Protocol Plain Language Summary

A clinical study to compare nemtabrutinib and venetoclax to standard treatments in people with blood cancer that stopped responding to treatment or came back after treatment (MK-1026-010)

Protocol Title: A Phase 3, Open-label, Randomized Study to Compare the Efficacy and Safety of Nemtabrutinib (MK-1026) Plus Venetoclax Versus Venetoclax Plus Rituximab in Participants With Relapsed/Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Following at Least 1 Prior Therapy (BELLWAVE-010)

Why is this study needed?

Researchers are looking for new ways to treat **chronic lymphocytic leukemia (CLL)** and **small lymphocytic lymphoma (SLL)** when either the cancer has come back after treatment **(relapsed)**, or current treatment has stopped working to slow or stop cancer growth **(refractory)**. CLL and SLL are types of blood cancer. With standard treatments, there is a high chance that CLL and SLL will get worse, or treatment will stop working.

Past studies have shown that the study treatment **nemtabrutinib** can slow tumor growth. More research is needed to learn if nemtabrutinib can slow cancer growth and increase how long people live compared to standard cancer treatments.

In this study, researchers want to know if **nemtabrutinib** is safe to take with **venetoclax** and how well people tolerate the treatments together. They also want to know if people who take nemtabrutinib and venetoclax live longer without their cancer getting worse compared to those who take standard treatments.

Who will take part in this study?

About 720 people at least 18 years of age who:

- Have been diagnosed with active CLL or SLL disease
- Did not respond to at least one prior treatment or prior treatment is no longer working
- Do not have another cancer that got worse or was treated in the past 3 years

How is this study designed?

Each person could be in the study for about 10 years. This study has 2 parts:

- **In Part 1**, 30 people will take **nemtabrutinib and venetoclax:**
  - The first 15 people who join the study will take venetoclax every morning and a **lower dose of nemtabrutinib** at least 10 hours later - researchers will review the safety
  - If the low dose is safe, the next 15 people will take venetoclax every morning and a **higher dose of nemtabrutinib** at least 10 hours later
  - Researchers will review the safety of both doses of nemtabrutinib and decide which dose to use in Part 2
- **In Part 2**, 690 people will have an equal chance of receiving either:
  - **Venetoclax** every morning and **nemtabrutinib** at least 10 hours later
  - **Venetoclax** every morning and **rituximab** or **rituximab biosimilar** (similar treatments made by a different company) once every 28 days (one cycle) for up to 6 cycles. This is a standard treatment for CLL and SLL.

During the study, both the person and the study doctor will know which treatment the person is getting (an open-label study). People will have blood and tissue tests, have imaging tests, and answer sets of questions during and after stopping treatment.

What treatments are being given during the study?

Nemtabrutinib added to venetoclax is being studied. This treatment is compared to the standard treatment, venetoclax plus rituximab. Venetoclax and nemtabrutinib are taken by mouth once a day.

Rituximab or rituximab biosimilar is given through a needle in a vein (IV infusion) once every 28 days (one cycle). Each person will take their assigned treatment for up to 2 years or until their cancer gets worse or they stop treatment for any reason. Each person may be followed for up to 10 years.

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

Main goals	How they will be measured
Part 1: • To learn about the safety and how well people tolerate nemtabrutinib and venetoclax • To decide which dose of nemtabrutinib to use in Part 2	Percent of people who during **Part 1**: • Had medical problems related to nemtabrunitib that prevents an increase in dose (**dose limiting toxicity**) • Had an **adverse event** (AE). An AE is any health problem that happens during a study. • Stopped study treatment due to an AE
Part 2: To learn if people who take nemtabrutinib and venetoclax live longer without the cancer getting worse compared to those who take venetoclax and rituximab	**Progression free survival**: the average length of time after the start of treatment in which people are alive, and their cancer does not grow or spread. Researchers will compare this throughout the study.
Other goals for Part 2 of the study	**How they will be measured**
To learn how many people who take nemtabrutinib and venetoclax have no detectable cancer cells in their bone marrow compared to those who take standard treatments	**Minimal residual disease**: lab test measurements that cannot find any cancer in bone marrow at 14 months after a person starts treatment
To learn how long people who take nemtabrutinib and venetoclax live compared to those who take standard treatments	**Overall survival**: the average length of time that people live from the start of treatment to their death from any cause. Researchers will compare this throughout the study.
To learn how many people who take nemtabrutinib and venetoclax have their cancer shrink or go away compared to those who take standard treatments	**Objective response**: the percent of people whose cancer responds (shrinks or goes away) to treatment. Researchers will compare this throughout the study.
To learn how long a person's cancer responds to treatment with nemtabrutinib and venetoclax compared to those who take standard treatments	**Duration of response**: the length of time from when a person's cancer first responds to treatment until their cancer gets worse or their death from any cause Researchers will compare this throughout the study.
To learn about the safety of nemtabrutinib and venetoclax and how well people tolerate them	Percent of people who: • Had an AE during or after they stopped their study treatment • Stopped study treatment due to an AE

What are the possible benefits and risks?

People in this study may or may not have their cancer stop growing or go away. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. The study can be stopped if the committee decides that the study treatment is not safe or does not show benefit. More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.