NOVARTIS

The effects and safety of LMB763 for people with diabetic kidney disease

Thank you!

Thank you to the participants who took part in the clinical trial for diabetic kidney disease. Every participant helped the researchers learn more about **LMB763**, also called nidufexor.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

Trial information

Trial number: CLMB763X2202
Drug studied: LMB763
Sponsor: Novartis

What was the main purpose of this trial?

The main purpose of this trial was to learn if LMB763 lowered signs of kidney damage in people with diabetic kidney disease when taken with standard treatments. This trial was also designed to learn more about the safety of LMB763. To find this out, researchers compared the effects of LMB763 to a placebo.

Diabetic kidney disease is a type of kidney disease caused by diabetes. High sugar and fat in the blood from diabetes can damage the kidneys over time. Damaged kidneys don't work as well to filter waste and extra fluid out of the blood.

LMB763 is a trial drug that may activate a certain protein that helps the kidneys work. Researchers think this may slow down kidney damage.

Placebo – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The main questions this trial was designed to answer:

- Did a sign of kidney damage go down in the participants who took LMB763?
- What medical problems did the participants have during this trial?
  Keeping track of the medical problems helped to learn about the safety of LMB763.

Main results: After 24 weeks, a sign of kidney damage went down more in participants who took LMB763 than those who took the placebo.

The researchers concluded there were no new safety concerns for LMB763.

How long was this trial?

The trial began in December 2018 and ended in May 2021. The total time planned for the participants to be in the trial was about 8 months.

The sponsor decided to end the trial early. The trial sponsor reviewed the data and concluded there was enough data to know if LMB763 had an effect on diabetic kidney disease. The decision to stop was not related to the safety of the trial drug.

Who was in this trial?

83 participants were in this trial – 60 men and 23 women. The participants were 36 to 75 years old. Their average age was 61.

82 participants reported their race as White, and 1 participant reported their race as Black or African American.

Every participant in this trial had diabetic kidney disease due to type 2 diabetes and:

- Did not have other kidney conditions or type 1 diabetes
- Did not have a kidney transplant
- Did not take certain medicines for diabetes

This trial took place in Argentina, Czech Republic, Germany, Jordan, Lebanon, Turkey, and the United States.

Visit **novctrd.com** for more information about:

- Who could and could not be in this trial
- Which medicines they could or could not take
- Reasons why the participants did not complete the trial

Use trial number **CLMB763X2202** to find the scientific summary.

What trial treatments did the participants take?

A computer program was used to randomly assign one of these treatments to each participant:

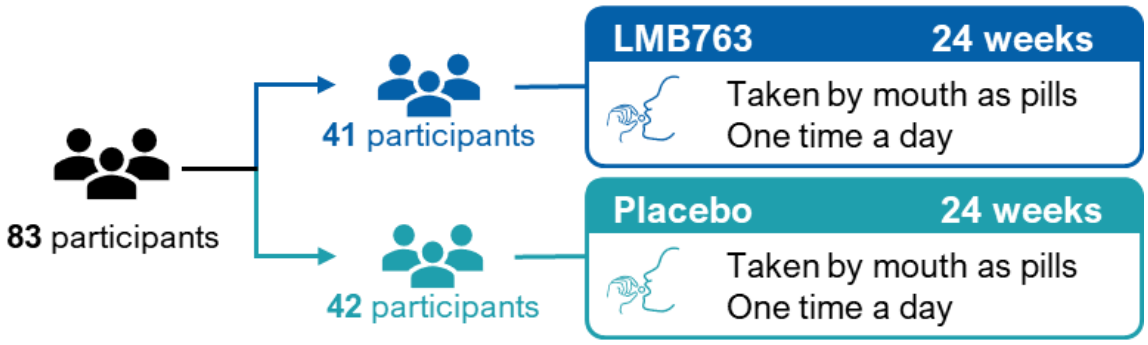
- **LMB763** – 50 milligrams (mg) by mouth as pills for 24 weeks
- **Placebo** – looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

All participants continued taking certain medicines for kidney disease.

Using a computer program to assign the treatments helped make sure the team compared the results as fairly as possible.

The participants and trial staff did not know what treatment each participant took during the trial. Some trials are done this way because knowing what treatment participants take can influence the results. Not knowing what treatment participants take helps make sure the results are looked at fairly.

The graphic below shows how many participants were assigned each treatment.



What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results.

Always talk to a doctor before making any changes to your health care.

Did a sign of kidney damage go down in the participants who took LMB763?

Yes, after 24 weeks, a sign of kidney damage went down more in participants who took LMB763 than those who took the placebo.

The trial doctors looked at signs of kidney damage using these 2 types of urine tests that measure levels of albumin:

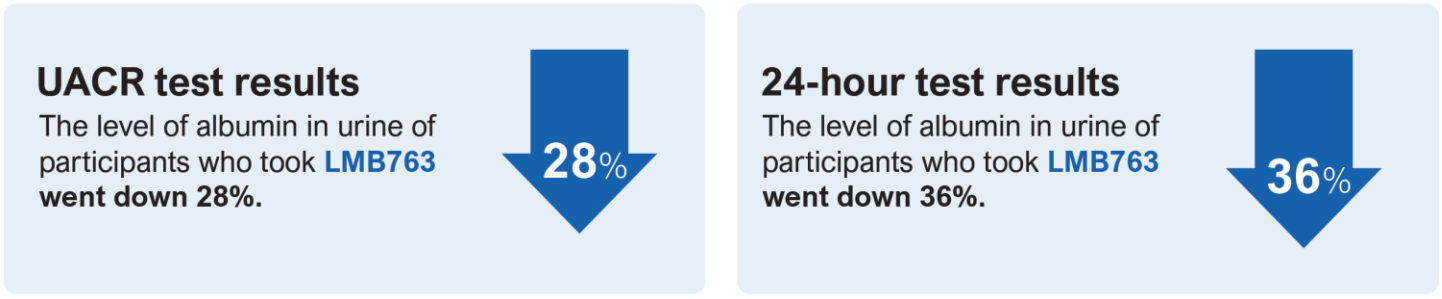
- The **urine albumin-creatinine ratio (UACR) test** compares the level of albumin in urine to the level of creatinine. Creatinine is a waste product healthy kidneys filter from the blood into urine.
- The **24-hour urinary albumin test** measures albumin in all urine collected over 24 hours.

Why measure albumin?
Albumin is the main protein in the blood. Very little albumin is normally found in urine.
A high level of albumin in urine is a sign of kidney damage.

On average, the researchers found that the level of albumin in the urine went down after taking LMB763 for 24 weeks. A **lower** level of albumin in urine is a sign that kidney damage is **slowing down**.

Did the level of albumin in urine go down?

The results below show the average change of albumin levels in the urine after 24 weeks. Results were adjusted for those who took the placebo.



A **lower** level of albumin in urine is a sign that kidney damage is **slowing down.**

What other results were learned?

Did LMB763 affect the participants' eGFR?

Estimated glomerular filtration rate, eGFR, is a blood test that shows how well the kidneys work to filter waste from the blood. A lower eGFR test result can be a sign of kidney damage. The trial staff measured the participants' eGFR many times during treatment.

When the researchers compared the eGFR results between the 2 groups after 24 weeks of treatment, they found there was no meaningful change. The researchers concluded that 24 weeks of treatment was too short of a timeframe to determine if LMB763 had an effect on eGFR.

Did LMB763 affect how well the kidneys controlled the level of water in the blood?

The trial staff compared the level of water in participants' urine to the level in their blood. If the water level in the blood is too high or too low, it means the kidneys aren't working well to control it. This is a sign of kidney damage.

When the researchers compared the level of water in the blood between the 2 groups, they found there was no meaningful change after 24 weeks.

Did LMB763 affect common measures of body weight and fat?

The trial staff took many body weight and fat measures related to type 2 diabetes, including:

- Body weight
- BMI – a health measure based on height and weight
- Waist size to hip size
- The levels of fats in the blood after the participants had not eaten for at least 6 hours.

When the researchers compared these measures of body weight and fat between the 2 groups, they found there was no meaningful change after 24 weeks.

What medical problems did the participants have during this trial?

Medical problems that happen during trials are called “adverse events”. Trial doctors looked for any adverse events during the visits to the trial site. The participants also reported adverse events.

Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they think the adverse events are not related to the trial treatments.

An adverse event is:

- Any **unwanted sign or symptom** that the participants have during a trial.
- Considered **serious** when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death

Adverse events **may** or **may not** be caused by treatments in the trial.

The adverse events in this section include those that happened during treatment and up to 1 month after treatment.

More than half of the participants reported adverse events (51 out of 83 participants). 4 participants reported adverse events that were considered serious. The most common adverse event was itchy skin. The researchers concluded there were no new safety concerns for LMB763.

What serious adverse events did the participants have?

2 of the 41 participants, or 5%, who took **LMB763** reported a total of 4 serious adverse events:

- **Bacterial skin infection** | erysipelas
- **Eczema** | dermatitis atopic
- **High blood sugar** | hyperglycemia
- **Kidneys suddenly stopped working as well** | acute kidney injury

2 of the 42 participants, or 5%, who took the **Placebo** reported 2 serious adverse events:

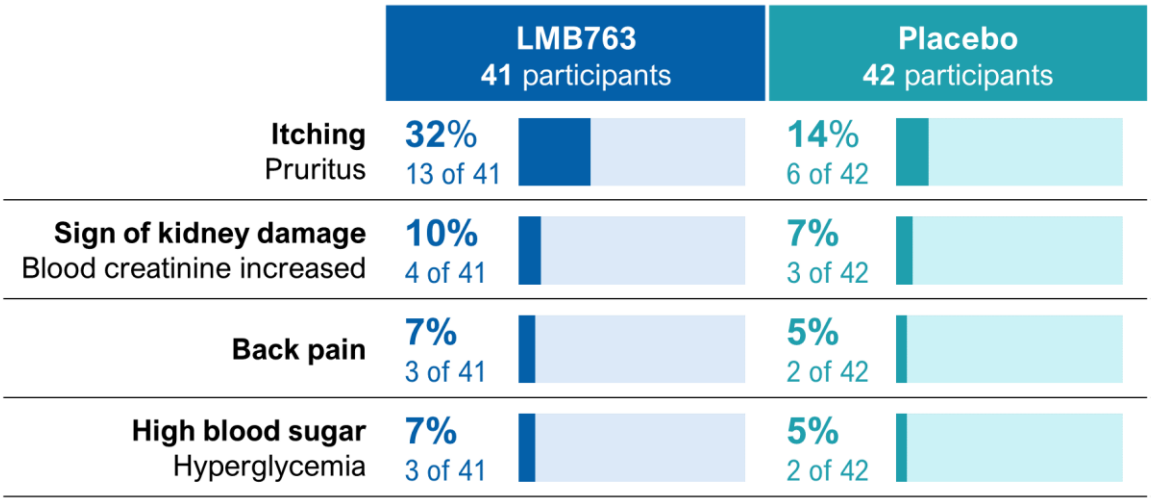
- **Mass or growth on kidney** | renal disorder
- **Too much fluid in the body** | hypervolemia

No other serious adverse events were reported, including no deaths.

What other adverse events did the participants have?

- **LMB763:** 28 of the 41 participants, or 71%, reported adverse events.
- **Placebo:** 23 of the 42 participants, or 60%, reported adverse events.

The table below shows the adverse events that happened in **5 or more participants.** Other adverse events were reported by fewer participants.



What was learned from this trial?

The researchers concluded that LMB763 lowered the participants' level of albumin in urine compared to placebo. The researchers also found that LMB763 did not have an effect on other signs of kidney damage, like eGFR and level of water in blood. More research is needed to know if LMB763 affects eGFR. LMB763 also did not have an effect on common measures of body weight and fat. The researchers found no new safety concerns for LMB763.

These are the results of a single trial. Other trials may have different results. This was one of many trials a drug goes through. This type of trial helped researchers learn about the safety of a trial drug in a small number of participants.

Where can I learn more about this and future trials?

For more information about this trial go to any of the following websites:

- **novctrd.com** – search using the study number **CLMB763X2202**
- **clinicaltrials.gov** – search using the number **NCT03804879**
- **clinicaltrialsregister.eu/ctr-search** – search using the number **2018-002491-40**

If more trials are planned, they will appear on the public websites above. When there, search for **LMB763, nidufexor, or diabetic nephropathy.**

Full trial title:
A randomized patient-and-physician blinded, placebo-controlled, 24-week study to assess the safety, tolerability and efficacy of LMB763 in patients with diabetic nephropathy

? If you participated in the trial and have **questions** about the results, please speak with the trial doctors or staff at your trial site.

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