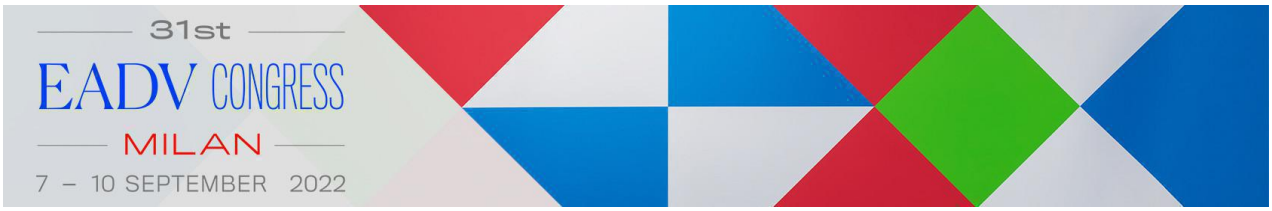

Abstract N°: 512

Title: GEM-3: A Phase 3 Study of Beremagene Geperpavec (B-VEC), an Investigational, Topical Gene Therapy, for the Treatment of Dystrophic Epidermolysis Bullosa (DEB)

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Introduction

Dystrophic epidermolysis bullosa (DEB) is a serious, ultra-rare genetic blistering disease caused by mutations in the *COL7A1* gene, encoding for type VII collagen (COL7) and leading to skin fragility and wounds. Patients with DEB require proactive management and care due to an increased risk of aggressive squamous cell carcinoma and a wide range of serious secondary complications, regardless of wound size or chronicity. A severe unmet need for therapies to treat the underlying cause of DEB remains. Beremagene geperpavec (B-VEC) is an investigational HSV-1-based topical, redosable gene therapy designed to restore functional COL7 protein by delivering the *COL7A1* gene. Here, the efficacy and safety of B-VEC in the phase 3 GEM-3 study for the treatment of DEB is described.

Materials and methods

GEM-3 is a Phase 3, multicenter, double-blind, placebo-controlled, intra-patient-randomized study (NCT04491604) that enrolled patients aged ≥6 months with confirmed *COL7A1* mutations. Each patient contributed 1 primary wound pair, randomized 1:1 to weekly treatment with B-VEC or placebo for 26 weeks (6 months). The B-VEC dose ranged from 4e8 - 1.2e9 PFU/wound determined by baseline wound size. The primary endpoint was complete wound healing at 6 months. Additional endpoints included complete wound healing at 3 months and change in pain associated with wound dressing changes. Complete wound healing was defined as 100% wound closure from exact wound area at baseline, specified as skin re-epithelialization without drainage.

Results

31 patients enrolled (ITT=31) with a mean (±SD) age of 17.2 (±10.7) and range of 1-44 years. At 6 months, B-VEC resulted in 67.4% complete wound healing compared to 21.6% for placebo (absolute difference (95% CI): 45.8% (23.6%-68.0%); $p<0.005$). At 3 months, 70.3% B-VEC treated wounds achieved complete wound healing vs 20.0% of placebo treated wounds (absolute difference (95% CI): 50.3% (28.7%-72.0%); $p<0.005$). Of the total wounds closed at 3 months, 66.7% (14/21) of B-VEC treated wounds were also closed at 6 months, as compared to 33.3% (2/6) for placebo ($p=0.02$). A trend towards decreased pain, consistent with wound healing, was observed in B-VEC treated vs placebo treated wounds. B-VEC was well-tolerated with no drug-related serious adverse events or discontinuations due to treatment.

Discussion

B-VEC treatment demonstrated a durable and significant improvement in complete wound healing at 3 and 6 months compared to placebo and was generally well-tolerated.

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