Regeneron Announces Positive Results from Phase 3 Optima Trial

An Update on the Regeneron Trial

By Dr Andrew Rankin, Trustee

On Wednesday 17 September 20205, Regeneron announced very positive results from their Phase 3 pivotal clinical trial in adults 18 and over with FOP. The trial tested two doses of garetosmab, 3 and 10 mg, versus a placebo via four-weekly intravenous infusions, for 56 weeks. The garestosmab demonstrated up to 99% reduction of abnormal bone formation compared with the placebo.

The trial has shown that garetosmab is the first and only experimental therapy to bring a drastic reduction in both the number and volume of abnormal bone formation (heterotopic ossification) in people living with FOP.

A pivotal trial is required by regulatory agencies such as the US Food and Drug Administration and the UK MHRA in order to approve a drug for marketing approval and for it to be allowed to be used in that country.

You can read the full press release here: https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-announces-positive-phase-3-trial-adults-ultra-rare

In summary, the key points:

- ✓ Both doses of garetosmab have proven to be highly effective in reducing the number of new bone lesions by greater than 90% compared to placebo.
- ✓ It has achieved a reduction of more than 99% of the total volume of new bone injuries.
- ✓ The increased dose of 10 mg/kg has also reduced painful flare-ups by 89%.
- ✓ The impact is such that the Independent Data Monitoring Committee has recommended that patients who were treated with placebo switch to garetosmab as soon as possible to obtain benefit.

Professor Richard Keen, who we know well from the Royal National Orthopaedic Hospital, stated that this trial results clearly illustrate the potential of garetosmab to alter the disease, reduce new lesions and notably is the first, and only investigational therapy to demonstrate a dramatic reduction in both the number and volume of abnormal bone lesions.

So, what was that dramatic reduction? Well, we're talking about 90 % or more reduction in bone formation however you measure it – number of new bone lesions, or volume of new bone. Importantly, secondary endpoint of flare-ups were also reduced up to 89% on the higher dose of garetosmab.

It will be interesting to see whether regulatory agencies will approve use for the lower or higher dose, because the higher dose has more effect in terms of the flare-ups, very similar in terms of bone formation, but it also has an increase in the adverse event of skin and soft tissue infections.

The skin and soft tissue infections, which are not generally serious, have been known from the previous studies with garetosmab; as has the epistaxis (which are nosebleeds); but there were no dose-dependent effects in this study of this other relatively minor epistaxis adverse event so it'll be interesting to see what dose gets approved. While I'm fairly confident that the drug will be approved in adults from the small amount of data so far presented by Regeneron, we must be cautious that Regeneron have only posted the highlights and we haven't seen all of the data that the regulatory agencies will review. So, it's only a matter of probability at the moment and not certainty that the drug will be approved.

The submission of the regulatory application for marketing authorisation of garetosmab for the treatment of FOP to the FDA is scheduled for the end of 2025, while global applications are scheduled for 2026. Garetosmab has rapid approval designation in the US and EU so, if approved, this could happen as quickly

as 6 months in those jurisdictions. We hope that the UK regulatory agency MHRA will piggyback on those applications to make available for adults with FOP in the UK as soon as possible in 2026/7.

The start of a critical Phase 3 study on garetosmab in adolescents and children with FOP, called OPTIMA 2 is also planned for 2026. This is paramount as we all realise that early intervention in children is critical to avoid the severe progressive impact of FOP from a young age. The success of garetosmab in this study marks a significant advancement for the potential treatment of FOP, offering hope to people affected by this difficult disease, both patients and, carers and families.

While regulatory approval is not assured, remembering the agencies will see full data that has not yet been released, we remain hopeful for a positive outcome within the next year.

We would like to thank everyone who contributed to this process, from researchers and doctors to patients and families who participated in the study, and the persistence and skill of the medical scientists at Regeneron and other companies around the globe.

These results are very exciting for us as a community, give a lot of hope as the first really active potential medicine for treating patients with FOP.

Let’s hope for favourable regulatory reviews, approval for marketing and an early paediatric clinical trial that also recruits in the UK.

Dr Andrew Rankin

FOP Friends Trustee

With thanks also to FOP Italia for part of the summary

Scan QR-code to read the full Regeneron Press Release: