

Understanding **ZIO-101** **(Darinaparsin)**



International Myeloma Foundation
12650 Riverside Drive, Suite 206
North Hollywood, CA 91607 USA

Telephone:

800-452-CURE (2873)

(USA & Canada)

818-487-7455

Fax: 818-487-7454

TheIMF@myeloma.org

www.myeloma.org



Table of Contents

Introduction	5
What is Multiple Myeloma?	5
What are the Stages of Multiple Myeloma?	6
What is Darinaparsin and How Does it Work?	8
What are the Possible Side Effects of Darinaparsin?	10
How is Darinaparsin Given?	11
What is the Dose and Schedule for Darinaparsin?	11
How Can I Receive Treatment with Darinaparsin?	11
About the IMF	12
Glossary	15



Introduction

You have been given this booklet to learn more about a new drug called Darinaparsin (S-dimethylarsino-glutathione, ZIO-101). After reading this booklet you should know:

- What Darinaparsin is
- How Darinaparsin works
- The possible side effects of Darinaparsin
- How Darinaparsin is given

This booklet is meant to provide you with general information only. It is not meant to replace the advice of your doctor or nurse. Your doctor or nurse can answer questions related to your specific treatment plan. All words that appear in **bold type** are defined in the glossary at the end of the booklet.

What is Multiple Myeloma?

Multiple myeloma (also known as myeloma or **plasma cell neoplasm**) is a malignancy of the **immunoglobulin- (antibody)** producing plasma cells found in the **bone marrow**. It is a hematologic malignancy resembling leukemia. However, the malignant plasma cells, or myeloma cells, rarely enter the bloodstream as in a true leukemia. Instead, the myeloma cells accumulate in the bone marrow, causing:

- Disruption of normal bone marrow function, most commonly giving rise to anemia (a low level of red blood cells in the bloodstream), although reduction in **white blood cell** and platelet counts can also occur

- Damage to bone surrounding accumulated myeloma cells
- Release of an abnormal protein, **monoclonal protein (M-protein)**, into the bloodstream
- Suppression of normal **immune functions**, observed as reduced levels of normal immunoglobulins and increased susceptibility to infection

Myeloma cells can also grow in the form of localized tumors or **plasmacytomas**. Plasmacytomas may be single or multiple and either medullary (confined within bone marrow and bone) or extramedullary (outside of the bone). When there are multiple plasmacytomas inside or outside bone, this condition is also called multiple myeloma.

The Stages of Multiple Myeloma

Stage I (low cell mass): Early disease. The bone structure appears normal or close to normal on x-ray images; the number of red blood cells and amount of calcium in the blood are normal or close to normal, and the amount of M-protein is very low.

Stage II (intermediate cell mass): An intermediate stage between stage I and III

Stage III (high cell mass): More advanced disease. One or more of the following are present:

- **Anemia**
- A high level of calcium in the blood

- More than 3 areas of advanced **lytic** bone lesions
- A high level of M-protein in the blood or urine

Multiple myeloma is a serious malignancy, but it is treatable. Many patients experience a series of responses, relapses, and remissions. With new treatments, the average survival of 5 years for patients diagnosed with multiple myeloma may be extended.

Following diagnosis, several options are available for initial or frontline therapy. For patients who may be candidates for high-dose therapy with transplant, various induction regimens can be considered, including Thalomid® (thalidomide) with dexamethasone, dexamethasone alone, or other dexamethasone-containing combinations. The combination of the **alkylating agent** melphalan plus prednisone, a simple oral therapy, is an option for patients not considering bone marrow (stem cell) transplant with intravenous high-dose melphalan. At the time of relapse,



newer agents are frequently required to achieve further response. Revlimid® (lenalidomide) is an important new agent available for use in this setting. Velcade® (bortezomib) is also an important new agent available for relapsed myeloma.

What is Darinaparsin and How Does it Work?

Darinaparsin (S-dimethylarsino-glutathione) is a novel, **organic** arsenic. Darinaparsin kills human myeloma cell lines grown in the laboratory. Darinaparsin is also active against human myelomas that have been transplanted into mice. Arsenic has been used in its **inorganic** form to treat various diseases for over 2000 years, even though it has been associated with undesirable side effects. As a form of organic arsenic, Darinaparsin represents a new class of **small molecule cancer therapy**.

The potential anti-myeloma effect of Darinaparsin may result from several activities:

- Disrupting the function of **mitochondria**, which are small structures within cells that provide energy, and are often referred to as the powerhouses of cells.
- Increasing the production of reactive oxygen species which can damage the DNA and protein of myeloma cells.
- Modifying the ability of myeloma cells to respond to factors in the bone marrow and blood that promote their growth.

- Inhibiting new blood vessel development (**anti-angiogenic activity**) on which myeloma and other cancer cells depend for their survival and growth.

The activity of Darinaparsin against cultured myeloma cells and transplanted tumors in laboratory models supports testing in patients with multiple myeloma. Two clinical studies are being conducted to evaluate different treatment schedules in patients with advanced/progressive myeloma who had received at least 2 prior therapies. A phase I/II study is investigating dosing with 300 mg/m² once daily for 5 consecutive days every 4 weeks (treatment week 1 and no treatment weeks 2, 3, 4). The phase II portion of this study is determining the preliminary efficacy and safety profile of this schedule.

The phase II study is investigating a different dosing schedule of Darinaparsin: 420 mg/m² twice a week every 3 weeks of a 4 week cycle (treatment weeks 1, 2, 3, and no treatment week 4). The purpose of this study is to determine preliminary efficacy and safety.

There have been 14 patients treated at 300 mg/m² once daily for 5 consecutive days every 4 weeks. In this group, 10 patients are evaluable for response, that is, they have received at least 2 cycles of therapy, and 4 of them have stable disease as their best response. Three patients have been treated at 420 mg/m² twice a week every 3 weeks of a 4 week cycle.

What are the Possible Side Effects of Darinaparsin?

Common **side effects** associated with Darinaparsin that have been seen in the phase I/II and phase II trials (both dosing schedules) include vomiting, fatigue, and pain at the site of infusion in patients receiving their treatment through a peripheral line. More serious side effects observed in a small number of patients include decreased blood cell counts, confusion, and dizziness. No clinically important neuropathy (nerve damage), bone marrow toxicity, or cardiotoxicity (heart toxicity) has been seen during the clinical trials so far. Your doctor or nurse can provide more information in greater detail about these and other possible side effects.

Because the safety information about Darinaparsin is derived from clinical trials, and these clinical trials are ongoing, no definitive conclusions about the side effects can yet be made.



How is Darinaparsin Given?

Darinaparsin is given as an **intravenous (I.V.) infusion**.

What is the Dose and Schedule for Darinaparsin?

The most effective dose and schedule for treating multiple myeloma with Darinaparsin is still being determined in clinical trials.

How Can I Receive Treatment with Darinaparsin?

At present, Darinaparsin is available to patients with multiple myeloma and other types of cancer who are willing to participate in clinical trials. For more information on how to enroll in a clinical trial, contact the IMF.

IMF hotline:

USA & Canada only: 800-452-CURE (2873)

Elsewhere: 818-487-7455

IMF Web site: www.myeloma.org

About the IMF

*“One person can make a difference,
Two can make a miracle.”*

Brian D. Novis
IMF Founder

Myeloma is a little-known, complex, and often misdiagnosed bone marrow cancer that attacks and destroys bone. Myeloma affects approximately 75,000 to 100,000 people in the United States, with approximately 20,000 new cases diagnosed each year. Although there is presently no known cure for myeloma, doctors have many approaches to help myeloma patients live better and longer.

The International Myeloma Foundation (IMF) was founded in 1990 by Brian and Susie Novis shortly after Brian’s myeloma diagnosis at the age of 33. It was Brian’s dream that future patients would have easy access to medical information and emotional support throughout their battle with myeloma. He established the IMF with the 3 goals of treatment, education, and research. He sought to provide a broad spectrum of services for patients, their families, friends, and health care providers. Although Brian died 4 years after his initial diagnosis, his dream didn’t. Today, the IMF reaches out to an international membership of more than 150,000. The IMF was the first organization dedicated solely to myeloma, and today it remains the largest.

The IMF provides programs and services to aid in the research, diagnosis, treatment, and management of myeloma. The IMF ensures that no one must brave the myeloma battle alone.

We care for patients today, while working toward tomorrow’s cure.

How Can the IMF Help You?

PATIENT EDUCATION

INFORMATION PACKAGE

Our free IMF InfoPack provides comprehensive information about myeloma, treatment options, disease management, and IMF services. It includes our acclaimed **Patient Handbook**.

INTERNET ACCESS

Log on to www.myeloma.org for 24-hour access to information about myeloma, the IMF, education, and support programs.

ONLINE MYELOMA FORUM

Join the IMF Internet Discussion Group at www.myeloma.org/listserve.html to share your thoughts and experiences.

MYELOMA MINUTE

Subscribe to this free weekly email newsletter for up-to-the-minute information about myeloma.

PATIENT & FAMILY SEMINARS

Meet with leading experts in myeloma treatment to learn more about recent advances in therapy and research.

MYELOMA MATRIX

On our website and in print, this document is a comprehensive guide to drugs in development for myeloma.

MYELOMA TODAY NEWSLETTER

Our quarterly newsletter is available free of charge by subscription.

SUPPORT

MYELOMA HOTLINE: 800-452-CURE (2873)

Toll-free throughout the United States and Canada, the IMF Hotline is staffed by trained information specialists and is in frequent interaction with members of our Scientific Advisory Board.

SUPPORT GROUPS

A worldwide network of more than 100 myeloma support groups holds regular meetings for members of the myeloma community. The IMF conducts annual retreats for myeloma support group leaders.

RESEARCH

BANK ON A CURE®

This DNA bank will provide genetic data for research in new drug development.

THE INTERNATIONAL STAGING SYSTEM (ISS)

This updated staging system for myeloma will enhance physicians' ability to select the most appropriate treatment for each patient.

RESEARCH GRANTS

Leading the world in collaborative research and achieving extraordinary results, the IMF Grant Program supports both junior and senior researchers working on a broad spectrum of projects. The IMF has attracted many young investigators into the field of myeloma who remain in the field and actively pursue a cure for the disease.

Glossary

Alkylating agent: A chemotherapy agent that prevents the growth and division of new cancer cells by inhibiting their ability to replicate DNA.

Anemia: A low level of red blood cells in the bloodstream.

Anti-angiogenic activity: Ability to inhibit new blood vessel development.

Antibody: A protein produced by some of the body's white blood cells that helps fight infection.

Bone marrow: A soft, spongy tissue found in most large bones that produces red and white blood cells and platelets.

Immune function: The functioning of the immune system; the system of white bloodcells and their properties that help the body resist infection and some cancers.

Immunoglobulin: An antibody.

Inorganic: Not formed by a living organism.

Intravenous (I.V.) infusion: Delivery of a drug or fluid into the body using a needle inserted into a vein.

Lysis (lytic): Dissolution or destruction of cells.

Mitochondria: Small structures within cells that provide energy.

Monoclonal protein (M protein): An abnormal protein produced by myeloma cells that accumulates in and damages bone and bone marrow. A high level of M protein indicates that myeloma cells are present in large numbers.

Multiple myeloma: A cancer arising from the plasma cells in the bone marrow. The plasma cells in patients with multiple myeloma form abnormal antibodies, possibly damaging the bone, bone marrow, and other organs.

Neoplasm: Cancer.

Organic: Formed by a living organism, i.e., an animal or plant.

Plasma cell: A type of white blood cell that produces antibodies.

Plasmacytoma: A tumor made up of cancerous plasma cells.

Side effect: An effect caused by treatment with a drug. The term usually refers to an unwanted effect, but some side effects may be beneficial.

White blood cell: A cell made by the bone marrow that helps fight infection and/or disease.