Protocol Plain Language Summary

A clinical study of zilovertamab vedotin with standard treatment in people with large B-Cell lymphoma (MK-2140-003)

Protocol Title: A Phase 2/3 Multicenter, Open-label, Randomized, Active-Control Study of Zilovertamab Vedotin (MK-2140) in Combination With Standard of Care in Participants With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (waveLINE-003)

Why is this study needed?

Researchers are looking for new ways to treat people with relapsed or refractory diffuse large B-cell lymphoma (**rrDLBCL**). rrDLBCL is a type of non-Hodgkin's lymphoma (a blood cancer) that has come back after responding to a prior treatment (**relapsed**) or has not responded to treatment (**refractory**). Responding to treatment refers to cancer shrinking or going away.

rrDLBCL is usually treated with a **standard treatment** of chemotherapy combined with immunotherapy. Chemotherapy uses medicines to destroy cancer cells and immunotherapy uses medicines that work with the immune system to fight cancer.

Researchers want to learn if adding zilovertamab vedotin to current standard treatments can help people with rrDLBCL. **Zilovertamab vedotin**, the study medicine, is a type of targeted therapy. A targeted therapy is a treatment that works to control how specific types of cancer cells grow and spread.

The purpose of this study is to learn what dose of zilovertamab vedotin is safe and well tolerated when given with standard treatment. Researchers also want to learn how long people who receive zilovertamab vedotin with the standard treatment live without their cancer getting worse.

Who will take part in this study?

Up to about 260 people will be in this study. They will be ages 18 years old and older, and:

- Have DLBCL that has come back or did not respond to at least 1 prior standard treatment (rrDLBCL)
- Do not have primary mediastinal B-cell lymphoma (a different type of blood cancer)

What treatments are being given during the study?

During this study, people may receive one or more of these treatments:

- **Zilovertamab vedotin**, the study medicine
- **R-GemOx**, a standard treatment of rituximab (an immunotherapy drug), gemcitabine (a chemotherapy drug), and oxaliplatin (a chemotherapy drug)
- **BR**, standard treatment of bendamustine (a chemotherapy drug) and rituximab (an immunotherapy drug)

All treatments, except bendamustine, will be given through a needle into a vein as an intravenous (IV) infusion once every 3 weeks for up to about 4 and a half months. Bendamustine, will be given as an IV infusion twice every 3 weeks on Days 1 and 2.

The researcher has decided not to continue the BR treatment for Part 2 of the study. All people who were assigned to receive BR before this decision will continue with this treatment until they leave the study or the study ends.

How is this study designed?

This study has 2 parts:

Part 1: Researchers will give the following treatments to different groups of people every 3 weeks for 18 weeks:

- Group 1: zilovertamab vedotin with R-GemOx
- Group 2: zilovertamab vedotin with BR

Researchers will start by giving some people zilovertamab vedotin at a lower dose with R-GemOx or BR. Researchers will check to see if there are any safety concerns before giving the next higher or lower dose of zilovertamab vedotin with R-GemOx or BR to a different group of people. This will continue until researchers determine the tolerated dose **(selected dose)** of zilovertamab vedotin that is safe to use in Part 2.

Part 2: People from Part 1 will receive one of these treatments every 3 weeks for 18 weeks:

- Zilovertamab vedotin with R-GemOx
- R-GemOx alone

People will have an equal chance of receiving either the selected dose of zilovertamab vedotin with a standard treatment (R-GemOx) or a standard treatment alone. Both the people in the study and researchers will know which treatment the person takes (**open-label study**). People may give bone marrow, blood, and urine samples, have imaging tests and physical examinations, and answer sets of questions about their health. People may be in this study for up to about 4 years.

What are the goals of this study and how will they be measured?

Main goals	How they will be measured
To learn about safety and how well people tolerate (handle) zilovertamab vedotin with R-GemOX or BR	The number of people who: • Had health problems related to the study medicine that prevented giving a higher dose (**dose limiting toxicity**) • Had an **adverse event (AE)**—an AE is a health problem that happens or worsens during a study • Stopped treatment due to an AE
To learn how cancer responds to the selected dose of zilovertamab vedotin with R-GemOX compared to R-GemOX	**Progression-free survival:** the length of time from when people join the study until the cancer grows or spreads, or death from any cause
Other goals	**How they will be measured**
To learn how cancer responds to the selected dose of zilovertamab vedotin with R-GemOX compared to R-GemOX	Researchers will measure responses during the study: • **Overall survival:** the length of time that people live from when they join the study until death from any cause • **Objective response rate:** the percent of people whose cancer responds to treatment (gets smaller or goes away) • **Duration of response**: the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause

What are the possible benefits and risks?

Clinical studies may have benefits and risks. People may benefit because the study treatment may treat cancer or stop it from getting worse. There may be risks because the study treatment may not work or may cause health problems.
This study has a group of experts, separate from the researchers, who oversee the benefits and risks. If they decide that the study [medicine/treatment] is not safe or doesn't show benefit, the study can be stopped. More information about the benefits and risks is in the protocol.