CLINICAL STUDY RESULTS

A rollover study to learn about the effects of palovarotene in people older than 14 years of age with fibrodysplasia ossificans progressiva (FOP) who have completed certain previous studies of palovarotene

Overall in this study, the results suggest that palovarotene was generally safe in treating participants with fibrodysplasia ossificans progressiva (FOP).
The results shown in this summary represent one clinical study. Other clinical studies may produce different results.

This lay summary was created by Ipsen with the assistance of a third-party writing service provider

CLIN-60120-452
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What was the study about?

The purpose of this study was to learn about the effects of palovarotene in adolescents and adults with fibrodysplasia ossificans progressiva (FOP).

FOP is a very rare genetic condition where soft tissues, like muscles and ligaments, are replaced by bone. People with FOP can experience flare-ups, which often lead to the formation of a lot of new bones in the soft tissues. This new bone can cause mobility loss when formed in areas of the body where it did not previously exist. Palovarotene has been developed to treat FOP. It works by blocking certain chemical signals that cause bone formation.

The effects of palovarotene were looked at in previous studies. This current study aimed to learn more about palovarotene's effects. The study also aimed to provide palovarotene to participants benefiting from treatment as per the physician's judgement until the drug became available or reimbursed in their country.

The aim of this study was to learn more about the effects of palovarotene in adolescents and adults with FOP.

The study took place between March 2022 and November 2024 at 13 study sites in 10 countries.

Who took part in this study?

59	31	28	22 YEARS
PARTICIPANTS	MEN	WOMEN	AVERAGE AGE

To take part in the study, participants had to:

- be aged at least 14 years,
- have participated and completed certain previous studies with palovarotene (Study PVO-1A-301 or Study PVO-1A-202/ PVO-1A-204),
- have consented to continue participation in this study and agreed to take measures to prevent pregnancy.

Participants could not take part in the study if:

- they had history of allergy or sensitivity to palovarotene and certain other drugs, or were unresponsive to prior treatment with palovarotene,
- they had health conditions such as allergy to retinoids, gelatine or did not respond to palovarotene treatment, or had received treatments that could affect their ability to take the study treatment.

What treatments were used in this study?

Palovarotene capsules were given by mouth with the following dose and timings

Chronic treatment
5 mg daily
(chronic treatment only during periods of no flare-ups)

Flare-up treatment
20 mg daily for 1 month followed by 10 mg daily for 2 months*
(treatment was continued for 3 months even if the symptoms resolved earlier)

Persistent flare-up treatment
Continued use of 10 mg once daily for a month following flare-up treatment

Intercurrent flare-up (new flare-up location or marked worsening of original flare-up) treatment
Restarted flare-up treatment for 3 months

*The flare-up treatment began at the start of the first symptom indicating a FOP flare-up or an event likely to lead to a flare-up.

This study had 3 types of visits:
Inclusion visit (Day 1): The study doctor checked if participants were eligible to take part in this study. This visit could correspond to the last visit in the previous study.

Treatment period visits:
Eligible participants were given a supply of palovarotene at each follow-up visit, every 6 months. Participants took palovarotene once every day, during this study.

- If a participant entered the study whilst having a flare-up, they continued and completed their flare-up treatment as planned in the previous study.

During the treatment period, participants completed follow-up visits. The visits could be completed at the study site, or remotely by video or phone call. Participants continued these follow-up visits until the study ended or until the participant left the study for any reason. The researchers monitored the health of the study participants during these visits.

This study was “open-label”. This means that the researchers and the participants knew what type and dosage of treatment was given to each participant.

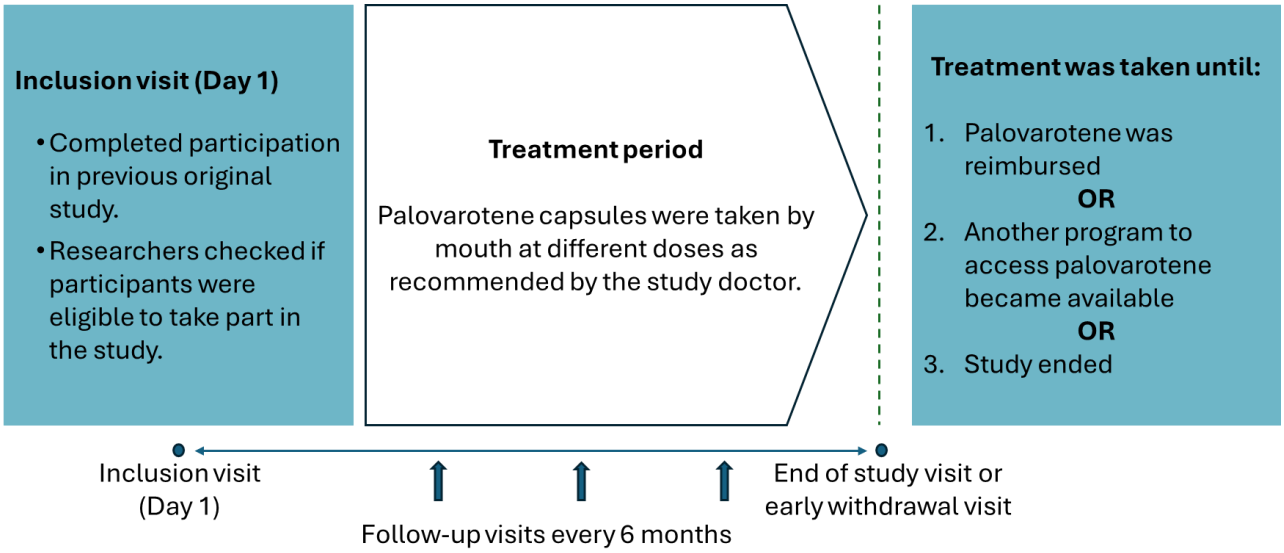
Since palovarotene was an investigational treatment, the participants continued the treatment until:

- it was reimbursed by a payer in their country,
- another program allowing access to palovarotene became available, or
- the study ended in November 2024.

Each participant could be in the study until November 2024 at the latest.

End of Study or Early Withdrawal visit:
Participants were asked to have an end of study visit when the study ended, or an early withdrawal visit if they left the study early. These visits could be an in-clinic visit or performed remotely. The participant’s health was monitored at this visit.

Participants were followed-up in-clinic or remotely for safety for 1 month after the last dose of palovarotene was received. If a participant stopped receiving palovarotene due to a safety concern, the participant was monitored for safety until the medical event was over or under control.



What researchers found out in the study?

No new safety findings were reported in this study.

What was learned about the safety of palovarotene in adolescents and adults with FOP?

During the study, participants were asked to report any 'adverse events', that is, if they felt unwell, had any kind of medical event, or noticed anything different about their bodies or health. Researchers recorded all adverse events reported by participants, whatever the cause.

The main purpose of this study was to analyse all 'adverse events' reported by participants. These adverse events included both serious and non-serious medical events, even those not related to the study drug. The full results of this study can be viewed on ClinicalTrials.gov and Clinicaltrialsregister.eu/ctr-search/search.

This lay summary also reports side effects. If the study doctor thinks an adverse event may be related to the study treatment, it is called a 'side effect'. A side effect is considered 'serious' when it is life-threatening, causes lasting problems, leads to hospitalisation, or is considered serious by the investigator. The side effects are reported in the following section of this summary – "How did the treatment make participants feel?".

What were the other findings in the study?

What was the efficacy of palovarotene on the movement of various joints in participants with FOP during the study?

Efficacy is a term used to describe how well a treatment works in a clinical study.

Researchers used the Cumulative Analogue Joint Involvement Scale (CAJIS), which is used to assess joint mobility in participants with FOP.

The results showed a slight increase in CAJIS score over the entire treatment period, which means there was a slight decrease in participants' mobility.

How did the treatment make participants feel?

- Adverse events that are life-threatening, cause lasting health problems or require an individual to go to the hospital are considered serious.
- 2% (1 out of 59) of participants in this study experienced a serious side effect.
- 2 participants died during the study.

Overall, 66% (39 out of 59) of participants experienced a side effect.

2% (1 out of 59) of participants stopped taking study treatment because of 2 side effects:

- abnormally dry skin that may affect the protective linings of the body (such as the mouth and eyes) and
- red and itchy skin.

2% (1 out of 59) of participants in this study experienced a serious side effect of slow bone healing after a bone fracture.

2 participants died in this study. Neither of these deaths were due to side effects.

The most commonly reported side effects that were reported by 5% or more of the participants are shown below.

Side Effects	All participants (59 Participants)
Any side effects	**66% (39 out of 59)** 
Dry skin	22% (13 out of 59) 
Allergic reaction	8% (5 out of 59) 
Flaky skin	7% (4 out of 59) 
Itching	7% (4 out of 59) 
Reddening of the skin	7% (4 out of 59) 
Dry lips	5% (3 out of 59) 
Injury to the outermost layer of the skin	5% (3 out of 59) 
Medical condition related to skin	5% (3 out of 59) 
Rash	5% (3 out of 59) 

More information

To learn more about this study, please visit:

- ClinicalTrials.gov and search for study NCT05027802 or
- Clinicaltrialsregister.eu/ctr-search/search and search for study 2021-002244-70

For more information about current treatments available, please speak to your healthcare provider. If you have any questions about this study, please contact the sponsor, Ipsen at:

clinical.trials@ipsen.com

Future research

There is future research planned on this topic.

Study identification and other information

FULL STUDY TITLE: Rollover study; multicentre, phase III, open-label study to further evaluate the safety and efficacy of palovarotene capsules in male and female participants aged ≥14 years with fibrodysplasia ossificans progressiva (FOP) who have completed study PVO-1A-301 or PVO-1A-202/PVO-1A-204 and may benefit from palovarotene therapy

STUDY NUMBERS: Europe: 2021-002244-70 | United States: NCT05027802

PROTOCOL: CLIN-60120-452

OTHER INFORMATION: Phase III studies can take several months to years to complete. Analysis of the study results will show how safe and/or efficacious a study treatment was during the study.

We thank all the volunteers who took part in this study. Without their support, advances in treatments for FOP would not be possible.

We would also like to thank the people who took the time to review this document to make it easier for a general audience to read.