ADORE, a clinical trial studying the effects of taking ruxolitinib with a new treatment in patients with myelofibrosis

Why is the trial needed?

Myelofibrosis (MF) is a bone marrow disorder where the blood cells are not produced at the right level. This leads to organs and tissues becoming enlarged, symptoms such as fatigue, and may eventually lead to complications like anemia, increased risk of infections, or clotting issues. The disease is typically diagnosed in older adults and cannot currently be cured. The treatment with ruxolitinib, already on the market, has helped many patients with MF. However, in MF, the body can become overactive, leading to too many signaling pathways. It has been reviewed, and Parts 2 and 3 will also include patients who receive ruxolitinib alone and 3 will also include patients who have received ruxolitinib for at least 12 weeks. This is to ensure enough patients take each of the treatments to be able to see if they are safe and effective.

What questions is ADORE trying to answer?

How could a new treatment work with ruxolitinib?

• Clinical trial: ADORE is for patients who are already taking the treatment ruxolitinib, but may also take another treatment. What is the study design?

To take part, participants must have all of the following:

1. Been taking the same dose of ruxolitinib for at least the last 4 weeks
2. Been taking ruxolitinib for at least 12 weeks
3. A low level of hemoglobin (the iron-rich protein that carries oxygen in your blood) and have had a confirmed diagnosis of blood cell abnormalities
4. Enlarged spleen, causing loss of appetite and belly pain
5. Symptoms, such as fatigue, weight loss and night sweats
6. A poor quality of life
7. Some patients’ MF gets worse over time despite taking ruxolitinib
8. Used to treat patients with MF for around a decade
9. An anticipated downside of ruxolitinib treatment is anemia
10. Shortness of breath and appetite loss

What is the effect of ruxolitinib on the body's tissues and organs?

Proteins known as JAKs send signals that are telling the body to make too many signals, they cause the body to make too many blood cells. Overactive signaling due to ERK proteins can turn on other signaling pathways, leading to better control of the cancer cells and their effects on the body. Rineterkib targets ERKs to help keep the production of p53 from working, so together ruxolitinib and rineterkib can make too much HDM2, which can turn on other signaling pathways.

Which treatments are being studied?

In Part 1 of the ADORE clinical trial, patients will be randomized to one of 5 possible new treatments:

- Ruxolitinib alone
- Ruxolitinib + rineterkib
- Ruxolitinib + siremadlin
- Ruxolitinib + erlotinib
- Ruxolitinib + nilotinib

If you have any questions, please contact:

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Do you have a patient who could participate in ADORE?

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