Protocol Plain Language Summary

A study to compare nemtabrutinib to standard cancer treatments in people with untreated blood cancer (MK-1026-008)

Protocol Title: A Phase 3, Randomized Study to Compare the Efficacy and Safety of Nemtabrutinib Versus Chemoimmunotherapy for Previously Untreated Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Without *TP53* Aberrations (BELLWAVE-008)

Why is this study needed?

Researchers are looking for new ways to treat people with **chronic lymphocytic leukemia (CLL)** or **small lymphocytic lymphoma (SLL)**. CLL and SLL are types of blood cancer. With standard treatments, there is a high chance that CLL or 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.

Researchers want to know if people who take nemtabrutinib compared to those who take the standard treatments in this study will live longer without their cancer growing, spreading or returning (**progression free survival**), live longer overall (**overall survival**) or have their cancer shrink or go away (**objective response**).

Who will take part in this study?

About 300 men and women at least 18 years of age with either CLL or SLL will take part in this study.

- Their blood cancer cells must not be missing part of chromosome 17 ("17p deletion") or have changes in the *TP53* gene ("*TP53* mutation")
- They must not have been treated previously for CLL or SLL

What treatments are being studied?

People will be assigned by chance to get one of the following treatments:

- The study treatment nemtabrutinib taken by mouth every day. This treatment continues until the cancer gets worse or they stop treatment for another reason
- The researcher's choice of 1 of 2 standard treatments. These standard treatments are given over time through a needle in a vein (IV infusion). Each person is treated for about 6 months (six 28-day cycles):
    - fludarabine and cyclophosphamide on Days 1, 2 and 3 of each cycle and rituximab or rituximab biosimilar (similar treatments made by a different company) on Day 1 of each cycle
    - bendamustine on Days 1 and 2 of each cycle and rituximab or rituximab biosimilar on Day 1 of each cycle

How is this study designed?

Each person could be in the study for about 6 to 8 years. Both the people in the study and the researcher will know which treatment participants are getting (an open-label study).

People will give blood samples, have biopsies (a sample of tissue is taken from the body and tested in a lab), imaging tests, and answer sets of questions before, during and after stopping treatment.

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

Main goal	How it will be measured
To learn how long people who take nemtabrutinib live without their cancer getting worse compared to those who take the standard treatments	**Progression free survival**: the average length of time from the start of treatment until a person's cancer gets worse or death from any cause. Researchers will compare this during the study at multiple time points.

Other goals	How they will be measured
To learn how long people who take nemtabrutinib live compared to those who take the standard treatments	**Overall survival**: the average length of time that people live from the start of treatment until death from any cause. Researchers will compare this after a certain number of deaths have been reported.
To learn how many people who take nemtabrutinib had their cancer shrink or go away compared to those who take standard treatment	**Objective response**: the percent of people whose cancer responds to treatment. Researchers will compare this during the study at an interim analysis.
To learn how long a person's cancer responds to treatment with nemtabrutinib compared to those who take the standard treatment	**Duration of response**: the length of time from when a person's cancer first responds to treatment until either their cancer gets worse or their death from any cause. Researchers will review this up to the end of the study.
To learn about the safety of nemtabrutinib and how well people managed (tolerated) the study treatment	Percent of people who: • had an **adverse event** during or after they stopped their study treatment - an adverse event is any health problem that happens during a study • stopped study treatment due to an adverse event

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. If the committee decides that the study treatment is not safe, the study can be stopped.

More information about the benefits and risks for a person is in the nemtabrutinib Investigator Brochure, MK-1026-008 Protocol and Informed Consent documents.