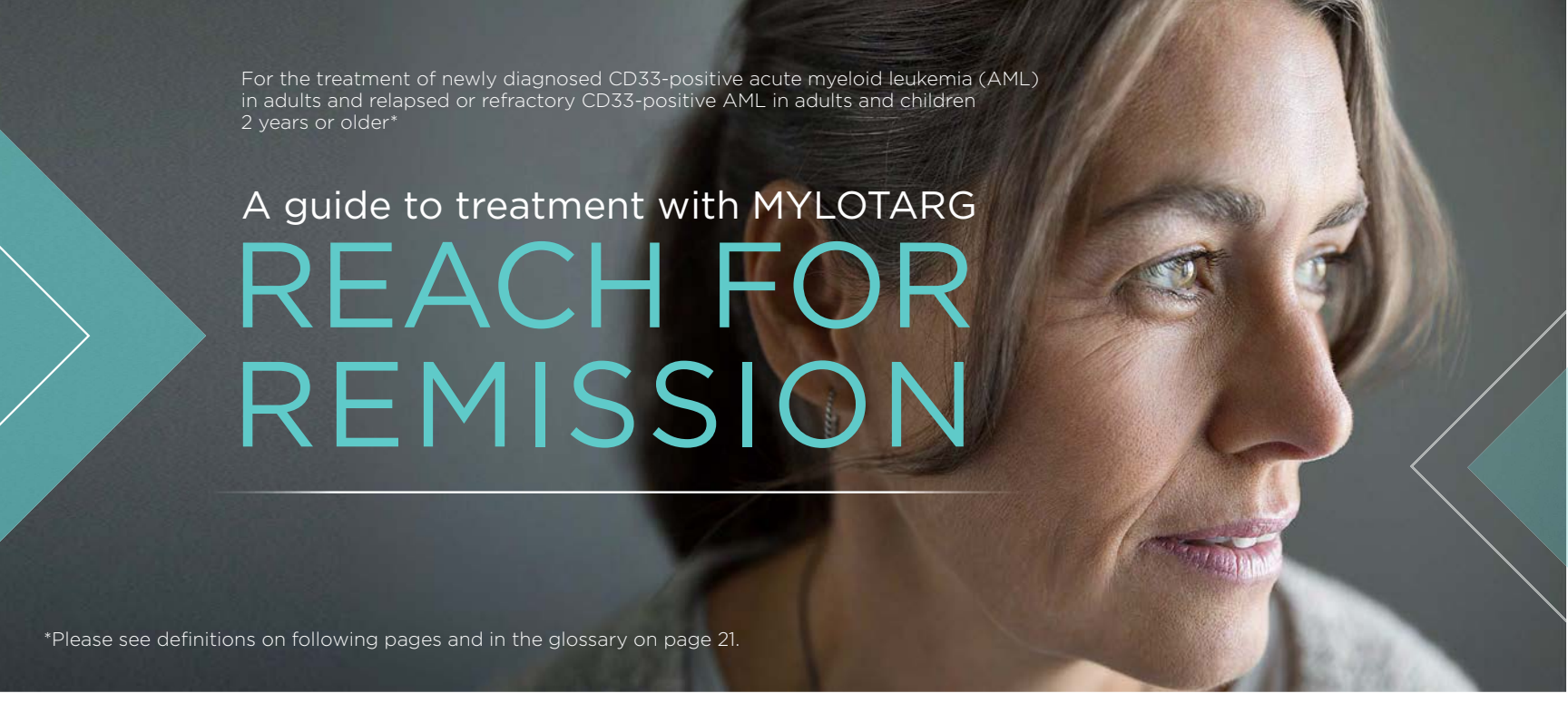

For the treatment of newly diagnosed CD33-positive acute myeloid leukemia (AML) in adults and relapsed or refractory CD33-positive AML in adults and children 2 years or older*

A guide to treatment with MYLOTARG

REACH FOR REMISSION

*Please see definitions on following pages and in the glossary on page 21.

What is MYLOTARG?

MYLOTARG™ (gemtuzumab ozogamicin) is a prescription medicine used to treat adults with newly diagnosed CD33-positive acute myeloid leukemia (AML) or patients over the age of 2 with CD33-positive AML whose disease returned or did not respond to previous treatment.

SELECTED SAFETY INFORMATION

WARNING: RISK OF LIVER PROBLEMS: MYLOTARG can cause liver problems that can be severe or life-threatening or lead to death, including a condition called veno-occlusive disease (VOD). If you have previously received or will be receiving a stem cell transplant, or you have a history of liver problems, you may be at an increased risk for VOD. Tell your doctor about any signs or symptoms of liver problems, including rapid weight gain, abdominal swelling (which may be painful), or yellowing of the whites of your eyes. Your doctor should do blood tests to check for liver problems before and regularly during your treatment. Liver problems may require dosing interruption or permanent discontinuation of MYLOTARG.

Please see additional Important Safety Information on page 20 and full Prescribing Information, including BOXED WARNING, at www.MylotargHCP.com.

MYLOTARG™
gemtuzumab ozogamicin INJECTION FOR IV INFUSION
4.5 mg single-dose vial

UNDERSTANDING AML

What is acute myeloid leukemia (AML)?

AML is a blood cancer in which the bone marrow makes too many abnormal blood cells, called leukemic blasts.

AML blocks the production of regular blood cells and can lead to lower numbers of healthy blood cells than normal, including:

- Low red blood cells (anemia)
- Low white blood cells (neutropenia)
- Low platelets (thrombocytopenia)

How common is AML?

AML is one of the most common types of acute leukemia in adults. While AML can affect both adults and children, people over the age of 65 are more likely to develop the disease. In 2018, there were approximately 19,500 new cases of AML.

SELECTED SAFETY INFORMATION

Contraindications: Do not take MYLOTARG™ (gemtuzumab ozogamicin) if you have a history of hypersensitivity to MYLOTARG or any of its ingredients.

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What are the goals of treatment for AML?

- Important goals of therapy include achieving and maintaining complete remission, whether you (or your child) are newly diagnosed or have been treated before
  - Complete remission (CR) means that leukemic blasts make up less than 5% of cells in your bone marrow, and blood cell counts are back to normal

	Understanding your diagnosis
Newly diagnosed	You have never been treated for AML.
Relapsed	You achieved remission with your previous cancer treatment, but your AML has returned.
Refractory	Your AML did not respond to previous cancer treatment.

SELECTED SAFETY INFORMATION

Infusion Reactions: You may experience reactions to MYLOTARG during or within 24 hours following your infusion. Reactions can be life-threatening or fatal. Your doctor may give you medicines before you receive MYLOTARG to decrease your chance of having a severe reaction. Tell your doctor or get medical help right away if you have fever, chills, low blood pressure, rapid heartbeat, rash, or breathing problems while receiving or after receiving MYLOTARG.

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TARGETING AML WITH MYLOTARG

MYLOTARG IS THE FIRST AND ONLY THERAPY APPROVED FOR AML THAT TARGETS A PROTEIN CALLED CD33

How MYLOTARG (gemtuzumab ozogamicin) works

- MYLOTARG is a type of medicine that uses an antibody to recognize a specific protein called CD33 that is found on the surface of both leukemia cells and healthy cells
- MYLOTARG attaches to the CD33 protein. It is thought to work in AML by delivering the anticancer drug into leukemia cells, causing damage that contributes to their death

Who can be treated with MYLOTARG

- Adults with newly diagnosed AML who tested positive for CD33
- Adults and children over 2 years old with relapsed or refractory AML who tested positive for CD33

MOST PATIENTS WITH AML (AROUND 90%) TESTED POSITIVE FOR THE CD33 PROTEIN

SELECTED SAFETY INFORMATION

Bleeding: Bleeding, which may be life-threatening or fatal, can occur with MYLOTARG. Call your doctor right away if you have unexpected bleeding, bruising, or blood in your urine or stools. Your doctor should do blood tests to check your blood cell counts frequently after your treatment. If you have low blood cell counts with MYLOTARG, your treatment may be interrupted or MYLOTARG may be permanently discontinued.

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MYLOTARG can be used in different circumstances

Newly diagnosed AML

- Adults with newly diagnosed CD33-positive AML and their healthcare team will decide whether chemotherapy will be given along with MYLOTARG

Relapsed or refractory AML

- Adults and children 2 years of age and older with relapsed or refractory CD33-positive AML will receive MYLOTARG alone

SELECTED SAFETY INFORMATION

Pregnancy: Avoid becoming pregnant during treatment with MYLOTARG. MYLOTARG can cause harm to an unborn baby. If you are able to become pregnant, you should use effective contraception during treatment with MYLOTARG and for at least 6 months after the last dose. If you are male and your partner is able to become pregnant, use effective contraception during treatment with MYLOTARG and for at least 3 months after the last dose.

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SIDE EFFECTS OF MYLOTARG

Serious side effects

MYLOTARG may cause serious side effects that can be severe, life-threatening, or even lead to death. These may include:

Liver problems, including a condition called hepatic veno-occlusive disease (VOD)

Bleeding

Infusion reactions (a type of allergic reaction)

Common side effects

The most common side effects experienced with MYLOTARG were:

- Bleeding
- Infection
- Fever
- Nausea
- Vomiting
- Constipation
- Rash
- Headache
- Mouth sores
- Increases in lab tests measuring liver function

SELECTED SAFETY INFORMATION

Heart Problems: Call your doctor right away if you feel dizzy, lightheaded, or faint or have very slow, very fast, or abnormal heartbeats. Your healthcare provider may check your heart during treatment with MYLOTARG. Tell your healthcare provider about all the medicines you take.

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These are not all of the possible side effects of MYLOTARG. Tell your healthcare provider if you have any side effect that bothers you or that does not go away. For more information, ask your doctor or pharmacist.

SELECTED SAFETY INFORMATION

Chromosomal Testing: Your healthcare provider may order tests (known as cytogenetic analyses) for chromosomal abnormalities that may be associated with your AML. Patients with certain chromosomal abnormalities may not benefit from adding MYLOTARG to chemotherapy. Based on your cytogenetic analysis, your healthcare provider may decide to stop treatment with MYLOTARG because its risks may outweigh its benefits.

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HOW **PATIENTS** IN THIS STUDY **RESPONDED**

MYLOTARG was studied in a clinical trial of newly diagnosed adults 50 to 70 years old. MYLOTARG added to chemotherapy was compared to treatment with chemotherapy only.

Of 271 patients in the study, 135 patients received MYLOTARG plus chemotherapy, and 136 received chemotherapy only.

What were the results with MYLOTARG plus chemotherapy compared to chemotherapy alone?

- MYLOTARG was evaluated based on **event-free survival**, which means that patients had achieved remission and were still alive without relapse
- The addition of **MYLOTARG NEARLY DOUBLED** the event-free survival in patients receiving MYLOTARG plus chemotherapy vs chemotherapy alone:

17.3 months with MYLOTARG plus chemotherapy VS **9.5** months with chemotherapy alone

- All patients in this study developed severe low white blood cell counts, low platelet counts, and low red blood cell counts

See pages 10-11 for information on how MYLOTARG is given.

SELECTED SAFETY INFORMATION

Common Side Effects: The most common side effects are bleeding, infection, fever, nausea, vomiting, constipation, rash, headache, mouth sores, and increases in lab tests measuring liver function.

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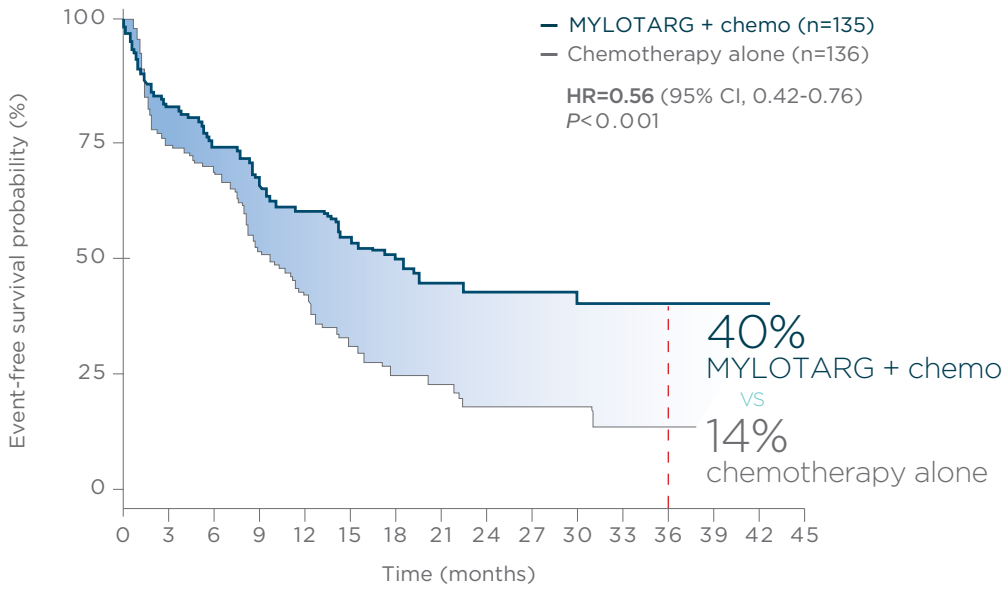
THE BENEFIT OF MYLOTARG WAS EVALUATED FOR OVER 3 YEARS

- The probability of being alive and in remission at 3 years was 40% with the addition of MYLOTARG vs 14% with chemotherapy alone, as shown in the graph below*



- The probability of being alive and in remission at 1 year was 59% with the addition of MYLOTARG vs 41% with chemotherapy alone
- The probability of being alive and in remission at 2 years was 42% with the addition of MYLOTARG vs 18% with chemotherapy alone

CI=confidence interval; HR=hazard ratio.
*This type of graph is called a Kaplan-Meier curve.
Please see definitions in the glossary on page 21

SELECTED SAFETY INFORMATION

Breastfeeding: Avoid breastfeeding during treatment with MYLOTARG and for at least 1 month after the final dose.

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4.5 mg single-dose vial

TAKING MYLOTARG WITH CHEMOTHERAPY FOR NEWLY DIAGNOSED CD33-POSITIVE AML

MYLOTARG is given by intravenous (IV) infusion. You will likely have to be admitted to the hospital for your infusion. The infusion typically takes about 2 hours.

Before starting treatment

Prior to your infusion, you will be given a steroid, acetaminophen, and an antihistamine to help reduce the chance of infusion reactions.

SELECTED SAFETY INFORMATION

WARNING: RISK OF LIVER PROBLEMS: MYLOTARG can cause liver problems that can be severe or life-threatening or lead to death, including a condition called veno-occlusive disease (VOD). If you have previously received or will be receiving a stem cell transplant, or you have a history of liver problems, you may be at an increased risk for VOD. Tell your doctor about any signs or symptoms of liver problems, including rapid weight gain, abdominal swelling (which may be painful), or yellowing of the whites of your eyes. Your doctor should do blood tests to check for liver problems before and regularly during your treatment. Liver problems may require dosing interruption or permanent discontinuation of MYLOTARG.

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How will I receive MYLOTARG as a newly diagnosed adult?

If your doctor has prescribed MYLOTARG in addition to chemotherapy:

- You will receive chemotherapy (2 different drugs) over a 1-week period. This is called **induction**
- During the same week, you will also receive MYLOTARG on Day 1, Day 4, and Day 7
- You may need a second round of induction chemotherapy, but MYLOTARG will not be added to the second round
- If you respond to induction, you may receive chemotherapy, with or without MYLOTARG, up to 2 more times. This is known as **consolidation**
- Your doctor will decide the number of treatments that is right for you

SELECTED SAFETY INFORMATION

Contraindications: Do not take MYLOTARG if you have a history of hypersensitivity to MYLOTARG or any of its ingredients.

Please see additional Important Safety Information on page 20, and full Prescribing Information, including BOXED WARNING, at www.MylotargHCP.com.

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HOW **PATIENTS** IN THIS STUDY **RESPONDED**

MYLOTARG compared to supportive care (SC) was studied in 237 newly diagnosed adults not receiving intensive chemotherapy who were over age 75 or age 61 to 75 with poor health.

Of 237 patients in the study, 118 received MYLOTARG and 119 received SC.

Common methods of SC for AML include taking antibiotics and receiving blood transfusions.

SELECTED SAFETY INFORMATION

Infusion Reactions: You may experience reactions to MYLOTARG during or within 24 hours following your infusion. Reactions can be life-threatening or fatal. Your doctor may give you medicines before you receive MYLOTARG to decrease your chance of having a severe reaction. Tell your doctor or get medical help right away if you have fever, chills, low blood pressure, rapid heartbeat, rash, or breathing problems while receiving or after receiving MYLOTARG.

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4.5 mg single-dose vial

WHAT WERE THE RESULTS WITH MYLOTARG COMPARED TO SC?

MYLOTARG helped patients live longer than a supportive care regimen

Median overall survival was 4.9 months with MYLOTARG vs 3.6 months with SC.

See pages 14-15 for information on how MYLOTARG is given.

SELECTED SAFETY INFORMATION

Bleeding: Bleeding, which may be life-threatening or fatal, can occur with MYLOTARG. Call your doctor right away if you have unexpected bleeding, bruising, or blood in your urine or stools. Your doctor should do blood tests to check your blood cell counts frequently after your treatment. If you have low blood cell counts with MYLOTARG, your treatment may be interrupted or MYLOTARG may be permanently discontinued.

Please see additional Important Safety Information on page 20, and full Prescribing Information, including BOXED WARNING, at www.MylotargHCP.com.

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4.5 mg single-dose vial

TAKING MYLOTARG WITHOUT CHEMOTHERAPY FOR NEWLY DIAGNOSED CD33-POSITIVE AML

MYLOTARG is given by IV infusion. The infusion typically takes about 2 hours, and you may be able to return home afterward.

Before starting treatment

Prior to your infusion, you will be given a steroid, acetaminophen, and an antihistamine to help reduce the chance of infusion reactions.

SELECTED SAFETY INFORMATION

Pregnancy: Avoid becoming pregnant during treatment with MYLOTARG. MYLOTARG can cause harm to an unborn baby. If you are able to become pregnant, you should use effective contraception during treatment with MYLOTARG and for at least 6 months after the last dose. If you are male and your partner is able to become pregnant, use effective contraception during treatment with MYLOTARG and for at least 3 months after the last dose.

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4.5 mg single-dose vial

How will I receive MYLOTARG as a newly diagnosed adult?

If your doctor has prescribed MYLOTARG without chemotherapy:

- MYLOTARG is given 2 times, approximately 7 days apart
- Your doctor may delay or skip a dose, based on your needs
- Depending how you respond to and tolerate MYLOTARG, it may then be given once a month for up to 8 months
- Your doctor will decide the number of treatments that is right for you

SELECTED SAFETY INFORMATION

Heart Problems: Call your doctor right away if you feel dizzy, lightheaded, or faint or have very slow, very fast, or abnormal heartbeats. Your healthcare provider may check your heart during treatment with MYLOTARG. Tell your healthcare provider about all the medicines you take.

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MYLOTARG HAS BEEN STUDIED IN PATIENTS WITH RELAPSED CD33-POSITIVE AML

HOW **PATIENTS** IN THIS STUDY **RESPONDED**

This study included 57 adult patients 22 to 80 years old with CD33-positive AML who had been treated for AML already, but whose disease returned (first relapse).

The study did not include patients who had AML related to previous blood cancer or to previous chemotherapy treatment, or patients who had already received a stem cell transplant.

WHAT WERE THE RESULTS WITH MYLOTARG IN ADULTS?

1 in 4 patients (26%) achieved a complete remission (CR) again

With MYLOTARG, patients who achieved remission stayed in remission for a median of 11.6 months

When you include patients with complete remission with low platelet counts (CRp), then 1 in 3 patients (33%) were able to achieve remission again

MYLOTARG IS ALSO APPROVED FOR USE IN CHILDREN OVER THE AGE OF 2 WITH RELAPSED OR REFRACTORY CD33-POSITIVE AML

See pages 18-19 for information on how MYLOTARG is given.

SELECTED SAFETY INFORMATION

Chromosomal Testing: Your healthcare provider may order tests (known as cytogenetic analyses) for chromosomal abnormalities that may be associated with your AML. Patients with certain chromosomal abnormalities may not benefit from adding MYLOTARG to chemotherapy. Based on your cytogenetic analysis, your healthcare provider may decide to stop treatment with MYLOTARG because its risks may outweigh its benefits.

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Complete remission means that leukemic blasts make up less than 5% of cells in your bone marrow and blood cell counts are back to normal

Complete remission with low platelet counts means that you have achieved complete remission, but your platelet counts are not yet back to normal

SELECTED SAFETY INFORMATION

Common Side Effects: The most common side effects are bleeding, infection, fever, nausea, vomiting, constipation, rash, headache, mouth sores, and increases in lab tests measuring liver function.

Please see additional Important Safety Information on page 20, and full Prescribing Information, including BOXED WARNING, at www.MylotargHCP.com.

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4.5 mg single-dose vial

TAKING MYLOTARG FOR RELAPSED OR REFRACTORY CD33-POSITIVE AML

MYLOTARG is given by IV infusion. The infusion typically takes about 2 hours, after which you (or your child) may be able to return home.

Before starting treatment

Prior to your infusion, you (or your child) will be given a steroid, acetaminophen, and an antihistamine to help reduce the chance of infusion reactions.

SELECTED SAFETY INFORMATION

Breastfeeding: Avoid breastfeeding during treatment with MYLOTARG and for at least 1 month after the final dose.

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4.5 mg single-dose vial

How will I (or my child) receive MYLOTARG for relapsed or refractory CD33-positive AML?

- MYLOTARG is given approximately every 3 days for 1 week
- Your doctor may delay a dose, based on your (or your child's) needs, and will decide on the number of treatments that is right for you (or your child)

SELECTED SAFETY INFORMATION

WARNING: RISK OF LIVER PROBLEMS: MYLOTARG can cause liver problems that can be severe or life-threatening or lead to death, including a condition called veno-occlusive disease (VOD). If you have previously received or will be receiving a stem cell transplant, or you have a history of liver problems, you may be at an increased risk for VOD. Tell your doctor about any signs or symptoms of liver problems, including rapid weight gain, abdominal swelling (which may be painful), or yellowing of the whites of your eyes. Your doctor should do blood tests to check for liver problems before and regularly during your treatment. Liver problems may require dosing interruption or permanent discontinuation of MYLOTARG.

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IMPORTANT SAFETY INFORMATION

INDICATIONS

MYLOTARG (gemtuzumab ozogamicin) is a prescription medicine used to treat adults with newly diagnosed CD33-positive acute myeloid leukemia (AML) or patients over the age of 2 with CD33-positive AML whose disease returned or did not respond to previous treatment.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF LIVER PROBLEMS: MYLOTARG can cause liver problems that can be severe or life-threatening or lead to death, including a condition called veno-occlusive disease (VOD). If you have previously received or will be receiving a stem cell transplant, or you have a history of liver problems, you may be at an increased risk for VOD. Tell your doctor about any signs or symptoms of liver problems, including rapid weight gain, abdominal swelling (which may be painful), or yellowing of the whites of your eyes. Your doctor should do blood tests to check for liver problems before and regularly during your treatment. Liver problems may require dosing interruption or permanent discontinuation of MYLOTARG.

Contraindications: Do not take MYLOTARG if you have a history of hypersensitivity to MYLOTARG or any of its ingredients.

Infusion Reactions: You may experience reactions to MYLOTARG during or within 24 hours following your infusion. Reactions can be life-threatening or fatal. Your doctor may give you medicines before you receive MYLOTARG to decrease your chance of having a severe reaction. Tell your doctor or get medical help right away if you have fever, chills, low blood pressure, rapid heartbeat, rash, or breathing problems while receiving or after receiving MYLOTARG.

Bleeding: Bleeding, which may be life-threatening or fatal, can occur with MYLOTARG. Call your doctor right away if you have unexpected bleeding, bruising, or blood in your urine or stools. Your doctor should do blood tests to check your blood cell counts frequently after your treatment. If you have low blood cell counts with MYLOTARG, your treatment may be interrupted or MYLOTARG may be permanently discontinued.

Pregnancy: Avoid becoming pregnant during treatment with MYLOTARG. MYLOTARG can cause harm to an unborn baby. If you are able to become pregnant, you should use effective contraception during treatment with MYLOTARG and for at least 6 months after the last dose. If you are male and your partner is able to become pregnant, use effective contraception during treatment with MYLOTARG and for at least 3 months after the last dose.

Heart Problems: Call your doctor right away if you feel dizzy, lightheaded, or faint or have very slow, very fast, or abnormal heartbeats. Your healthcare provider may check your heart during treatment with MYLOTARG. Tell your healthcare provider about all the medicines you take.

Chromosomal Testing: Your healthcare provider may order tests (known as cytogenetic analyses) for chromosomal abnormalities that may be associated with your AML. Patients with certain chromosomal abnormalities may not benefit from adding MYLOTARG to chemotherapy. Based on your cytogenetic analysis, your healthcare provider may decide to stop treatment with MYLOTARG because its risks may outweigh its benefits.

Common Side Effects: The most common side effects are bleeding, infection, fever, nausea, vomiting, constipation, rash, headache, mouth sores, and increases in lab tests measuring liver function.

Breastfeeding: Avoid breastfeeding during treatment with MYLOTARG and for at least 1 month after the final dose.

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4.5 mg single-dose vial

GLOSSARY

AML: Acute myeloid leukemia. AML is a blood cancer in which the bone marrow makes too many abnormal blood cells, called leukemic blasts. AML blocks the production of regular blood cells and can lead to lower numbers of healthy blood cells than normal, including low red blood cells, low white blood cells, and low platelets.

CD33: A protein that is found on the surface of leukemia cells and some healthy cells.

Complete remission (CR): When leukemia cells make up less than 5% of cells in your bone marrow and blood cell counts are back to normal.

Complete remission with low platelet counts (CRp): When you have achieved complete remission, but your platelet counts are not yet back to normal.

Confidence interval: A reflection of accuracy of the study results.

Event-free survival: The length of time patients who achieve remission remain alive without relapse.

Hazard ratio: Compares the chances of an event occurring at any given time between the two treatment groups in the study.

Kaplan-Meier curve: A Kaplan-Meier curve uses information about patients in a clinical trial to determine the chance of events over time. In this case, the curves represent patients treated with MYLOTARG vs patients who received a different treatment. The "y," or vertical axis, measures the percentage of patients estimated to be alive in the clinical trial. The "x," or horizontal axis, tracks time, in this case, measured in months. All patients enter the study alive, so the curves start at 100% for month 0 and decline over time.

Median: The midpoint in a range of numbers, where exactly half of the numbers are below and half of the numbers are above that point.

Newly diagnosed AML: You have never been treated for AML.

***P* value:** Shows how likely it is that the difference in results between the groups occurred by chance alone.

Relapsed AML: You achieved remission with your previous cancer treatment, but your AML has returned.

Refractory AML: Your AML did not respond to previous cancer treatment.

Please see Important Safety Information on page 20, and full Prescribing Information, including BOXED WARNING, at www.MylotargHCP.com.

VISIT **MYLOTARG.COM**
TO LEARN MORE

FOR ADDITIONAL SUPPORT, VISIT
PFIZERONCOLOGYTOGETHER.COM
OR CALL **1-877-744-5675**

SELECTED SAFETY INFORMATION

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4.5 mg single-dose vial

Pfizer Oncology

PP-MYL-USA-0250

February 2019

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MYLOTARG safely and effectively. See full prescribing information for MYLOTARG.

MYLOTARG™ (gemtuzumab ozogamicin) for injection, for intravenous use
Initial U.S. Approval: 2000

WARNING: HEPATOTOXICITY

See full prescribing information for complete boxed warning.

Hepatotoxicity, including severe or fatal hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), has been reported in association with the use of MYLOTARG. (5.1, 6.1)

---------- RECENT MAJOR CHANGES ----------

Dosage and Administration, Recommended Dosage (2.2)	4/2018
Dosage and Administration, Instructions for Reconstitution, Dilution, and Administration (2.4)	4/2018

----------INDICATIONS AND USAGE----------

MYLOTARG is a CD33-directed antibody-drug conjugate indicated for:

- treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults (1.1).
- treatment of relapsed or refractory CD33-positive AML in adults and in pediatric patients 2 years and older (1.2).

---------- DOSAGE AND ADMINISTRATION ----------

- Newly-diagnosed, de novo AML (combination regimen):
  - *Induction:* 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine (2.2).
  - *Consolidation:* 3 mg/m^2 on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine. (2.2).
- Newly-diagnosed AML (single-agent regimen):
  - *Induction:* 6 mg/m^2 (not limited to one 4.5 mg vial) on Day 1 and 3 mg/m^2 (not limited to one 4.5 mg vial) on Day 8 (2.2).
  - *Continuation:* For patients without evidence of disease progression following induction, up to 8 continuation courses of MYLOTARG 2 mg/m^2 (not limited to one 4.5 mg vial) on Day 1 every 4 weeks (2.2).
- Relapsed or refractory AML (single-agent regimen):
  - 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 (2.2).
- Premedicate with a corticosteroid, antihistamine, and acetaminophen 1 hour prior to MYLOTARG (2.1).

---------- DOSAGE FORMS AND STRENGTHS ----------

For Injection: 4.5 mg as a lyophilized cake or powder in a single-dose vial for reconstitution and dilution (3).

---------- CONTRAINDICATIONS ----------

Hypersensitivity to MYLOTARG or any of its components (4).

---------- WARNINGS AND PRECAUTIONS ----------

- Infusion related reactions (including anaphylaxis): Premedicate with a corticosteroid, acetaminophen, and diphenhydramine. Monitor patients during and for at least 1 hour after the end of the infusion. Interrupt the infusion, administer steroids or antihistamines, or permanently discontinue treatment as necessary (2.1, 5.2, and 6).
- Hemorrhage: Severe, including fatal, hemorrhage may occur when MYLOTARG is used at recommended doses. Monitor platelet counts frequently (5.3 and 6.1).
- Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception (5.6, 8.1, and 8.3).

---------- ADVERSE REACTIONS ----------

The most common adverse reactions (greater than 15%) were hemorrhage, infection, fever, nausea, vomiting, constipation, headache, increased AST, increased ALT, rash, and mucositis (6).

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------

Lactation: Advise not to breastfeed (8.2).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 4/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: HEPATOTOXICITY

Hepatotoxicity, including severe or fatal hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), has been reported in association with the use of MYLOTARG as a single agent, and as part of a combination chemotherapy regimen. Monitor frequently for signs and symptoms of VOD after treatment with MYLOTARG. (5.1 and 6.1)

1 INDICATIONS AND USAGE

1.1 Newly-Diagnosed CD33-positive Acute Myeloid Leukemia (AML)

MYLOTARG is indicated for the treatment of newly-diagnosed CD33-positive acute myeloid leukemia in adults.

1.2 Relapsed or Refractory CD33-positive AML

MYLOTARG is indicated for the treatment of relapsed or refractory CD33-positive acute myeloid leukemia in adults and in pediatric patients 2 years and older.

2 DOSAGE AND ADMINISTRATION

2.1 Premedication and Special Considerations

- Premedicate adults with acetaminophen 650 mg orally and diphenhydramine 50 mg orally or intravenously 1 hour prior to MYLOTARG dosing and 1 mg/kg methylprednisolone or an equivalent dose of an alternative corticosteroid within 30 minutes prior to infusion of MYLOTARG. Premedicate children with acetaminophen 15 mg/kg (maximum of 650 mg), diphenhydramine 1 mg/kg (maximum of 50 mg), and 1 mg/kg methylprednisolone orally or intravenously; additional doses of acetaminophen and diphenhydramine may be administered every 4 hours after the initial pretreatment dose. Repeat with the same dose of methylprednisolone or an equivalent corticosteroid for any sign of an infusion reaction, such as fever, chills, hypotension, or dyspnea during the infusion or within 4 hours afterwards *[see Warnings and Precautions (5.2)]*.
- Use appropriate measures to prevent tumor lysis syndrome.
- For patients with hyperleukocytosis (leukocyte count greater than or equal to 30 Gi/L), cytoreduction is recommended prior to administration of MYLOTARG.

2.2 Recommended Dosage

Newly-Diagnosed De Novo CD33-positive AML (combination regimen)

A treatment course including MYLOTARG in combination therapy for adults with newly-diagnosed de novo CD33-positive AML consists of 1 induction cycle and 2 consolidation cycles *[see Clinical Studies (14.1)]*.

For the induction cycle, the recommended dose of MYLOTARG is 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7 in combination with daunorubicin and cytarabine. For patients requiring a second induction cycle, do NOT administer MYLOTARG during the second induction cycle.

For the consolidation cycles, the recommended dose of MYLOTARG is 3 mg/m^2 on Day 1 (up to one 4.5 mg vial) in combination with daunorubicin and cytarabine.

Newly-Diagnosed CD33-positive AML (single-agent regimen)

A treatment course of MYLOTARG as a single agent for adults with newly-diagnosed CD33-positive AML consists of 1 cycle of induction and up to 8 cycles of continuation therapy *[see Clinical Studies (14.1)]*.

For the induction cycle, the recommended dose of MYLOTARG is 6 mg/m^2 (not limited to one 4.5 mg vial) as a single agent on Day 1, and 3 mg/m^2 (not limited to one 4.5 mg vial) on Day 8.

For continuation, the recommended dose of MYLOTARG is 2 mg/m^2 (not limited to one 4.5 mg vial) as a single agent on Day 1 every 4 weeks.

Relapsed or Refractory CD33-positive AML (single-agent regimen)

The recommended dose of MYLOTARG as a single agent for treatment of relapsed or refractory CD33-positive AML is 3 mg/m^2 (up to one 4.5 mg vial) on Days 1, 4, and 7. Treatment in the relapsed or refractory setting consists of a single course of MYLOTARG *[see Clinical Studies (14.1)]*.

2.3 Dosage Modifications for Toxicities

Monitor blood counts frequently through resolution of cytopenias. Monitor blood counts and chemistries at least three times per week through recovery from treatment-related toxicities. Management of some adverse reactions *[see Warnings and Precautions (5)* and *Adverse Reactions (6)]* may require dose interruptions or permanent discontinuation of MYLOTARG Table 1 shows the dose modification guidelines for hematologic and nonhematologic toxicities.

Table 1. Dosage Modifications for Hematologic and Nonhematologic Toxicities

Hematologic and Nonhematologic Toxicities	Recommended Action
For patients receiving MYLOTARG in combination therapy	
Persistent thrombocytopenia	• If platelet count does not recover to greater than or equal to 100 Gi/L within 14 days following the planned start date of the consolidation cycle (14 days after hematologic recovery following previous cycle), discontinue MYLOTARG (do not administer MYLOTARG in the consolidation cycles).
Persistent neutropenia	• If neutrophil count does not recover to greater than 0.5 Gi/L within 14 days following the planned start date of the consolidation cycle (14 days after hematologic recovery following previous cycle), discontinue MYLOTARG (do not administer MYLOTARG in the consolidation cycles).
For all patients receiving MYLOTARG (Monotherapy or in Combination)	
VOD	• Discontinue MYLOTARG *[see Warnings and Precautions (5.1)]*.
Total bilirubin greater than 2 × ULN, or AST and/or ALT greater than 2.5 × ULN	• Delay treatment with MYLOTARG until recovery of total bilirubin to less than or equal to 2 × ULN and AST and ALT to less than or equal to 2.5 × ULN prior to each dose. • Omit scheduled dose if delayed more than 2 days between sequential infusions.
Infusion-related reactions	• Interrupt the infusion and institute appropriate medical management. • Administer acetaminophen, diphenhydramine and/or methylprednisolone, if needed (see Section 2.1) • Provide supportive care measures as needed. • For mild, moderate or severe infusion related reactions, once symptoms resolve, consider resuming the infusion at no more than half the rate at which the reaction occurred. Repeat the procedure above in the event of recurrence of symptoms. • Permanently discontinue MYLOTARG upon occurrence of a severe infusion reaction or for any life-threatening infusion reaction *[see Warnings and Precautions (5.2)]*.
Other severe or life-threatening non-hematologic toxicities	• Delay treatment with MYLOTARG until recovery to a severity of no more than mild. • Omit scheduled dose if delayed more than 2 days between sequential infusions.

Abbreviations: ALT=alanine aminotransferase; AST=aspartate aminotransferase; VOD=veno-occlusive disease; ULN=upper limit of normal.

2.4 Instructions for Reconstitution, Dilution, and Administration

Use appropriate aseptic technique for the reconstitution and dilution procedures. Protect the reconstituted and diluted MYLOTARG solution from light.

Reconstitution

- MYLOTARG is a cytotoxic drug. Follow applicable special handling and disposal procedures.[1]
- Calculate the dose (mg) and number of vials of MYLOTARG required.
- Prior to reconstitution, allow drug product vials to reach ambient temperature for approximately 5 minutes.
- Reconstitute each vial with 5 mL of Sterile Water for Injection, USP to obtain a concentration of 1 mg/mL of MYLOTARG that delivers 4.5 mL (4.5 mg).
- Gently swirl the vial to aid dissolution. DO NOT SHAKE.
- Inspect the reconstituted solution for particulates and discoloration. The reconstituted solution may contain small white to off-white, opaque to translucent, and amorphous to fiber-like particles.
- MYLOTARG contains no bacteriostatic preservatives.
- Use reconstituted solution immediately or after being refrigerated at 2-8°C (36-46°F) for up to 1 hour. **PROTECT FROM LIGHT. DO NOT FREEZE**.

Dilution

- Calculate the required volume of the reconstituted solution needed to obtain the appropriate dose according to patient body surface area. Withdraw this amount from the vial(s) using a syringe. PROTECT FROM LIGHT. Discard any unused reconstituted solution left in the vial.

Doses must be mixed to a concentration between 0.075 mg/mL to 0.234 mg/mL according to the following instructions:

- Doses less than 3.9 mg must be prepared for administration by syringe. Add the reconstituted MYLOTARG solution to a syringe with 0.9% Sodium Chloride Injection to a final concentration between 0.075 mg/mL to 0.234 mg/mL. PROTECT FROM LIGHT.
- Doses greater than or equal to 3.9 mg are to be diluted in a syringe or an IV bag in an appropriate volume of 0.9% Sodium Chloride Injection to ensure a final concentration between 0.075 mg/mL to 0.234 mg/mL. PROTECT FROM LIGHT.
- Gently invert the infusion container to mix the diluted solution. DO NOT SHAKE.
- Following dilution with 0.9% Sodium Chloride Injection, MYLOTARG solution should be infused immediately. If not used immediately, store at room temperature (15-25°C; 59-77°F) for up to 6 hours, which includes the 2-hour infusion time and 1-hour, if needed, to allow the refrigerated diluted solution to equilibrate to room temperature. The diluted solution can be refrigerated at 2-8°C (36-46°F) for up to 12 hours which includes up to 1-hour in the vial post-reconstitution. PROTECT FROM LIGHT and DO NOT FREEZE.

Administration

- **Use an in-line 0.2 micron polyethersulfone (PES) filter for infusion of MYLOTARG.**
- Protect the intravenous bag from light using a light-blocking cover during infusion. The infusion line does not need to be protected from light.
- Infuse the diluted solution over 2 hours.
- Do not mix MYLOTARG with, or administer as an infusion with, other medicinal products.

3. DOSAGE FORMS AND STRENGTHS

For injection: 4.5 mg as a white to off-white lyophilized cake or powder in a single-dose vial for reconstitution and further dilution.

4. CONTRAINDICATIONS

MYLOTARG is contraindicated in patients with a history of hypersensitivity to the active substance in MYLOTARG or any of its components or to any of the excipients. Reactions have included anaphylaxis *[see Warnings and Precautions (5.2)* and *Adverse Reactions (6)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity, Including Veno-occlusive Liver Disease (VOD)

Hepatotoxicity, including life-threatening and sometimes fatal hepatic VOD events, have been reported in patients receiving MYLOTARG as a single agent or as part of a combination chemotherapy regimen *[see Adverse Reactions (6)]*.

In ALFA-0701, VOD events were reported in 6/131 (5%) patients during or following treatment with MYLOTARG, or following later hematopoietic stem cell transplantation (HSCT). The median time from the MYLOTARG dose to onset of VOD was 9 days (range: 2-298 days), with 5 events occurring within 28 days of any dose of MYLOTARG and 1 event occurring greater than 28 days after the last dose of MYLOTARG. Three of the 6 VOD events were fatal. VOD was also reported in 2 patients in the control arm of ALFA-0701 after receiving MYLOTARG as a therapy for relapsed AML.

In MyloFrance-1 (MYLOTARG 3 mg/m^2 on Days 1, 4 and 7), VOD events were reported in none of the 57 patients during or following treatment, or following HSCT after completion of MYLOTARG treatment.

Based on an analysis across trials, the risk of VOD was higher in adult patients who received higher doses of MYLOTARG as monotherapy, in patients with moderate or severe hepatic impairment prior to receiving MYLOTARG, in patients treated with MYLOTARG after HSCT, and in patients who underwent HSCT after treatment with MYLOTARG. Patients who had moderate/severe hepatic impairment prior to treatment with MYLOTARG were 8.7 times more likely to develop VOD compared to patients without moderate/severe hepatic impairment at baseline. Patients treated with MYLOTARG for relapse after HSCT were 2.6 times more likely to develop VOD compared to patients without prior HSCT. Patients who underwent HSCT following MYLOTARG treatment were 2.9 times more likely to develop VOD after HSCT compared to patients without HSCT following MYLOTARG treatment. Although no relationship was found between VOD and time of HSCT relative to higher MYLOTARG monotherapy doses, the

ALFA-0701 study recommended an interval of 2 months between the last dose of MYLOTARG and HSCT. In MyloFrance-1, no patients underwent HSCT within 3.5 months of MYLOTARG therapy.

Assess ALT, AST, total bilirubin, and alkaline phosphatase prior to each dose of MYLOTARG. After treatment with MYLOTARG, monitor frequently for signs and symptoms of VOD; these may include elevations in ALT, AST, total bilirubin, hepatomegaly (which may be painful), rapid weight gain, and ascites. Monitoring only total bilirubin may not identify all patients at risk of VOD. For patients who develop abnormal liver tests, more frequent monitoring of liver tests and clinical signs and symptoms of hepatotoxicity is recommended. For patients who proceed to HSCT, monitor liver tests frequently during the post-HSCT period, as appropriate.

Manage signs or symptoms of hepatic toxicity by dose interruption or discontinuation of MYLOTARG *[see Dosage and Administration (2.3)]*. In patients who experience VOD, discontinue MYLOTARG and treat according to standard medical practice.

5.2 Infusion-Related Reactions (Including Anaphylaxis)

Life-threatening or fatal infusion related-reactions can occur during or within 24 hours following infusion of MYLOTARG *[see Adverse Reactions (6)]*. Signs and symptoms of infusion-related reactions may include fever, chills, hypotension, tachycardia, hypoxia and respiratory failure.

Premedicate prior to MYLOTARG infusion *[see Dosage and Administration (2.1)]*. Monitor vital signs frequently during infusion. Interrupt infusion immediately for patients who develop evidence of infusion reaction, especially dyspnea, bronchospasm, or hypotension. Monitor patients during and for at least 1 hour after the end of the infusion or until signs and symptoms completely resolve. Discontinue use of MYLOTARG in patients who develop signs or symptoms of anaphylaxis, including severe respiratory symptoms or clinically significant hypotension *[see Dosage and Administration (2.2)]*.

5.3 Hemorrhage

MYLOTARG is myelosuppressive and can cause fatal or life-threatening hemorrhage due to prolonged thrombocytopenia. In ALFA-0701, (MYLOTARG in combination with chemotherapy), all grades and Grade 3-4 bleeding events were reported in 118/131 (90%) and 27/131 (21%) patients, respectively. Fatal bleeding events (including cerebral hematoma, intracranial hematoma, and subdural hematoma) occurred in 4/131 (3%) patients. Thrombocytopenia with platelet counts less than 50 Gi/L persisting more than 42 days occurred in 19 (19%) patients in the induction phase *[see Adverse Reactions (6)]*. The proportion of patients with persistent thrombocytopenia increased with progressive treatment phases and was higher in patients treated with MYLOTARG plus chemotherapy than with chemotherapy alone *[see Adverse Reactions (6)]*.

In AML-19 (MYLOTARG monotherapy at 6 mg/m^2 Day 1 and 3 mg/m^2 Day 8), all grades and Grade 3 or higher bleeding were reported in 28/111 (25%) and 14/111 (13%) patients, respectively. Fatal bleeding occurred in 1/111 (1%). In MyloFrance-1 (MYLOTARG 3 mg/m^2 as monotherapy), Grade 3 bleeding was reported in 4/57 (7%) patients, but no patient experienced Grade 4 hemorrhage.

Assess blood counts prior to each dose of MYLOTARG and monitor blood counts frequently after treatment with MYLOTARG until resolution of cytopenias. Monitor patients for signs and symptoms of bleeding during treatment with MYLOTARG. Manage severe bleeding, hemorrhage or persistent thrombocytopenia using dose delay or permanent discontinuation of MYLOTARG *[see Dosage and Administration (2.2)]*, and provide supportive care per standard practice.

5.4 QT Interval Prolongation

QT interval prolongation has been observed in patients treated with other drugs containing calicheamicin. When administering MYLOTARG to patients who have a history of or predisposition for QTc prolongation, who are taking medicinal products that are known to prolong QT interval, and in patients with electrolyte disturbances, obtain electrocardiograms (ECGs) and electrolytes prior to the start of treatment and as needed during administration.

5.5 Use in AML with Adverse-Risk Cytogenetics

In subgroup analyses in ALFA-0701, the addition of MYLOTARG to standard combination chemotherapy did not improve event-free survival in the subgroup of patients having adverse-risk cytogenetics (HR 1.11; 95% CI: 0.63, 1.95). For patients being treated with MYLOTARG in combination with daunorubicin and cytarabine for newly-diagnosed de novo AML, when cytogenetics testing results become available consider whether the potential benefit of continuing treatment with MYLOTARG outweighs the risks for the individual patient.

5.6 Embryo-Fetal Toxicity

Based on its mechanism of action and findings from animal studies, MYLOTARG can cause embryo-fetal harm when administered to a pregnant woman. In animal studies, gemtuzumab ozogamicin caused embryo-fetal toxicity, starting at a dose that was approximately 0.4 times the exposure in patients at the maximum recommended dose, based on the area under the concentration-time curve (AUC). Advise females of reproductive potential to use effective contraception during treatment with MYLOTARG and for at least 6 months after the final dose of MYLOTARG. Advise males with female partners of reproductive potential to use effective contraception during treatment with MYLOTARG and for at least 3 months after the last dose of MYLOTARG. Apprise pregnant women of the potential risk to the fetus. Advise women to contact their healthcare provider if they become pregnant or if pregnancy is suspected during treatment with MYLOTARG *[see Use in Specific Populations (8.1, 8.3), Clinical Pharmacology (12.1),* and *Nonclinical Toxicology (13.1)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions associated with MYLOTARG are discussed in detail in other sections of the prescribing information:

- Hepatotoxicity, including VOD *[see Warnings and Precautions (5.1)]*
- Infusion related reactions *[see Warnings and Precautions (5.2)]*
- Hemorrhage *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Combination Therapy in Newly-Diagnosed De Novo CD33-positive AML

The safety evaluation of MYLOTARG (3 mg/m^2 Day 1, 4 and 7 in combination with daunorubicin and cytarabine [DA]) in adults is based on data from ALFA-0701 for 131 patients treated with MYLOTARG plus DA and in 137 patients treated with DA alone *[see Clinical Studies (14.1)]*. In this study, 123 patients received all 3 fractionated doses of MYLOTARG and 7 patients missed at least 1 dose, with a mean total dose administered during induction of 14.51 mg (range: 4.6-18.0). MYLOTARG was received by 91 (70%) patients in the MYLOTARG arm during Consolidation 1 and 64 (49%) patients in the MYLOTARG arm during Consolidation 2.

Safety data consisting of selected TEAEs considered most important for understanding the safety profile of MYLOTARG as well as all adverse events (AEs) that led to the permanent discontinuation of treatment were retrospectively collected. The selected TEAEs consisted of all grades hemorrhages, all grades VOD, and severe infections.

Discontinuation due to any adverse reaction occurred in 31% of patients in the MYLOTARG arm versus 7% in the DA arm. The most frequent (greater than or equal to 1%) adverse reactions for patients treated with MYLOTARG that led to permanent discontinuation were thrombocytopenia (15%), VOD (3%), and septic shock (2%).

Fatal adverse reactions occurred in 8 patients (6%) in the MYLOTARG arm versus 3 patients (2%) in the DA arm. In the MYLOTARG arm, 3 patients died of VOD, 4 patients died of hemorrhage-related events (CNS hemorrhage, hemorrhagic shock), and 1 patient died of suspected cardiac cause. In the DA arm, 3 patients died of sepsis.

Table 2. Selected Grade 3 and Higher Adverse Reactions in Patients with Newly-Diagnosed De Novo AML in ALFA-0701

	MYLOTARG + Daunorubicin + Cytarabine (n, %)	Daunorubicin + Cytarabine (n, %)
Induction	N = 131	N = 137
Infection[a]	61 (47%)	53 (39%)
Hemorrhage[b]	24 (18%)	12 (9%)
Veno-occlusive liver disease[c]	3 (2%)	0
Consolidation 1	N = 91	N = 103
Infection[a]	50 (55%)	43 (42%)
Hemorrhage[b]	5 (5%)	0
Veno-occlusive liver disease[c]	0	0
Consolidation 2	N = 64	N = 107
Infection[a]	32 (50%)	54 (50%)
Hemorrhage[b]	4 (6%)	0
Veno-occlusive liver disease[c]	0	0

Abbreviations: AML=acute myeloid leukemia; N=number of patients; PT=preferred term.
[a] Infection is a grouped term consisting of multiple preferred terms.
[b] Hemorrhage is a grouped term consisting of multiple preferred terms.
[c] Veno-occlusive liver disease includes the following reported PTs: Veno-occlusive liver disease, veno-occlusive disease.

All patients in ALFA-0701 developed severe neutropenia, thrombocytopenia and anemia. The incidence of Grade 3-4 thrombocytopenia that was prolonged in the absence of active leukemia was higher in patients treated with MYLOTARG (Table 3).

Table 3: Prolonged Cytopenias[a] in ALFA-0701

	MYLOTARG + Daunorubicin + Cytarabine (n/N, %)	Daunorubicin + Cytarabine (n/N, %)
Induction		
Prolonged thrombocytopenia	19/101 (19%)	7/97 (7%)
Prolonged neutropenia	3/106 (3%)	0/101 (0%)
Consolidation 1		
Prolonged thrombocytopenia	21/87 (24%)	6/91 (7%)
Prolonged neutropenia	3/88 (3%)	1/97 (1%)
Consolidation 2		
Prolonged thrombocytopenia	22/62 (35%)	25/103 (24%)
Prolonged neutropenia	1/62 (2%)	2/105 (2%)

[a] Platelets less than 50 Gi/L or neutrophils less than 0.5 Gi/L lasting past cycle Day 42 in the absence of active leukemia.

Table 4 summarizes shifts in selected chemistry abnormalities by treatment arm for patients treated in ALFA-0701.

Table 4. ALFA-0701 – Chemistry Laboratory Values: Shifts in Subjects with Baseline Grade 2 or Lower Values

	MYLOTARG + Daunorubicin + Cytarabine		Daunorubicin + Cytarabine	
Laboratory Abnormality	**Subjects (n) with baseline Grade less than or equal to 2**	**Progressed to Grade greater than or equal to 3 (n, %)**	**Subjects (n) with baseline Grade less than or equal to 2**	**Progressed to Grade greater than or equal to 3 (n, %)**
Hypophosphatemia	117	75 (64%)	127	52 (41%)
Hypokalemia	127	73 (57%)	133	41 (31%)
Hyponatremia	129	57 (44%)	134	36 (27%)
Alkaline phosphatase increased	120	16 (13%)	128	7 (5%)
Aspartate aminotransferase increased	126	18 (14%)	132	11 (8%)
Alanine aminotransferase increased	124	13 (10%)	132	20 (15%)
Blood bilirubin increased	119	9 (8%)	126	5 (4%)

Monotherapy for Newly-Diagnosed CD33-positive AML

The safety evaluation of MYLOTARG (6 mg/m^2 then 3 mg/m^2, with 7 days between the doses) as monotherapy is based on a randomized, open-label, Phase 3 trial of MYLOTARG (N=118) versus best supportive care (BSC) (N=119) in patients with previously untreated AML who were considered ineligible for intensive chemotherapy in Study AML-19 *[see Clinical Studies (14.1)]*.

The overall incidence of any Grade adverse reactions reported in AML-19 was 87% in the MYLOTARG arm and 90% in the BSC arm. The incidence of Grade greater than or equal to 3 adverse reactions was 61% in the MYLOTARG arm and 68% in the BSC arm. Death due to any Adverse Event was reported in the MYLOTARG arm of 19 (17%) compared to the BSC arm of 23 (20%).

Table 5. Selected Adverse Reactions in AML-19

	MYLOTARG n=111		Best Supportive Care n=114	
	Any Grade	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
Liver	57 (51%)	8 (7%)	52 (46%)	7 (6%)
Fatigue	51 (46%)	13 (12%)	69 (61%)	24 (21%)
Infection	49 (44%)	39 (35%)	48 (42%)	39 (34%)
Cardiac	31 (28%)	7 (6%)	37 (33%)	16 (14%)
Bleeding	28 (25%)	14 (13%)	34 (30%)	14 (12%)
Febrile neutropenia	20 (18%)	20 (18%)	27 (24%)	27 (24%)
Metabolic	18 (16%)	4 (4%)	17 (15%)	7 (6%)
Renal	7 (6%)	4 (4%)	9 (8%)	5 (4%)

Monotherapy for Relapsed or Refractory CD33-positive AML

The adverse reactions described in this section reflect exposure to MYLOTARG 3 mg/m^2 on Days 1, 4 and 7 as monotherapy in 57 patients with relapsed AML treated on MyloFrance-1 *[see Clinical Studies (14.1)]*. All 57 (100%) patients received the 3 planned doses of MYLOTARG.

During the treatment period, Grade 3 treatment-emergent adverse events (TEAEs) that occurred in greater than 1% patients included sepsis (32%), fever (16%), rash (11%), pneumonia (7%), bleeding (7%), mucositis (4%), pain (4%), diarrhea (2%), headaches (2%), tachycardia (2%), and lung edema (2%). No Grade 4 toxicity was observed. All grade TEAEs that occurred in greater than 15% of patients included fever (79%), infection (42%), increased AST (40%), bleeding (23%), nausea and vomiting (21%), constipation (21%), mucositis (21%), headache (19%), increased ALT (16%), and rash (16%). No infectious deaths occurred. Grade 1 or 2 hyperbilirubinemia developed in 4 (7%) patients. No episodes of VOD occurred. Seven patients received HSCT after MYLOTARG treatment. Three patients received an allogeneic BMT and 4 patients were treated with autologous BMT. No patients developed VOD following HSCT.

6.2 Postmarketing Experience

The following adverse drug reactions have been identified during post-approval use of MYLOTARG. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders: Neutropenic colitis*

Infections and Infestations: fungal lung infections including Pulmonary mycosis and Pneumocystis jirovecii pneumonia*; and bacterial infections including Stenotrophomonas infection

Renal and Urinary Disorders: Hemorrhagic cystitis[1]

Respiratory, Thoracic and Mediastinal Disorders: Interstitial pneumonia[1]

* including fatal events

6.3 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Immunogenicity of MYLOTARG was not studied in clinical trials using the recommended dose regimens.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action and findings from animal studies *[see Clinical Pharmacology (12.1)* and *Nonclinical Toxicology (13.1)]*, MYLOTARG can cause embryo-fetal harm when administered to a pregnant woman. There are no available data on MYLOTARG use in pregnant women to inform a drug-associated risk of major birth defects and miscarriage. In rat embryo-fetal development studies, gemtuzumab ozogamicin caused embryo-fetal toxicity at maternal systemic exposures that were greater than or equal to 0.4 times the exposure in patients at the maximum recommended dose, based on AUC *(see Data)*. If MYLOTARG is used during pregnancy, or if the patient becomes pregnant while taking MYLOTARG, advise the patient of the potential risk to a fetus.

Adverse outcomes in pregnancy occur regardless of the health of the mother or the use of medications. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In an embryo-fetal development study in rats, pregnant animals received daily intravenous doses up to 1.2 mg/m^2/day gemtuzumab ozogamicin during the period of organogenesis. Embryo-fetal toxicities including fetal growth retardation as evidenced by decreased live fetal weights, incidence of fetal wavy ribs and delayed skeletal ossification were observed at greater than or equal to 0.15 mg/m^2/day. Increased embryo-fetal lethality and fetal morphological anomalies (digital malformations, absence of the aortic arch, anomalies in the long bones in the forelimbs, misshapen scapula, absence of a vertebral centrum, and fused sternebrae) were observed at greater than or equal to 0.36 mg/m^2/day. All doses with embryo-fetal effects were observed in the presence of maternal toxicity that included decreases in gestational body weight gain, food consumption, and gravid uterine weight. The lowest dose at which embryo-fetal effects were observed in rats (0.15 mg/m^2/day) was 0.4 times the exposure in patients at the maximum recommended human dose, based on AUC.

8.2 Lactation

Risk Summary

There are no data on the presence of gemtuzumab ozogamicin or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for adverse reactions in breastfed infants, women should not breastfeed during treatment with MYLOTARG and for at least 1 month after the final dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Based on animal studies, MYLOTARG can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)* and *Nonclinical Toxicology (13.1)]*. Verify the pregnancy status of females of reproductive potential prior to initiating MYLOTARG.

Contraception

Females

Advise females of reproductive potential to avoid becoming pregnant while receiving MYLOTARG. Advise females of reproductive potential to use effective contraception during treatment with MYLOTARG and for at least 6 months after the last dose *[see Nonclinical Toxicology (13.1)]*.

Males

Advise males with female partners of reproductive potential to use effective contraception during treatment with MYLOTARG and for at least 3 months after the last dose *[see Nonclinical Toxicology (13.1)]*.

Infertility

Females

Based on findings in animals, MYLOTARG may impair fertility in females of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

Males

Based on findings in animals, MYLOTARG may impair fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and efficacy of MYLOTARG in combination with daunorubicin and cytarabine have not been established in the pediatric patients with newly-diagnosed de novo AML.

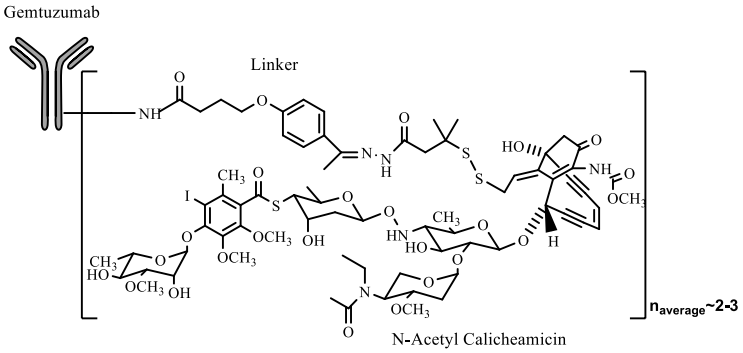
The safety and efficacy of MYLOTARG as a single agent in the pediatric patients with relapsed or refractory AML is supported by a single-arm trial in 29 patients in the following age groups: 1 patient 1 month to less than 2 years old, 13 patients 2 years to less than 12 years old, and 15 patients 12 years to 18 years old. A literature review included an additional 96 patients with ages ranging from 0.2 to 21 years. No differences in efficacy and safety were observed by age.

8.5 Geriatric Use

Use of MYLOTARG in combination with daunorubicin and cytarabine in newly-diagnosed adult patients with de novo AML is supported by a randomized, controlled trial that included 50 patients greater than or equal to 65 years old. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Use of MYLOTARG monotherapy in newly-diagnosed adult patients with AML is supported by a randomized controlled trial with 118 patients treated with MYLOTARG. All patients were over the age of 60 years and 65% of patients were above 75 years. No overall differences in effectiveness were observed by age.

Use of MYLOTARG as single-agent treatment of relapsed or refractory AML is supported by a single-arm trial that included 27 patients 65 years or older. No overall differences in effectiveness were observed between these patients and younger patients. Elderly patients experienced a higher rate of fever and severe or greater infections.

11. DESCRIPTION



Gemtuzumab ozogamicin is an antibody-drug conjugate (ADC) composed of the CD33-directed monoclonal antibody (hP67.6; recombinant humanized immunoglobulin [Ig] G4, kappa antibody produced by mammalian cell culture in NSO cells) that is covalently linked to the cytotoxic agent N-acetyl gamma calicheamicin. Gemtuzumab ozogamicin consists of conjugated and unconjugated gemtuzumab. The conjugated molecules differ in the number of activated calicheamicin derivative moieties attached to gemtuzumab. The number of conjugated calicheamicin derivatives per gemtuzumab molecule ranges from predominantly zero to 6, with an average of 2 to 3 moles of calicheamicin derivative per mole of gemtuzumab.

MYLOTARG (gemtuzumab ozogamicin) for Injection is supplied as a sterile, white to off-white, preservative-free lyophilized cake or powder for intravenous administration. Each single-dose vial delivers 4.5 mg gemtuzumab ozogamicin. Inactive ingredients are dextran 40 (41.0 mg), sodium chloride (26.1 mg), sodium phosphate dibasic anhydrous (2.7 mg), sodium phosphate monobasic monohydrate (0.45 mg), and sucrose (69.8 mg). After reconstitution with 5 mL of Sterile Water for Injection USP, the concentration is 1 mg/mL of gemtuzumab ozogamicin with a deliverable volume of 4.5 mL (4.5 mg).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Gemtuzumab ozogamicin is a CD33-directed antibody-drug conjugate (ADC). The antibody portion (hP67.6) recognizes human CD33 antigen. The small molecule, N-acetyl gamma calicheamicin, is a cytotoxic agent that is covalently attached to the antibody via a linker. Nonclinical data suggest that the anticancer activity of gemtuzumab ozogamicin is due to the binding of the ADC to CD33-expressing tumor cells, followed by internalization of the ADC-CD33 complex, and the intracellular release of N-acetyl gamma calicheamicin dimethyl hydrazide via hydrolytic cleavage of the linker. Activation of N-acetyl gamma calicheamicin dimethyl hydrazide induces double-strand DNA breaks, subsequently inducing cell cycle arrest and apoptotic cell death.

12.2 Pharmacodynamics

Saturation of a high percentage of CD33 antigenic sites is presumed to be required for maximum delivery of calicheamicin to leukemic blast cells. Near maximal peripheral CD33 saturation was observed across studies after gemtuzumab ozogamicin dosing at dose levels of 2 mg/m^2 and above.

At 9 mg/m^2 gemtuzumab ozogamicin (2 doses, 14 days apart), the risk for VOD increases as the C_{max} of the first dose of gemtuzumab ozogamicin increases. The increase in VOD is more prominent in patients with prior stem cell transplantation.

12.3 Pharmacokinetics

There are no clinical PK data for the fractionated regimen. When gemtuzumab ozogamicin is administered at 9 mg/m^2 (2 doses, 14 days apart), the C_{max} following the first dose for patients who received 9 mg/m^2 gemtuzumab ozogamicin was 3.0 mg/mL and increased to 3.6 mg/mL after the second dose.

Distribution

N-acetyl gamma calicheamicin dimethyl hydrazide is approximately 97% bound to human plasma proteins in vitro. Population PK analyses found the total volume of distribution of hP67.6 antibody (sum of V1 [6.31 L] and V2 [15.1 L]) to be approximately 21.4 L in patients.

Elimination

The clearance (CL) value of hP67.6 from plasma was 0.35 L/h after the first dose and 0.15 L/h after the second dose, a decrease of roughly 60%. The terminal plasma half-life ($t_{½}$) for hP67.6 was 62 hours after the first dose and 90 hours after the second dose.

Metabolism

In vitro studies demonstrated that N-acetyl gamma calicheamicin dimethyl hydrazide is extensively metabolized, primarily via nonenzymatic reduction of the disulfide moiety.

Specific Populations

Age, race, sex, mild or moderate renal impairment (creatinine clearance [CLcr] 30-89 mL/min calculated by the Cockcroft-Gault equation) or mild hepatic impairment had no clinically significant effect on the pharmacokinetics of gemtuzumab ozogamicin. The pharmacokinetics of gemtuzumab ozogamicin in patients with severe renal impairment (CLcr 15-29 mL/min) or moderate (total bilirubin greater than 1.5x to 3.0x ULN) and severe hepatic impairment (total bilirubin greater than 3x ULN) is unknown.

Drug Interaction Studies

No clinical drug interaction studies have been performed.

In vitro studies

At clinically relevant concentrations, gemtuzumab ozogamicin had a low potential to:

- *Inhibit CYP450 Enzymes*: CYP1A2, CYP2A6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and CYP3A4/5.

At clinically relevant concentrations, N-acetyl gamma calicheamicin dimethyl hydrazide had a low potential to:

- *Inhibit CYP450 Enzymes*: CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and CYP3A4/5.
- *Induce CYP450 Enzymes*: CYP1A2, CYP2B6, and CYP3A4.
- *Inhibit UGT Enzymes*: UGT1A1, UGT1A4, UGT1A6, UGT1A9, and UGT2B7.
- *Inhibit Drug Transporters*: P-gp (P-glycoprotein), breast cancer resistance protein (BCRP), organic anion transporter (OAT)1 and OAT3, organic cation transporter (OCT)2, and organic anion transporting polypeptide (OATP)1B1 and OATP1B3.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Formal carcinogenicity studies have not been conducted with gemtuzumab ozogamicin. In toxicity studies, rats were dosed weekly for 6 weeks with gemtuzumab ozogamicin at doses up to 7.2 mg/m^2/week. After 6 weeks of dosing, rats developed oval cell hyperplasia in the liver, which is considered a potentially preneoplastic finding, at 7.2 mg/m^2/week (approximately 16 times the exposure in patients at the maximum recommended dose, based on AUC). Other preneoplastic or neoplastic changes observed with other antibody-calicheamicin conjugates in rats included basophilic and/or eosinophilic altered cell foci and hepatocellular adenomas. The relevance of these animal findings to humans is uncertain.

Gemtuzumab ozogamicin was clastogenic in vivo in the bone marrow of mice that received single doses greater than or equal to 22.1 mg/m^2. This is consistent with the known induction of DNA breaks by calicheamicin. N-acetyl gamma calicheamicin dimethyl hydrazide (the released cytotoxic agent) was mutagenic in the bacterial reverse mutation assay and clastogenic in the in vitro micronucleus assay in human TK6 cells.

In a female fertility study, female rats were administered daily intravenous doses of gemtuzumab ozogamicin up to 1.08 mg/m^2 for 14 days before mating with untreated male rats. Significant decreases in the numbers of corpora lutea and implants were observed at 1.08 mg/m^2, and dose-related decreases and increases in the number of live and dead embryos were observed at doses tested (approximately 0.4 times the exposure in patients at the maximum recommended dose, based on AUC). Increased embryofetal lethality at ≥0.36 mg/m^2 was observed in the presence of maternal toxicity that included decreases in gestational body weight and food consumption. Additional findings in female reproductive organs (ovarian atrophy and decreased numbers of follicles associated with atrophy of the uterus, vagina and mammary glands) occurred in rats and monkeys after dosing with other antibody-calicheamicin conjugates.

Fertility was assessed in male rats administered daily intravenous doses of gemtuzumab ozogamicin from 0.12 to 1.08 mg/m^2 for 28 days, followed by mating with untreated females, either at the end of the dosing period or after a 9-week drug-free period. Male fertility index was decreased at doses ≥0.12 mg/m^2 (approximately 1.2 times the exposure in patients at the maximum recommended dose, based on AUC). Effects on testes and epididymides occurred at ≥0.12 mg/m^2, including smaller size and lower weights in addition to adverse effects on sperm. Partial recovery was noted for some effects. Additional effects in male reproductive organs occurred in repeat-dose toxicology studies and included effects on mammary gland, testes, and epididymides in rats at ≥2.4 mg/m^2/week and effects on testes and epididymides in monkeys at 21.6 mg/m^2/week. Testicular effects in male monkeys with other antibody-calicheamicin conjugates included degeneration of seminiferous tubules and decreased epididymidal sperm, which did not reverse following a 6-week drug-free period.

14 CLINICAL STUDIES

14.1 Newly-Diagnosed CD33-positive AML

Study ALFA-0701

MYLOTARG in combination with chemotherapy was investigated in ALFA-0701 (NCT00927498), a multicenter, randomized, open-label Phase 3 study of 271 patients with newly-diagnosed de novo AML age 50 to 70 years. Patients were randomized (1:1) to receive induction therapy consisting of daunorubicin (60 mg/m^2 on Days 1 to 3) and cytarabine (200 mg/m^2 on Days 1 to 7) (DA) with (n=135) or without (n=136) MYLOTARG 3 mg/m^2 (up to maximum of one vial) on Days 1, 4, and 7. Patients who did not achieve a response after first induction could receive a second induction with daunorubicin and cytarabine alone. Patients with response received consolidation therapy with 2 courses of treatment including daunorubicin (60 mg/m^2 on Day 1 of consolidation course 1; 60 mg/m^2 on Days 1 and 2 of consolidation course 2) and cytarabine (1 g/m^2 every 12 hours on Days 1 to 4) with or without MYLOTARG 3 mg/m^2 (up to a maximum of one vial) on Day 1 according to their initial randomization. Patients who experienced remission were also eligible for allogeneic transplantation. An interval of at least 2 months between the last dose of MYLOTARG and transplantation was recommended.

The median age of the patients was 62 years (range, 50-70), 137 female and 134 male, and 88% had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 to 1 at baseline. Baseline characteristics were balanced between treatment arms with the exception

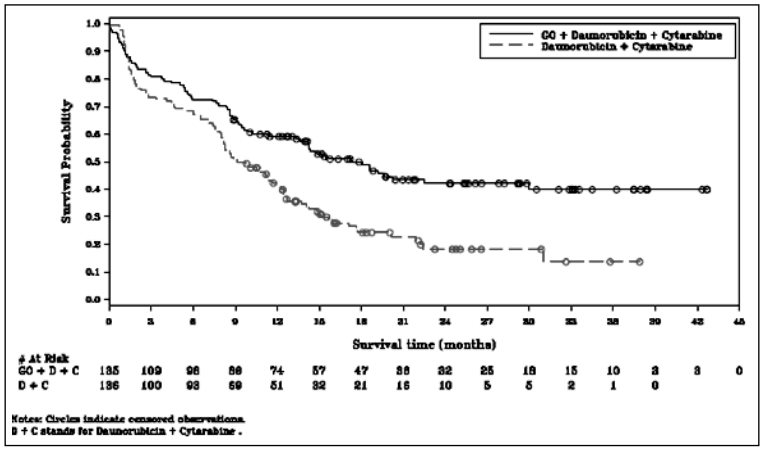
of gender as a higher percentage of males were enrolled in the MYLOTARG arm (55%) than in the DA alone arm (44%). Overall, 59%, 65%, and 70% of patients had documented favorable/intermediate risk and 33%, 27%, and 21% had poor/adverse disease by the National Comprehensive Cancer Network (NCCN), European LeukemiaNet (ELN), and cytogenetic risk classifications, respectively. CD33 expression on AML blasts by flow cytometry harmonized from local laboratory results was determined in 194/271 (72%) patients overall. Few patients (14%) had low CD33 expression (less than 30% of blasts), and none had no expression of CD33.

Efficacy was established on the basis of event-free survival (EFS), measured from the date of randomization until induction failure, relapse, or death by any cause. Per protocol, induction failure was defined as failure to achieve CR or CRp in induction, and date of induction failure was defined as date of marrow evaluation after the last course of induction. Median EFS was 17.3 months in the MYLOTARG arm versus 9.5 months in the control arm; hazard ratio (HR) 0.56 (95% CI: 0.42-0.76); 2-sided p less than 0.001 by log-rank test.

In an exploratory analysis of EFS defined as failure to achieve CR in induction, relapse, or death from any cause and using the date of randomization as the date of induction failure, median EFS was 13.6 months for MYLOTARG + DA and 8.8 months for DA with HR 0.68 (95% CI: 0.51-0.91).

The Kaplan-Meier plot for per-protocol EFS is shown in Figure 1. There was no statistically significant difference between treatment arms in overall survival.

Figure 1. Kaplan-Meier Plot of Event-Free Survival (mITT Population) ALFA-0701 Trial



Abbreviations: C=cytarabine; D=daunorubicin; GO=gemtuzumab ozogamicin; mITT=modified intent-to-treat.

Study AML-19

MYLOTARG single-agent therapy was evaluated in Study AML-19 (NCT00091234), a multicenter, randomized, open-label Phase 3 study comparing MYLOTARG to best supportive care (BSC) for patients with newly-diagnosed AML who were a) greater than 75 years of age or b) 61 to 75 years of age with a World Health Organization performance status (WHO PS) greater than 2 or were unwilling to receive intensive chemotherapy. Patients were randomized 1:1 and stratified by age (61-75 vs 76-80 years vs ≥ 81 years), CD33 positivity of bone marrow blasts (less than 20 % vs 20-80% vs greater than 80% vs unknown), initial white blood cell count (less than 30 vs greater than or equal to 30 x 10^9/L), WHO PS (0-1 vs 2 vs 3-4), and institution.

During induction, MYLOTARG 6 mg/m^2 was given on Day 1 and MYLOTARG 3 mg/m^2 was given on Day 8. Patients with no evidence of disease progression or significant toxicities after MYLOTARG induction received continuation therapy as outpatients with up to 8 courses of treatment including MYLOTARG 2 mg/m^2 on Day 1 every 4 weeks. Patients continued therapy if they did not experience significant toxicities, relapse, or disease progression. BSC included standard supportive care measures and hydroxyurea or other anti-metabolites for palliative purposes.

In total, 118 patients were randomized to treatment with MYLOTARG and 119 patients to BSC. Overall, the median age of patients was 77 years (range, 62-88 years), and most patients (65%) had a WHO PS of 0 to 1 at baseline. Baseline characteristics were balanced between treatment arms with the exception of gender and cytogenetics. Compared to the BSC arm, the MYLOTARG arm had a higher percentage of females (52% vs 39%) and patients with favorable/intermediate risk cytogenetics (50% vs 38%). The proportion with adverse cytogenetics was similar between arms (28% vs 27%). Fewer patients on the MYLOTARG arm had missing cytogenetics data (22% vs 35%). CD33 expression on AML blasts by flow cytometry at a centralized location was determined in 235/237 (99%) patients; 10% had CD33 expression less than 20%.

The efficacy of MYLOTARG was established on the basis of improvement in overall survival (OS). The hazard ratio (HR) for OS was 0.69 (95% CI: 0.53-0.90) (2-sided p=0.005 by log-rank test). Median OS was 4.9 months in the MYLOTARG arm versus 3.6 months in the control arm.

14.2 Relapsed or refractory CD33-positive AML

Study MyloFrance-1

The efficacy of MYLOTARG as a single agent was evaluated in MyloFrance-1 a phase 2, single-arm, open-label study in adults with CD33-positive AML in first relapse. Patients with secondary leukemia or a prior autologous or allogeneic stem cell transplantation were excluded. Study treatment included a single course of MYLOTARG 3 mg/m^2 on Days 1, 4, and 7. Consolidation therapy consisted of cytarabine intravenously every 12 hours for 3 days. The cytarabine dose was 3 g/m^2 for patients less than 55 years old and 1 g/m^2 for patients 55 years or older and/or patients with a creatinine clearance below 50 mL/minute. Hematopoietic stem cell transplantation (HSCT) was allowed after treatment with MYLOTARG, but it was recommended to delay HSCT by at least 90 days following MYLOTARG.

There were 57 patients treated with MYLOTARG. Overall, the median age of patients was 64 years (range 22-80 years). The median duration of first remission was 10 months. Forty-four (78%) patients had intermediate-risk and 12 (22%) poor-risk cytogenetics.

The efficacy of MYLOTARG was established on the basis of complete remission (CR) rate and duration of remission. Fifteen (26%; 95% CI 16% - 40%) patients achieved CR following a single course of MYLOTARG. Median relapse-free survival, measured from the first documentation of CR to the date of relapse or death, was 11.6 months.

15 REFERENCES

1. OSHA Hazardous Drugs. OSHA. [Accessed on June 9, 2017, from http://www.osha.gov/SLTC/hazardousdrugs/index.html]

16 HOW SUPPLIED/STORAGE AND HANDLING

MYLOTARG (gemtuzumab ozogamicin) for Injection is a white to off-white lyophilized cake or powder supplied in a carton (NDC 0008-4510-01) containing one 4.5 mg single-dose vial *[see Dosage and Administration (2)]*.

16.1 Storage and Handling

Refrigerate (2-8°C; 36-46°F) MYLOTARG vials and store in the original carton to protect from light. DO NOT FREEZE.

MYLOTARG is a cytotoxic drug. Follow applicable special handling and disposal procedures.[1]

17. PATIENT COUNSELING INFORMATION

Hepatotoxicity, Including Veno-occlusive Liver Disease (VOD)

Inform patients that liver problems, including severe, life-threatening, or fatal VOD may develop during MYLOTARG treatment. Prior to receiving MYLOTARG, inform patients who previously received, or will receive an HSCT that they may be at increased risk for developing VOD. Inform patients that the risk of developing VOD after an allogeneic HSCT is increased after receiving treatment with MYLOTARG. Inform patients that signs or symptoms of liver toxicity, including rapid weight gain, right upper quadrant pain and tenderness, hepatomegaly, and ascites should be monitored regularly during treatment, but these symptoms may not identify all patients at risk or prevent the complications of liver toxicity. Inform patients that liver problems may require dosing interruption or permanent discontinuation of MYLOTARG *[see Warnings and Precautions (5.1)]*.

Hemorrhage

Inform patients that decreased platelet counts, which may be life-threatening, may develop during MYLOTARG treatment and that complications associated with decreased platelet counts may include bleeding/hemorrhage events, which may be life-threatening or fatal. Inform patients to report signs and symptoms of bleeding/hemorrhage during treatment with MYLOTARG. Inform patients that severe bleeding/hemorrhage may require dosing interruption or permanent discontinuation of MYLOTARG *[see Warnings and Precautions (5.3)]*.

Infusion Related Reactions

Advise patients to contact their health care provider if they experience signs and symptoms of infusion related reactions, including symptoms such as fever, chills, rash, or breathing problems *[see Warnings and Precautions (5.2)]*.

Pregnancy and Breastfeeding

Advise men and women of reproductive potential to use effective contraception during MYLOTARG treatment and for at least 3 and 6 months, respectively, after the last dose *[see Use in Specific Populations (8.3)]*. Advise women of childbearing potential to avoid becoming pregnant while receiving MYLOTARG. Advise women to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with MYLOTARG. Inform the patient of the potential hazard to the fetus *[see Warnings and Precautions (5.6)* and *Use in Specific Populations (8.1)]*. Advise women against breastfeeding while receiving MYLOTARG and for 1 month after the last dose *[see Use in Specific Populations (8.2)]*.

This product's label may have been updated. For full prescribing information, please visit www.mylotarg.com.

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