

Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients.

The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Inotuzumab Ozogamicin (PF-05208773)

Protocol Number: B1931030

Dates of Study: 01 July 2019 to 21 September 2022

Title of this Study: A Study of Two Inotuzumab Ozogamicin (InO) Doses in Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia Transplant Eligible Patients

[A Phase 4, Open-Label, Randomized Study of Two Inotuzumab Ozogamicin Dose Levels in Adult Patients With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia Eligible for Hematopoietic Stem Cell Transplantation and Who Have Risk Factor(s) for Veno-Occlusive Disease]

Date(s) of this Report: 20 September 2023



– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is B-Cell Acute Lymphoblastic Leukemia (ALL)?

B-cell acute lymphoblastic leukemia is a type of acute lymphoblastic leukemia (ALL) that develops when many immature white blood cells, known as B-cell lymphoblasts, in the bloodstream and bone marrow are overproduced and begin to change (mutate) abnormally. Researchers are looking to provide better medical care for patients with either relapsed (which means that there was response to the most recent treatment, but the cancer came back) or refractory (which means that there was no response, or the disease got worse while receiving the most recent treatment) B-Cell ALL.

What is Inotuzumab ozogamicin (InO)?

InO (Besponsa™ [beh-SPON-suh]) is a medicine that is currently approved in countries including the United States, those within the European Union, Switzerland, Japan, Canada, and Australia for the treatment of adults with relapsed or refractory cluster of differentiation-22 (CD22) positive ALL. InO includes an antibody that attaches to B cells or B lymphocytes (a type of white blood cells) with a protein called CD22. Patients with CD22-positive ALL have this protein on their leukemia cells. Once attached to the leukemia cells, the drug delivers a substance into the cells and causes the cell to die.

What was the purpose of this study?

The main purpose of this study is to see how the safety and anti-cancer activity of a lower dose of InO compares to the approved dose of InO for patients with relapsed or refractory ALL who may be at higher risk for severe liver problems after InO treatment and stem cell transplant (a treatment provided to replace the cancer cells with healthy cells). The

severe liver problems occur due to blockage in the liver blood vessels (called venoocclusive disease [VOD]). VOD is a well-recognized complication of stem cell transplant and InO. The risk of VOD appears to be higher in patients who proceed to stem cell transplant after InO therapy, especially for patients who are aged 55 years or more, have had a prior stem cell transplant, have had more than 1 prior treatment for their cancer, or have had liver problems.

This study is different from regular medical care. The purpose of regular medical care is to improve or otherwise manage the health, but the purpose of research is to gather information to advance science and medicine and does not replace your regular medical care.

Researchers wanted to know:

- **How safe was the treatment with different dose levels of InO in participants with relapsed or refractory B-cell acute lymphoblastic leukemia to reduce the risk of VOD?**
- **How effective was treatment with different dose levels of InO in participants with relapsed or refractory B-cell acute lymphoblastic leukemia?**

What happened during the study?

How was the study done?

This was an “open-label” study. This means researchers and participants knew what study medication each patient was receiving.




Researchers tested 2 doses levels of InO in participants with relapsed or refractory B-cell ALL who were eligible for hematopoietic stem cell transplant (HSCT) and who had higher risks for developing VOD post-HSCT after InO treatment, as shown below:




Participants were treated with InO at a starting dose of 1.8 mg/m²/cycle (Dose Level 1, the approved dose) or 1.2 mg/m²/cycle (Dose Level 2, the reduced dose) administered over 3 divided doses. Each dose was given weekly on Day 1, 8, and 15, making up one cycle of treatment. A cycle will last approximately 21 to 28 days. After the significant disappearance of the signs and symptoms (CR/CRi) was achieved in participants, the dose was reduced. CR is complete remission based on the disappearance of leukemia by standard microscopy. CRi is complete remission with incomplete recovery of normal blood cells.

For participants leading to HSCT, no more than 2 cycles were recommended. Additional third cycle was planned for those patients who did not achieve CR/CRi and for participants who had very low levels of cancer cells detected (minimal residual disease [MRD] positive) in the body after 2 cycles. Patients who did not achieve CR/CRi within 3 cycles discontinued treatment. Patients who became ineligible for HSCT could receive up to 6 cycles (Figure 1).

Figure 1. Dosing for Each Cycle

One treatment cycle = 21 to 28 days

Dose Level 1 (InO 1.8 mg/m ² /cycle)				
Cycles 1		After CR/CRi achieved	Cycles 2	Cycles ≥3*
Day 1	Days 8 and 15		Day 1, 8 and 15	
 0.8 mg/m ²	 0.5 mg/m ²		 0.5 mg/m ²	Participants who did not achieve CR/CRi*

Dose Level 2 (InO 1.2 mg/m ² /cycle)				
Cycles 1		After CR/CRi achieved	Cycles 2	Cycles ≥3*
Day 1	Days 8 and 15		Day 1, 8 and 15	
 0.6 mg/m ²	 0.3 mg/m ²		 0.3 mg/m ²	Participants who did not achieve CR/CRi*

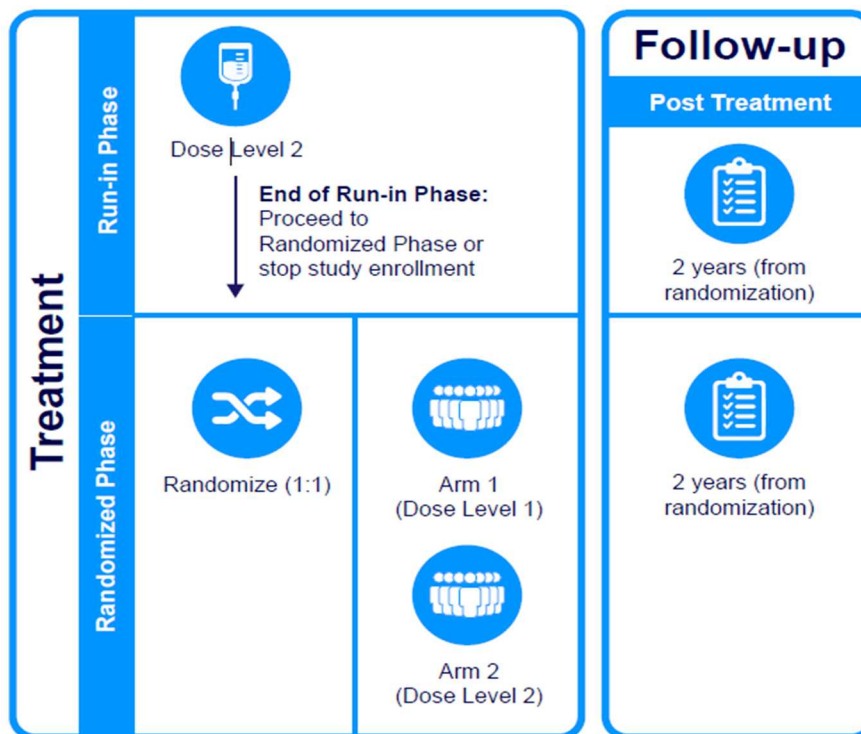
* For patients proceeding to HSCT, 2 cycles were recommended; a third cycle was planned for those patients who did not achieve CR/CRi and MRD-negativity after 2 cycles (maximum of 4 cycles). Patients who did not achieve CR/CRi within 3 or 4 cycles discontinued the treatment.

Overall, the study consisted of a Screening Visit, Treatment Period and Follow-up Period as shown in Figure 2.

All participants were “screened” to see if they qualify to be in the study. Participants who qualified for treatment after screening entered the Treatment Period. To ensure the safety of participants, dosing was done in 2 phases, as follows:

- Run-in Phase: up to 22 participants were treated and all received the lower dose of 1.2 mg/m²/cycle (dose level 2). This stage of the study was used to confirm that the lower dose achieves sufficient efficacy.
- Randomized Phase: up to 80 participants were enrolled to receive the study drug by chance at either the approved dose (dose level 1) or the lower dose. 38 participants received InO starting dose of 1.8 mg/m²/cycle and 42 participants received InO starting dose of 1.2 mg/m²/cycle.

Figure 2. Study B1931030: Study Flow Diagram



Researchers then compared the results of study participants taking 1.2 mg/m²/cycle (run-in phase), 1.2 mg/m²/cycle (randomized phase), 1.2 mg/m²/cycle (run-in and randomized phase), and 1.8 mg/m²/cycle (randomized phase).

Where did this study take place?

The Sponsor ran this study at 33 locations in 8 countries.

When did this study take place?

It began 01 July 2019 and ended 21 September 2022.

Who participated in this study?

The study included participants who have relapsed or refractory B-Cell CD22-positive ALL, who were eligible for stem cell transplant, who were at least 55 years or more, and had a prior stem cell transplant, had more than 1 prior treatment for cancer, or had liver problems.

- A total of 56 men participated
- A total of 46 women participated
- All participants were between the ages 18 to 75 years.

Participants were to be treated until

- their cancer got worse,
- they left the study by their own choice,
- they had unacceptable medical problems, or
- the study ended.

Of the 102 participants who started the study, 60 (58.8%) participants finished the treatment phase, and 42 (41.2%) participants did not finish the study. The most common reasons for stopping the treatment were because their cancer got worse, and the participants passed away during this study.

How long did the study last?

The time participants were in the study, depended on their number of treatment cycles and follow-up time. The entire study took 3 years to complete.

When the study ended in September 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How safe was the treatment with different dose levels of InO in participants with relapsed or refractory B-cell acute lymphoblastic leukemia to reduce the risk of VOD?

The overall safety for both InO dose levels was generally manageable in adult participants with relapsed or refractory B-cell ALL eligible for HSCT and who had risk factors for VOD.

In total, VOD (during study treatment, post HSCT, and overall) was reported in 10 (9.8%) participants out of 102 (2 [9.1%] in 1.2 mg/m²/cycle [run-in phase], 6 [14.3%] in 1.2 mg/m²/cycle [randomized phase], 8 [12.5%] in 1.2 mg/m²/cycle [run-in and randomized phase], and 2 [5.3%] in 1.8 mg/m²/cycle [randomized phase]). All participants developed VOD after post-study HSCT.

The post-study HSCT VOD rate was 2 (20.0%) out of 10 participants in 1.2 mg/m²/cycle (run-in phase), 6 (28.6%) out of 21 participants in 1.2 mg/m²/cycle (randomized phase), 8 (25.8%) out of 31 participants in 1.2 mg/m²/cycle (run-in and randomized phase), and 2 (16.7%) out of 12 participants in 1.8 mg/m²/cycle (randomized phase).

There were no new safety issues or signals identified in both dose levels relevant to InO therapy.

How effective was treatment with different dose levels of InO in participants with relapsed or refractory B-cell acute lymphoblastic leukemia?

The significant disappearance of the signs and symptoms (CR/CRi) leukemia in response to treatment observed in run-in phase and randomized phase are:

Run-in Phase: The CR/CRi rate was 11 out of 22 participants (50%) for 1.2 mg/m²/cycle.

Randomized Phase: The CR/CRi rates was 35 out of 42 participants (83.3%) for 1.2 mg/m²/cycle and was 26 out of 38 participants (68.4%) for 1.8 mg/m²/cycle (randomized phase).

Run-in and Randomized phase: The CR/CRi rate for 1.2 mg/m²/cycle was 46 out 64 participants (71.9%).

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

95 out of 102 (93.1%) participants in this study had at least 1 medical problem. A total of 14 (13.7%) participants left the study because of

medical problems. The most common medical problems – those reported by more than 10% of participants – are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 10% of participants are listed.
- The **2nd** column tells how many of the 22 participants taking 1.2 mg/m²/cycle in the run-in phase reported each medical problem. Next to this number is the percentage of the 22 participants taking 1.2 mg/m²/cycle in the run-in phase who reported the medical problem.
- The **3rd** column tells how many of the 42 participants taking 1.2 mg/m²/cycle in the randomized phase reported each medical problem. Next to this number is the percentage of the 42 participants taking 1.2 mg/m²/cycle in the randomized phase who reported the medical problem.
- The **4th** column tells how many of the 64 participants taking 1.2 mg/m²/cycle in the run-in + randomized phase reported each medical problem. Next to this number is the percentage of the 64 participants taking 1.2 mg/m²/cycle in the run-in + randomized phase who reported the medical problem.
- The **5th** column tells how many of the 38 participants taking 1.8 mg/m²/cycle in the randomized phase reported each medical problem. Next to this number is the percentage of the 38 participants taking 1.8 mg/m²/cycle in the randomized phase who reported the medical problem.

- The **6th** column tells how many of the total 102 participants reported each medical problem. Next to this number is the percentage of the 102 participants who reported the medical problem.
- Using these instructions, you can see that 21 out of the 22 (95.5%) participants in run-in phase taking 1.2 mg/m²/cycle reported low blood platelet count (thrombocytopenia), 16 out of the 42 (38.1%) participants in randomized phase taking 1.2 mg/m²/cycle and 20 out of the 64 (31.3%) participants in run-in and randomized phase reported low neutrophil levels (neutropenia), and 13 out of the 38 (34.2%) participants in randomized phase taking 1.8 mg/m²/cycle reported low blood platelet count (thrombocytopenia). A total of 32 out of the 102 (31.4%) participants taking the study medication reported low blood platelet count (thrombocytopenia).

Table 1. Commonly reported medical problems by study participants reported for more than 10% of study participant with relapsed or refractory B-cell acute lymphoblastic leukemia

Medical Problem	1.2 mg/m ² /cycle (Run- in) (22 Participa nts)	1.2 mg/m ² /cyc le (Randomiz ed) (42 Participant s)	1.2 mg/m ² /cy cle (Run- in + Randomiz ed) (64 Participan ts)	1.8 mg/m ² /cyc le (Randomiz ed) (38 Participant s)	Total (102 Participa nts)
Low blood platelet count (Thrombocytopenia)	5 (22.7)	14 (33.3)	19 (29.7)	13 (34.2)	32 (31.4)
Low neutrophil levels (Neutropenia)	4 (18.2)	16 (38.1)	20 (31.3)	10 (26.3)	30 (29.4)
Fever associated with low levels of white blood cell (Febrile neutropenia)	4 (18.2)	6 (14.3)	10 (15.6)	8 (21.1)	18 (17.6)

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Medical Problem	1.2 mg/m ² /cycle (Run- in) (22 Participants)	1.2 mg/m ² /cycle (Randomiz- ed) (42 Participants)	1.2 mg/m ² /cycle (Run- in + Randomiz- ed) (64 Participants)	1.8 mg/m ² /cycle (Randomiz- ed) (38 Participants)	Total (102 Participants)
Low red blood cell count (Anemia)	2 (9.1)	9 (21.4)	11 (17.2)	6 (15.8)	17 (16.7)
Fever (Pyrexia)	6 (27.3)	7 (16.7)	13 (20.3)	4 (10.5)	17 (16.7)
Increased liver enzyme in blood (aspartate aminotransferase [AST])	4 (18.2)	3 (7.1)	7 (10.9)	8 (21.1)	15 (14.7)

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Low white blood cell levels (Leukopenia)	2 (9.1)	6 (14.3)	8 (12.5)	6 (15.8)	14 (13.7)
Increased liver enzyme in blood (Alanine aminotransferas e [ALT])	5 (22.7)	5 (11.9)	10 (15.6)	3 (7.9)	13 (12.7)

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Increased liver enzyme in blood (Gamma-glutamyl transferase [GGT])	1 (4.5)	4 (9.5)	5 (7.8)	6 (15.8)	11 (10.8)
Liver disease due to blockage in the liver blood vessels (Venoocclusive liver disease)	2 (9.1)	6 (14.3)	8 (12.5)	2 (5.3)	10 (9.8)

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Medical Problem	1.2 mg/m ² /cycle (Run- in) (22 Participants)	1.2 mg/m ² /cycle (Randomiz- ed) (42 Participants)	1.2 mg/m ² /cycle (Run- in + Randomiz- ed) (64 Participants)	1.8 mg/m ² /cycle (Randomiz- ed) (38 Participants)	Total (102 Participants)
Increased lactate dehydrogenase (LDH) in blood	2 (9.1)	3 (7.1)	5 (7.8)	4 (10.5)	9 (8.8)
Nosebleed (Epistaxis)	3 (13.6)	2 (4.8)	5 (7.8)	4 (10.5)	9 (8.8)
Decreased white blood cells (Neutrophil) count	4 (18.2)	1 (2.4)	5 (7.8)	4 (10.5)	9 (8.8)
Vomiting	1 (4.5)	5 (11.9)	6 (9.4)	3 (7.9)	9 (8.8)

Table 1. Commonly reported medical problems by study participants reported for more than 10% of study participant with relapsed or refractory B-cell acute lymphoblastic leukemia

Medical Problem	1.2 mg/m ² /cycle (Run-in) (22 Participants)	1.2 mg/m ² /cycle (Randomized) (42 Participants)	1.2 mg/m ² /cycle (Run-in + Randomized) (64 Participants)	1.8 mg/m ² /cycle (Randomized) (38 Participants)	Total (102 Participants)
Stomach pain	2 (9.1)	5 (11.9)	7 (10.9)	1 (2.6)	8 (7.8)
Headache	0	4 (9.5)	4 (6.3)	4 (10.5)	8 (7.8)
Nausea	0	5 (11.9)	5 (7.8)	3 (7.9)	8 (7.8)
Hard stool (Constipation)	1 (4.5)	2 (4.8)	3 (4.7)	4 (10.5)	7 (6.9)
Disease progression (cancer got worse)	3 (13.6)	1 (2.4)	4 (6.3)	2 (5.3)	6 (5.9)

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Medical Problem	1.2 mg/m ² /cycle (Run- in) (22 Participa nts)	1.2 mg/m ² /cyc le (Randomiz ed) (42 Participant s)	1.2 mg/m ² /cy cle (Run- in + Randomiz ed) (64 Participan ts)	1.8 mg/m ² /cyc le (Randomiz ed) (38 Participant s)	Total (102 Participa nts)
Low platelet count	3 (13.6)	0	3 (4.7)	3 (7.9)	6 (5.9)
Lung infection (Pneumonia)	3 (13.6)	1 (2.4)	4 (6.3)	0	4 (3.9)

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

A total of 64 out of 102 participants (62.7%) had serious medical problems.

- 15 of 22 participants (68.2%) in the 1.2 mg/m²/cycle (run-in phase) had serious medical problems. The most commonly reported problems were fever associated with low levels of white blood cell and cancer got worse.
- 28 of 42 participants (66.7%) participants in the 1.2 mg/m²/cycle (randomized phase) had serious medical problems. The most frequently reported problem was VOD.
- 43 of 64 participants (67.2%) in the 1.2 mg/m²/cycle (run-in and randomized phase) had serious medical problems. The most frequently reported problems were VOD and fever associated with low levels of white blood cell.
- 21 of 38 participants (55.3%) in the 1.8 mg/m²/cycle (randomized phase) had serious medical problems. The most frequently reported problem was fever associated with low levels of white blood cell.

25 out of 102 participants (24.5%) had treatment-related serious medical problems. The most commonly reported serious medical problem was febrile neutropenia (9 participants).

64 out of 102 participants (62.7%) died during the study, of which 12 died within 63 days of first dose and 28 died within 63 days of last dose.

Overall, 19 participants (18.6%) died as their cancer got worse and 6 participants (5.9%) died due to study treatment toxicity. The most common cause of death was medical problem not related to study medication (30 [29.4%] participants).

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

[www.pfizer.com/research/
research_clinical_trials/trial_results](http://www.pfizer.com/research/research_clinical_trials/trial_results)

Use the protocol number
B1931030

The full scientific report of this study is available online at:

www.clinicaltrials.gov

Use the study identifier
NCT03677596

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study,
thank you for volunteering.

We do research to try to find the
best ways to help patients, and you
helped us to do that!