

In patients with progressive familial intrahepatic cholestasis (PFIC)...

FINDINGS OVER TIME: RESULTS FROM A LIVMARLI STUDY

What MARCH-PFIC and MARCH-ON tell us about patients treated with LIVMARLI for up to 2 years

How LIVMARLI was studied

In a 6-month clinical study called MARCH-PFIC, 93 patients with PFIC were treated with either LIVMARLI or placebo.* The purpose of the study was to find out if LIVMARLI helped reduce levels of cholestatic pruritus (itch) and bile acids in the blood (known as serum bile acids, or sBA).† After 6 months, patients had the option to enter a long-term follow-up study (called MARCH-ON).

The study assessed changes in:



Cholestatic pruritus



Serum bile acids (sBA)



Growth (height and weight)



Bilirubin levels



Liver enzymes (ALT and AST)

Patients in the MARCH studies were split into multiple cohorts, or groups‡:

PFIC2 Group

Only included patients with PFIC2§

All-PFIC Group

Included patients with PFIC2, as well as patients with PFIC1, PFIC3, PFIC4, or PFIC6¶

During the first 6 months of treatment:

57%

of patients who took LIVMARLI experienced an improvement in cholestatic pruritus vs 27% of those who took placebo (8 of 14 vs 4 of 15 patients)

45%

of patients who took LIVMARLI had reductions in sBA vs 7% of those who took placebo (5 of 11 vs 1 of 15 patients)

64%

of patients who took LIVMARLI experienced an improvement in cholestatic pruritus vs 29% of those who took placebo (21 of 33 vs 8 of 28 patients)

50%

of patients who took LIVMARLI had reductions in sBA vs 7% of those who took placebo (15 of 30 vs 2 of 28 patients)

Improvements were maintained through 2 years in patients who remained on treatment in the long-term MARCH-ON study

The most commonly reported side effects were gastrointestinal (GI) events like diarrhea and stomach pain. Other common side effects included fat-soluble vitamin (FSV) deficiency, liver test abnormalities, bone fractures, and rectal bleeding.

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

*The MARCH-PFIC study was a multicenter, double-blind study, meaning the study was run in many locations and patients and doctors were not aware which patients received LIVMARLI and which received placebo. After 26 weeks, patients who chose to remain on treatment only took LIVMARLI. Placebo looked and tasted like a "real" treatment but did not have any active medicine.

†Improvements in cholestatic pruritus defined as a reduction in Itch Reported Outcome (ItchRO) score of 1 or more. ItchRO is a tool designed to measure itch severity over time based on a 5-point scale. Reduction in sBA level was defined as having an average (at Weeks 18, 22, and 26) of less than 102 µmol/L or an average decrease of 75% or more from the start of treatment.

‡Other patients with less common or more variable forms of PFIC were also studied.

§The PFIC2 group included 31 patients; 14 received LIVMARLI, 17 received placebo.

¶The All-PFIC group included 64 patients; 33 received LIVMARLI, 31 received placebo.

INDICATION

LIVMARLI (maralixibat) oral solution and tablets are a prescription medicine used to treat cholestatic pruritus (itch) in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

LIVMARLI is not for use in PFIC type 2 patients who have a severe defect in the bile salt export pump (BSEP) protein.

It is not known if LIVMARLI is safe and effective in children with PFIC who are under 12 months of age. It is not known if LIVMARLI is safe and effective in adults who are 65 years of age and older.

Please see additional Important Safety Information for LIVMARLI throughout and full Prescribing Information, including Patient Information and Instructions for Use.

IMPORTANT SAFETY INFORMATION

What are the possible side effects of LIVMARLI (maralixibat) oral solution and tablets?

LIVMARLI can cause serious side effects, including:

- **Liver injury.** Changes in certain liver tests are common in patients with PFIC but may worsen during treatment. These changes may be a sign of liver injury and can be serious or may lead to liver transplant or death.

 **Livmarli**[®]
(maralixibat) oral solution or tablets

What study data tell us about additional benefits over time

Studies also looked at whether reducing cholestatic pruritus with LIVMARLI led to other improvements beyond the itch. What they found was that patients whose cholestatic pruritus improved with LIVMARLI also saw improvements in the level of bilirubin in their blood, as well as improvements in their growth.

The importance of bilirubin



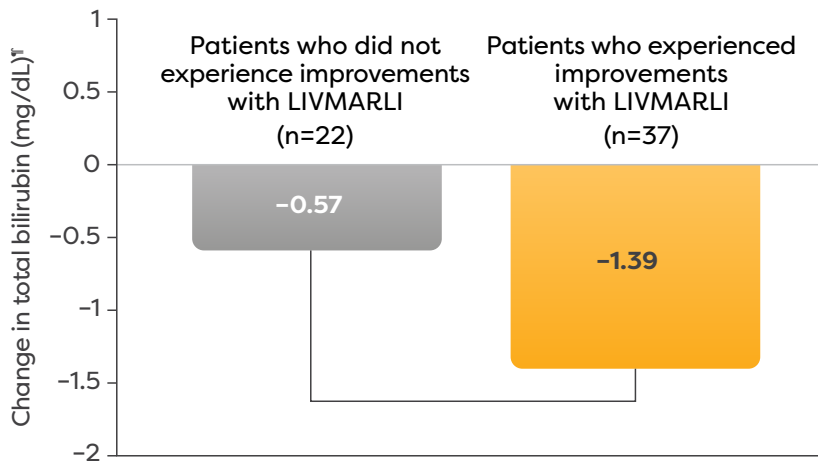
Bilirubin forms when your body breaks down red blood cells and they're removed from the liver in bile. If bile is not flowing properly, bilirubin can build up in the blood.



Doctors can check bilirubin levels to detect, monitor, and understand liver injury or disease.

Changes in total bilirubin levels with LIVMARLI

Change in bilirubin from start of study[†]



Those who saw improvements in cholestatic pruritus with LIVMARLI also had more than twice the reduction in bilirubin compared with those who did not, on average.

[†]Based on average total bilirubin value at Weeks 18, 22, and 26.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of LIVMARLI (maralixibat) oral solution and tablets?

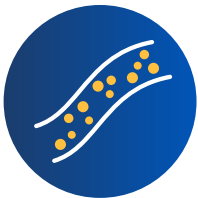
Your health care provider should do blood tests and physical exams before starting and during treatment with LIVMARLI to check your liver function. Tell your health care provider right away if you get any signs or symptoms of liver problems, including:

- nausea or vomiting
- your skin or the white part of your eye turns yellow
- dark or brown urine
- pain on the right side of your stomach (abdomen)
- fullness, bloating, or fluid in your stomach area (ascites)
- loss of appetite
- bleeding or bruising more easily than normal, including vomiting blood

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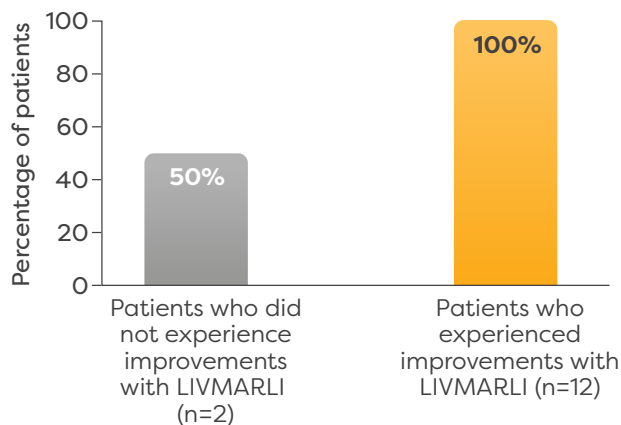
Maintenance of normal bilirubin levels and changes in high bilirubin levels over time



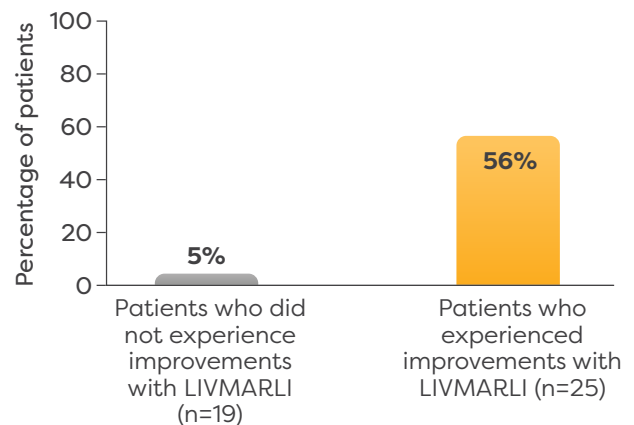
Among patients who saw improvements in itch with LIVMARLI, **all who started with normal total bilirubin levels kept those levels normal after 26 weeks.** In comparison, half of the patients who did not have improvements in itch saw their bilirubin stay within normal levels.^{#**}

About half of patients who saw improvements in itch with LIVMARLI also saw their high total bilirubin levels return to normal after 26 weeks. Among patients who did not see improvements in itch, only 5% had normal total bilirubin levels after 26 weeks.^{#**}

Patients with normal bilirubin levels that stayed normal throughout the study**



Patients with high bilirubin levels that became normal with LIVMARLI treatment**



[#]Based on average total bilirubin value at Weeks 18, 22, and 26.

^{**}Normal bilirubin defined as ≤ 1.2 mg/dL and high bilirubin defined as > 1.2 mg/dL as measured by a blood test.

IMPORTANT SAFETY INFORMATION (cont'd)

What are the possible side effects of LIVMARLI (maralixibat) oral solution and tablets?

- **Stomach and intestinal (gastrointestinal) problems.** LIVMARLI can cause stomach and intestinal problems, including diarrhea and stomach pain during treatment. Diarrhea can also cause the loss of too much body fluid (severe dehydration). Your health care provider may advise you to monitor for new or worsening stomach problems, including stomach pain, diarrhea, blood in your stool, or vomiting

Tell your health care provider right away if you have any new or worsening signs or symptoms of stomach and intestinal problems, including:

- diarrhea
- more frequent bowel movements than usual
- stools that are black, tarry, or sticky, or have blood or mucous
- severe stomach-area pain or tenderness
- vomiting
- urinating less often than usual
- dizziness
- headache

- A condition called **Fat-Soluble Vitamin (FSV) Deficiency caused by low levels of certain vitamins (vitamin A, D, E, and K) stored in body fat.** FSV deficiency is common in patients with PFIC but may worsen during treatment. Your health care provider should do blood tests before starting and during treatment, and may monitor for bone fractures and bleeding, which are common side effects

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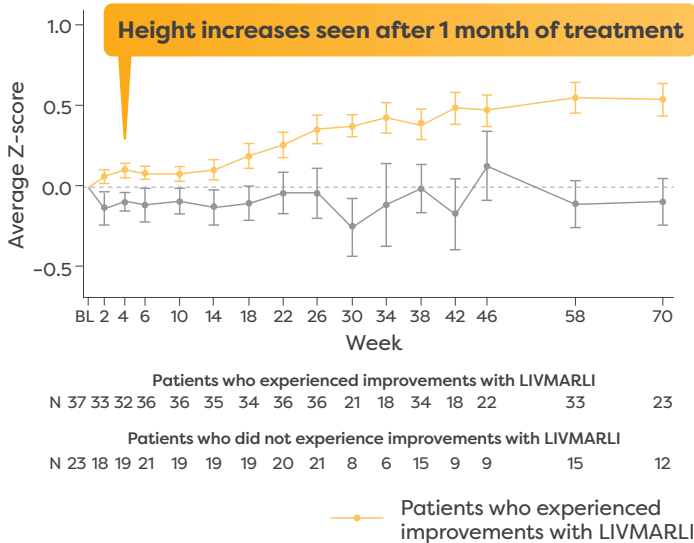
How LIVMARLI affected height and weight

Results from MARCH-PFIC and MARCH-ON showed that patients who experienced improvements in cholestatic pruritus **were also more likely to grow in height and gain weight over time.**

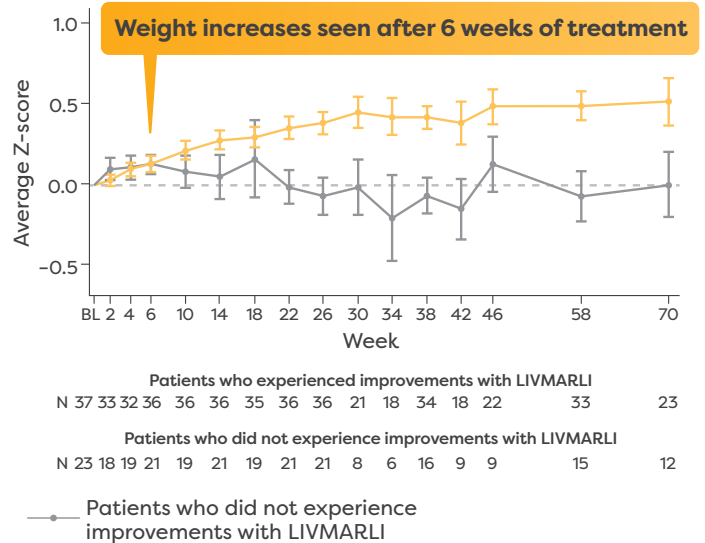
Height and weight were measured as a **Z-score**, which shows how someone compares with **the average** for their age and sex.

Changes in growth (height and weight)

Change in height from start of study^{††}



Change in weight from start of study^{††}



^{††}Changes reported from the All-PFIC group.

Patients with PFIC who felt cholestatic pruritus relief with LIVMARLI started growing taller in just 1 month and gaining weight in 6 weeks. Improvements in height and weight continued for more than a year.

Discover more about LIVMARLI at LIVMARLI.com

IMPORTANT SAFETY INFORMATION (cont'd)

Tell your health care provider about all medicines that you take, as LIVMARLI may interact with other medicines. If you take a medicine that lowers cholesterol by binding bile acids, such as cholestyramine, colestevlam, or colestipol, take LIVMARLI at least 4 hours before or 4 hours after you take that medicine.

Your health care provider may change your dose, or temporarily or permanently stop treatment with LIVMARLI if you have certain side effects.

LIVMARLI is available in oral solution and tablet formulations. Take LIVMARLI exactly as your health care provider tells you to and do not change your dose unless you are instructed to. In patients with PFIC, LIVMARLI is taken by mouth, 2 times each day, 30 minutes before a meal. For the oral solution, be sure to use the provided oral dosing dispenser to accurately measure the dose of medicine.

These are not all of the possible side effects of LIVMARLI. For more information, ask your health care provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

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