Protocol Plain Language Summary

A clinical study of zilovertamab vedotin alone and with nemtabrutinib to treat B-cell malignancies (MK-2140-006)

Protocol Title: A Multicenter, Open-label, Phase 2 Basket Study to Evaluate the Safety and Efficacy of MK-2140 as a Monotherapy and in Combination in Participants With Aggressive and Indolent B-cell Malignancies (waveLINE-006)

Why is this study needed?

Researchers are looking for new ways to treat certain **relapsed or refractory B-cell malignancies.** A **B-cell malignancy** is cancer in a type of white blood cell (called B-cells). **Relapsed** means the cancer has come back after treatment. **Refractory** means the cancer did not **respond** (get smaller or go away) to treatment. The certain types of B-cell malignancy in this study are:

- Mantle cell lymphoma (MCL)
- Richter transformation (RT)
- Chronic lymphocytic leukemia (CLL)
- Follicular lymphoma (FL)

Zilovertamab vedotin and **nemtabrutinib**, the study medicines, are targeted therapies. **Targeted therapy** is a treatment that works to control how specific types of cancer cells grow and spread.

The goal of this study is to learn about the safety and how well people tolerate zilovertamab vedotin alone or with nemtabrutinib. Researchers also want to learn how many people have the cancer respond to treatment.

Who will take part in this study?

About 275 people with certain types of B-cell malignancy will be in this study. They will be at least 18 years old and:

- Have MCL, RT, FL, or CLL that came back after treatment or did not respond to treatment
- Have not received an organ transplant

What treatments are being given during the study?

People will receive one or both of these treatments:

- **Zilovertamab vedotin**
- **Nemtabrutinib**

People will receive zilovertamab vedotin through a needle into a vein as an intravenous (IV) infusion. People will take nemtabrutinib by mouth as tablets. People will continue their treatment until the cancer gets worse or they don't tolerate it.

How is this study designed?

A person may be in this study for up to about 5 and a half years.

Both the people in the study and researchers will know which treatment the person takes (**open-label study**). During the study, people may give blood and urine samples, have tumor and imaging tests, have bone marrow biopsies and physical examinations, and answer sets of questions about their health.

People will be placed into groups based on their type of B-cell malignancy and the number of treatments they previously received:

Group	Type of B-cell malignancy	Number of previous treatments	Treatment
A	MCL	2	**Zilovertamab vedotin** once every 3 weeks
B	RT	1	**Zilovertamab vedotin** once every 3 weeks
C	MCL	1	**Zilovertamab vedotin** once every 3 weeks **with nemtabrutinib** everyday
D	FL or CLL	2	People will have an equal chance of receiving either: • **Zilovertamab vedotin** once every 3 weeks • **Zilovertamab vedotin** 2 times every 3 weeks
E	FL	2	**Zilovertamab vedotin** at the best dose and schedule for FL based on data from Group D
F	CLL	2	**Zilovertamab vedotin** at the best dose and schedule for CLL based on data from Group D

In **Group A**, people with MCL have previously received a type of targeted therapy called an irreversible Bruton tyrosine kinase inhibitor (BTKi). In **Group C**, people with MCL have not previously received another type of targeted therapy called a reversible BTKi.

Researchers will give a few people in Group C a starting dose level of zilovertamab vedotin with nemtabrutinib. They will check for any safety concerns or medical problems and adjust the dose level of zilovertamab vedotin if needed. This will help researchers decide which dose level of zilovertamab vedotin with nemtabrutinib to give to the rest of the people in Group C.

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

Main goals	How they will be measured
To learn about the **safety** and how well people **tolerate** zilovertamab vedotin alone or with nemtabrutinib	The number of people in Groups C and D who: • Had an **adverse event (AE)**—an AE is a health problem that happens or worsens during the study • Stopped treatment due to an AE
To learn about the **dose-limiting toxicity (DLT)** of zilovertamab vedotin with nemtabrutinib	The number of people who have a DLT during the first 8 weeks of treatment. A **DLT** is a medical problem related to study medicine that prevents giving a higher dose or may prevent giving the same dose. This will be measured only for the few people in Group C that receive a starting dose level
To learn the **objective response rate (ORR)** of people who receive zilovertamab vedotin alone or with nemtabrutinib	**ORR** is the number of people whose cancer responds (gets smaller or goes away)to treatment during the study

Other goals	How they will be measured
To learn the **duration of response (DOR)** of people who receive zilovertamab vedotin alone or with nemtabrutinib	**DOR** is the length of time from when the cancer first responds to treatment until the cancer grows, spreads, or death from any cause

To learn about the **safety** and how well people **tolerate** zilovertamab vedotin alone	The number of people in Groups A, B, E, and F who: • Had an AE during the study • Stopped treatment due to an AE

What are the possible benefits and risks?

Clinical studies may have benefits and risks. People may benefit because the study medicines may treat B-cell malignancies or stop it from getting worse. There may be risks because the study medicines may not work or may cause health problems. More details about the possible benefits and risks are in the protocol.