NON-INTERVENTIONAL (NI) STUDY REPORT
INTERIM REPORT #1

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	20 February 2019
EU Post Authorization Study (PAS) register number	EUPAS23056
Active substance	Inotuzumab ozogamicin
Medicinal product	Inotuzumab ozogamicin (Besponsa®)
Research question and objectives	Research question: What are the toxicities after HSCT in adult and pediatric patients who receive inotuzumab ozogamicin? Objectives: 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; • Timing of inotuzumab ozogamicin treatment prior to HSCT; • Transplant-related mortality (TRM) (non-relapse mortality), non-transplant related mortality (NTRM), relapse, and overall survival (OS); • Post-HSCT adverse events of interest including hepatic veno-occlusive disease /sinusoidal obstruction syndrome (VOD/SOS); and

	• Cause of death (COD).
Author	Kofi Asomaning, PhD Epidemiology Lead, Pfizer Inc., 500 Arcola Road, Collegeville, PA 19426, USA

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1. ABSTRACT

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).

Date:

20 February 2019

Name and affiliation of the Main Author:

Kofi Asomaning PhD, Epidemiology Lead, Pfizer Inc.

Keywords:

Inotuzumab ozogamicin, post-HSCT toxicities, VOD, transplant-related mortality (TRM; non-relapse mortality), non-transplant related mortality (NTRM).

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 clinical trials, inotuzumab ozogamicin has been associated with severe, life-threatening, and potentially fatal adverse events, including hepatotoxicity and hepatic VOD/sinusoidal obstruction syndrome (SOS). In pivotal study B1931022, inotuzumab ozogamicin was associated with the occurrence of VOD/SOS, particularly following HSCT. Among the 79 patients 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 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 ALL. The following post-marketing requirement (PMR 3259-1) was agreed with the US FDA:

> "Characterize toxicity after HSCT in adult and pediatric patients who receive inotuzumab ozogamicin. Include hepatic VOD, TRM (non-relapse 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 five years."

This non-interventional study is being conducted to fulfill this PMR and is designated as a PASS.

Research Question and Objectives:

Research question:

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

Objectives:

Based on collected data obtained from the 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;
- Timing of inotuzumab ozogamicin treatment prior to HSCT;
- TRM (non-relapse mortality), NTRM, relapse, and OS;
- Post HSCT adverse events (AEs) of interest including hepatic VOD/SOS;
- COD.

Study Design:

This non-interventional PASS uses de-identified healthcare data from the CIBMTR database. The study will evaluate safety outcomes post-HSCT in patients with B-cell precursor ALL who have been treated with inotuzumab ozogamicin prior to HSCT. The study will utilize 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).

Setting:

The data source is the CIBMTR database. CIBMTR is a collaboration between the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin (MCW). CIBMTR facilitates critical observational and interventional research through scientific and statistical expertise, a large network of transplant centers, and a unique and extensive clinical outcomes database. CIBMTR is also mandated by the U.S. Health Resources and Services Administration (HRSA) to collect data from all patients undergoing allogeneic HSCT in the US.

The CIBMTR receives data for approximately 23,000 new HSCT recipients annually, as well as follow-up data on previously reported patients. In 2014-2016, a total of 2,506 US patients with B-cell ALL (1,984 adults [age ≥ 18] and 522 pediatric [age < 18 at the time of HSCT]), who underwent their first allogeneic HSCT, registered and 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). The TED data set is an internationally accepted standard data set that contains a limited number of key variables for all consecutive HSCT recipients. The CRF captures additional patient-, disease-, and treatment-related data in a subset of patients. (i.e., the CRF does not include data from all patients in the registry).

Subjects and Study Size (including dropouts):

The study population will include all adult and pediatric US patients with B-cell ALL treated with inotuzumab ozogamicin who proceeded to HSCT and whose data are available in the CIBMTR database. Data from pediatric patients will be included in accordance with the agreement reached during negotiation of the PMR with the FDA.

Data from all available adult (age ≥ 18) and pediatric (age < 18 at the time of HSCT) US patients with B-cell ALL in the CIBMTR database treated with inotuzumab ozogamicin and underwent allogeneic HSCT during the accrual period will be included in the analysis.

Variables and Data Sources:

There will be no hypothesis testing in this study. All statistical analyses will be descriptive. Data from all patients who proceed to HSCT will be obtained using routine CIBMTR data collection forms, as well as additional forms to specifically collect inotuzumab ozogamicin data.

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

1. Patient-, disease- and HSCT-related characteristics, including details of all prior therapies;
2. Timing of inotuzumab ozogamicin treatment in relation to HSCT;
3. Transplant-related mortality (non-relapse mortality), NTRM, post-transplant relapse, and post-transplant OS in the first 100 days;
4. Post-HSCT AEs of interest, including VOD/SOS in the first 100 days;
5. COD.

Data will be presented for adult and pediatric patients, separately and combined. Due to the low number of patients in the adult and pediatric cohorts, and the different nature inherent in these two groups, univariate analyses were not performed in this report. As more patients accrue, CIBMTR expects to perform univariate analysis.

Patients who received a prior allogeneic HSCT for B-cell ALL will be presented separately from those patients who were undergoing their first allogeneic HSCT for B-cell ALL since the underlying disease, risk for relapse and post-HSCT complications are different for patients with a prior allogeneic HSCT for B-cell ALL than for patients undergoing their first allogeneic HSCT for B-cell ALL.

Results:

Between 18 August 2017 and 17 August 2018, 30 patients (26 adults and 4 pediatric) were accrued. The data lock date, when data collection forms were last evaluated, was 11 December 2018.

Of the 30 patients, 29 patients were undergoing their first allogeneic HSCT for B-cell ALL (26 adults and 3 pediatrics) and 1 pediatric patient had received a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin.

The pediatric patient who had a prior allogeneic HSCT for B-cell ALL before receiving inotuzumab ozogamicin will be described separately (i.e., the data from this patient is not included in the tables presented in Section 10 of this interim report) since the underlying disease, risk for relapse and post-HSCT complications are different for patients with a prior HSCT than for patients undergoing their first allogeneic HSCT for B-cell ALL. Data for this patient is summarized in the narrative below.

Patient who had a prior allogeneic HSCT for B-cell ALL

The patient who had a prior allogeneic HSCT for B-cell ALL was a pediatric patient (11 years old at time of HSCT) and had $\geq$ 3 comorbidities, including mild hepatic disease, prior to HSCT. The patient had a Lansky performance score of 100 (normal), with no history of proven invasive fungal infection and was in the 3rd (or greater) complete remission (CR) at the time of HSCT. The graft source was bone marrow (BM) from an unrelated donor. The patient was given a myeloablative conditioning regimen of busulfan and cyclophosphamide, and also received a regimen of tacrolimus (Tac) and methotrexate (MTX) for GVHD prophylaxis. The duration from ALL diagnosis, which preceded the prior HSCT for this patient, to HSCT was 59 months and the duration from ALL diagnosis to the first dose of inotuzumab ozogamicin was 56 months.

This patient experienced severe VOD/SOS at 0.33 months after the 2nd allogeneic HSCT. This patient also experienced septic shock at 0.76 months post-HSCT and acute renal failure requiring dialysis post-HSCT. The patient died due to VOD/SOS at 0.82 months post-HSCT.

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

In total, 29 patients (26 adults and 3 pediatric patients with a median age of 37 years) underwent their first allogeneic HSCT for B-cell ALL after treatment with inotuzumab ozogamicin.

Prior to transplant, 4 patients were in front-line therapy; 3 patients were in Salvage 1; 4 patients were in Salvage 2; and 15 patients were in Salvage > 2. Data was not available for 3 patients.

As of the data lock date, post-transplant follow-up information was available for 20/29 (69%) patients:

- 14/20 patients did not experience post-HSCT relapse; of these:

  - 3/14 patients (2 adults and 1 pediatric patient) died in remission, and their causes of death were due to:
    - Infection at 0.62 months post-HSCT (adult patient)
    - Hemorrhage at 0.79 months post-HSCT (adult patient)
    - Thrombotic microangiopathy (TMA) at 8.05 months post-HSCT (pediatric patient)

- 6/20 patients experienced post-HSCT relapse; of these:
  - 4/6 patients (3 adults and 1 pediatric patient) died after post-HSCT relapse of ALL; causes of death were due to the following:
    - Primary disease at 2.46 months post-HSCT (pediatric patient)
    - Primary disease at 6.34 months post-HSCT (adult patient)
    - Primary disease at 7.10 months post-HSCT (adult patient)
    - Primary disease at 10.12 months post-HSCT (adult patient)
- 2/20 patients experienced post-transplant VOD/SOS; of these:
  - 1 case was mild (1 adult patient)
  - 1 case was severe (1 adult patient)
- 12/20 patients reported receiving liver toxicity prophylaxis with ursodiol
- 1/20 patients reported receiving liver toxicity prophylaxis with defibrotide
- 1/20 patients reported receiving liver toxicity prophylaxis with ursodiol and defibrotide

Follow-up for the remaining 9 patients will be conducted for subsequent interim reports.

Discussion:

Between 18 August 2017 and 17 August 2018, 30 patients (26 adults and 4 pediatrics) were accrued. Of the 30 patients, 29 patients were undergoing their first allogeneic HSCT for B-cell ALL (26 adults and 3 pediatrics) and 1 pediatric patient had received a prior HSCT before receiving inotuzumab ozogamicin.

Post-transplant follow-up information was available for 20/29 (69%) of the patients undergoing their first allogeneic HSCT for B-cell ALL. Of these 20 patients, post-transplant VOD/SOS occurred in 2 patients, post-transplant mortality occurred in 7 patients TRM occurred in 3 patients. Three deaths occurred within the first 100 days post-transplant.

The 1 pediatric patient who had received a prior allogeneic HSCT for ALL developed VOD/SOS after a second allogeneic transplant and died 0.82 months post-HSCT.

Given the relatively small number of patients accrued for this interim report, it was not possible to make any conclusions regarding the time to event endpoints or the association between patient baseline characteristics, pre-HSCT exposure to inotuzumab ozogamicin, patient characteristics at the time of HSCT and the occurrence of post-transplant VOD/SOS.

Names and Affiliations of Principal Investigators:

Name, degree(s)	Title	Affiliation	Address
Kofi Asomaning, PhD	Epidemiology Lead	Pfizer Inc	500 Arcola Road, Collegeville, PA 19426, USA
Mary Horowitz, MD	Lead Senior Director/ Cofounder	CIBMTR	Froedtert and the Medical College of Wisconsin Clinical Cancer Center, 9200 W. Wisconsin Avenue Suite C5500, Milwaukee, WI 53226, USA
Wael Saber, MD	Scientific Director	CIBMTR	Froedtert and the Medical College of Wisconsin Clinical Cancer Center, 9200 W. Wisconsin Avenue Suite C5500, Milwaukee, WI 53226, USA

CIBMTR: Center for International Blood and Marrow Transplant Research

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ABT	Antibody based therapy
ADC	antibody-drug conjugate
AE's	adverse events
ALL	acute lymphoblastic leukemia
ANC	absolute neutrophil count
AST	atate aminotransferase
BM	bone marrow
BOOP	bronchiolitis obliterans organizing pneumonia
CD22	cluster of differentiation 22
CI	confidence interval
CIBMTR	Center for International Blood and Marrow Transplant Research
COD	cause of death
COP/BOOP	cryptogenic organizing pneumonia/bronchiolitis obliterans organizing pneumonia
CR	complete remission
CNS	central nervous system
CRF	Comprehensive Report Form
CRi	complete remission with incomplete hematologic recovery
CSA	cyclosporine
EU	European Union
FAS	full analysis set
FDA	Food and Drug Administration
GVHD	graft-versus-host disease
HLA	human leukocyte antigen
HRSA	Health Resources and Services Administration
HSCT	hematopoietic stem cell transplantation
HCT-CI	Hematopoietic Cell Transplantation Comorbidity Index
HTN	hypertension
IPN	interstitial pneumonitis
IRB	Institutional Review Board
IV	intravenous
MCW	Medical College of Wisconsin
MMF	mycophenolate mofetil
MRD	minimal residual disease
MTX	methotrexate
N/A	not applicable
NMDP	National Marrow Donor Program
NTRM	non-transplant related mortality
OS	overall survival
PAS	post-authorization study
PASS	post-authorization safety study
PMR	post-marketing requirement
PTSD	post-traumatic stress disorder
SAP	statistical analysis plan
SIRS	systemic inflammatory response syndrome
SOS	sinusoidal obstruction syndrome
Tac	tacrolimus
TBI	total body irradiation
TED	transplant essential data
TMA	thrombotic microangiopathy
TRM	transplant related mortality

Abbreviation	Definition
US	United States
VOD	veno-occlusive disease

3. INVESTIGATORS

3.1. Principal Investigators

Table 1 shows the principal Investigator(s) for Study B1931028.

Table 1. Study B1931028: Principal Investigators

Name, degree(s)	Title	Affiliation	Address
Kofi Asomaning, PhD	Epidemiology Lead	Pfizer Inc	500 Arcola Road, Collegeville, PA 19426, USA
Mary Horowitz, MD	Lead Senior Director/ Cofounder	CIBMTR	Froedtert and the Medical College of Wisconsin Clinical Cancer Center, 9200 W. Wisconsin Avenue Suite C5500, Milwaukee, WI 53226, USA
Wael Saber, MD	Scientific Director	CIBMTR	Froedtert and the Medical College of Wisconsin Clinical Cancer Center, 9200 W. Wisconsin Avenue Suite C5500, Milwaukee, WI 53226, USA

CIBMTR: Center for International Blood and Marrow Transplant Research

4. OTHER RESPONSIBLE PARTIES

Not applicable.

5. MILESTONES

Table 2 shows the milestones for Study B1931028.

Table 2. Study B1931028: Study Milestones

Milestone	Planned date	Actual date
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
End of data collection	17 August 2022	
Interim study report #1 (covering a study period of 18 August 2017 - 17 August 2018)	28 February 2019	20 February 2019
Interim report 2 (covering a study period of 18 August 2017 - 17 August 2019)	28 February 2020	
Interim report 3 (covering a study period of 18 August 2017 - 17 August 2020)	28 February 2021	
Interim report 4 (covering a study period of 18 August 2017 - 17 August 2021)	28 February 2022	
Final study report (covering a study period of 18 August 2017 - 17 August 2022)	28 February 2023	

EU, European Union; FDA, Food and Drug Administration; PAS, post authorization study.

6. RATIONALE AND BACKGROUND

Inotuzumab ozogamicin is an ADC composed of a CD22-directed monoclonal antibody that is covalently linked to N-acetyl-gamma-calicheamicin dimethylhydrazide.

In the US, inotuzumab ozogamicin was approved by the FDA on 17 August 2017 for the treatment of adults with relapsed or refractory B-cell precursor ALL.

ALL is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the BM, peripheral blood, and other organs (Jabbour EJ et al, 2005). ALL represents approximately 20% of leukemias among adults and 80% of acute leukemias in children (Jabbour EJ et al, 2005). 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) (Howlander N et al, 2015). 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 (Howlander N et al, 2015). The B-cell subtype accounts for approximately 75% of ALL cases in adults and approximately 88% in children (American Cancer Society, 2015; National Comprehensive Cancer Network, 2014). 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 (Ma H et al, 2014).

Inotuzumab ozogamicin has been associated with severe, life-threatening, and sometimes fatal AEs, including hepatotoxicity and hepatic VOD/SOS. In Phase 3 Study B1931022, VOD/SOS occurred during inotuzumab treatment and, more frequently, after subsequent treatment with 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 three chemotherapy regimens (80.7% vs 29.4%). While HSCT after treatment with inotuzumab ozogamicin appeared to be associated with long-term survival, post-HSCT toxicity especially VOD/SOS and TRM (non-relapse mortality) was higher in patients treated with inotuzumab ozogamicin than with treating physicians' choice of chemotherapy. Specifically, among the 79 patients 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 TRM (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 is designated as a PASS and is a PMR (PMR 3259-1) by the FDA. The PMR wording which was agreed with the FDA is as follows:

> "Characterize toxicity after HSCT in adult and pediatric patients who receive inotuzumab ozogamicin. Include hepatic VOD, TRM (non-relapse 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 five 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 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;
- Timing of inotuzumab ozogamicin treatment prior to HSCT;
- TRM (non-relapse mortality), NTRM, relapse, and OS;
- Post-HSCT adverse events of interest including hepatic VOD/SOS;
- COD.

8. AMENDMENTS AND UPDATES

There have been no amendments to the Study B1931028 protocol since the original version was submitted to the FDA on 22 January 2018.

9. RESEARCH METHODS

9.1. Study Design

The protocol for Study B1931028 is included in Appendix 1. This non-interventional PASS will use de-identified healthcare data from the CIBMTR database. The study will evaluate safety outcomes post-HSCT in patients who have relapsed or refractory B-cell precursor ALL who have been treated with inotuzumab ozogamicin prior to proceeding to HSCT. The study will utilize 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).

9.2. Setting

The study population will include 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 will be included in accordance with the agreement reached during negotiation of the PMR with the FDA.

9.3. Subjects

9.3.1. Inclusion Criteria

Patients must meet all the following inclusion criteria to be eligible for inclusion in the study:

1. 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.
2. At least 1 dose of inotuzumab ozogamicin prior to proceeding to HSCT.
3. Received HSCT from a US transplant center.

9.3.2. Exclusion Criteria

Only data from patients who have consented will be used in this study.

9.4. Variables

Definition of exposures, outcomes, and other variables including measured risk factors, co-morbidities, co-medications, etc. with operational definitions and measurement; potential confounding variables and effect modifiers are included in the Statistical Analysis Plan (SAP) (see Appendix 2).

9.5. Data Sources and Measurement

This non-interventional PASS uses de-identified healthcare data from the CIBMTR database. CIBMTR is a collaboration between the NMDP/Be The Match and the MCW. CIBMTR facilitates critical observational and interventional research through scientific and statistical expertise, a large network of transplant centers, and a unique and extensive clinical outcomes database. CIBMTR is also mandated by the US HRSA to collect data from all patients undergoing allogeneic HSCT in the US.

The CIBMTR receives data for approximately 23,000 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] and 522 pediatric [age < 18 at time of transplantation]) B-cell ALL patients in the US who underwent their first allogeneic HSCT registered and provided consent to CIBMTR for research.

The CIBMTR collects data on two levels, using a TED form and a CRF. The TED data set is an internationally accepted standard data set that contains a limited number of key variables for all consecutive transplant recipients. 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 > 90% of cases submitted to CIBMTR annually.

All patients are registered with a Pre-TED form. In this study, all patients will be selected for the CRF level of data collection.

The CIBMTR data collection forms used for Study B1931028 are shown in Appendix 3.

9.6. Bias

Not applicable.

9.7. Study Size

Data (TED- and CRF-level) from all US patients in the CIBMTR database treated with inotuzumab ozogamicin during the accrual period (18 August 2017 up to and including 17 August 2018 for Study B1931028 Interim CSR #1) will be included in the analysis.

9.8. Data Transformation

Detailed methodology for data transformations are documented in the SAP, which is dated, filed and maintained by the Sponsor (see Appendix 2).

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

1. Patient-, disease- and HSCT-related characteristics, including details of all prior anti-cancer therapies;
2. Timing of inotuzumab ozogamicin treatment prior to HSCT;
3. TRM (non-relapse mortality), NTRM, relapse, and OS in the first 180 days;
4. Post-HSCT AEs of interest, including VOD/SOS in the first 100 days;
5. COD.

Data will be presented for adults, pediatrics, and adults and pediatrics combined.

The study 'baseline' time point is the date of the 'current' HSCT i.e., a pediatric patient will be defined as a patient who is < 18 years at the time of HSCT, regardless of whether they become > 18 years of age during the 5-year follow-up for Study B1931028. There is no minimum age requirement for this study.

Data for the PASS regarding post-HSCT adverse events of interest in patients treated with inotuzumab ozogamicin were collected from the CIBMTR database using the standard and supplemental forms shown in Table 3.

Table 3. Study B1931028: Post-HSCT Adverse Events of Interest in Patients with B-Cell Precursor ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT

Variable	Data Source (CIBMTR form)
Infection up to day 100	Post HSCT Follow-up Data, Post-Transplant Essential Data
GVHD	
VOD up to day 100	Post HSCT Follow-up Data, Post-Transplant Essential Data, VOD/SOS Supplemental Data Collection Form
Secondary Malignancy	Post HSCT Follow-up Data, Post-Transplant Essential Data
ORGAN DYSFUNCTION	
Pulmonary adverse events	
IPN/Idiopathic pneumonia syndrome	Post HSCT Follow-up Data, Post-Transplant Essential Data
Bronchiolitis obliterans	
COP/BOOP	
Diffuse alveolar hemorrhage	
Cardiovascular disease	
Arrhythmia	Post HSCT Follow-up Data, Post-Transplant Essential Data
Congestive heart failure	
Coronary artery disease	
Myocardial infarction/unstable angina	
HTN requiring therapy	
TMA	
Renal adverse events	
Acute renal failure requiring dialysis	Post HSCT Follow-up Data, Post-Transplant Essential Data
Musculoskeletal dysfunction	
Avascular necrosis	Post HSCT Follow-up Data, Post-Transplant Essential Data
Endocrine dysfunction	
Diabetes/hyperglycemia requiring chronic treatment	Post HSCT Follow-up Data, Post-Transplant Essential Data
Growth hormone deficiency/short stature	
Hypothyroidism requiring replacement therapy	
Pancreatitis	
Neurologic/psychiatric	
Depression requiring therapy	Post HSCT Follow-up Data, Post-Transplant Essential Data
Anxiety requiring therapy	
CNS hemorrhage and stroke	
Post-traumatic stress disorder (PTSD) requiring therapy	

BOOP, bronchiolitis obliterans organizing pneumonia; COP, cryptogenic organizing pneumonia; CNS, central nervous system; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplant; IPN, interstitial pneumonitis; PTSD, Post-traumatic stress disorder; TMA, Thrombotic microangiopathy; VOD, veno-occlusive disease.

9.9. Statistical Methods

9.9.1. Main Summary Measures

Assessments will include the following:

1. Patient-, disease- and HSCT-related characteristics, including details of all prior anti-cancer therapies;

2. Timing of inotuzumab ozogamicin treatment prior to HSCT (last dose of inotuzumab ozogamicin to the date of HSCT);

3. 180-day incidence of TRM, NTRM, post-transplant relapse, post-transplant OS, and post-inotuzumab ozogamicin survival;

4. Post-HSCT AEs of interest, including VOD/SOS in the first 100 days post-HSCT (Table 3);

5. COD.

Data will be collected from the CIBMTR database using the following forms:

- Pre-Transplant Essential Data;
- Recipient Baseline Data;
- ALL Pre-HSCT Data;
- ALL Post-HSCT Data;
- Inotuzumab Ozogamicin (Besponsa) Supplemental Data Collection;
- Post HSCT Follow-up Data;
- Post-Transplant Essential Data;
- VOD/SOS Supplemental Data Collection; and
- Recipient Death Data.

9.9.1.1. Transplant-Related Mortality (TRM)

TRM (which can also be referred to as non-relapse mortality) will be defined as 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 will be censored at the date that the patient was last known to be alive. The duration (in months) of TRM will be 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 will be defined as 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 will be censored at the date that the patient was last known to be alive. The duration (in months) of

NTRM will be 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 will be defined as 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 will be censored at the date that the patient was last known to be alive. The duration (in months) of relapse will be 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 will be defined as the time from HSCT to death due to any cause. In the absence of confirmation of death, post-transplant OS will be censored at the date that the patient was last known to be alive. The duration (months) of post-transplant OS will be 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 will be defined as 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 will be censored at the date that the patient was last known to be alive. The duration (months) of post-inotuzumab ozogamicin survival will be 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 will be defined as the time from HSCT to date of last contact. The duration (months) of post-HSCT follow-up will be calculated as follows: [date of last contact − date of HSCT + 1]/30. 4375.

9.9.1.7. Covariates

Covariates related to patient-, disease- and HSCT-related characteristics as well as pre-HSCT therapy will be included in the analysis.

9.9.1.8. Subgroups

Exploratory subgroup analysis will be 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;

Additional subgroup analyses may also be explored.

9.9.2. Main Statistical Methods

All analyses will be based on descriptive statistics (i.e., no hypothesis testing is planned). P-values may be provided, but no definite conclusions will be made based on p-values, and no adjustments for multiplicity will be applied. Additional analyses may be performed if deemed appropriate.

9.9.2.1. Time-to-Event Endpoints

Time-to-event endpoints (e.g., post-transplant OS and post-inotuzumab ozogamicin survival) will be summarized using the Kaplan-Meier method. Median event time will be summarized with the confidence interval (CI) calculated using the method described by Brookmeyer R and Crowley J (1982).

9.9.2.1.1. Competing-Risks Analyses

TRM, NTRM, and post-transplant relapse will be summarized using competing-risks analyses. Competing-risks analyses will evaluate the hazard of events in the presence of potentially competing events. The cumulative incidence of events will be summarized with the CI calculated based on the cumulative incidence function using the SAS macro by Lin G et al (2012), which is based on the method described by Kalbfleisch JD and Prentice RL (1980).

9.9.2.2. Categorical Variables

Categorical variables will be summarized using counts and percentages. Appropriate confidence intervals will be calculated using the normal approximation or the exact method.

The categorical variables will be compared using the risk difference with CI calculated using the normal approximation or the exact method (Collett D, 1991). In addition, categorical variables may be compared using chi-square or Fisher's exact tests.

9.9.2.3. Continuous Variables

Continuous variables will be summarized using descriptive statistics (mean, standard deviation, median, minimum, maximum and number of patients).

Continuous variables will be compared using the mean difference with CI calculated based on the t-distribution. In addition, continuous variables may be compared using the Wilcoxon rank-sum test.

9.9.3. Missing Values

Missing dates (except for death dates) will be 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 is missing for any date used in a calculation, the 1st of the month will be used to replace the missing date unless the calculation results in a negative time duration (e.g., date of onset cannot be prior to day one date). In this case, the date resulting in 0 time duration will be used;

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

- If these conventions produce a date that results in a negative time to event, then the time to event will be reset to 1 day.

Missing death dates will be handled by the following conventions:

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

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

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

For time-to-event endpoints, patients who have not yet experienced the event of interest will be censored.

There are no plans for imputation of missing values for other variables; all missing values will be excluded from analyses.

9.9.4. Sensitivity Analyses

Not applicable.

9.9.5. Amendments to Statistical Analysis Plan

The original SAP dated 15 January 2018 was amended twice (version 2 and 3).

Major changes from the original version of the SAP to SAP version 2.0 (dated 06 July 2018) are summarized as follows:

- The definitions of transplant-related mortality (TRM) and non-transplant related mortality (NTRM) are revised to allow deaths within the first 28 days post-transplant to be considered as an event for TRM (non-relapse mortality);

- An alternative method to estimate the cumulative incidence rate of NTRM, with its CI, is added.

Major changes from SAP version 2.0 to SAP version 3.0 (dated 20 February 2019) are summarized as follows:

- The full analysis set (FAS) will be only used for analyses of pre- and at-HSCT variables.

- The post-transplant evaluable set is 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, ≥1) and for patients undergoing allogeneic HSCT were removed. Separate analyses were conducted for patients undergoing first, second, third (if applicable) allogeneic HSCT for B-cell ALL, and patients undergoing 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.

9.10. Quality Control

Centers contributing data to the CIBMTR database report longitudinal data on all transplants. Compliance and accuracy of data is ensured by computerized record checks, physician review of data, and on-site audits. Observational studies conducted by the CIBMTR are performed in compliance with all applicable federal regulations pertaining to the protection of human research participants. Protected health information used in the performance of such research is collected and maintained in CIBMTR's capacity as a Public Health Authority under the Health Insurance Portability and Accountability Act Privacy Rule.

9.11. Protection of Human Subjects

9.11.1. Patient Information and Consent

All parties will ensure protection of patients' personal data. Patient identifiers will not be included on any data forms, reports, publications, or in any other disclosures, except where required by law. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of patients' personal data.

Only data from patients who have consented will be used in this study. CIBMTR will obtain patient consent as per standard practice.

9.11.2. Institutional Review Board (IRB)

Studies conducted by the CIBMTR are performed under the guidance and review of the IRB of the NMDP.

The CIBMTR will be responsible for confirmation of patient consent to participate in the Research Database. This study will follow the standard CIBMTR consent procedures and will use the standard CIBMTR consent forms. In addition, due to supplemental data collection, CIBMTR will obtain IRB approval of the study protocol and protocol amendments. CIBMTR's informed consent forms for participation in the Research Database Protocol are already IRB-approved.

9.11.3. Ethical Conduct of Study

The study is being conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor. CIBMTR follows generally accepted research practices.

10. RESULTS

10.1. Participants

Between 18 August 2017 and 17 August 2018, 30 patients (26 adults and 4 pediatric) were accrued. The data lock date, when data collection forms were last evaluated, was 11 December 2018.

Of the 30 patients, 29 patients were undergoing their first allogeneic HSCT for B-cell ALL (26 adults and 3 pediatrics) and 1 pediatric patient had received a prior HSCT before receiving inotuzumab ozogamicin.

The pediatric patient who had a prior HSCT before receiving inotuzumab ozogamicin will be described separately (i.e., the data from this patient is not included in the tables presented in Section 10 of this interim report) since the underlying disease, risk for relapse and post-HSCT complications are different for patients with a prior HSCT than for patients undergoing their first allogeneic HSCT for B-cell ALL. Data for this patient is summarized in the narrative below.

Patient who had a prior allogeneic HSCT for B-cell ALL

The patient who had a prior allogeneic HSCT for B-cell ALL was a pediatric patient (11 years old at time of HSCT) and had $\geq$ 3 comorbidities, including mild hepatic disease, prior to HSCT. The patient had a Lansky performance score of 100 (Normal), with no history of proven invasive fungal infection and was in the 3rd (or greater) complete remission at time of HSCT. The graft source was bone marrow from an unrelated donor. The patient was given a myeloablative conditioning regimen of busulfan and cyclophosphamide, and also received a regimen of Tac and MTX for GVHD prophylaxis. The duration from ALL diagnosis, which preceded the prior HSCT for this patient, to HSCT was 59 months and the duration from ALL diagnosis to the first dose of inotuzumab ozogamicin was 56 months.

This patient experienced severe VOD/SOS at 0.33 months after the 2nd allogeneic HSCT. This patient also experienced septic shock at 0.76 months post-HSCT and acute renal failure requiring dialysis post-HSCT. The patient died due to VOD/SOS at 0.82 months post-HSCT.

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

In total, 29 patients (26 adults and 3 pediatric patients with a median age of 37 years) underwent their first allogeneic HSCT for B-cell ALL after treatment with inotuzumab ozogamicin.

Prior to transplant, 4 patients were in front-line therapy; 3 patients were in Salvage 1; 4 patients were in Salvage 2; and 15 patients were in Salvage > 2. Data was not available for 3 patients.

As of the data lock date, post-transplant follow-up information was available for 20/29 (69%) patients:

- 14/20 patients did not experience post-HSCT relapse; of these:
    - 3/14 patients (2 adults and 1 pediatric patient) died in remission, and their causes of death were due to:
        - Infection at 0.62 months post-HSCT (adult patient)
        - Hemorrhage at 0.79 months post-HSCT (adult patient)
        - TMA at 8.05 months post-HSCT (pediatric patient)
- 6/20 patients experienced post-HSCT relapse; of these:
    - 4/6 patients (3 adults and 1 pediatric patient) died after post-HSCT relapse of ALL; causes of death were due to the following:
        - Primary disease at 2.46 months post-HSCT (pediatric patient)
        - Primary disease at 6.34 months post-HSCT (adult patient)
        - Primary disease at 7.10 months post-HSCT (adult patient)
        - Primary disease at 10.12 months post-HSCT (adult patient)
- 2/20 patients experienced post-transplant VOD/SOS; of these:
    - 1 case was mild (1 adult patient)
    - 1 case was severe (1 adult patient)
- 12/20 patients reported receiving liver toxicity prophylaxis with ursodiol
- 1/20 patients reported receiving liver toxicity prophylaxis with defibrotide
- 1/20 patients reported receiving liver toxicity prophylaxis with ursodiol and defibrotide

Follow-up for the remaining 9 patients will be conducted for subsequent interim reports.

10.2. Descriptive Data

10.2.1. Subject Evaluation Groups

Table 4 summarizes the completeness of follow-up (completeness index) in patients who underwent their first allogeneic HSCT. 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, and 6-month follow-up forms submitted by transplant centers.

Table 4. Study B1931028: Completeness Index[a] (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

Time	Pediatric Patients (N = 3), %	Adult Patients (N = 17), %	Overall (N = 20), %
1-month	100	100	100
100-day	100	100	100
6-month	100	86	88

[a] Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. Lancet 2002; 359: 1309-10.

10.2.2. Summary of Demographic Characteristics and Other Baseline Characteristics

10.2.2.1. Demographic Characteristics

Table 5 summarizes the demographic characteristics, baseline characteristics, and comorbid conditions. Among all 29 patients, the median age was 37 years (range: 9-70 years).

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Number of centers	2	14	16
Age, years			
1-9	2	0	2
10-17	1	0	1
18-29	0	5	5
30-39	0	7	7
40-49	0	7	7
50-59	0	2	2
≥ 60	0	5	5
Median	9	44	37
Range	(9-13)	(18-70)	(9-70)

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Race			
Caucasian	3	20	23
African–American	0	1	1
Asian / Pacific Islander	0	2	2
Not reported	0	3	3
Weight, kg			
Median	27	82	81
Range	(24-83)	(50-134)	(24-134)
Body mass index, kg/m^2			
Median	15	29	29
Range	(15-34)	(20-41)	(15-41)
Body surface area, m^2			
Median	1	2	2
Range	(0.9-1.9)	(1.5-2.6)	(0.9-2.6)
Height, cm			
Median	132	170	165
Range	(128-157)	(154-185)	(128-185)
Gender			
Male	2	14	16
Female	1	12	13
Sorror HCT-CI[a]			
0	1	4	5
1-2	1	6	7
≥ 3	1	16	17
Arrhythmia[b]			
No	2	25	27
Yes	1	1	2
Cardiac disease[c]			
No	3	25	28
Yes	0	1	1
Cerebrovascular disease[d]			
No	3	25	28
Yes	0	1	1
Hepatic disease, mild[e]			
No	3	18	21
Yes	0	8	8

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Hepatic disease, moderate to severe[f]			
No	3	24	27
Yes	0	2	2
Lines of salvage therapy prior to transplant			
N/A; CIBMTR form[g] not yet received	0	2	2
Not reported	0	1	1
Induction	2	2	4
Salvage 1	0	3	3
Salvage 2	0	4	4
Salvage >2	1	14	15
N	3	24	27
Median	1	4	4
Range	(1-12)	(1-7)	(1-12)
Lines of salvage therapy prior to inotuzumab ozogamicin			
N/A; CIBMTR forms[g] not yet received	0	2	2
Not reported	0	1	1
N	3	23	26
Median	0	3	3
Range	(0-5)	(0-4)	(0-5)
AST, prior to transplant, units/L			
N/A; CIBMTR form[h] not yet received	0	2	2
N	3	24	27
Median	1.5	0.9	0.9
Range	(0.9-2.1)	(0.3-1.6)	(0.3-2.1)
Total serum bilirubin, prior to transplant, mg/dL			
N/A; CIBMTR form[h] not yet received	0	2	2
N	3	24	27
Median	0.5	0.4	0.4
Range	(0.4-0.9)	(0.2-1.5)	(0.2-1.5)
Platelets, $\times 10^9$/L			
N/A; CIBMTR form[h] not yet received	0	2	2
N	3	24	27
Median	169	141	141
Range	(25-257)	(28-239)	(25-257)

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Neutrophils, × 10^9/L			
N/A; CIBMTR form[h] not yet received	0	2	2
N	3	24	27
Median	57	55	55
Range	(35-67)	(13-90)	(13-90)
Hemoglobin, g/dL			
N/A; CIBMTR form[h] not yet received	0	2	2
N	3	24	27
Median	13	13	13
Range	(9-15)	(6-16)	(6-16)
White blood cells, at diagnosis of ALL, × 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
Not reported	1	0	1
N	2	24	26
Median	N/A	10	9
Range	(0-10)	(0-308)	(0-308)
Blasts in blood, at diagnosis of ALL, × 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
< 1%	0	4	4
≥ 1%	0	18	18
Not reported	3	2	5
N	0	22	22
Median	N/A	42	42
Range	N/A	(0-95)	(0-95)
Blasts in BM, at diagnosis of ALL, × 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
< 50%	1	3	4
≥ 50%	1	18	19
Not reported	1	3	4
N	2	21	23
Median	N/A	88	88
Range	(10-88)	(5-99)	(5-99)

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
White blood cells, at last evaluation prior to start of conditioning regimen, × 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
N	3	24	27
Median	6.3	3.6	3.6
Range	(1.6-6.4)	(0.8-7.4)	(0.8-7.4)
Blasts in blood, at last evaluation prior to conditioning regimen, x 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
< 1%	1	21	22
≥ 1%	1	1	2
Not reported	1	2	3
N	2	22	24
Median	N/A	0	0
Range	(0-4)	(0-2)	(0-4)
Blasts in bone marrow, at last evaluation prior to conditioning regimen, × 10^9/L			
N/A; CIBMTR form[g] not yet received	0	2	2
< 5%	1	24	25
≥ 5%	1	0	1
Not reported	1	0	1
N	2	24	26
Median	N/A	1	1
Range	(0-94)	(0-4)	(0-94)
Performance scale used			
Karnofsky	0	26	26
90-100	0	15	15
10-80	0	11	11
Lansky	3	0	3
90-100	1	0	1
10-80	2	0	2
History of proven invasive fungal infection			
No	2	24	26
Yes	1	1	2
Not reported	0	1	1

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Disease status of ALL prior to conditioning regimen			
1st complete remission	1	5	6
2nd complete remission	2	13	15
≥ 3rd complete remission	0	3	3
1st relapse	0	2	2
≥ 3rd relapse	0	1	1
Primary induction failure	0	2	2
Prior HSCT			
No	3	26	29
Time from diagnosis to HSCT, months			
3-5	1	4	5
6-11	0	3	3
≥ 12	2	19	21
Median	92	27	28
Range	(5-92)	(4-87)	(4-92)
Time from diagnosis to first dose of inotuzumab ozogamicin, months			
< 3	1	3	4
3-5	0	2	2
6-11	0	3	3
≥ 12	2	18	20
Median	79	26	29
Range	(2-89)	(1-83)	(1-89)
GVHD prophylaxis			
Ex-vivo T-cell depletion	2	0	2
Post-transplant cyclophosphamide	1	9	10
Tac + MMF ± others	0	4	4
Tac + MTX ± others	0	8	8
Tac ± others	0	2	2
CSA + MMF ± others	0	2	2
CSA + MTX ± others	0	1	1
Conditioning regimen intensity[i]			
Myeloablative	2	13	15
Reduced intensity	1	13	14
Dual alkylators used in conditioning regimen[j]			
Yes	2	3	5
No	1	23	24

Table 5. Study B1931028: Summary of Demographic Characteristics, Baseline Characteristics, and Comorbid Conditions (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Busulfan used in conditioning regimen			
Yes	0	5	5
No	3	21	24
Thiotepa used in conditioning regimen			
Yes	2	2	4
No	1	24	25
Product type			
BM	1	4	5
Peripheral blood stem cells	2	17	19
Cord blood	0	5	5
Donor type			
HLA-identical sibling	0	6	6
Other related	1	6	7
Unrelated	2	14	16

Abbreviations: ALL, acute lymphoblastic leukemia; AST: aspartate transaminase; BM: bone marrow; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; CSA, cyclosporine; GVHD, graft-versus-host disease; HLA, human leukocyte antigen; HCT-CI, Hematopoietic Cell Transplantation Comorbidity Index; N/A; not applicable; MMF, mycophenolate mofetil; MTX, methotrexate; Tac, tacrolimus; TBI, total body irradiation.

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] For example, 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] 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

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

[g] 2011 Pre-transplant ALL-specific form

[h] 2000 Recipient baseline form

[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.

10.2.3. Summary of Treatment

10.2.3.1. Therapies Prior to Inotuzumab Ozogamicin Treatment

Table 6 summarizes the therapies received prior to inotuzumab ozogamicin treatment.

Table 6. Study B1931028: Summary of Therapies Received Prior to Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of treatment regimen(s) prior to receiving inotuzumab ozogamicin			
N/A; CIBMTR form[a] not yet received	0	2	2
Not reported	0	1	1
No	2	2	4
Yes	1	21	22
1	0	4	4
2	0	4	4
3	0	9	9
4	0	4	4
5	1	0	1
Number of patients receiving at least 1 treatment regimen prior to receiving inotuzumab ozogamicin	1	21	22
Prior HSCT			
No	1	21	22
CNS prophylaxis			
Yes	0	14	14
No	1	3	4
Not reported	0	4	4
Lines of therapy prior to transplant			
Salvage 1	0	3	3
Salvage 2	0	4	4
Salvage > 2	1	14	15

Table 6. Study B1931028: Summary of Therapies Received Prior to Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Purpose of therapy prior to receiving inotuzumab ozogamicin			
Induction	0	5	5
Consolidation	0	3	3
Maintenance	0	8	8
Treatment for disease relapse	1	5	6
Radiation therapy prior to receiving inotuzumab ozogamicin			
Yes	0	2	2
No	1	19	20
Regimens given for front-line therapy, prior to receiving inotuzumab ozogamicin			
Chemotherapy	1	10	11
Chemotherapy + ABT	0	5	5
Chemotherapy + ABT / Chemotherapy + TKI	0	1	1
Chemotherapy + TKI	0	2	2
TKI	0	1	1
Chemotherapy / Chemotherapy	0	1	1
Chemotherapy / ABT	0	1	1
Regimens given for consolidation therapy, prior to receiving inotuzumab ozogamicin			
None	1	11	12
Chemotherapy	0	3	3
Chemotherapy + TKI	0	3	3
Chemotherapy + ABT	0	2	2
Chemotherapy + ABT / Chemotherapy	0	1	1
Chemotherapy + ABT / Chemotherapy + ABT	0	1	1
Regimens given for maintenance therapy, prior to receiving			

Table 6. Study B1931028: Summary of Therapies Received Prior to Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
inotuzumab ozogamicin			
None	1	12	13
Chemotherapy	0	5	5
Chemotherapy + TKI	0	3	3
Chemotherapy + ABT	0	1	1
Regimens given for disease relapse, prior to receiving inotuzumab ozogamicin			
None	0	15	15
Chemotherapy	0	1	1
ABT	0	1	1
Chemotherapy / Chemotherapy	0	1	1
ABT / Chemotherapy	0	1	1
ABT / Chemotherapy / Chemotherapy / Chemotherapy	0	1	1
Chemotherapy / Chemotherapy / ABT / Chemotherapy	1	0	1
TKI / Chemotherapy + TKI / TKI	0	1	1

Abbreviations: ABT: antibody-based therapy; ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CNS, central nervous system; HSCT, hematopoietic stem cell transplantation, ABT, anti-body therapy (includes blinatumomab, rituximab, ofatumumab); TKI, tyrosine-kinase inhibitor (includes dasatinib, imatinib, nilotinib, ponatinib).
Note: One patient received inotuzumab ozogamicin for a second HSCT for B-cell ALL, and was excluded from this table.
[a] 2011 Pre-transplant ALL-specific form
Note: Forward slash lines ("/") denote separate lines of therapy.

10.2.3.2. Inotuzumab Ozogamicin Treatment Prior to HSCT

Table 7 summarizes inotuzumab ozogamicin treatment prior to HSCT.

Table 7. Study B1931028: Summary of Inotuzumab Ozogamicin Treatment Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	**3**	**26**	**29**
Number of treatment regimen(s) prior to receiving inotuzumab ozogamicin			
N/A; CIBMTR form[a] not yet received	0	2	2
0	2	2	4
1	0	4	4
2	0	4	4
3	0	9	9
4	0	4	4
≥ 5	1	0	1
Not reported	0	1	1
Number of cycles of inotuzumab ozogamicin			
1	0	7	7
2	3	12	15
≥ 3	0	7	7
Regimen containing inotuzumab ozogamicin			
N/A; CIBMTR form[a] not yet received	0	2	2
Single agent	1	12	13
Combined with chemotherapy	1	6	7
Combined with chemotherapy + ABT	1	2	3
Combined with chemotherapy + TKI	0	3	3
Not reported	0	1	1
Response to treatment containing inotuzumab ozogamicin			
CR	3	12	15
CRi[b]	0	6	6
No CR/CRi	0	7	7
Not reported	0	1	1
MRD responders rate			
Positive	0	9	9
Negative	3	13	16
Not reported	0	4	4

Table 7. Study B1931028: Summary of Inotuzumab Ozogamicin Treatment Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
MRD method of testing			
Flow cytometry	3	11	14
Not reported	0	15	15
MRD testing method and results in responders			
Flow cytometry	3	11	14
Negative	3	9	12
Positive	0	2	2
Not reported	0	15	15
Negative	0	4	4
Positive	0	7	7
Not reported	0	4	4
Time from last dose of inotuzumab ozogamicin to HSCT, months			
Median	1.3	1.9	1.9
Range	(1.1-2.3)	(0.4-6.1)	(0.4-6.1)

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, Complete remission; CRi, Complete remission with incomplete hematologic recovery; HSCT, hematopoietic stem cell transplantation; MRD, minimal residual disease.

[a] 2011 Pre-transplant ALL-specific form

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

Table 8 summarizes inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included only inotuzumab ozogamicin.

Table 8. Study B1931028: Summary of Inotuzumab Ozogamicin Doses Prior to HSCT Among Patients Whose Treatment Regimen Included Only Inotuzumab Ozogamicin (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	1	12	13
Number of patients who received 1 cycle of inotuzumab ozogamicin	0	5	5
Inotuzumab ozogamicin combined dose, all cycles			
0.8	0	1	1
1.8	0	2	2
2.1	0	1	1
3.6	0	1	1
Number of patients who received 2 cycles of inotuzumab ozogamicin	1	4	5
Inotuzumab ozogamicin combined dose, all cycles			
3	0	1	1
3.3	0	2	2
3.6	1	0	1
5.8	0	1	1
Number of patients who received 3 cycles of inotuzumab ozogamicin	0	3	3
Inotuzumab ozogamicin combined dose, all cycles			
4.9	0	1	1
9.2	0	1	1
Not reported	0	1	1

Note: This cohort includes patients who belonged to the "Single agent" category described in the variable "Regimen containing inotuzumab ozogamicin" form.

Table 9 summarizes inotuzumab ozogamicin doses prior to HSCT among patients whose treatment regimen included other agents.

Table 9. Study B1931028: Summary of Inotuzumab Ozogamicin Doses Prior to HSCT Among Patients Whose Treatment Regimen Included Other Agents (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	2	11	13
Number of patients who received 1 cycle of inotuzumab ozogamicin	0	2	2
Inotuzumab ozogamicin combined dose, all cycles			
0.6	0	1	1
2.3	0	1	1
Number of patients who received 2 cycles of inotuzumab ozogamicin	2	6	8
Inotuzumab ozogamicin combined dose, all cycles			
1.5	0	3	3
2.1	0	1	1
2.4	1	0	1
2.8	0	2	2
3.3	1	0	1
Number of patients who received 3 cycles of inotuzumab ozogamicin	0	3	3
Inotuzumab ozogamicin combined dose, all cycles			
5.1	0	2	2
5.4	0	1	1

Note: This cohort of patients are the patients who belonged to the "Combined with chemotherapy", "Combined with chemotherapy + TKI", "Combined with chemotherapy + ABT" categories described in the variable "Regimen containing inotuzumab ozogamicin" form.

10.2.3.3. Treatments at Time of HSCT

Table 10 summarizes the treatments received at the time of HSCT, except for drugs given for conditioning regimen, among patients who have received inotuzumab ozogamicin treatment.

Table 10. Study B1931028: Summary of Treatments Received at Time of HSCT, Except for Drugs Given for Conditioning Regimen, Among Patients who Received Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Number of patients	3	26	29
Liver toxicity prophylaxis			
N/A; CIBMTR form[a] not yet received	0	12	12
No specific therapy used to prevent liver toxicity	1	1	2
Ursodiol	0	12	12
Ursodiol + Defibrotide	1	0	1
Defibrotide	1	0	1
Not reported	0	1	1
Antibacterial infection prophylaxis			
N/A; CIBMTR form[b] not yet received	0	10	10
No antibacterial infection prophylaxis used	1	8	9
Levofloxacin IV or oral	1	6	7
Bactrim (Sulfamethoxazole-Trimethoprim)	0	1	1
Ceftaroline	1	0	1
Ciprofloxacin + Cefepime	0	1	1
Antiviral infection prophylaxis			
N/A; CIBMTR form[b] not yet received	0	10	10
Acyclovir	1	11	12
Valacyclovir (Valtrex)	0	3	3
Ganciclovir	0	1	1
Valganciclovir	1	1	2
Cidofovir	1	0	1

Table 10. Study B1931028: Summary of Treatments Received at Time of HSCT, Except for Drugs Given for Conditioning Regimen, Among Patients who Received Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)	Adult Patients (≥ 18 years)	All Patients
Antifungal infection prophylaxis			
N/A; CIBMTR form[b] not yet received	0	10	10
No antifungal infection prophylaxis used	0	1	1
Fluconazole (Diflucan)	2	7	9
Posaconazole (Noxafil)	1	3	4
Caspofungin (Cancidas)	0	2	2
Micafungin (Mycamine)	0	2	2
Nystatin	0	1	1
Anti-pneumocystis infection prophylaxis			
N/A; CIBMTR form[b] not yet received	0	10	10
No anti-pneumocystis infection prophylaxis used	0	7	7
Trimethoprime/Sulfamethoxazole (Bactrim, Septra)	2	5	7
Pentamidine, inhaled	0	2	2
Pentamidine, IV	1	0	1
Atovaquone (Mepron)	0	1	1
Dapsone	0	1	1
GVHD prophylaxis			
Ex-vivo T-cell depletion	2	0	2
Post-transplant cyclophosphamide	1	9	10
Tac + MMF ± others	0	4	4
Tac + MTX ± others	0	8	8
Tac ± others	0	2	2
CSA + MMF ± others	0	2	2
CSA + MTX ± others	0	1	1

Abbreviations: CIBMTR: Center for International Blood and Marrow Transplant Research; CSA: cyclosporine; GVHD: graft-versus-host disease; IV: intravenous; MMF: mycophenolate mofetil; MTX: methotrexate; N/A: not applicable; Tac: Tacrolimus.
Note: One patient received inotuzumab ozogamicin for a second HSCT for B-cell ALL, and was excluded from this table.
[a] 2450 Post-TED 100-day form or 2100 Post-transplant 100-day form
[b] 2100 Post-transplant 100-day form

10.2.3.4. Post-HSCT Therapies

Table 11 summarizes the post-HSCT therapies following inotuzumab ozogamicin treatment.

Table 11. Study B1931028: Summary of Post-HSCT Therapies Following Inotuzumab Ozogamicin in Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with follow-up[a]	3	17	20
Systemic therapy given for reasons other than relapse, persistent, or MRD			
None	3	15	18
Ponatinib	0	2	2
Systemic therapy given for relapsed, persistent, or MRD			
No systemic therapy given for this purpose	3	13	16
Chemotherapy + Hydroxyurea	0	1	1
Chemotherapy	0	1	1
Blinatumomab	0	1	1
Cytarabine	0	1	1
Radiation therapy given for reasons other than relapse, persistent, or MRD			
None	3	17	20

Abbreviations: MRD, minimal residual disease
[a] 2450 Post-TED 100-day form or 2100 Post-transplant 100-day form

10.2.4. Post-Transplant Overall Survival

Table 12 summarizes post-transplant OS.

Table 12. Study B1931028: Summary of Post-Transplant Overall Survival[a] (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[b]	3	17	20
Number of deaths	2	5	7
Cause of death[c]			
Primary disease	1	3	4
TMA	1	0	1
Infection	0	1	1
Hemorrhage	0	1	1
Time from transplant to death, months			
0.62	0	1	1
0.79	0	1	1
2.46	1	0	1
6.34	0	1	1
7.1	0	1	1
8.05	1	0	1
10.12	0	1	1

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; TMA, thrombotic microangiopathy; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.

[a] Post-Transplant Overall Survival: 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.

[b] 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.

[c] Only the primary cause of death is reported.

10.2.5. Post-Inotuzumab Ozogamicin Survival

Table 13 summarizes OS after receiving inotuzumab ozogamicin.

Table 13. Study B1931028: Summary of Post-Inotuzumab Ozogamicin Survival[a] (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[b]	3	26	29
Number of deaths	2	5	7
Cause of death[c]			
Primary disease	1	3	4
TMA	1	0	1
Infection	0	1	1
Hemorrhage	0	1	1
Time from first dose of inotuzumab ozogamicin to death, months			
3.38	0	1	1
4.11	0	1	1
9.33	0	1	1
9.82	0	1	1
10.91	1	0	1
12.52	0	1	1
15.41	1	0	1

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; TMA, thrombotic microangiopathy; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.

[a] Post-Inotuzumab Ozogamicin Survival: 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.

[b] 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.

[c] Only the primary cause of death is reported.

10.2.6. Transplant-Related Mortality (Post-Transplant Non-Relapse Mortality)

Table 14 summarizes TRM.

Three patients (1 pediatric, 2 adult) died in remission. The causes of death were TMA (1 pediatric), infection (1 adult), and hemorrhage (1 adult).

Table 14. Study B1931028: Summary of Transplant-Related Mortality (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[a]	3	17	20
Number of patients with post-transplant mortality	1	2	3

Table 14. Study B1931028: Summary of Transplant-Related Mortality (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with competing risks[b]	1	5	6
Time from transplant to TRM, months			
0.62	0	1	1
0.79	0	1	1
8.05	1	0	1

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; TRM: transplant related mortality, VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for transplant-related mortality is defined as post-transplant relapse.

10.2.7. Non-Transplant-Related Mortality

Table 15 summarizes NTRM.

Table 15. Summary of Non-Transplant-Related Mortality (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[a]	3	17	20
Number of patients with NTRM	1	3	4
Number of patients with competing risks[b]	1	2	3
Time from transplant to NTRM, months			
2.46	1	0	1
6.34	0	1	1
7.10	0	1	1
10.12	0	1	1

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; NTRM: non-tranplant related mortality; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for non-transplant related mortality is defined as transplant-related mortality.

10.2.8. Post-Transplant Relapse

Table 16 summarizes post-transplant relapse.

Table 16. Study B1931028: Summary of Post-Transplant Relapse (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[a]	3	17	20
Number of patients with post-transplant relapse	1	5	6
Number of patients with competing risks[b]	1	2	3
Time from transplant to relapse, months			
1.61	0	1	1
1.87	0	1	1
2.20	1	0	1
3.52	0	1	1
5.22	0	1	1
5.88	0	1	1

[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for relapse is defined as transplant-related mortality.

10.2.9. 100-Day Post-HSCT Adverse Events of Interest Including Hepatic VOD/SOS

Table 17 summarizes the 100-day post-HSCT Aes (including hepatic VOD/SOS).

Table 17. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with post-transplant follow-up[a]	3	17	20
Viral infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
Yes	1	9	10
No	2	7	9
Bacterial infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
Yes	0	8	8
No	3	8	11
Fungal infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
Yes	0	1	1
No	3	15	18

Table 17. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Systemic Inflammatory Response Syndrome (SIRS) development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	3	3
Yes	0	1	1
No	3	12	15
Not reported	0	1	1
Septic shock development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	3	3
Yes	0	1	1
No	3	12	15
Not reported	0	1	1
Maximum grade of acute GVHD[c]			
N/A; CIBMTR form[b] not yet received	0	1	1
None	1	12	13
Grade I	1	2	3
Grade III	0	2	2
Grade IV	1	0	1
Time from HSCT to date of maximum acute GVHD, months			
N	2	4	6
Median	N/A	1.8	1.4
Range	(0.4-1.4)	(1-2.8)	(0.4-2.8)
Chronic GVHD[d]			
No	2	15	17
Yes	1	2	3
Time from HSCT to chronic GVHD diagnosis, months			
N	1	2	3
Median	3	3	3
Range	N/A	(3-3)	(3-3)
VOD/SOS[e]			
No	3	15	18
Yes	0	2	2
Time from HSCT to VOD/SOS diagnosis, months			
N	0	2	1
Median	N/A	N/A	0.5
Range	N/A	(0.5-2.6)	(0.3-2.6)
Secondary malignancy			
No	3	16	19
Yes[f]	0	1	1

Table 17. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Time from HSCT to secondary malignancy, months			
N	0	1	1
Median	N/A	4	4
Range	N/A	N/A	N/A
Pulmonary AEs[g]			
IPN / Idiopathic pneumonia syndrome			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	15	18
Yes	0	1	1
Bronchiolitis obliterans			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
COP/BOOP			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Diffuse alveolar hemorrhage			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Cardiovascular AEs			
Arrhythmia			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	15	18
Yes	0	1	1
Congestive heart failure			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	15	18
Yes	0	1	1
Coronary artery disease			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Myocardial infarction or unstable angina			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Hypertension (HTN) requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	2	15	17
Yes	1	1	2
TMA			
N/A; CIBMTR form[b] not yet received	0	1	1
No	2	15	17
Yes	1	1	2

Table 17. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Renal AEs			
Acute renal failure requiring dialysis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	15	18
Yes	0	1	1
Musculoskeletal AEs			
Avascular necrosis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Endocrine dysfunction			
Diabetes or hyperglycemia requiring chronic treatment			
N/A; CIBMTR form[b] not yet received	0	1	1
No	2	16	18
Yes	1	0	1
Growth hormone deficiency or short stature			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Hypothyroidism requiring replacement therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Pancreatitis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
Neurologic or psychiatric AEs			
Depression requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	2	16	18
Yes	1	0	1
Anxiety requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	2	16	18
Yes	1	0	1
CNS hemorrhage and stroke			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19
PTSD requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	3	16	19

Abbreviations: AEs, adverse events; ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; COP/BOOP, cryptogenic organizing pneumonia / bronchiolitis

Table 17. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)

obliterans organizing pneumonia; CNS, central nervous system; GVHD, graft-versus-host disease; HSCT, hematopoietic cell transplantation; HTN, hypertension; IPN, interstitial pneumonitis; N/A, not applicable; PTSD, post-traumatic stress disorder; TMA, thrombotic microangiopathy; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.

[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.

[b] 2100 Post-transplant 100-day form

[c] 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.

[d] Chronic GVHD was evaluated up to 1 year post-transplant.

[e] VOD/SOS was evaluated up to 100 days post-transplant.

[f] Secondary malignancy was squamous cell cancer of the skin.

[g] Remaining adverse events evaluated up to 100 days post-transplant.

10.2.10. Venoocclusive Disease

Table 18 shows a summary of VOD/SOS in patients who received inotuzumab ozogamicin prior to first allogeneic HSCT for ALL.

Table 18. Study B1931028: VOD/SOS in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)		Adult Patients (≥ 18 years)		All Patients	
	Defibrotide[a] (N = 2)	No defibrotide (N = 1)	Defibrotide (N = 0)	No defibrotide (N = 26)	Defibrotide (N = 2)	No defibrotide (N = 27)
Number of patients with post-transplant follow-up[b]	2	1	0	17	2	18
Number of patients with post-transplant VOD/SOS[c]	0	0	0	2	0	2
Time to post-transplant VOD/SOS, days						
Median	N/A	N/A	N/A	N/A	N/A	N/A
Range	N/A	N/A	N/A	(14-79)	N/A	(14-79)
Grade of VOD/SOS[d]						
No VOD/SOS	2	1	0	15	2	16
Mild	0	0	0	1	0	1
Severe	0	0	0	1	0	1
Liver toxicity prophylaxis						
N/A; CIBMTR form[e] not yet received	0	0	0	2	0	2
None (or no additional)	0	1	0	1	0	2
Ursodiol	0	0	0	12	0	12
Ursodiol + Defibrotide	1	0	0	0	1	0
Defibrotide	1	0	0	0	1	0
Not reported	0	0	0	2	0	2
Treatment for VOD/SOS						
N/A; no VOD/SOS	2	1	0	15	2	16
None	0	0	0	0	0	0
Defibrotide + Diuretics + Ursodiol	0	0	0	1	0	1
Diuretics	0	0	0	1	0	1
Post-VOD/SOS survival						
N/A; no VOD/SOS	2	1	0	15	2	16
Alive	0	0	0	2	0	2
Dead	0	0	0	0	0	0

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; N/A, not applicable; SOS, sinusoidal obstruction syndrome; VOD, veno-occlusive disease.

Table 18. Study B1931028: VOD/SOS in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)		Adult Patients (≥ 18 years)		All Patients	
	Defibrotide[a] (N = 2)	No defibrotide (N = 1)	Defibrotide (N = 0)	No defibrotide (N = 26)	Defibrotide (N = 2)	No defibrotide (N = 27)

[a] Measures whether defibrotide was given as part of liver toxicity prophylaxis
[b] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[c] VOD/SOS was evaluated up to 100 days post-transplant.
[d] "Mild VOD/SOS" is VOD/SOS with no other organ involvement. "Severe VOD/SOS" is VOD/SOS with multiple organ dysfunction.
[e] F2450 Post-TED 100-day form or F2100 Post-transplant 100-day form version 4.

10.2.10.1. Association of Baseline Characteristics, Pre-HSCT Exposure to Inotuzumab Ozogamicin and Patient Characteristics at the Time of HSCT with Occurrence of Transplant VOD/SOS

Given the relatively small number of patients accrued, we were unable to conduct any analyses to determine the association of baseline characteristics, Pre-HSCT exposure to inotuzumab ozogamicin and patient characteristics at the time of HSCT with occurrence of post-transplant VOD/SOS.

10.2.11. Post-HSCT Clinical Status

Table 19 shows a summary of post-HSCT clinical status following inotuzumab ozogamicin treatment.

Table 19. Study B1931028: Summary of Post-HSCT Clinical Status Following Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Number of patients with follow-up	3	17	20
Best response to HSCT			
Continued CR[a]	3	13	16
CR[b]	0	2	2
Not in CR	0	1	1
Not reported	0	1	1
Granulopoiesis / neutrophil recovery[c,d]			
Yes	3	16	19
No	0	1	1
Time to event, days			
Median	17	19	19
Range	(12-19)	(12-41)	(12-41)
Megakaryopoiesis / platelet recovery[d,e]			
Yes	1	15	16
No	2	2	4
Time to event, days			
Median	14	29	28
Range	N/A	(18-67)	(14-67)
Engraftment syndrome[d]			
N/A; CIBMTR form[f] not yet received	0	1	1
No	3	16	19
Weight, kg, most recent post-HSCT			
N/A; CIBMTR form[f] not yet received	0	1	1
Not reported	1	7	8
N	2	9	11
Median	N/A	81	79
Range	(24-63)	(52-306)	(24-306)

Table 19. Study B1931028: Summary of Post-HSCT Clinical Status Following Inotuzumab Ozogamicin Treatment (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 3)	Adult Patients (≥ 18 years) (N = 26)	All Patients (N = 29)
Height (cm) most recent post-HSCT			
N/A; CIBMTR form[f] not yet received	0	1	1
Not reported	1	16	17
N	2	0	2
Median, cm	N/A	N/A	N/A
Range, cm	(130-156)	N/A	(130-156)
Performance scale and status, post-HSCT			
N/A; CIBMTR form[f] not yet received	0	1	1
Karnofsky	4	16	20
90-100	2	2	4
10-80	0	8	8
Not reported	1	6	7
Total inpatient days in first 100 days post-HSCT[g]			
N/A; CIBMTR form[f] not yet received	0	1	1
Not reported	0	3	3
N	3	13	16
Median	47	35	39
Range	(30-70)	(7-89)	(7-89)
Time from HSCT to date of last contact, months			
Median	6	6	6
Range	(2-8)	(0.6-12)	(0.6-12)
< 3	1	2	3
3-5	0	9	9
6-11	2	6	8

Abbreviations: CR, complete remission; CIBMRT, Center for International Blood and Marrow Transplant Research

[a] Continued complete remission defined as a patient who was transplanted in complete remission and the complete remission was sustained post-transplant.

[b] Complete remission 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.

[c] Absolute neutrophil count (ANC) $\geq$ 500/mm^3 achieved and sustained for 3 lab values

[d] Outcome evaluated up to 100 days post-transplant.

[e] Initial platelet count $\geq$ 20 x 10^9/L achieved

[f] 2100 Post-transplant 100-day form

[g] The form asks for the number of inpatient days in the first 100 days (day 0 to day 100) post-HSCT.

11. DISCUSSION

11.1. Key Results

Between 18 August 2017 and 17 August 2018, 30 patients (26 adults and 4 pediatric) were accrued. The data lock date, when data collection forms were last evaluated, was 11 December 2018.

Of the 30 patients, 29 patients were undergoing their first allogeneic HSCT for B-cell ALL (26 adults and 3 pediatrics) and 1 pediatric patient had received a prior HSCT before receiving inotuzumab ozogamicin.

The pediatric patient who had a prior HSCT before receiving inotuzumab ozogamicin will be described separately (i.e., the data from this patient is not included in the tables presented in Section 10 of this interim report) since the underlying disease, risk for relapse and post-HSCT complications are different for patients with a prior HSCT than for patients undergoing their first allogeneic HSCT for B-cell ALL. Data for this patient is summarized in the narrative below.

Patient who had a prior allogeneic HSCT for B-cell ALL

The patient who had a prior allogeneic HSCT for B-cell ALL was a pediatric patient (11 years old at time of HSCT) and had ≥ 3 comorbidities, including mild hepatic disease, prior to HSCT. The patient had a Lansky performance score of 100 (Normal), with no history of proven invasive fungal infection and was in the 3rd (or greater) complete remission at time of HSCT. The graft source was BM from an unrelated donor. The patient was given a myeloablative conditioning regimen of busulfan and cyclophosphamide, and also received a regimen of tacrolimus and methotrexate for GVHD prophylaxis. The duration from ALL diagnosis, which preceded the prior HSCT for this patient, to HSCT was 59 months and the duration from ALL diagnosis to the first dose of inotuzumab ozogamicin was 56 months.

This patient experienced severe VOD/SOS at 0.33 months after the 2nd allogeneic HSCT. This patient also experienced development of septic shock at 0.76 months post-HSCT and acute renal failure requiring dialysis post-HSCT. The patient died due to VOD/SOS at 0.82 months post-HSCT.

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

In total, 29 patients (26 adults and 3 pediatric patients with a median age of 37 years) underwent their first allogeneic HSCT for B-cell ALL after treatment with inotuzumab ozogamicin.

Prior to transplant, 4 patients were in front-line therapy; 3 patients were in Salvage 1; 4 patients were in Salvage 2; and 15 patients were in Salvage > 2. Data was not available for 3 patients.

As of the data lock date, post-transplant follow-up information was available for 20/29 (69%) patients:

- 14/20 patients did not experience post-HSCT relapse; of these:
    - 3/14 patients (2 adults and 1 pediatric patient) died in remission, and their causes of death were due to:
        - Infection at 0.62 months post-HSCT (adult patient)
        - Hemorrhage at 0.79 months post-HSCT (adult patient)

        - Thrombotic microangiopathy (TMA) at 8.05 months post-HSCT (pediatric patient)

- 6/20 patients experienced post-HSCT relapse; of these:
    - 4/6 patients (3 adults and 1 pediatric patient) died after post-HSCT relapse of ALL; causes of death were due to the following:
        - Primary disease at 2.46 months post-HSCT (pediatric patient)
        - Primary disease at 6.34 months post-HSCT (adult patient)
        - Primary disease at 7.10 months post-HSCT (adult patient)
        - Primary disease at 10.12 months post-HSCT (adult patient)
- 2/20 patients experienced post-transplant VOD/SOS; of these:
    - 1 case was mild (1 adult patient)
    - 1 case was severe (1 adult patient)
- 12/20 patients reported receiving liver toxicity prophylaxis with ursodiol
- 1/20 patients reported receiving liver toxicity prophylaxis with defibrotide
- 1/20 patients reported receiving liver toxicity prophylaxis with ursodiol and defibrotide

Follow-up for the remaining 9 patients will be conducted for subsequent interim reports.

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 will be analyzed. Not all CIBMTR centers agree to provide additional patient data (CRF data) and therefore some US patients who received HSCT after inotuzumab ozogamicin treatment are expected to be "missing" from the CIBMTR database. Also, not all centers agree to provide supplemental information (i.e., the supplemental inotuzumab ozogamicin form); therefore, some US patients who received HSCT after inotuzumab ozogamicin treatment are "missing" from the study.

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

11.3. Interpretation

Given the relatively small number of patients for which data was available between 18 August 2017 and 17 August 2018, interpretation of the study results is limited.

11.4. Generalizability

This study is generalizable to post-HSCT B-cell precursor ALL patients following treatment with inotuzumab ozogamicin in the US. Since supportive treatment for B-cell ALL and post-HSCT adverse events 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 adverse events, 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

Between 18 August 2017 and 17 August 2018, 30 patients (26 adults and 4 pediatrics) were accrued. Of the 30 patients, 29 patients were undergoing their first allogeneic HSCT for B-cell ALL (26 adults and 3 pediatrics) and 1 pediatric patient had received a prior HSCT before receiving inotuzumab ozogamicin.

Post-transplant follow-up information was available for 20/29 (69%) of the patients undergoing their first allogeneic HSCT for B-cell ALL. Of these 20 patients, post-transplant VOD/SOS occurred in 2 patients, post-transplant mortality occurred in 7 patients and TRM occurred in 3 patients. Three deaths occurred within the first 100 days post-transplant.

The 1 pediatric patient who had received a prior allogeneic HSCT for ALL developed VOD/SOS after a second allogeneic transplant and died 0.82 months post-HSCT.

Given the relatively small number of patients accrued for this interim report, it was not possible to make any conclusions regarding the time to event endpoints or the association between patient baseline characteristics, pre-HSCT exposure to inotuzumab ozogamicin, patient characteristics at the time of HSCT and the occurrence of post-transplant VOD/SOS.

14. REFERENCES

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15. LIST OF SOURCE TABLES AND FIGURES

Not applicable.

16. SUPPLEMENTAL TABLES

The following supplemental tables are provided:

Table 20. Summary of Post-Transplant Overall Survival[a] in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

Table 21. Summary of Post-Transplant Overall Survival[a] in Patients in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

Table 22. Summary of Post-Inotuzumab Ozogamicin Survival[a] in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

Table 23. Summary of Post-Inotuzumab Ozogamicin Survival[a] in Patients in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

Table 20. Summary of Post-Transplant Overall Survival[a] in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[b]	2	14	16
Number of deaths	1	5	6
Cause of death[c]			
Primary disease	1	3	4
Infection	0	1	1
Hemorrhage	0	1	1
Time from transplant to death, months			
0.62	0	1	1
0.79	0	1	1
2.46	1	0	1
6.34	0	1	1
7.1	0	1	1
10.12	0	1	1

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome

[a] Post-Transplant Overall Survival: 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.

[b] 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.

[c] Only the primary cause of death is reported.

Table 21. Summary of Post-Transplant Overall Survival[a] in Patients in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Number of patients with post-transplant follow-up[b]	1	3	4
Number of deaths	1	0	1
Cause of death[c]			
TMA	1	0	1
Time from transplant to death, months			
8.05	1	0	1

Abbreviations: HSCT, hematopoietic stem cell transplantation; TMA, thrombotic microangiopathy

[a] Post-Transplant Overall Survival: 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.

[b] 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.

[c] Only the primary cause of death is reported.

Table 22. Summary of Post-Inotuzumab Ozogamicin Survival[a] in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[b]	2	14	16
Number of deaths	1	5	6
Cause of death[c]			
Primary disease	1	3	4
Infection	0	1	1
Hemorrhage	0	1	1
Time from first dose of inotuzumab ozogamicin to death, months			
3.38	0	1	1
4.11	0	1	1
9.33	0	1	1
9.82	0	1	1
12.52	0	1	1
15.41	1	0	1

Abbreviations: ALL, acute lymphoblastic leukemia; HSCT, hematopoietic stem cell transplantation
[a] Post-Inotuzumab Ozogamicin Survival: 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.
[b] 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.
[c] Only the primary cause of death is reported.

Table 23. Summary of Post-Inotuzumab Ozogamicin Survival[a] in Patients in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Number of patients with post-transplant follow-up[b]	1	3	4
Number of deaths	1	0	1
Cause of death[c]			
TMA	1	0	1
Time from first dose of inotuzumab ozogamicin to death, months			
10.91	1	0	1

Abbreviations: HSCT, hematopoietic stem cell transplantation; TMA, thrombotic microangiopathy
[a] Post-Inotuzumab Ozogamicin Survival: 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.
[b] 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.
[c] Only the primary COD is reported.

Table 24. Summary of Transplant-Related Mortality in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[a]	2	14	16
Number of patients with post-transplant mortality	0	2	2
Number of patients with competing risks[b]	1	5	6
Time from transplant to TRM, months			
0.62	0	1	1
0.79	0	1	1

Abbreviations: ALL, acute lymphoblastic leukemia; CHSCT, hematopoietic stem cell transplantation; TRM, transplant-related mortality; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for TRM is defined as post-transplant relapse.

Table 25. Summary of Transplant-Related Mortality in Patients in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Number of patients with post-transplant follow-up[a]	1	3	4
Number of patients with post-transplant mortality	1	0	1
Number of patients with competing risks[b]	0	0	0
Time from transplant to TRM, months			
8.05	1	0	1

Abbreviations: HSCT, hematopoietic stem cell transplantation; TRM, transplant-related mortality.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for TRM is defined as post-transplant relapse.

Table 26. Summary of Non-Transplant-Related Mortality in Patients who had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[a]	2	14	16
Number of patients with post-transplant mortality	1	3	4
Number of patients with competing risks[b]	0	2	2
Time from transplant to TRM, months			
1.87	0	1	1
2.2	1	0	1
3.52	0	1	1
5.88	0	1	1

Abbreviations: HSCT, hematopoietic stem cell transplantation; TRM, transplant-related mortality; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.
Note: There were no patients who were in 1st complete remission prior to HSCT who experienced NTRM, so this table was omitted in this report.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for NTRM is defined as TRM.

Table 27. Summary of Post-Transplant Relapse in Patients Who Had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[a]	2	14	16
Number of patients with post-transplant relapse	1	5	6
Number of patients with competing risks[b]	0	2	2
Time from transplant to relapse, months			
1.61	0	1	1
1.87	0	1	1
2.20	1	0	1
3.52	0	1	1
5.22	0	1	1
5.88	0	1	1

Abbreviations: ALL, acute lymphoblastic leukemia; HSCT, hematopoietic stem cell transplantation.
Note: There were no patients who were in 1st complete remission prior to HSCT who experienced post-HSCT relapse, so this table was omitted in this report.
[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[b] The competing risk for relapse is defined as TRM.

Table 28. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and Had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Number of patients with post-transplant follow-up[a]	2	14	16
Viral infection, up to day 100			
Yes	1	8	9
No	1	6	7
Bacterial infection, up to day 100			
Yes	0	7	7
No	2	7	9
Fungal infection, up to day 100			
Yes	0	1	1
No	2	13	15
SIRS development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	2	2
Yes	0	1	1
No	2	10	12
Not reported	0	1	1
Septic shock development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	2	2
Yes	0	1	1
No	2	10	12
Not reported	0	1	1
Maximum grade of acute GVHD[b]			
None	1	6	7
Grade I	1	2	3
Grade III	0	2	2
Not reported	0	4	4
Time from HSCT to date of maximum acute GVHD, months			
N	1	4	5
Median	1.4	1.8	1.4
Range	N/A	(1-2.8)	(1-2.8)
Chronic GVHD[c]			
No	2	12	14
Yes	0	2	2

Table 28. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and Had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Time from HSCT to chronic GVHD diagnosis, months			
N	0	2	2
Median	N/A	N/A	N/A
Range	N/A	(3-3)	(3-3)
VOD/SOS[d]			
No	2	12	14
Yes	0	2	2
Time from HSCT to VOD/SOS diagnosis, months			
N	0	2	2
Median	N/A	N/A	N/A
Range	N/A	(0.5-2.6)	(0.5-2.6)
Secondary malignancy			
No	2	13	15
Yes[e]	0	1	1
Time from HSCT to secondary malignancy, months			
N	0	1	1
Median	N/A	4	4
Range	N/A	N/A	N/A
Pulmonary AEs[f]			
IPN / Idiopathic pneumonia syndrome			
No	2	13	15
Yes	0	1	1
Bronchiolitis obliterans			
No	2	14	16
COP/BOOP			
No	2	14	16
Diffuse alveolar hemorrhage			
No	2	14	16
Cardiovascular AEs			
Arrhythmia			
No	2	13	15
Yes	0	1	1
Congestive heart failure			
No	2	13	15
Yes	0	1	1
Coronary artery disease			
No	2	14	16

Table 28. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and Had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
Myocardial infarction or unstable angina			
No	2	14	16
HTN requiring therapy			
No	2	14	16
Thrombotic microangiopathy (TMA)			
No	2	13	15
Yes	0	1	1
Renal AEs			
Acute renal failure requiring dialysis			
No	2	13	15
Yes	0	1	1
Musculoskeletal AEs			
Avascular necrosis			
No	2	14	16
Endocrine dysfunction			
Diabetes or hyperglycemia requiring chronic treatment			
No	2	14	16
Growth hormone deficiency or short stature			
No	2	14	16
Hypothyroidism requiring replacement therapy			
No	2	14	16
Pancreatitis			
No	2	14	16
Neurologic or psychiatric AEs			
Depression requiring therapy			
No	2	14	16
Anxiety requiring therapy			
No	2	14	16
CNS hemorrhage and stroke			
No	2	14	16

Table 28. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and Had Relapsed or Refractory B-Cell ALL Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 2)	Adult Patients (≥ 18 years) (N = 21)	All Patients (N = 23)
PTSD requiring therapy			
No	2	14	16

Abbreviations: AEs, adverse events; ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; COP/BOOP, cryptogenic organizing pneumonia / bronchiolitis obliterans organizing pneumonia; CNS, central nervous system; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; IPN, interstitial pneumonitis; N/A, not applicable; PTSD, post-traumatic stress disorder; SIRS, Systemic Inflammatory Response Syndrome; SOS, hepatic sinusoidal obstruction syndrome; VOD/SOS, veno-occlusive disease / sinusoidal obstruction syndrome.
Note: One patient received inotuzumab ozogamicin for a second HSCT for B-cell ALL, and was excluded from this table. This patient died due to transplant-related mortality, and cause of death attributed to VOD/SOS, 0.82 months post-HSCT.

[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.

[b] Acute GVHD grading follows the Consensus criteria, according to 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.

[c] Chronic GVHD was evaluated up to 1 year post-transplant.

[d] VOD/SOS was evaluated up to 100 days post-transplant.

[e] Secondary malignancy was squamous cell cancer of the skin.

[f] Remaining adverse events evaluated up to 100 days post-transplant.

Table 29. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Number of patients with post-transplant follow-up[a]	1	3	4
Viral infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
Yes	0	1	1
No	1	1	2
Bacterial infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
Yes	0	1	1
No	1	1	2
Fungal infection, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
SIRS development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Septic shock development, up to day 100			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Maximum grade of acute GVHD[c]			
N/A; CIBMTR form[b] not yet received	0	1	1
None	0	2	2
Grade IV	1	0	1
Time from HSCT to date of maximum acute GVHD, months			
N	1	0	1
Median	0.4	N/A	0.4
Range	N/A	N/A	N/A
Chronic GVHD[d]			
No	0	3	3
Yes	1	0	1
Time from HSCT to chronic GVHD diagnosis, months			
N	1	0	1
Median	3	N/A	3
Range	N/A	N/A	N/A
VOD/SOS[e]			
No	1	3	4
Secondary malignancy			
No	1	3	4

Table 29. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Pulmonary AEs[f]			
IPN / Idiopathic pneumonia syndrome			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Bronchiolitis obliterans			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
COP/BOOP			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Diffuse alveolar hemorrhage			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Cardiovascular AEs			
Arrhythmia			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Congestive heart failure			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Coronary artery disease			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Myocardial infarction or unstable angina			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
HTN requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	0	1	1
Yes	1	1	2
TMA			
N/A; CIBMTR form[b] not yet received	0	1	1
No	0	2	2
Yes	1	0	1
Renal AEs			
Acute renal failure requiring dialysis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3

Table 29. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
Musculoskeletal AEs			
Avascular necrosis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Endocrine dysfunction			
Diabetes or hyperglycemia requiring chronic treatment			
N/A; CIBMTR form[b] not yet received	0	1	1
No	0	2	2
Yes	1	0	1
Growth hormone deficiency or short stature			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Hypothyroidism requiring replacement therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Pancreatitis			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3
Neurologic or psychiatric AEs			
Depression requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	0	2	2
Yes	1	0	1
Anxiety requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	0	2	2
Yes	1	0	1
CNS hemorrhage and stroke			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3

Table 29. 100-Day Post-HSCT Adverse Events of Interest in Patients with B-Cell ALL who Received Inotuzumab Ozogamicin Therapy and in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years) (N = 1)	Adult Patients (≥ 18 years) (N = 5)	All Patients (N = 6)
PTSD requiring therapy			
N/A; CIBMTR form[b] not yet received	0	1	1
No	1	2	3

Abbreviations: AEs, adverse events; ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; COP/BOOP, cryptogenic organizing pneumonia / bronchiolitis obliterans organizing pneumonia; CNS, central nervous system; GVHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; IPN, interstitial pneumonitis; N/A, not applicable; PTSD, post-traumatic stress disorder; SIRS, Systemic Inflammatory Response Syndrome; SOS, hepatic sinusoidal obstruction syndrome; TMA, thrombotic microangiopathy; VOD, veno-occlusive disease.

[a] 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 completed a follow-up form are not included in the data and estimates shown in this table.

[b] 2100 Post-transplant 100-day form

[c] Acute GVHD grading follows the Consensus criteria, according to 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.

[d] Chronic GVHD was evaluated up to 1 year post-transplant.

[e] VOD/SOS was evaluated up to 100 days post-transplant.

[f] Remaining adverse events evaluated up to 100 days post-transplant

Table 30. Summary of Post-Transplant VOD/SOS, in Patients who had Relapsed or Refractory B-cell ALL Prior to HSCT, (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients, (< 18 years)		Adult Patients (≥ 18 years)		All Patients	
	Defibrotide[a] (N = 2)	No defibrotide (N = 0)	Defibrotide (N = 0)	No defibrotide (N = 21)	Defibrotide (N = 2)	No defibrotide (N = 21)
Number of patients with post-transplant follow-up[b]	2	0	0	14	2	14
Number of patients with post-transplant VOD/SOS[c]	0	0	0	2	0	2
Time to post-transplant VOD/SOS, days						
N	0	0	0	2	0	2
Median	N/A	N/A	N/A	N/A	N/A	N/A
Range	N/A	N/A	N/A	(14-79)	N/A	(14-79)
Grade of VOD/SOS[d]						
No VOD/SOS	2	0	0	12	2	12
Mild	0	0	0	1	0	1
Severe	0	0	0	1	0	1
Liver toxicity prophylaxis						
N/A; CIBMTR form[e] not yet received	0	0	0	3	0	3
None	0	0	0	1	0	1
Ursodiol	0	0	0	10	0	10
Ursodiol + Defibrotide	1	0	0	0	1	0
Defibrotide	1	0	0	0	1	0
Treatment for VOD/SOS						
N/A; no VOD/SOS	2	0	0	12	2	12
None	0	0	0	0	0	0
Defibrotide + Diuretics + Ursodiol	0	0	0	1	0	1
Diuretics	0	0	0	1	0	1
Post-VOD/SOS survival						
N/A; no VOD/SOS	2	0	0	12	2	12
Alive	0	0	0	2	0	2
Dead	0	0	0	0	0	0

Abbreviations: ALL, acute lymphoblastic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; HSCT, hematopoietic stem cell transplantation; N/A, not applicable; SOS, sinusoidal obstruction syndrome; VOD, veno-occlusive disease.

[a] Defibrotide use was considered if used for liver toxicity prophylaxis

[b] 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

Table 30. Summary of Post-Transplant VOD/SOS, in Patients who had Relapsed or Refractory B-cell ALL Prior to HSCT, (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients, (< 18 years)		Adult Patients (≥ 18 years)		All Patients	
	Defibrotide[a] (N = 2)	No defibrotide (N = 0)	Defibrotide (N = 0)	No defibrotide (N = 21)	Defibrotide (N = 2)	No defibrotide (N = 21)

biennially thereafter until death. Patients who have not completed a follow-up form are not included in the data and estimates shown in this table.
[c] VOD/SOS was evaluated up to 100 days post-transplant. Defibrotide use was considered if used for liver toxicity prophylaxis
[d] "Mild VOD/SOS" is VOD /SOS with no other organ involvement. "Severe VOD/SOS" is VOD/SOS with multiple organ dysfunction.
[e] F2450 Post-TED 100-day form or F2100 Post-transplant 100-day form version 4.

Table 31. Summary of Post-Transplant VOD/SOS, in Patients who were in First Complete Remission Prior to HSCT (Patients Undergoing First Allogeneic HSCT for B-cell ALL)

	Pediatric Patients (< 18 years)		Adult Patients (≥ 18 years)		All Patients	
	Defibrotide[a] (N = 0)	No defibrotide (N = 1)	Defibrotide (N = 0)	No defibrotide (N = 5)	Defibrotide (N = 0)	No defibrotide (N = 6)
Number of patients with post-transplant follow-up[b]	0	1	0	3	0	4
Number of patients with post-transplant VOD/SOS[c]	0	0	0	0	0	0
Liver toxicity prophylaxis						
None	0	1	0	0	0	1
Ursodiol	0	0	0	2	0	2
Not reported	0	0	0	1	0	1

Abbreviations: HSCT, hematopoietic stem cell transplantation; SOS, sinusoidal obstruction syndrome; VOD, veno-occlusive disease.
[a] Defibrotide use was considered if used for liver toxicity prophylaxis.
[b] 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 completed a follow-up form are not included in the data and estimates shown in this table.
[c] VOD/SOS was evaluated up to 100 days post-transplant. Defibrotide use was considered if used for liver toxicity prophylaxis.

17. APPENDICES

17.1. Appendix 1

Study B1931028 protocol

17.2. Appendix 2

Study B1931028 SAP version 3.0 dated 20 February 2019

17.3. Appendix 3

CIBMTR data collection forms:

- Pre-Transplant Essential Data
- Recipient Baseline Data
- ALL Pre-HSCT Data
- ALL Post-HSCT Data
- Inotuzumab Ozogamicin (Besponsa) Supplemental Data Collection
- Post HSCT Follow-up Data
- Post-Transplant Essential Data
- VOD/SOS Supplemental Data Collection Form
- Recipient Death Data