Protocol Plain Language Summary

A clinical study of bomedemstat for people with essential thrombocythemia (MK-3543-006)

Protocol title: A Phase 3, Randomized, Open-label, Active-Comparator-Controlled Clinical Study to Evaluate the Safety and Efficacy of Bomedemstat (MK-3543/IMG-7289) versus Best Available Therapy (BAT) in Participants With Essential Thrombocythemia who have an Inadequate Response to or are Intolerant of Hydroxyurea

Why is this study needed?

Researchers are looking for new ways to treat **essential thrombocythemia (ET)**. ET is a rare type of blood cancer in which the body makes too many platelets. Platelets are cells that help blood to clot. Some people with ET have a high risk (chance) of having blood clots or bleeding problems.

Bomedemstat is a **study treatment** designed to treat ET. The purpose of this study is to learn if bomedemstat works better than standard treatment for ET to:

- Lower the number of platelets
- Lower the number of white blood cells (if a person's white blood cells were increased)
- Prevent blood clots, major bleeding problems, or ET leading to other blood diseases

Who will take part in this study?

About 300 people with ET will be in this study. They will be 18 years old or older and:

- Previously received a standard treatment for ET, called hydroxyurea that did not work to lower the number of platelets, or they did not tolerate it
- Have not had certain other cancers in the last 2 years

What treatments are being studied?

People will receive one of these treatments (one treatment at a time):

- **Bomedemstat**: The study treatment taken by mouth once a day
- **Standard treatment**: A standard treatment for ET based on the researcher's choice of anagrelide, busulfan, interferon alfa/pegylated interferon alfa, or ruxolitinib.
    - Anagrelide, busulfan, and ruxolitinib are taken by mouth
    - Interferon alfa/pegylated interferon alfa are given as a shot under the skin

How is this study designed?

This study has 2 parts:

- **Part 1 (about 1 year)**: People will have an equal chance of receiving either bomedemstat or standard treatment. After 1 year, researchers will review the data for safety and how well treatments worked.
- **Part 2 (up to 2 years)**: People will continue to receive treatment.

In both Part 1 and Part 2, researchers may raise or lower the amount of treatment that a person takes based on the person's platelet and other blood cell levels.

Both the people in the study and the researcher will know which study treatment a person is getting (open-label study). During the study, people will have bone marrow biopsies, urine and blood tests, a heart test (called electrocardiogram or ECG), physical examinations, and answer questions about their health. People may be in this study for up to 3 years.

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

Main goal	How it will be measured
To learn if more people who take bomedemstat have a better **response** compared to those who take standard treatment	The number of people who have a response that begins by week 24 of treatment and lasts until at least week 48. A **response** is when a person has all of these: • The number of platelets go down to a healthy number • The number of white blood cells (WBCs) go down to a healthy number, if their WBCs were high • No blood clots, major bleeding, or ET leading to other blood diseases at 1 year
Other goals	**How they will be measured**
To learn **how long the response lasts** for people who take bomedemstat and those who take standard treatment	The length of time from start of response until **any** of these happen: • The number of platelets go back up to a high number • The number of WBCs go back up to a high number • A person has blood clots, major bleeding, or ET leading to other blood diseases
To learn about the **ET symptoms** of people who take bomedemstat and those who take standard treatment	People will answer questions to measure their ET symptoms including **fatigue** (feeling weak and tired). Researchers will measure the change in scores during the study.
To learn about the **length of remission** (no signs of cancer) for people who take bomedemstat and those who take standard treatment	**Length of remission** is the length of time from when a person's platelets and WBCs go down to a healthy number until they go back up to a higher number due to ET. They must not have bleeding, clotting or progression to another blood disorder during this time.
To learn about **certain events related to blood clotting** of people who take bomedemstat and those who take standard treatment	The number of people who have any of these: • Blood clots • Major bleeding • ET leading to other blood diseases
To learn about the **event-free survival (EFS)** of people who take bomedemstat and those who take standard treatment	**EFS** is the length of time people live without having blood clots, major bleeding, ET leading to other blood diseases, or death from any cause
To learn about **safety** and how well people **tolerate** bomedestat	The number of people who: • Had an **adverse event (AE)** – An AE is a health problem that happens or worsens during a 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 medicine may treat ET or stop it from getting worse. There may be risks because the study medicine 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 is not safe or doesn't show benefit, the study can be stopped. More information about the benefits and risks is in the protocol.