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Siga's Mpox Pill Fails In Academic Trial

by Elizabeth Cairns

The commercial implications of the miss are hard to call, but separate trials could offer hope.

The World Health Organization (WHO) having this week declared mpox a public health emergency, now is not the time for a trial failure. Unfortunately *SIGA Technologies, Inc*'s antiviral TPOXX (tecovirimat) has failed to distinguish itself from placebo in a study conducted by the US National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID), the organization said on 15 August.

The PALM 007 study, conducted in 800 hospitalized clade I mpox patients in the Democratic Republic of the Congo (DRC), aimed to prove a benefit for TPOXX, given orally for two weeks, on the primary endpoint of improvement in time to lesion resolution within 28 days. It was part of a global initiative to address the 2022 mpox outbreak in the DRC; the country is also the main locus of the current surge, with more than 15,600 cases and 537 deaths so far this year.

Key Takeaways

- A NIAID-sponsored trial of Siga's TPOXX showed that the antiviral failed to speed healing from the virus.
- The product is already approved for mpox in the EU and the UK.
- Further trials with different designs are ongoing.

No such benefit occurred. Siga said that patients in the placebo arm had much more favorable outcomes than those in the observational studies from the DRC that were used to

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plan PALM 007. The NIAID pointed out that the study's 1.7% overall mortality among enrollees, regardless of whether they received the drug or not, was much lower than the mpox mortality rate of 3.6% or higher reported among all cases in the DRC, suggesting that the care the patients received in hospital had a major effect.

Further Studies

A minor plus is that what Siga call a "meaningful improvement" was seen with the drug in patients whose symptoms began less than a week before randomization, and in those with severe or greater disease, which WHO defines as 100 or more skin lesions. Siga believes this is reason enough to start further trials in similar patients. Safety was also good.

But the study's overall miss is disappointing, not least because TPOXX is already used for mpox. It is authorized in the EU and the UK for the treatment of mpox, smallpox, cowpox and vaccinia complications. In the US and Canada it is approved solely to treat smallpox, a virus that no longer naturally occurs, but which does still exist in a handful of lab facilities. Tecovirimat targets and inhibits the activity of the orthopoxvirus VP37 protein which is highly conserved in all members of the orthopoxvirus genus.

The PALM 007 study was not intended to gain US approval for TPOXX for mpox treatment.

Monkeypox: Siga Says FDA Hasn't Indicated Emergency Use Authorization An Option for Tpoxx

By Sarah Karlin-Smith

05 Aug 2022

Siga CSO Dennis Hruby talked with the *Pink Sheet* about the company's plans for development of Tpoxx for monkeypox in the US. If the necessary emergency declaration is made that would let FDA issue EUAs, the company would likely try to apply with its current clinical trial-less data set.

Read the full article here

Other mpox studies are underway. Four randomized clinical trials are currently enrolling patients: STOMP in the US and other countries; UNITY in Switzerland, Brazil and Argentina; Platinum-CAN in Canada; and EPOXI in the EU. Siga says that the designs of these trials differ from that of PALM 007 – for example, to date the other four trials have enrolled no children and a much higher percentage of immunocompromised patients, such as those living with HIV.

How much the trial failure might hurt TPOXX's sales is unclear; the company is private and does not disclose detailed product-level sales; neither do equity analysts cover it. In the first six months of 2024 Siga said it had product revenues of $45m, which included oral TPOXX deliveries to the US Strategic National Stockpile and the US Department of Defense, none of which would be intended for mpox.

The sales figure also includes shipments of TPOXX pills to “eleven international customers”, which might include mpox sales.