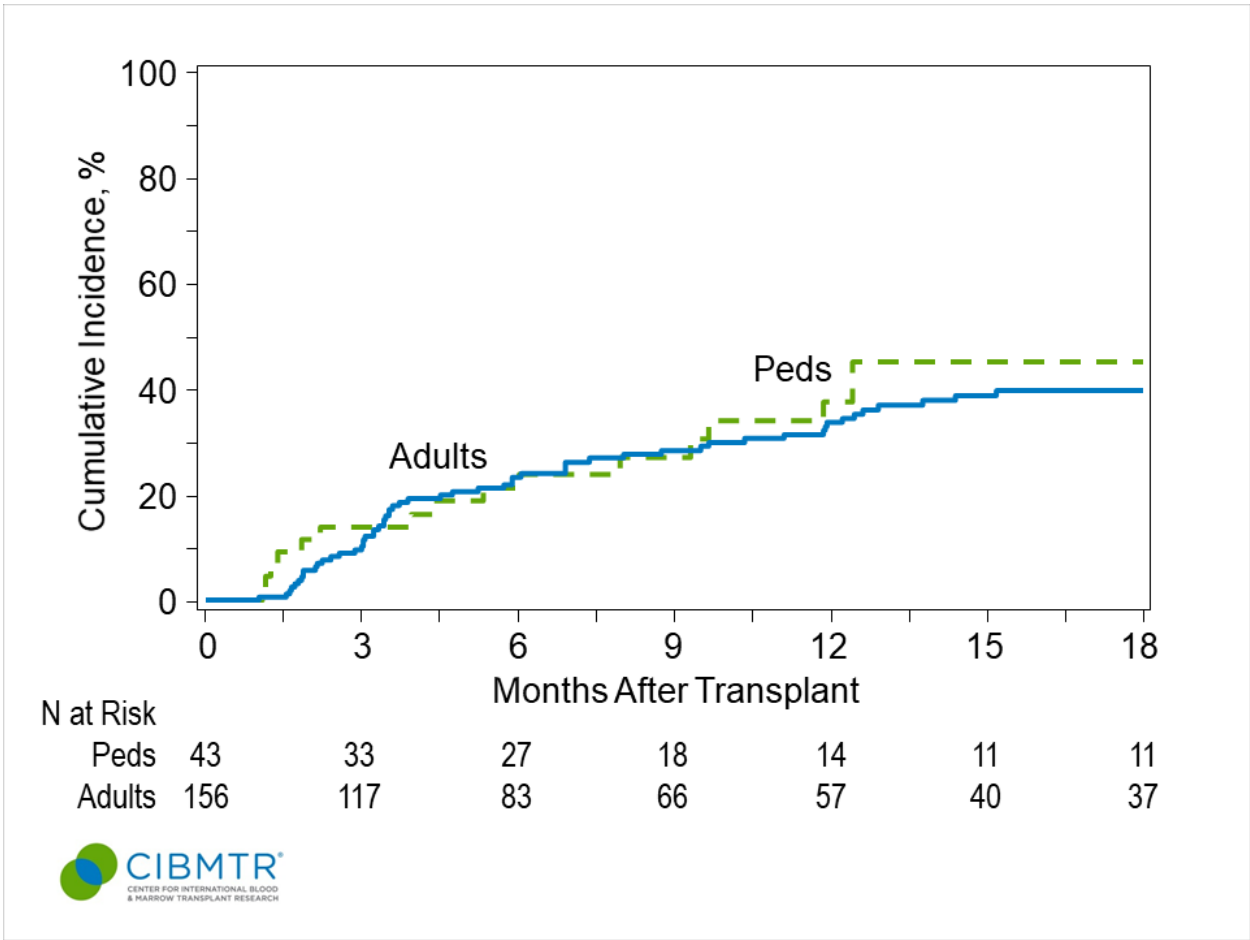


### 16.1.11. R/R subset post-transplant relapse

**Table 63. Post-transplant relapse within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Post-transplant relapse (95% CI) | | | |
| 6 months | 21 (10-35)% | 24 (17-30)% | 23 (17-29)% |
| 12 months | NE | 34 (26-42)% | 35 (28-42)% |
| 18 months | NE | 40 (32-48)% | 41 (34-48)% |
| No. patients with post-transplant relapse within 12 months | 16 | 57 | 73 |
| No. patients with competing risk (transplant-related mortality) | 5 | 37 | 42 |
| Time from transplant to post-transplant relapse, no. (%), months | | | |
| < 3 | 6 (38) | 16 (28) | 22 (30) |
| 3-5 | 3 (19) | 20 (35) | 23 (32) |
| 6-11 | 5 (31) | 14 (25) | 19 (26) |
| 12-18 | 2 (13) | 7 (12) | 9 (12) |
| Median (95% CI) | 4.85 (1.84-9.66) | 3.71 (3.32-6.05) | 3.94 (3.42-6.01) |
| Range | (1.08-12.42) | (1.02-15.18) | (1.02-15.18) |
| Mean | 5.76 | 5.83 | 5.81 |
| Standard deviation | 4.28 | 4.09 | 4.1 |

**Figure 18 Post-transplant relapse within 18 months in patients who had relapsed or refractory B-cell ALL prior to HSCT**

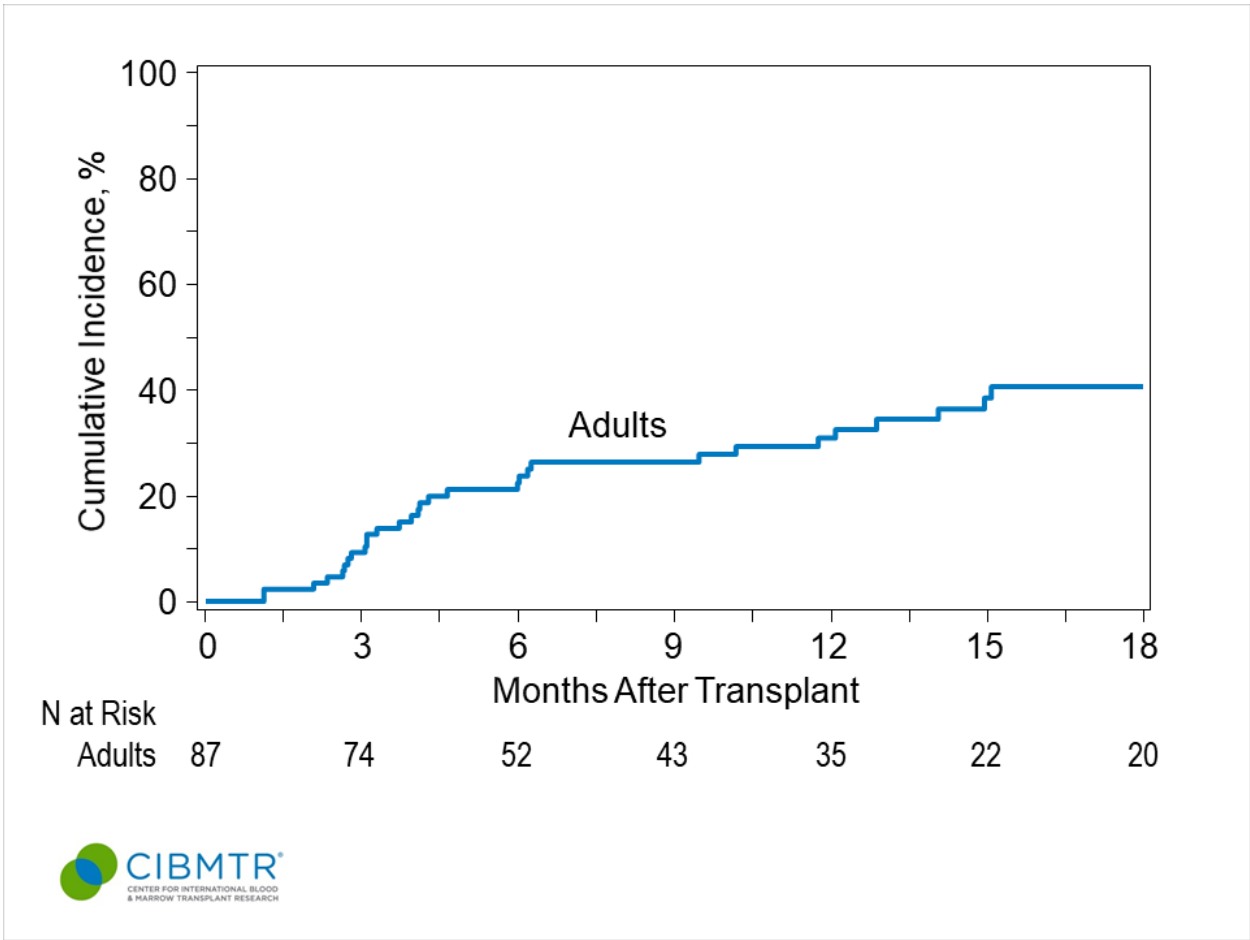


### 16.1.12. Remission subset post-transplant relapse

**Table 64. Post-transplant relapse within 18 months in patients in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Post-transplant relapse (95% CI) | | | |
| 6 months | NE | 22 (14-32)% | 24 (16-33)% |
| 12 months | NE | 31 (21-42)% | 31 (22-42)% |
| 18 months | NE | 41 (29-53)% | 40 (29-52)% |
| No. patients with post-transplant relapse within 18 months | 3 | 30 | 33 |
| No. patients with competing risk (transplant-related mortality) | 1 | 12 | 13 |
| Time from transplant to post-transplant relapse, no. (%), months | | | |
| < 3 | 1 (33) | 8 (27) | 9 (27) |
| 3-5 | 2 (67) | 11 (37) | 13 (39) |
| 6-11 | 0 | 6 (20) | 6 (18) |
| 12-18 | 0 | 5 (17) | 5 (15) |
| Median (95% CI) | 5.26 (1.97-5.29) | 4.09 (3.09-6.18) | 4.11 (3.09-6.01) |
| Range | (1.97-5.29) | (1.12-15.08) | (1.12-15.08) |
| Mean | 4.17 | 5.99 | 5.82 |
| Standard deviation | 1.91 | 4.35 | 4.2 |

**Figure 19 Post-transplant relapse within 18 months in adults in first complete remission prior to HSCT**



### 16.1.13. R/R subset adverse events

**Table 65. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Viral infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 16 (37) | 69 (44) | 85 (43) |
| No | 20 (47) | 82 (53) | 102 (51) |
| Not reported | 6 (14) | 4 (3) | 10 (5) |
| Bacterial infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 13 (30) | 88 (56) | 101 (51) |
| No | 23 (53) | 63 (40) | 86 (43) |
| Not reported | 6 (14) | 4 (3) | 10 (5) |
| Fungal infection, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 4 (9) | 15 (10) | 19 (10) |
| No | 32 (74) | 136 (87) | 168 (84) |
| Not reported | 6 (14) | 4 (3) | 10 (5) |
| SIRS development, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 2 (5) | 8 (5) | 10 (5) |
| No | 40 (93) | 146 (94) | 186 (93) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Septic shock, up to day 100 | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 4 (9) | 24 (15) | 28 (14) |
| No | 38 (88) | 130 (83) | 168 (84) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Maximum grade of acute GVHD, up to day 100 [a] | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| None | 25 (58) | 74 (47) | 99 (50) |
| I | 3 (7) | 16 (10) | 19 (10) |
| II | 7 (16) | 43 (28) | 50 (25) |
| III | 4 (9) | 11 (7) | 15 (8) |
| IV | 3 (7) | 10 (6) | 13 (7) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Time from HSCT to date of maximum acute GVHD, months | | | |
| Number evaluable | 17 | 79 | 96 |
| Median | 0.9 | 1.4 | 1.3 |
| Range | (0.5-2.1) | (0.4-3.2) | (0.4-3.2) |
| Mean | 1 | 1.5 | 1.4 |
| Standard deviation | 0.4 | 0.6 | 0.6 |

**Table 65. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| Chronic GVHD, up to 1 year post-transplant | | | |
| Yes | 4 (9) | 39 (25) | 43 (22) |
| No | 38 (88) | 112 (72) | 150 (75) |
| Not reported | 1 (2) | 5 (3) | 6 (3) |
| Time from HSCT to chronic GVHD, months | | | |
| Number evaluable | 4 | 39 | 43 |
| Median | 5.3 | 7 | 6.9 |
| Range | (3.8-7.1) | (2-13.9) | (2-13.9) |
| Mean | 5.4 | 7 | 6.9 |
| Standard deviation | 1.6 | 3 | 2.9 |
| VOD/SOS within 100 days post-transplant | | | |
| Yes | 13 (30) | 27 (17) | 40 (20) |
| No | 30 (70) | 127 (81) | 157 (79) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Time from HSCT to VOD/SOS, months | | | |
| Number evaluable | 13 | 27 | 40 |
| Median | 0.4 | 0.4 | 0.4 |
| Range | (0.2-0.8) | (0.2-2.6) | (0.2-2.6) |
| Mean | 0.4 | 0.6 | 0.6 |
| Standard deviation | 0.2 | 0.6 | 0.5 |
| Secondary malignancy | | | |
| Yes [b] | 0 | 2 (1) | 2 (1) |
| No | 37 (86) | 150 (96) | 187 (94) |
| Not reported | 6 (14) | 4 (3) | 10 (5) |
| Time from HSCT to secondary malignancy, months | | | |
| Number evaluable | 0 | 2 | 2 |
| Median | NE | NE | NE |
| Range | NE | (4-21) | (4-21) |
| Mean | NE | 12 | 12 |
| Standard deviation | NE | 12 | 12 |
| **Pulmonary AEs within 100 days post-transplant** | | | |
| IPN / Idiopathic pneumonia syndrome | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 5 (12) | 11 (7) | 16 (8) |
| No | 37 (86) | 142 (91) | 179 (90) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Bronchiolitis obliterans | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 1 (1) | 1 (1) |
| No | 42 (98) | 154 (99) | 196 (98) |

**Table 65. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| COP/BOOP | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |
| Diffuse alveolar hemorrhage | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 5 (3) | 5 (3) |
| No | 42 (98) | 150 (96) | 192 (96) |
| **Cardiovascular AEs within 100 days post-transplant** | | | |
| Arrhythmia | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 7 (4) | 7 (4) |
| No | 42 (98) | 147 (94) | 189 (95) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Congestive heart failure | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 1 (1) | 1 (1) |
| No | 42 (98) | 154 (99) | 196 (98) |
| Coronary artery disease | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |
| Myocardial infarction or unstable angina | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 1 (1) | 1 (1) |
| No | 42 (98) | 154 (99) | 196 (98) |
| Hypertension (HTN) requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 3 (7) | 8 (5) | 11 (6) |
| No | 38 (88) | 147 (94) | 185 (93) |
| Not reported | 1 (2) | 0 | 1 (1) |
| Thrombotic microangiopathy (TMA) | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 1 (2) | 4 (3) | 5 (3) |
| No | 41 (95) | 151 (97) | 192 (96) |
| **Renal AEs within 100 days post-transplant** | | | |
| Acute renal failure requiring dialysis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 4 (9) | 16 (10) | 20 (10) |
| No | 38 (88) | 139 (89) | 177 (89) |

**Table 65. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |
| **Musculoskeletal AEs within 100 days post-transplant** | | | |
| Avascular necrosis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 1 (1) | 1 (1) |
| No | 42 (98) | 154 (99) | 196 (98) |
| **Endocrine dysfunction within 100 days post-transplant** | | | |
| Diabetes or hyperglycemia requiring chronic treatment | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 1 (2) | 7 (4) | 8 (4) |
| No | 41 (95) | 148 (95) | 189 (95) |
| Growth hormone deficiency or short stature | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |
| Hypothyroidism requiring replacement therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |
| Pancreatitis | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |
| Depression requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 2 (1) | 2 (1) |
| No | 41 (95) | 152 (97) | 193 (97) |
| Not reported | 1 (2) | 1 (1) | 2 (1) |
| Anxiety requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 2 (5) | 3 (2) | 5 (3) |
| No | 40 (93) | 150 (96) | 190 (95) |
| Not reported | 0 | 2 (1) | 2 (1) |
| CNS hemorrhage and stroke | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 1 (2) | 3 (2) | 4 (2) |
| No | 41 (95) | 152 (97) | 193 (97) |
| PTSD requiring therapy | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 0 | 0 | 0 |
| No | 42 (98) | 155 (99) | 197 (99) |

**Table 65. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with post-transplant follow-up** | **43** | **156** | **199** |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table.

Outcomes are not evaluable (NE) if sample size is < 20.

All events were evaluated up to 100 days post-transplant unless noted otherwise. Data are simple proportions.

[a] Acute GVHD grading follows the Consensus criteria (Przepiorka D, Weisdorf D, Martin P, et al. [1995] 1994 Consensus Conference on Acute GVHD Grading. Bone Marrow Transplant 15:825–828.) Acute GVHD was evaluated up to 100 days post-transplant.

[b] Secondary malignancy reported for n=2 patients was squamous cell cancer of the skin and non-Hodgkin lymphoma.

### 16.1.14. Remission subset adverse events

**Table 66. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Viral infection, up to day 100 | | | |
| Yes | 4 (44) | 38 (44) | 42 (44) |
| No | 4 (44) | 46 (53) | 50 (52) |
| Not reported | 1 (11) | 3 (3) | 4 (4) |
| Bacterial infection, up to day 100 | | | |
| Yes | 1 (11) | 37 (43) | 38 (40) |
| No | 7 (78) | 47 (54) | 54 (56) |
| Not reported | 1 (11) | 3 (3) | 4 (4) |
| Fungal infection, up to day 100 | | | |
| Yes | 0 | 7 (8) | 7 (7) |
| No | 8 (89) | 77 (89) | 85 (89) |
| Not reported | 1 (11) | 3 (3) | 4 (4) |
| SIRS development, up to day 100 | | | |
| Yes | 2 (22) | 1 (1) | 3 (3) |
| No | 7 (78) | 86 (99) | 93 (97) |
| Septic shock, up to day 100 | | | |
| Yes | 2 (22) | 10 (11) | 12 (13) |
| No | 7 (78) | 77 (89) | 84 (88) |
| Maximum grade of acute GVHD, up to day 100 [a] | | | |
| None | 5 (56) | 36 (41) | 41 (43) |
| I | 1 (11) | 10 (11) | 11 (11) |
| II | 2 (22) | 29 (33) | 31 (32) |
| III | 0 | 6 (7) | 6 (6) |
| IV | 1 (11) | 6 (7) | 7 (7) |
| Time from HSCT to date of maximum acute GVHD, months | | | |
| Number evaluable | 4 | 50 | 54 |
| Median | 1.5 | 1.3 | 1.3 |
| Range | (0.4-2.9) | (0.5-3) | (0.4-3) |
| Mean | 1.6 | 1.4 | 1.4 |
| Standard deviation | 1 | 0.6 | 0.6 |
| Chronic GVHD, up to 1 year post-transplant | | | |
| Yes | 2 (22) | 27 (31) | 29 (30) |
| No | 7 (78) | 59 (68) | 66 (69) |
| Not reported | 0 | 1 (1) | 1 (1) |

**Table 66. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Time from HSCT to chronic GVHD, months | | | |
| Number evaluable | 2 | 27 | 29 |
| Median | NE | 8.4 | 8.4 |
| Range | (3.3-12.4) | (2.2-30.6) | (2.2-30.6) |
| Mean | 7.9 | 10.3 | 10.1 |
| Standard deviation | 6.5 | 6.3 | 6.2 |
| VOD/SOS within 100 days post-transplant | | | |
| Yes | 3 (33) | 8 (9) | 11 (11) |
| No | 6 (67) | 79 (91) | 85 (89) |
| Time from HSCT to VOD/SOS, months | | | |
| Number evaluable | 3 | 8 | 11 |
| Median | 0.3 | 0.5 | 0.5 |
| Range | (0.3-0.4) | (0.4-3) | (0.3-3) |
| Mean | 0.4 | 1.1 | 0.9 |
| Standard deviation | 0.1 | 1 | 0.9 |
| Secondary malignancy | | | |
| Yes [b] | 0 | 4 (5) | 4 (4) |
| No | 8 (89) | 80 (92) | 88 (92) |
| Not reported | 1 (11) | 3 (3) | 4 (4) |
| Number evaluable | NE | 4 | 4 |
| Median | NE | 5 | 5 |
| Range | NE | (2-11) | (2-11) |
| Mean | Ne | 6 | 6 |
| Standard deviation | NE | 4 | 4 |
| **Pulmonary AEs within 100 days post-transplant** | | | |
| IPN / Idiopathic pneumonia syndrome | | | |
| Yes | 0 | 4 (5) | 4 (4) |
| No | 9 | 83 (95) | 92 (96) |
| Bronchiolitis obliterans | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| COP/BOOP | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Diffuse alveolar hemorrhage | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |

**Table 66. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| **Cardiovascular AEs within 100 days post-transplant** | | | |
| Arrhythmia | | | |
| Yes | 0 | 1 (1) | 1 (1) |
| No | 9 | 85 (98) | 94 (98) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Congestive heart failure | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Coronary artery disease | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Myocardial infarction or unstable angina | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Hypertension (HTN) requiring therapy | | | |
| Yes | 3 (33) | 5 (6) | 8 (8) |
| No | 6 (67) | 81 (93) | 87 (91) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Thrombotic microangiopathy (TMA) | | | |
| Yes | 1 (11) | 4 (5) | 5 (5) |
| No | 8 (89) | 83 (95) | 91 (95) |
| **Renal AEs within 100 days post-transplant** | | | |
| Acute renal failure requiring dialysis | | | |
| Yes | 1 (11) | 5 (6) | 6 (6) |
| No | 8 (89) | 82 (94) | 90 (94) |
| **Musculoskeletal AEs within 100 days post-transplant** | | | |
| Avascular necrosis | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| **Endocrine dysfunction within 100 days post-transplant** | | | |
| Diabetes or hyperglycemia requiring chronic treatment | | | |
| Yes | 1 (11) | 2 (2) | 3 (3) |
| No | 8 (89) | 85 (98) | 93 (97) |
| Growth hormone deficiency or short stature | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Hypothyroidism requiring replacement therapy | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |

**Table 66. 100-Day post-HSCT adverse events of interest in patients with B-cell ALL who received inotuzumab ozogamicin and were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Pancreatitis | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| Depression requiring therapy | | | |
| Yes | 1 (11) | 0 | 1 (1) |
| No | 8 (89) | 87 | 95 (99) |
| Anxiety requiring therapy | | | |
| Yes | 1 (11) | 1 (1) | 2 (2) |
| No | 8 (89) | 86 (99) | 94 (98) |
| CNS hemorrhage and stroke | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |
| PTSD requiring therapy | | | |
| Yes | 0 | 0 | 0 |
| No | 9 | 87 | 96 |

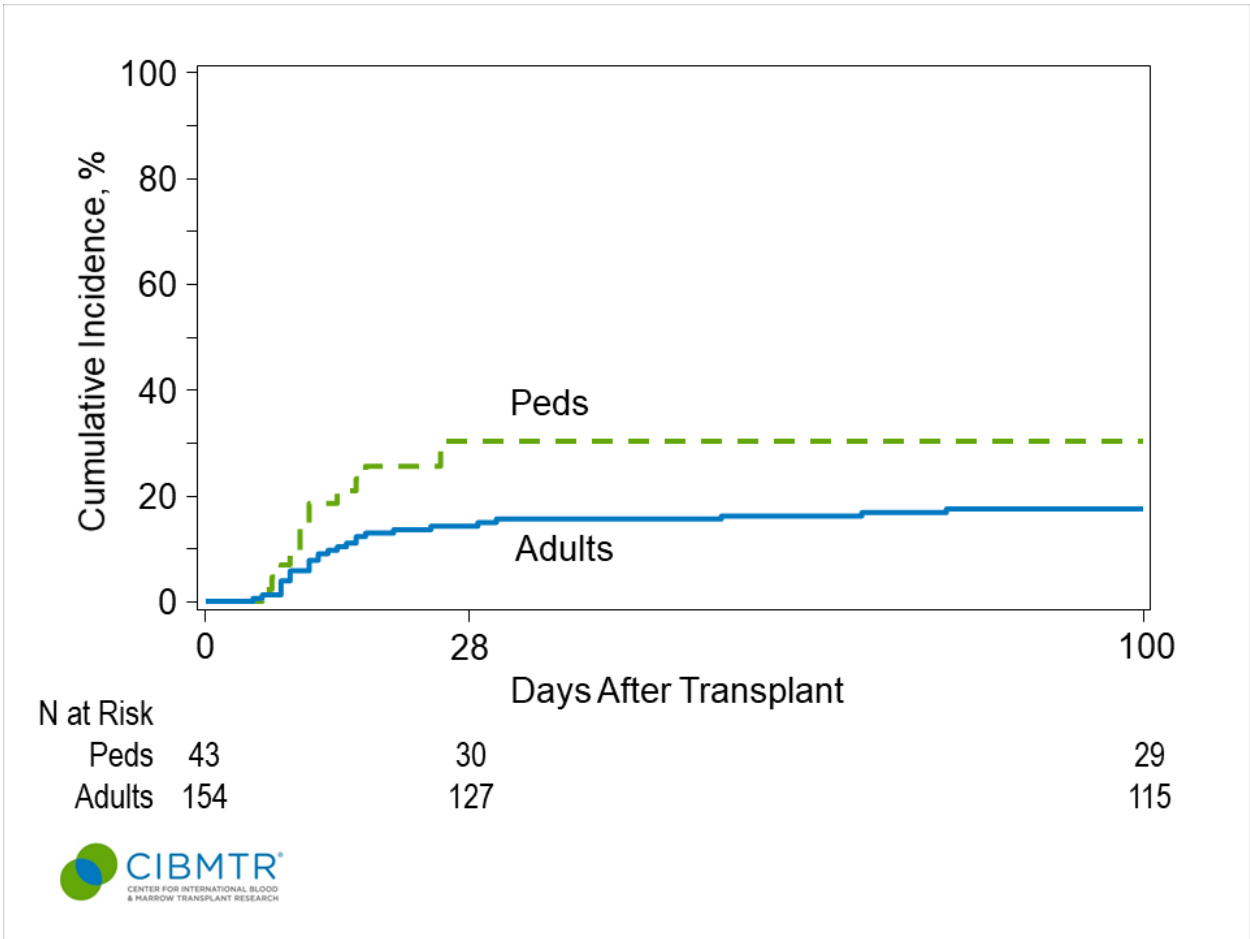
Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table.
Outcomes are not evaluable (NE) if sample size is < 20.
All events were evaluated up to 100 days post-transplant unless noted otherwise.
[a] Acute GVHD grading follows the Consensus criteria (Przepiorka D, Weisdorf D, Martin P, et al. [1995] 1994 Consensus Conference on Acute GVHD Grading. Bone Marrow Transplant 15:825–828.) Acute GVHD was evaluated up to 100 days post-transplant.
[b] Secondary malignancies reported were acute myeloid leukemia, other acute leukemia, basal cell skin malignancy, and myelodysplastic syndrome.

### 16.1.15. R/R subset VOD rates

**Table 67. Post-transplant VOD/SOS within 100 days in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with relapsed or refractory B-cell ALL and with post-transplant follow-up** | **43** | **156** | **199** |
| Veno-occlusive disease, (95% CI) | | | |
| 100 days | 30 (17-45)% | 18 (12-24)% | 20 (15-26)% |
| Number of patients with veno-occlusive disease | 13 | 27 | 40 |
| Number of patients with competing risk (death without VOD) | 1 | 12 | 13 |
| Time from transplant to veno-occlusive disease, no. (%), months | | | |
| < 3 | 13 | 27 | 40 |
| Median (95% CI) | 0.36 (0.26 - 0.56) | 0.39 (0.3 - 0.56) | 0.38 (0.33-0.53) |
| Range | (0.2-0.82) | (0.16-2.6) | (0.16-2.6) |
| Mean | 0.43 | 0.64 | 0.57 |
| Standard deviation | 0.2 | 0.62 | 0.53 |

**Figure 20 Post-transplant VOD/SOS within 100 days in patients who had relapsed or refractory B-cell ALL prior to HSCT**

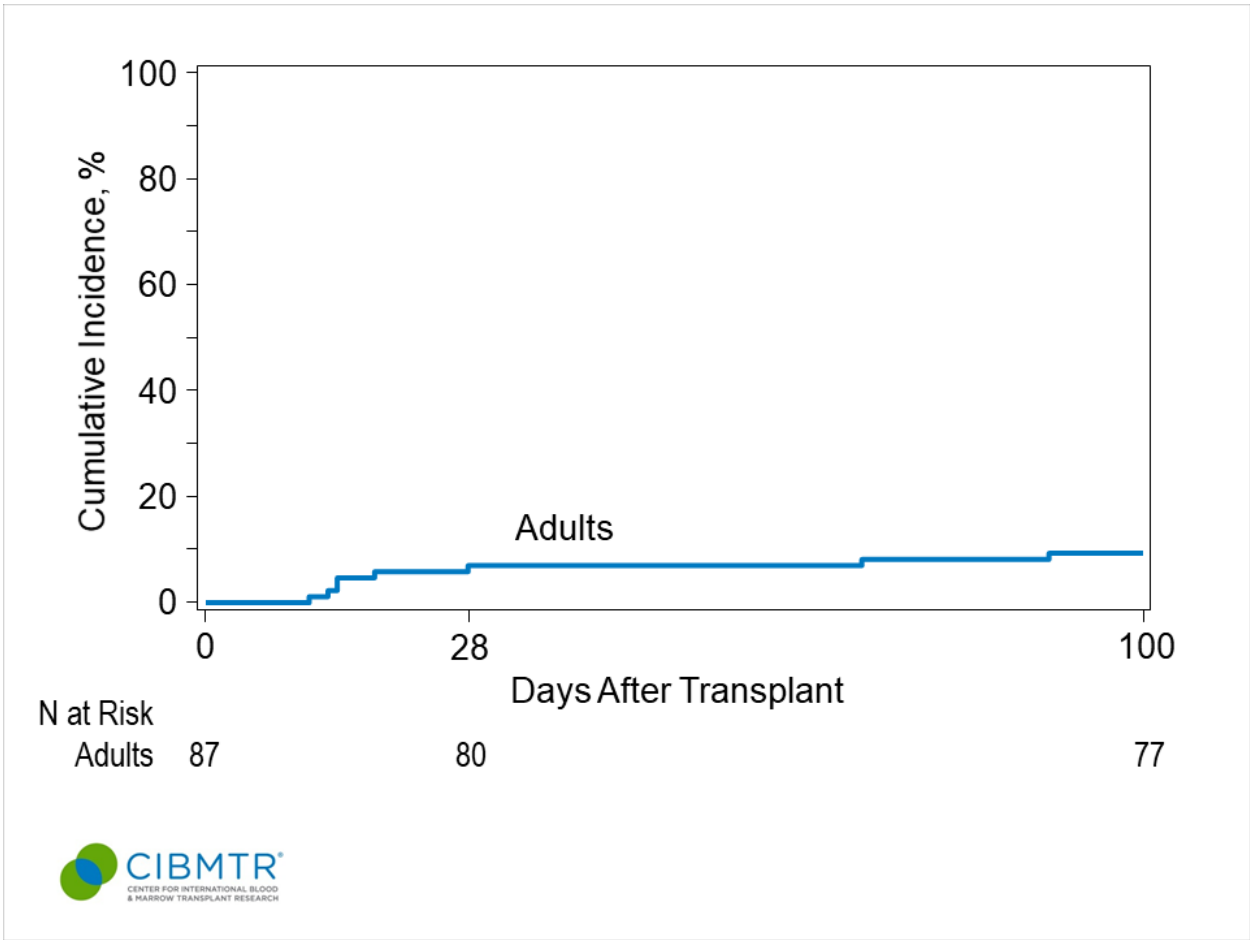


### 16.1.16. Remission subset VOD rates

**Table 68. Post-transplant VOD/SOS within 100 days, in patients who were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients in first complete remission prior to HSCT and with post-transplant follow-up** | **9** | **87** | **96** |
| Veno-occlusive disease, (95% CI) | | | |
| 100 days | NE | 9 (4-16)% | 11 (6-19)% |
| Number of patients with veno-occlusive disease | 3 | 8 | 11 |
| Number of patients with competing risk (death without VOD) | 0 | 1 | 1 |
| Time from transplant to veno-occlusive disease, no. (%), months | | | |
| < 3 | 3 | 8 | 11 |
| Median | 0.33 (0.3-0.43) | 0.53 (0.43-2.96) | 0.46 (0.36-2.30) |
| Range | (0.3-0.43) | (0.36-2.96) | (0.3-2.96) |
| Mean | 0.35 | 1.06 | 0.87 |
| Standard deviation | 0.07 | 1 | 0.9 |

**Figure 21 Post-transplant VOD/SOS within 100 days in adults in first complete remission prior to HSCT**



## 16.1.17. R/R subset VOD characteristics

**Table 69. VOD characteristics within 100 days post-transplant, with and without and defibrotide as liver toxicity prophylaxis, in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 years) No. (%) | | Adult patients (≥ 18 years) No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | Defibrotide | No defibrotide | Defibrotide | No defibrotide | Defibrotide | No defibrotide |
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and post-transplant follow-up** | **19** | **24** | **17** | **139** | **36** | **163** |
| Number of patients with post-transplant VOD/SOS | 5 | 8 | 6 | 21 | 11 | 29 |
| Time to post-transplant VOD/SOS, days | | | | | | |
| Median | 11 | 12 | 13 | 12 | 11 | 12 |
| Range | (8-17) | (6-25) | (6-31) | (5-79) | (6-31) | (5-79) |
| Mean | 11 | 14 | 17 | 20 | 14 | 19 |
| Standard deviation | 3 | 8 | 11 | 21 | 8 | 18 |
| Grade of VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 14 (74) | 16 (67) | 11 (65) | 118 (85) | 25 (69) | 134 (82) |
| Mild VOD/SOS (no other organs involved within 60 days of VOD/SOS diagnosis) | 4 (21) | 2 (8) | 2 (12) | 7 (5) | 6 (17) | 9 (6) |
| Severe VOD/SOS (multiple organ dysfunction within 60 days of VOD/SOS diagnosis) | 1 (5) | 6 (25) | 4 (24) | 14 (10) | 5 (14) | 20 (12) |
| Liver toxicity prophylaxis | | | | | | |
| None (or no additional) | 0 | 5 (21) | 0 | 10 (7) | 0 | 15 (9) |
| Ursodiol | 0 | 15 (63) | 0 | 121 (87) | 0 | 136 (83) |
| Ursodiol + defibrotide | 10 (53) | 0 | 12 (71) | 0 | 22 (61) | 0 |
| Ursodiol + defibrotide + others | 9 (47) | 0 | 4 (24) | 0 | 13 (36) | 0 |
| Ursodiol + others | 0 | 3 (13) | 0 | 4 (3) | 0 | 7 (4) |
| Defibrotide | 0 | 0 | 1 (6) | 0 | 1 (3) | 0 |
| Not reported | 0 | 1 (4) | 0 | 4 (3) | 0 | 5 (3) |
| Treatment for VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 14 (74) | 16 (67) | 11 (65) | 118 (85) | 25 (69) | 134 (82) |
| None | 0 | 0 | 2 (12) | 2 (1) | 2 (6) | 2 (1) |
| Defibrotide | 0 | 1 (4) | 1 (6) | 2 (1) | 1 (3) | 3 (2) |

**Table 69. VOD characteristics within 100 days post-transplant, with and without and defibrotide as liver toxicity prophylaxis, in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 years) No. (%) | | Adult patients (≥ 18 years) No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | Defibrotide | No defibrotide | Defibrotide | No defibrotide | Defibrotide | No defibrotide |
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and post-transplant follow-up** | **19** | **24** | **17** | **139** | **36** | **163** |
| Defibrotide + ursodiol | 1 (5) | 0 | 0 | 0 | 1 (3) | 0 |
| Defibrotide + ursodiol + diuretics | 1 (5) | 2 (8) | 0 | 4 (3) | 1 (3) | 6 (4) |
| Diuretics | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics + heparin | 1 (5) | 1 (4) | 0 | 2 (1) | 1 (3) | 3 (2) |
| Defibrotide + ursodiol + methylprednisolone + N-acetylcysteine + rifaximin/lactulose | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Defibrotide + diuretics | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Defibrotide + ursodiol + methylprednisolone + diuretics + N-acetylcysteine + tissue plasminogen activator | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Not reported | 2 (11) | 4 (17) | 3 (18) | 6 (4) | 5 (14) | 10 (6) |
| Post-VOD/SOS survival | | | | | | |
| N/A; no VOD/SOS | 14 (74) | 16 (67) | 11 (65) | 118 (85) | 25 (69) | 134 (82) |
| Alive | 3 (16) | 4 (17) | 3 (18) | 8 (6) | 6 (17) | 12 (7) |
| Dead | 2 (11) | 4 (17) | 3 (18) | 13 (9) | 5 (14) | 17 (10) |

### 16.1.18. Remission subset VOD characteristics

**Table 70. VOD characteristics within 100 days post-transplant, with and without and defibrotide as liver toxicity prophylaxis, in patients who were in first complete remission prior to HSCT**

| | Pediatric patients < 18 years, No. (%) | | Adult patients ≥ 18 years, No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | Defibrotide | No defibrotide | Defibrotide | No defibrotide | Defibrotide | No defibrotide |
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and post-transplant follow-up** | 4 | 5 | 5 | 82 | 9 | 87 |
| Number of patients with post-transplant VOD/SOS | 2 | 1 | 2 | 6 | 4 | 7 |
| Time to post-transplant VOD/SOS, days | | | | | | |
| Median | NE | 13 | NE | 14 | 40 | 14 |
| Range | (9-10) | NE | (70-90) | (11-28) | (9-90) | (11-28) |
| Mean | 10 | 13 | 80 | 16 | 45 | 16 |
| Standard deviation | 1 | NE | 14 | 6 | 42 | 6 |
| Grade of VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 2 (50) | 4 (80) | 3 (60) | 76 (93) | 5 (56) | 80 (92) |
| Mild VOD/SOS (no other organs involved within 60 days of VOD/SOS diagnosis) | 1 (25) | 1 (20) | 2 (40) | 4 (5) | 3 (33) | 5 (6) |
| Severe VOD/SOS (multiple organ dysfunction within 60 days of VOD/SOS diagnosis) | 1 (25) | 0 | 0 | 2 (2) | 1 (11) | 2 (2) |
| Liver toxicity prophylaxis | | | | | | |
| None (or no additional) | 0 | 1 (20) | 0 | 4 (5) | 0 | 5 (6) |
| Ursodiol | 0 | 4 (80) | 0 | 76 (93) | 0 | 80 (92) |
| Ursodiol + defibrotide | 1 (25) | 0 | 3 (60) | 0 | 4 (44) | 0 |
| Ursodiol + defibrotide + others | 2 (50) | 0 | 1 (20) | 0 | 3 (33) | 0 |
| Ursodiol + others | 0 | 0 | 0 | 2 (2) | 0 | 2 (2) |
| Defibrotide | 1 (25) | 0 | 1 (20) | 0 | 2 (22) | 0 |
| Treatment for VOD/SOS | | | | | | |
| N/A; no VOD/SOS | 2 (50) | 4 (80) | 3 (60) | 76 (93) | 5 (56) | 80 (92) |
| Defibrotide + ursodiol + diuretics | 0 | 0 | 0 | 1 (1) | 0 | 1 (1) |
| Not reported | 2 (50) | 1 (20) | 2 (40) | 5 (6) | 4 (44) | 6 (7) |

**Table 70. VOD characteristics within 100 days post-transplant, with and without and defibrotide as liver toxicity prophylaxis, in patients who were in first complete remission prior to HSCT**

| | Pediatric patients < 18 years, No. (%) | | Adult patients ≥ 18 years, No. (%) | | All patients No. (%) | |
|---|---|---|---|---|---|---|
| | Defibrotide | No defibrotide | Defibrotide | No defibrotide | Defibrotide | No defibrotide |
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and post-transplant follow-up** | 4 | 5 | 5 | 82 | 9 | 87 |
| Post-VOD/SOS survival | | | | | | |
| N/A; no VOD/SOS | 2 (50) | 4 (80) | 3 (60) | 76 (93) | 5 (56) | 80 (92) |
| Alive | 1 (25) | 1 (20) | 0 | 2 (2) | 1 (11) | 3 (3) |
| Dead | 1 (25) | 0 | 2 (40) | 4 (5) | 3 (33) | 4 (5) |

## 16.1.19. R/R post-HSCT clinical status

**Table 71. Post-HSCT clinical status, in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with follow-up** | **43** | **156** | **199** |
| Best response to HSCT | | | |
| Continued complete remission (CR)[a] | 42 (98) | 138 (88) | 180 (90) |
| CR | 0 | 11 (7) | 11 (6) |
| Not in CR | 1 (2) | 4 (3) | 5 (3) |
| Not reported | 0 | 3 (2) | 3 (2) |
| Granulopoiesis / neutrophil recovery[b] | | | |
| Yes | 42 (98) | 145 (93) | 187 (94) |
| No | 0 | 5 (3) | 5 (3) |
| Not reported | 1 (2) | 6 (4) | 7 (4) |
| Time from HSCT to granulopoiesis/neutrophil recovery, days | | | |
| Number evaluable | 42 | 145 | 187 |
| Median | 17 | 17 | 17 |
| Range | (5-30) | (9-52) | (5-52) |
| Mean | 18 | 18 | 18 |
| Standard deviation | 6 | 7 | 6 |
| Megakaryopoiesis / platelet recovery[c] | | | |
| Yes | 36 (84) | 124 (79) | 160 (80) |
| No | 7 (16) | 26 (17) | 33 (17) |
| Not reported | 0 | 6 (4) | 6 (3) |
| Time from HSCT to megakaryopoiesis/platelet recovery, days | | | |
| Number evaluable | 36 | 124 | 160 |
| Median | 33 | 28 | 29 |
| Range | (13-89) | (13-95) | (13-95) |
| Mean | 36 | 32 | 33 |
| Standard deviation | 18 | 16 | 16 |
| Engraftment syndrome within 100 days post-transplant | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Yes | 10 (23) | 13 (8) | 23 (12) |
| No | 32 (74) | 140 (90) | 172 (86) |
| Not reported | 0 | 2 (1) | 2 (1) |
| Time from HSCT to engraftment syndrome, days | | | |
| Number evaluable | 10 | 13 | 23 |
| Median | 13 | 14 | 13 |
| Range | (9-23) | (2-42) | (2-42) |
| Mean | 14 | 15 | 15 |
| Standard deviation | 5 | 9 | 7 |

**Table 71. Post-HSCT clinical status, in patients who had relapsed or refractory B-cell ALL prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with follow-up** | **43** | **156** | **199** |
| Weight, most recent post-HSCT, kg | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Not reported | 0 | 4 (3) | 4 (2) |
| Number evaluable | 42 | 151 | 193 |
| Median | 37 | 77 | 73 |
| Range | (8-104) | (40-199) | (8-199) |
| Mean | 41 | 82 | 73 |
| Standard deviation | 23 | 25 | 30 |
| Height, most recent post-HSCT, cm | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Not reported | 13 (30) | 154 (99) | 167 (84) |
| Number evaluable | 29 | 1 | 30 |
| Median | 127 | 173 | 129 |
| Range | (87-173) | NE | (87-173) |
| Mean | 131 | 173 | 132 |
| Standard deviation | 26 | NE | 27 |
| Performance scale and status, post-HSCT | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| Karnofsky | | | |
| 90-100 | 1 (2) | 53 (34) | 54 (27) |
| 10-80 | 5 (12) | 50 (32) | 55 (28) |
| Not reported | 36 (84) | 52 (33) | 88 (44) |
| Total inpatient days in first 100 days post-HSCT [d] | | | |
| N/A; CIBMTR Form 2100 not yet received | 1 (2) | 1 (1) | 2 (1) |
| < g30 | 10 (23) | 66 (42) | 76 (38) |
| 30-59 | 21 (49) | 46 (29) | 67 (34) |
| 60-100 | 4 (9) | 21 (13) | 25 (13) |
| Not reported | 7 (16) | 22 (14) | 29 (15) |
| Number evaluable | 35 | 133 | 168 |
| Median | 37 | 30 | 31 |
| Range | (21-80) | (6-94) | (6-94) |
| Mean | 41 | 36 | 37 |
| Standard deviation | 15 | 21 | 20 |
| Time from HSCT to date of last contact, months | | | |
| < 3 | 7 (16) | 26 (17) | 33 (17) |
| 3-5 | 4 (9) | 29 (19) | 33 (17) |
| 6-11 | 12 (28) | 30 (19) | 42 (21) |
| ≥ 12 | 20 (47) | 71 (46) | 91 (46) |
| Number evaluable | 43 | 156 | 199 |
| Median | 10.12 | 8.79 | 9.82 |
| Range | (0.92-50.66) | (0.36-50.79) | (0.36-50.79) |
| Mean | 14.8 | 13.85 | 14.05 |
| Standard deviation | 12.85 | 12.26 | 12.37 |

## 16.1.20. Remission post-HSCT clinical status

**Table 72. Post-HSCT clinical status, in patients who were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with follow-up** | **9** | **87** | **96** |
| Best response to HSCT | | | |
| Continued complete remission (CR)[a] | 9 | 87 | 96 |
| Granulopoiesis / neutrophil recovery[b] | | | |
| Yes | 9 | 85 (98) | 94 (98) |
| No | 0 | 2 (2) | 2 (2) |
| Time from HSCT to granulopoiesis/neutrophil recovery, days | | | |
| Number evaluable | 9 | 85 | 94 |
| Median | 21 | 16 | 17 |
| Range | (12-31) | (10-38) | (10-38) |
| Mean | 21 | 17 | 17 |
| Standard deviation | 7 | 5 | 5 |
| Megakaryopoiesis / platelet recovery[c] | | | |
| Yes | 8 (89) | 76 (87) | 84 (88) |
| No | 0 | 9 (10) | 9 (9) |
| Not reported | 1 (11) | 2 (2) | 3 (3) |
| Time from HSCT to megakaryopoiesis/platelet recovery, days | | | |
| Number evaluable | 8 | 76 | 84 |
| Median | 31 | 27 | 28 |
| Range | (17-49) | (12-97) | (12-97) |
| Mean | 33 | 30 | 30 |
| Standard deviation | 11 | 15 | 15 |
| Engraftment syndrome within 100 days post-transplant | | | |
| Yes | 1 (11) | 5 (6) | 6 (6) |
| No | 8 (89) | 82 (94) | 90 (94) |
| Time from HSCT to engraftment syndrome, days | | | |
| Number evaluable | 1 | 5 | 6 |
| Median | 12 | 16 | 15 |
| Range | NE | (12-20) | (12-20) |
| Mean | 12 | 16 | 15 |
| Standard deviation | NE | 4 | 4 |
| Weight, most recent post-HSCT, kg | | | |
| Number evaluable | 9 | 87 | 96 |
| Median | 45 | 83 | 81 |
| Range | (23-84) | (24-163) | (23-163) |
| Mean | 50 | 86 | 82 |
| Standard deviation | 20 | 24 | 26 |

**Table 72. Post-HSCT clinical status, in patients who were in first complete remission prior to HSCT**

| | Pediatric patients (< 18 y) No. (%) | Adults (≥ 18 y) No. (%) | All patients No. (%) |
|---|---|---|---|
| **Number of patients with relapsed or refractory B-cell ALL prior to HSCT and with follow-up** | **9** | **87** | **96** |
| Height, most recent post-HSCT, cm | | | |
| Not reported | 3 (33) | 87 | 90 (94) |
| Number evaluable | 6 | NE | 6 |
| Median | 150 | NE | 150 |
| Range | (119-168) | NE | (119-168) |
| Mean | 148 | NE | 148 |
| Standard deviation | 16 | NE | 16 |
| Performance scale and status, post-HSCT | | | |
| Karnofsky | | | |
| 90-100 | 0 | 37 (43) | 37 (39) |
| 10-80 | 1 (11) | 34 (39) | 35 (36) |
| Not reported | 8 (89) | 16 (18) | 24 (25) |
| Total inpatient days in first 100 days post-HSCT [d] | | | |
| < 30 | 2 (22) | 53 (61) | 55 (57) |
| 30-59 | 5 (56) | 14 (16) | 19 (20) |
| 60-100 | 2 (22) | 10 (11) | 12 (13) |
| Not reported | 0 | 10 (11) | 10 (10) |
| Number evaluable | 9 | 77 | 86 |
| Median | 39 | 23 | 23 |
| Range | (28-93) | (7-92) | (7-93) |
| Mean | 47 | 30 | 32 |
| Standard deviation | 22 | 19 | 20 |
| Time from HSCT to date of last contact, months | | | |
| < 3 | 0 | 7 (8) | 7 (7) |
| 3-5 | 2 (22) | 14 (16) | 16 (17) |
| 6-11 | 3 (33) | 21 (24) | 24 (25) |
| ≥ 12 | 4 (44) | 45 (52) | 49 (51) |
| Number evaluable | 9 | 87 | 96 |
| Median | 11.99 | 12.19 | 12.17 |
| Range | (4.11-35.88) | (0.53-54.08) | (0.53-54.08) |
| Mean | 15.8 | 14.5 | 14.62 |
| Standard deviation | 11.67 | 11.19 | 11.18 |

## 16.2. Subset 3: Relapsed/refractory with inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)

### 16.2.1. Subset 3 demographics

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| No. of centers | 17 | 38 | 48 |
| Age, years, no. (%) | | | |
| < 1 | 1 (3) | 0 | 1 (1) |
| 1-9 | 18 (53) | 0 | 18 (14) |
| 10-17 | 15 (44) | 0 | 15 (12) |
| 18-29 | 0 | 26 (27) | 26 (20) |
| 30-39 | 0 | 18 (19) | 18 (14) |
| 40-49 | 0 | 21 (22) | 21 (16) |
| 50-59 | 0 | 15 (16) | 15 (12) |
| ≥ 60 | 0 | 16 (17) | 16 (12) |
| Number evaluable | 34 | 96 | 130 |
| Median | 8.5 | 42.5 | 31.5 |
| Range | (0-17) | (18-75) | (0-75) |
| Mean | 8.6 | 42.6 | 33.8 |
| Standard deviation | 5.2 | 15.9 | 20.4 |
| Race, no. (%) | | | |
| White | 28 (82) | 69 (72) | 97 (75) |
| Black or African American | 0 | 9 (9) | 9 (7) |
| Asian/Native Hawaiian and other Pacific Islander | 1 (3) | 11 (11) | 12 (9) |
| Others | 2 (6) | 0 | 2 (2) |
| Not reported | 3 (9) | 7 (7) | 10 (8) |
| Weight, kg | | | |
| Number evaluable | 34 | 96 | 130 |
| Median | 31 | 88 | 79 |
| Range | (8-88) | (32-182) | (8-182) |
| Mean | 37 | 92 | 78 |
| Standard deviation | 22 | 29 | 37 |
| Body mass index, $kg/m^2$, no. (%) | | | |
| N/A; BMI does not apply to pediatric patients | 34 | 0 | 34 (26) |
| Underweight | 0 | 5 (5) | 5 (4) |
| Healthy weight | 0 | 16 (17) | 16 (12) |
| Overweight | 0 | 25 (26) | 25 (19) |
| Obese | 0 | 50 (52) | 50 (38) |
| Number evaluable | 34 | 96 | 130 |
| Median | 18.9 | 30.3 | 27.3 |
| Range | (15.1-28.7) | (12.2-62.5) | (12.2-62.5) |
| Mean | 20.1 | 31.4 | 28.4 |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| Standard deviation | 4.2 | 9.2 | 9.5 |
| Body surface area, $m^2$ | | | |
| Number evaluable | 34 | 96 | 130 |
| Median | 1.1 | 2 | 1.9 |
| Range | (0.4-2.1) | (1.2-3) | (0.4-3) |
| Mean | 1.1 | 2.1 | 1.8 |
| Standard deviation | 0.5 | 0.3 | 0.6 |
| Height, cm | | | |
| Number evaluable | 34 | 96 | 130 |
| Median | 132.5 | 171 | 167.8 |
| Range | (67-176) | (152-190) | (67-190) |
| Mean | 128.1 | 170.9 | 159.7 |
| Standard deviation | 30.5 | 8.6 | 25.5 |
| Sex, no. (%) | | | |
| Male | 16 (47) | 55 (57) | 71 (55) |
| Female | 18 (53) | 41 (43) | 59 (45) |
| Sorror HCT-CI, no. (%) [a] | | | |
| 0 | 12 (35) | 12 (13) | 24 (18) |
| 1-2 | 14 (41) | 34 (35) | 48 (37) |
| 3-4 | 7 (21) | 32 (33) | 39 (30) |
| 5 | 1 (3) | 11 (11) | 12 (9) |
| 6 | 0 | 1 (1) | 1 (1) |
| 7 | 0 | 3 (3) | 3 (2) |
| Not reported | 0 | 3 (3) | 3 (2) |
| Arrhythmia, no. (%) [b] | | | |
| Yes | 1 (3) | 9 (9) | 10 (8) |
| No | 33 (97) | 84 (88) | 117 (90) |
| Not reported | 0 | 3 (3) | 3 (2) |
| Cardiac disease, no. (%) [c] | | | |
| Yes | 0 | 5 (5) | 5 (4) |
| No | 34 | 88 (92) | 122 (94) |
| Not reported | 0 | 3 (3) | 3 (2) |
| Cerebrovascular disease, no. (%) [d] | | | |
| Yes | 0 | 4 (4) | 4 (3) |
| No | 34 | 89 (93) | 123 (95) |
| Not reported | 0 | 3 (3) | 3 (2) |
| Hepatic disease, no. (%) | | | |
| Moderate/severe [e] | 4 (12) | 4 (4) | 8 (6) |
| Mild [f] | 9 (26) | 21 (22) | 30 (23) |
| No hepatic disease | 21 (62) | 68 (71) | 89 (68) |
| Not reported | 0 | 3 (3) | 3 (2) |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| Lines of salvage therapy prior to transplant, no. (%) [g] | | | |
| Salvage 1 | 6 (18) | 16 (17) | 22 (17) |
| Salvage 2 | 2 (6) | 31 (32) | 33 (25) |
| Salvage > 2 | 26 (76) | 49 (51) | 75 (58) |
| Number evaluable | 34 | 96 | 130 |
| Median | 5.5 | 4 | 4 |
| Range | (2-14) | (2-7) | (2-14) |
| Mean | 5.9 | 3.8 | 4.3 |
| Standard deviation | 3.4 | 1.4 | 2.3 |
| Lines of salvage therapy prior to inotuzumab ozogamicin, no. (%) | | | |
| No treatment given | 1 (3) | 1 (1) | 2 (2) |
| First line | 5 (15) | 18 (19) | 23 (18) |
| Salvage 1 | 2 (6) | 30 (31) | 32 (25) |
| Salvage 2 | 8 (24) | 28 (29) | 36 (28) |
| Salvage > 2 | 18 (53) | 19 (20) | 37 (28) |
| Number evaluable | 34 | 96 | 130 |
| Median | 4.5 | 2 | 3 |
| Range | (0-13) | (0-6) | (0-13) |
| Mean | 4.6 | 2.6 | 3.2 |
| Standard deviation | 3.1 | 1.4 | 2.1 |
| Aspartate transaminase (AST), prior to transplant, no. (%) | | | |
| Normal | 14 (41) | 62 (65) | 76 (58) |
| Abnormal | 20 (59) | 33 (34) | 53 (41) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Number evaluable | 34 | 95 | 129 |
| Median | 1.2 | 0.9 | 0.9 |
| Range | (0.3-3.6) | (0.4-2.9) | (0.3-3.6) |
| Mean | 1.3 | 1 | 1.1 |
| Standard deviation | 0.7 | 0.5 | 0.6 |
| Total serum bilirubin, prior to transplant, no. (%) | | | |
| Normal | 33 (97) | 86 (90) | 119 (92) |
| Abnormal | 1 (3) | 8 (8) | 9 (7) |
| Not reported | 0 | 2 (2) | 2 (2) |
| Number evaluable | 34 | 94 | 128 |
| Median | 0.3 | 0.4 | 0.4 |
| Range | (0-1.1) | (0.2-1.7) | (0-1.7) |
| Mean | 0.4 | 0.5 | 0.5 |
| Standard deviation | 0.3 | 0.3 | 0.3 |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| Platelets, × $10^9$/L, prior to transplant, no. (%) | | | |
| Not reported | 1 (3) | 5 (5) | 6 (5) |
| Number evaluable | 33 | 91 | 124 |
| Median | 128 | 106 | 114.5 |
| Range | (10-310) | (11-316) | (10-316) |
| Mean | 134.3 | 118.2 | 122.5 |
| Standard deviation | 73.7 | 69.1 | 70.4 |
| Neutrophils, prior to transplant, × $10^9$/L, no. (%) | | | |
| Not reported | 2 (6) | 3 (3) | 5 (4) |
| Number evaluable | 32 | 93 | 125 |
| Median | 47 | 54 | 53 |
| Range | (20-86) | (4-95) | (4-95) |
| Mean | 51.3 | 53.2 | 52.7 |
| Standard deviation | 17.9 | 17.5 | 17.6 |
| Hemoglobin, prior to transplant, g/dL, no. (%) | | | |
| Number evaluable | 34 | 96 | 130 |
| Median | 11.7 | 12.4 | 12.2 |
| Range | (6.7-16.3) | (8-17.7) | (6.7-17.7) |
| Mean | 11.6 | 12.3 | 12.1 |
| Standard deviation | 1.7 | 2.1 | 2 |
| White blood cell (WBC) count at diagnosis, × $10^9$/L, no. (%) | | | |
| Not reported | 8 (24) | 13 (14) | 21 (16) |
| Number evaluable | 26 | 83 | 109 |
| Median | 12.9 | 13.6 | 13.3 |
| Range | (0.4-525) | (0.8-368) | (0.4-525) |
| Mean | 61.6 | 60.6 | 60.9 |
| Standard deviation | 118.9 | 93.5 | 99.5 |
| Blasts in blood, at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | |
| < 1% | 1 (3) | 6 (6) | 7 (5) |
| ≥ 1% | 20 (59) | 71 (74) | 91 (70) |
| Not reported | 13 (38) | 19 (20) | 32 (25) |
| Number evaluable | 21 | 77 | 98 |
| Median | 46 | 51 | 48.5 |
| Range | (0-98) | (0-99) | (0-99) |
| Mean | 50.1 | 48.9 | 49.1 |
| Standard deviation | 32.6 | 34.6 | 34 |
| Blasts in bone marrow, at diagnosis of B-cell ALL, × $10^9$/L, no. (%) | | | |
| < 50% | 2 (6) | 4 (4) | 6 (5) |
| 50-89% | 7 (21) | 34 (35) | 41 (32) |
| ≥ 90% | 12 (35) | 38 (40) | 50 (38) |
| Not reported | 13 (38) | 20 (21) | 33 (25) |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| Number evaluable | 21 | 76 | 97 |
| Median | 92 | 89.5 | 90 |
| Range | (21-98) | (2-100) | (2-100) |
| Mean | 82.3 | 81.2 | 81.5 |
| Standard deviation | 21.4 | 20.5 | 20.6 |
| White blood cell (WBC) count prior to transplant, $\times 10^9$/L, no. (%) | | | |
| Number evaluable | 34 | 96 | 130 |
| Median | 3.6 | 3.6 | 3.6 |
| Range | (0.4-11.8) | (0.4-8.9) | (0.4-11.8) |
| Mean | 4.1 | 3.8 | 3.9 |
| Standard deviation | 2.6 | 1.9 | 2.1 |
| Blasts in blood prior to transplant, $\times 10^9$/L, no. (%) | | | |
| < 1% | 23 (68) | 67 (70) | 90 (69) |
| ≥ 1% | 0 | 4 (4) | 4 (3) |
| Not reported | 11 (32) | 25 (26) | 36 (28) |
| Number evaluable | 23 | 71 | 94 |
| Median | 0 | 0 | 0 |
| Range | (0-0) | (0-2) | (0-2) |
| Mean | 0 | 0.08 | 0.06 |
| Standard deviation | 0 | 0.37 | 0.32 |
| Blasts in bone marrow, prior to transplant, $\times 10^9$/L, no. (%) | | | |
| < 5% | 27 (79) | 84 (88) | 111 (85) |
| Not reported | 7 (21) | 12 (13) | 19 (15) |
| Number evaluable | 27 | 84 | 111 |
| Median | 0 | 1 | 1 |
| Range | (0-3) | (0-4) | (0-4) |
| Mean | 0.52 | 1.15 | 1 |
| Standard deviation | 0.8 | 1.2 | 1.14 |
| Extramedullary disease, at diagnosis of B-cell ALL, no. (%) | | | |
| Yes | 5 (15) | 11 (11) | 16 (12) |
| No | 16 (47) | 76 (79) | 92 (71) |
| Unknown | 2 (6) | 7 (7) | 9 (7) |
| Not reported | 11 (32) | 2 (2) | 13 (10) |
| Extramedullary disease, at last evaluation prior to transplant, no. (%) | | | |
| Yes | 1 (3) | 3 (3) | 4 (3) |
| No | 33 (97) | 91 (95) | 124 (95) |
| Unknown | 0 | 2 (2) | 2 (2) |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| Performance score prior to transplant, no. (%) | | | |
| Karnofsky, 90-100 | 3 (9) | 48 (50) | 51 (39) |
| Karnofsky, 10-80 | 0 | 44 (46) | 44 (34) |
| Karnofsky, not reported | 0 | 4 (4) | 4 (3) |
| Lansky, 90-100 | 28 (82) | 0 | 28 (22) |
| Lansky, 10-80 | 3 (9) | 0 | 3 (2) |
| History of proven invasive fungal infection, no. (%) | | | |
| Yes | 6 (18) | 2 (2) | 8 (6) |
| No | 28 (82) | 93 (97) | 121 (93) |
| Not reported | 0 | 1 (1) | 1 (1) |
| Disease status prior to transplant, no. (%) | | | |
| CR2 | 18 (53) | 72 (75) | 90 (69) |
| CR3+ | 16 (47) | 15 (16) | 31 (24) |
| REL1 | 0 | 6 (6) | 6 (5) |
| REL3+ | 0 | 1 (1) | 1 (1) |
| PIF | 0 | 2 (2) | 2 (2) |
| Prior autologous HSCT, no. (%) | | | |
| No | 34 | 96 | 130 |
| Time from diagnosis to HSCT, months, no. (%) | | | |
| < 3 | 1 (3) | 0 | 1 (1) |
| 6-11 | 4 (12) | 20 (21) | 24 (18) |
| ≥ 12 | 16 (47) | 59 (61) | 75 (58) |
| Outliers[h] | 13 (38) | 17 (18) | 30 (23) |
| Number evaluable | 21 | 79 | 100 |
| Median | 22.14 | 20.27 | 20.81 |
| Range | (2.89-47.57) | (6.21-46.39) | (2.89-47.57) |
| Mean | 25.88 | 21.64 | 22.53 |
| Standard deviation | 15.06 | 10.99 | 12 |
| Time from diagnosis to first dose of inotuzumab ozogamicin, months, no. (%) | | | |
| < 3 | 1 (3) | 2 (2) | 3 (2) |
| 3-5 | 0 | 6 (6) | 6 (5) |
| 6-11 | 6 (18) | 15 (16) | 21 (16) |
| ≥ 12 | 13 (38) | 54 (56) | 67 (52) |
| Outliers[h] | 11 (32) | 13 (14) | 24 (18) |
| Not reported | 3 (9) | 6 (6) | 9 (7) |
| Number evaluable | 20 | 77 | 97 |
| Median | 20.16 | 17.12 | 17.51 |
| Range | (0.3-46.09) | (1.81-44.06) | (0.3-46.09) |
| Mean | 23.12 | 18.96 | 19.82 |
| Standard deviation | 14.97 | 11.06 | 12 |

**Table 73. Characteristics of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| Characteristic | Peds | Adults | Total |
|---|---|---|---|
| **No. of patients** | **34** | **96** | **130** |
| GVHD prophylaxis, no. (%) | | | |
| Ex-vivo T-cell depletion | 4 (12) | 1 (1) | 5 (4) |
| Cyclophosphamide ± others | 11 (32) | 42 (44) | 53 (41) |
| Tac + MMF ± others (not Cy) | 3 (9) | 13 (14) | 16 (12) |
| Tac + MTX ± others (not Cy, MMF) | 3 (9) | 31 (32) | 34 (26) |
| Tac ± others (not Cy, MMF, MTX) | 0 | 3 (3) | 3 (2) |
| CsA + MMF ± others (not Cy, Tac) | 6 (18) | 1 (1) | 7 (5) |
| CsA + MTX ± others (not Cy, Tac, MMF) | 6 (18) | 5 (5) | 11 (8) |
| Not reported | 1 (3) | 0 | 1 (1) |
| Conditioning regimen intensity, no. (%) [i] | | | |
| Myeloablative | 33 (97) | 49 (51) | 82 (63) |
| RIC/NMA | 1 (3) | 47 (49) | 48 (37) |
| Dual alkylators used in conditioning regimen, no. (%)[j] | | | |
| Yes | 8 (24) | 9 (9) | 17 (13) |
| No | 26 (76) | 87 (91) | 113 (87) |
| Busulfan used in conditioning regimen, no. (%) | | | |
| Yes | 4 (12) | 14 (15) | 18 (14) |
| No | 30 (88) | 82 (85) | 112 (86) |
| Thiotepa used in conditioning regimen, no. (%) | | | |
| Yes | 8 (24) | 8 (8) | 16 (12) |
| No | 26 (76) | 88 (92) | 114 (88) |
| Product type, no. (%) | | | |
| BM | 19 (56) | 15 (16) | 34 (26) |
| PBSC | 7 (21) | 76 (79) | 83 (64) |
| UCB | 8 (24) | 5 (5) | 13 (10) |
| Donor type, no. (%) | | | |
| HLA-identical sibling | 5 (15) | 23 (24) | 28 (22) |
| Other related | 12 (35) | 29 (30) | 41 (32) |
| Unrelated | 17 (50) | 44 (46) | 61 (47) |
| Follow-up, median (range), months | 15.18 (3.52-50.66) | 23.66 (3.61-48.26) | 21.36 (3.52-50.66) |

Note: Median and range values are calculated using only patients with complete data for that variable.
[a] Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. Blood 2004; 104:961-8.
[b] History of atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment.
[c] History of coronary artery disease (one or more vessel-coronary artery stenosis requiring medical treatment, stent, or bypass graft), congestive heart failure, myocardial infarction, OR ejection fraction ≤ 50% on the most recent test.
[d] History of transient ischemic attack, subarachnoid hemorrhage or cerebrovascular accident.
[e] Liver cirrhosis, bilirubin > 1.5 × upper limit of normal, or AST/ALT > 2.5 × upper limit of normal.
[f] Chronic hepatitis, bilirubin > upper limit of normal to 1.5 × upper limit of normal, or AST/ALT > upper limit of normal to 2.5 × upper limit of normal at the time of transplant OR any history of hepatitis B or hepatitis C infection.
[g] The lines of therapy prior to a specified event are defined as follows. “No treatment given” means no lines of therapy given prior to specified event; “First line” means 1 line of therapy; “Salvage 1” means 2 lines of therapy; “Salvage 2” means 3 lines of therapy; “Salvage > 2” means 4 (or more) lines of therapy.
[h] Outliers are defined as patients who underwent HSCT in CR1 more than 12 months after disease diagnosis, or patients who underwent HSCT for all other disease statuses more than 48 months after disease diagnosis.

[i] Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. Biol Blood Marrow Transplant 2009;15:1628-33.
[j] Dual alkylators were defined as the conditioning regimen including one of the following pairs of treatments: busulfan + cyclophosphamide; busulfan + melphalan; cyclophosphamide + melphalan; busulfan + thiotepa; or cyclophosphamide + thiotepa.

### 16.2.2. Subset 3 post-transplant overall survival

**Table 74. Post-transplant overall survival within 18 months of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **33** | **93** | **126** |
| Post-transplant overall survival (95% CI) | | | |
| 6 months | 79 (63-91)% | 65 (55-74)% | 69 (60-76)% |
| 12 months | NE | 46 (35-57)% | 53 (44-62)% |
| 18 months | NE | 42 (31-53)% | 50 (41-60)% |
| Number of deaths within 18 months | 8 | 48 | 56 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 5 (63) | 16 (33) | 21 (38) |
| New malignancy | 0 | 0 | 0 |
| GVHD | 0 | 7 (15) | 7 (13) |
| VOD/SOS | 1 (13) | 6 (13) | 7 (13) |
| Interstitial pneumonitis | 0 | 1 (2) | 1 (2) |
| Infection | 1 (13) | 5 (10) | 6 (11) |
| Septic shock | 0 | 1 (2) | 1 (2) |
| Thrombotic microangiopathy (TMA) | 0 | 0 | 0 |
| Hemorrhage | 0 | 4 (8) | 4 (7) |
| Organ failure | 1 (13) | 7 (15) | 8 (14) |
| Graft failure | 0 | 1 (2) | 1 (2) |
| Other | 0 | 0 | 0 |
| Time from transplant to death, no. (%) months | | | |
| < 3 | 6 (75) | 15 (31) | 21 (38) |
| 3-5 | 1 (13) | 17 (35) | 18 (32) |
| 6-11 | 1 (13) | 14 (29) | 15 (27) |
| 12-18 | 0 | 2 (4) | 2 (4) |
| Median (95% CI) | 2.38 (1.12-10.12) | 4.19 (3.35-5.75) | 3.93 (2.92-5.06) |
| Range | (0.92-10.12) | (0.36-15.21) | (0.36-15.21) |
| Mean | 3.2 | 5.04 | 4.78 |
| Standard deviation | 2.95 | 3.42 | 3.4 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-transplant overall survival is time from HSCT to death from any cause. Patients are censored at the last date that the patient was known to be alive. There are no competing risks.

### 16.2.3. Subset 3 post-transplant overall mortality

**Table 75. Post-transplant overall mortality within 18 months of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimen)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **Number of patients with post-transplant follow-up** | **33** | **93** | **126** |
| Post-transplant overall mortality (95% CI) | | | |
| 6 months | 21 (9-37)% | 35 (26-45)% | 31 (24-40)% |
| 12 months | NE | 54 (43-65)% | 47 (38-56)% |
| 18 months | NE | 58 (47-69)% | 50 (40-59)% |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.

Outcomes are not evaluable (NE) if sample size is < 20.

Post-transplant overall mortality is time from HSCT to death from any cause. Patients are censored at the last date that the patient was known to be alive. There are no competing risks.

### 16.2.4. Subset 3 post-inotuzumab overall survival

**Table 76. Overall survival within 18 months of first dose of inotuzumab ozogamicin in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with follow-up and CIBMTR Form 2541 and date of first dose of inotuzumab ozogamicin provided** | **32** | **90** | **122** |
| Post-inotuzumab ozogamicin overall survival (95% CI) | | | |
| 6 months | 78 (62-90)% | 84 (76-91)% | 83 (75-89)% |
| 12 months | NE | 53 (42-64)% | 60 (50-69)% |
| 18 months | NE | 46 (35-57)% | 53 (43-62)% |
| Number of deaths within 18 months | 8 | 44 | 52 |
| Primary cause of death, no. (%) | | | |
| Recurrence of B-cell ALL | 5 (63) | 14 (32) | 19 (37) |
| GVHD | 0 | 7 (16) | 7 (13) |
| VOD/SOS | 1 (13) | 6 (14) | 7 (13) |
| Interstitial pneumonitis | 0 | 1 (2) | 1 (2) |
| Infection | 1 (13) | 5 (11) | 6 (12) |
| Septic shock | 0 | 1 (2) | 1 (2) |
| Thrombotic microangiopathy | 0 | 0 | 0 |
| Hemorrhage | 0 | 3 (7) | 3 (6) |
| Organ failure | 1 (13) | 6 (14) | 7 (13) |
| Graft failure | 0 | 1 (2) | 1 (2) |
| Other | | | |
| Time from first dose of inotuzumab ozogamicin to death, no. (%), months | | | |
| < 3 | 0 | 1 (2) | 1 (2) |
| 3-5 | 7 (88) | 13 (30) | 20 (38) |
| 6-11 | 0 | 25 (57) | 25 (48) |
| 12-18 | 1 (13) | 5 (11) | 6 (12) |
| Median (95% CI) | 4.39 (4.04-12.85) | 7.23 (6.54-9.3) | 6.78(5.65-8.74) |
| Range | (4.04-12.85) | (1.94-15.47) | (1.94-15.47) |
| Mean | 5.63 | 7.92 | 7.57 |
| Standard deviation | 2.99 | 3.19 | 3.24 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-inotuzumab ozogamicin survival is time from first dose of inotuzumab ozogamicin to death from any cause. Patients are censored at the last date that the patient was known to be alive. There are no competing risks.

### 16.2.5. Subset 3 transplant-related mortality

**Table 77. Transplant-related mortality within 18 months in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **33** | **93** | **126** |
| Transplant-related mortality (95% CI) | | | |
| 6 months | 9 (2-21)% | 22 (14-31)% | 18 (12-26)% |
| 12 months | NE | 26 (17-36)% | 22 (15-29)% |
| 18 months | NE | NE | 23 (16-31)% |
| No. patients with TRM within 18 months | 3 | 24 | 27 |
| No. patients with competing risk (post-transplant relapse) within 18 months | 14 | 35 | 49 |
| Primary cause of death, among patients with TRM, no. (%) | | | |
| GVHD | 0 | 5 (21) | 5 (19) |
| VOD/SOS | 1 (33) | 5 (21) | 6 (22) |
| Interstitial pneumonitis | 0 | 1 (4) | 1 (4) |
| Infection | 1 (33) | 2 (8) | 3 (11) |
| Septic shock | 0 | 1 (4) | 1 (4) |
| Thrombotic microangiopathy (TMA) | 0 | 0 | 0 |
| Hemorrhage | 0 | 3 (13) | 3 (11) |
| Organ failure | 1 (33) | 6 (25) | 7 (26) |
| Graft failure | 0 | 1 (4) | 1 (4) |
| Other | 0 | 0 | 0 |
| Time from transplant to TRM, no. (%), months | | | |
| < 3 | 3 | 13 (54) | 16 (59) |
| 3-5 | 0 | 7 (29) | 7 (26) |
| 6-11 | 0 | 3 (13) | 3 (11) |
| 12-18 | 0 | 1 (4) | 1 (4) |
| Median (95% CI) | 2.3 (0.92-2.92) | 2.25 (1.84-3.98) | 2.30 (1.84-3.88) |
| Range | (0.92-2.92) | (0.36-13.08) | (0.36-13.08) |
| Mean | 2.05 | 3.72 | 3.53 |
| Standard deviation | 1.03 | 3.33 | 3.19 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.

Outcomes are not evaluable (NE) if sample size is < 20.

Transplant-related mortality (post-transplant non-relapse mortality) is time from HSCT to death within the first 28 days post-HSCT, or death from any cause without prior relapse/progression post-HSCT.

### 16.2.6. Subset 3 non-transplant-related mortality

**Table 78. Non-transplant-related mortality within 18 months in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **33** | **93** | **126** |
| Non-transplant-related mortality (95% CI) | | | |
| 6 months | 0.1 (0.0-0.2)% | 0.1 (0.1-0.2)% | 0.1 (0.1-0.2) |
| 12 months | NE | 0.3 (0.2-0.4)% | 0.3 (0.2-0.3) |
| 18 months | NE | NE | 0.3 (0.2-0.4) |
| No. patients with NTRM within 18 months | 5 | 24 | 29 |
| No. patients with competing risk (transplant-related mortality) | 3 | 24 | 27 |
| Time from transplant to NTRM, no. (%), months | | | |
| < 3 | 3 (60) | 2 (8) | 5 (17) |
| 3-5 | 1 (20) | 10 (42) | 11 (38) |
| 6-11 | 1 (20) | 11 (46) | 12 (41) |
| 12-18 | 0 | 1 (4) | 1 (3) |
| Median (95% CI) | 2.46 (1.12-10.12) | 5.88 (4.7-7.39) | 5.49 (4.17-7.23) |
| Range | (1.12-10.12) | (2.23-15.21) | (1.12-15.21) |
| Mean | 3.9 | 6.36 | 5.94 |
| Standard deviation | 3.62 | 3.04 | 3.22 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Non-transplant-related mortality is time from HSCT to death after the first 28 days post-HSCT from any cause after prior relapse/progression post-HSCT.

### 16.2.7. Subset 3 post-transplant relapse

**Table 79. Post-transplant relapse within 18 months in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **33** | **93** | **126** |
| Post-transplant relapse (95% CI) | | | |
| 6 months | 25 (11-41)% | 27 (19-37)% | 18 (12-26)% |
| 12 months | NE | 34 (24-44)% | 22 (15-29)% |
| 18 months | NE | NE | 23 (16-31)% |
| No. patients with post-transplant relapse within 18 months | 14 | 35 | 49 |
| No. patients with competing risk (transplant-related mortality) | 3 | 24 | 27 |
| Months from transplant to post-transplant relapse, no. (%) | | | |
| < 3 | 6 (43) | 10 (29) | 16 (33) |
| 3-5 | 2 (14) | 15 (43) | 17 (35) |
| 6-11 | 4 (29) | 5 (14) | 9 (18) |
| 12-18 | 2 (14) | 5 (14) | 7 (14) |
| Median (95% CI) | 4.63 (1.38-11.86) | 3.45 (3.06-5.88) | 3.51 (3.05-5.88) |
| Range | (1.08-12.42) | (1.02-14.39) | (1.02-14.39) |
| Mean | 5.58 | 5.23 | 5.33 |
| Standard deviation | 4.45 | 3.98 | 4.07 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table. Patients with a reported outcome event beyond 18 months post-transplant (or post-inotuzumab ozogamicin) are not shown in this table, as follow-up among survivors in the population is approximately 18 months post-transplant.
Outcomes are not evaluable (NE) if sample size is < 20.
Post-transplant relapse is time from HSCT to first relapse post-HSCT without death post-relapse, or with death after the first 28 days post-HSCT.

### 16.2.8. Subset 3 VOD rates

**Table 80. Veno-occlusive disease within 100 days in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Pediatric patients (< 18 y) | Adults (≥ 18 y) | All patients |
|---|---|---|---|
| **No. patients with post-transplant follow-up** | **33** | **93** | **126** |
| Veno-occlusive disease | | | |
| 100 days (95% CI) | 30 (16-47)% | 17 (10-26)% | 21 (14-28)% |
| No. patients with veno-occlusive disease | 10 | 16 | 26 |
| No. patients with competing risk (death without VOD) | 1 | 6 | 7 |
| Time from transplant to veno-occlusive disease, no. (%), months | | | |
| < 3 | 10 | 16 | 26 |
| Median (95% CI) | 0.34 (0.23-0.82) | 0.48 (0.36-0.79) | 0.41 (0.33-0.56) |
| Range | (0.2-0.82) | (0.16-2.3) | (0.16-2.3) |
| Mean | 0.41 | 0.67 | 0.57 |
| Standard deviation | 0.23 | 0.58 | 0.49 |

Notes: The CIBMTR collects follow-up data at specific time points post-HSCT, specifically at 100 days, 6 months and annually until year 6 post-HSCT and biennially thereafter until death. Patients who have not yet completed a follow-up form are not included in the data and estimates shown in this table.
VOD is the occurrence of veno-occlusive disease/sinusoidal obstruction syndrome reported on the CIBMTR Form 2100. VOD is only considered within the first 100 days post-HSCT. Death without VOD is the competing risk.

### 16.2.9. Subset 3 outcomes

**Table 81. Outcomes by lines of therapy of relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Salvage 1 (N = 21) | | Salvage 2 (N = 31) | | Salvage > 2 (N = 74) | |
|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Overall survival | 21 | | 31 | | 74 | |
| 6 months | | NE | | NE | | 73 (62-82)% |
| 1 year | | NE | | NE | | 58 (47-70)% |
| 18 months | | NE | | NE | | 54 (42-66)% |
| Overall mortality | 21 | | 31 | | 74 | |
| 6 months | | NE | | NE | | 27 (18-38)% |
| 1 year | | NE | | NE | | 42 (30-53)% |
| 18 months | | NE | | NE | | 46 (34-58)% |
| Overall survival post first dose of inotuzumab | 20 | | 28 | | 74 | |
| 6 months | | NE | | 89 (75-98)% | | 82 (73-90)% |
| 1 year | | NE | | NE | | 66 (54-77)% |
| 18 months | | NE | | NE | | 57 (45-69)% |
| Transplant-related mortality | 21 | | 31 | | 74 | |
| 6 months | | NE | | NE | | 15 (8-24)% |
| 1 year | | NE | | NE | | 18 (10-28)% |
| 18 months | | NE | | NE | | NE |
| Non-transplant-related mortality | 21 | | 31 | | 74 | |
| 6 months | | NE | | NE | | 12(6-21) |
| 1 year | | NE | | NE | | 24(15-34) |
| 18 months | | NE | | NE | | NE |
| Relapse | 21 | | 31 | | 74 | |
| 6 months | | NE | | NE | | 26 (16-36)% |
| 1 year | | NE | | NE | | 37 (26-48)% |
| 18 months | | NE | | NE | | NE |
| Post-HSCT VOD/SOS | 21 | | 31 | | 74 | |
| 100-day | | NE | | 26 (12-43)% | | 19 (11-29)% |

### 16.2.10. VOD and therapy in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)

**Table 82. VOD by lines of therapy prior to transplant in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Lines of salvage therapy prior to transplant | | | |
|---|---|---|---|---|
| **VOD** | **Salvage 1** | **Salvage 2** | **Salvage > 2** | **Total** |
| No | 17 (81) | 23 (74) | 60 (81) | 100 (79) |
| Yes | 4 (19) | 8 (26) | 14 (19) | 26 (21) |

**Table 83. VOD by number of cycles of inotuzumab in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | 1 Cycle | | 2 Cycles | | ≥ 3 Cycles | |
|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 42 | | 60 | | 23 | |
| 100-day | | 24 (12-38)% | | 17 (8-27)% | | NE |

**Table 84. VOD by cumulative inotuzumab dose in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | < 1.8 mg/m² | | 1.8-2.7 mg/m² | | 2.8-3.2 mg/m² | | ≥ 3.3 mg/m² | |
|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 32 | | 27 | | 11 | | 46 | |
| 100-day | | 25 (12-41)% | | 22 (9-40)% | | NE | | 15 (6-27)% |

**Table 85. VOD by lines of therapy prior to inotuzumab in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Lines of salvage therapy prior to inotuzumab | | | | |
|---|---|---|---|---|---|
| **VOD** | **First line** | **Salvage 1** | **Salvage 2** | **Salvage ≥ 2** | **Total** |
| **No** | 18 (81) | 23 (77) | 29 (83) | 29 (78) | 99 (80) |
| **Yes** | 4 (18) | 7 (23) | 6 (17) | 8 (22) | 25 (20) |

**Table 86. VOD rates by remission type in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | CR2 (N = 87) | | Advanced (N = 39) | |
|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 87 | | 39 | |
| 100-day | | 21 (13-30)% | | 21 (9-35)% |

**Table 87. VOD rates by time from last inotuzumab dose to first alloHSCT in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | < 1 (N = 19) | | 1-1.6 (N = 48) | | 1.7-3 (N = 35) | | > 3 (N = 21) | |
|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 19 | | 48 | | 35 | | 21 | |
| 100-day | | NE | | 21 (11-33)% | | 31 (17-48)% | | NE |

**Table 88. VOD rates by study year in relapsed or refractory B-cell ALL patients who received inotuzumab ozogamicin prior to first alloHSCT and proceeded to HSCT without any intervening therapies (excluding conditioning regimens)**

| | Aug 2017-Aug 2018 | | Aug 2018-Aug 2019 | | Aug 2019-Aug 2020 | | Aug 2020-Aug 2021 | | Aug 2021-Aug 2022 | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Outcomes** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** | **N** | **Prob (95% CI)** |
| Post-HSCT VOD/SOS | 29 | | 29 | | 30 | | 25 | | 13 | |
| 100-day | | 14 (4-29)% | | 28 (13-45)% | | 20 (8-36)% | | 16 (4-33)% | | NE |

# Document Approval Record

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