Oleogel-S10 (Birch Triterpenes)

BACKGROUNDER

At Amryt Pharma, we strive to transform the lives of people with rare, debilitating conditions, such as Epidermolysis Bullosa (EB), and those who care for them. Oleogel-S10 (Birch Triterpenes) previously AP101 is Amryt's lead development candidate, a potential treatment for wounds associated with EB, a rare and distressing genetic skin disorder affecting young children and adults for which there is currently no approved treatment available. Oleogel-S10 is currently in a Phase 3 clinical trial (EASE trial) and in October 2020 positive topline data was presented at the European Association of Dermatology and Venerology (EADV Virtual 2020).

- Primary endpoint met– patients treated with Oleogel-S10 experienced an increase in speed of wound healing when compared with the control group (p=0.013)
- Oleogel-S10 demonstrated a good safety profile and was well tolerated

Oleogel-S10, a topical therapeutic gel, has the potential to be the first treatment approved for EB.

What is Oleogel-S10?

- Oleogel-S10 is an innovative topical wound treatment
- It is a sterile gel that is applied to the skin and is formulated to contain two ingredients, birch triterpenes derived from birch bark (10 percent) and sunflower oil (90 percent).
- Filsuvez® has been selected as the brand name for the product. Amryt does not have regulatory approval for Filsuvez® to treat EB. The product has been granted Rare Pediatric Disease Designation and has also received a Fast Track Designation from the U.S. Food and Drug Administration.

How Oleogel-S10 works

Oleogel-S10 accelerates wound closure by exerting effects on different wound healing phases. In vitro and ex-vivo tests showed that birch triterpenes modulate immune inflammatory mediators, key players in the inflammation phase in wound healing. Formation of a new skin barrier involves the proliferation, migration, and adhesion, of new skin cells (keratinocytes) to make up the outer layer of the skin – the epidermis. Birch triterpenes support the differentiation of these cells, thereby promoting wound healing.

How Oleogel-S10 is used

A generous layer of gel is applied to the wound surface and covered by a sterile non-adhesive wound dressing or, applied to the dressing so that the gel is in direct contact with the wound. The gel should be reapplied at each wound dressing change according to the individual's regular routine until the wound is healed.

EASE trial

The EASE trial (NCT03068780) is the largest ever global Phase 3 trial conducted in patients with EB, initiated in 58 sites in 28 countries. It comprises a 3 month double-blind randomised controlled phase followed by a 24 month open-label, single-arm phase.

- Patients with EB target wounds of between 10 and 50cm^2 in size that were present for > 21 days and < 9 months were randomised in the double-blind phase to study treatment in a 1:1 ratio and wound dressings applied according to standard of care.
- 223 patients were enrolled into the trial including 156 pediatric patients. Of those that completed the double-blind phase, 100% entered the open label safety follow up phase.

The primary endpoint of the trial was to compare the efficacy of Oleogel-S10 versus control gel according to the proportion of patients with complete closure of the target wound within 45 days of treatment.

Trial results

The highlights of the EASE study results are presented below. Please see the attached press release for further information.

- The primary endpoint of the trial was met with statistical significance
- The proportion of patients with first complete closure of EB target wound within 45 days was 41.3% in the Oleogel-S10 group and 28.9% in the control group (p value=0.013)
- This translates to a 44% increase in the probability of target wound closure with Oleogel-S10 compared to the control gel
- The proportion of Recessive Dystrophic EB ("RDEB") patients with first complete closure of EB target wound within 45 days was 44.0% in the Oleogel-S10 group and 26.2% in the control group (nominal p value=0.008)
- This translates to a 72% increase in the probability of target wound closure with Oleogel-S10 compared to the control gel in RDEB patients
- A greater reduction in pain associated with dressing changes was observed in the Oleogel-S10 treatment group at each time point compared with the control group. At Day 14, this difference was nominally significant (p value=0.02)
- There was a greater reduction in total body wound burden as measured by EB Disease Activity and Scarring Index ("EBDASI") and total body surface area of EB partial thickness wounds with Oleogel-S10 although the differences were not statistically significant
- Oleogel-S10 had an acceptable safety profile and was well tolerated when compared with the control gel

Regulatory submissions for Oleogel-S10 in EB

- Oleogel-S10 has received a Fast Track Designation from the U.S. Food and Drug Administration.
- Regulatory submissions in the US and the EU are expected to be filed by late Q1 2021
- Oleogel-S10 has received Rare Pediatric Disease Designation from the FDA. This means that if an NDA for Oleogel-S10 is approved, the Company expects to be eligible to apply for a Rare Pediatric Disease Priority Review Voucher that can be used, sold or transferred

- Oleogel-S10 has been granted Orphan Drug status for the treatment of EB in the EU and the US
- Should Oleogel-S10 be granted approval, it should be entitled to Orphan Drug exclusivity for the treatment of EB, extending seven years in the US and ten years in the EU from the date of approval in the respective jurisdictions

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