Trial in Progress: Phase 2a CROSSWALK-c Trial – Crovalimab for Vaso-Occlusive Episodes in SCD

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Trial in Progress: Phase 2a CROSSWALK-c Trial – Crovalimab for Vaso-Occlusive Episodes in SCD

Alexandre Sostelly, PhD7, Pablo Bartolucci, MD, PhD9,10

Background

• Sickle cell disease (SCD) is a group of autosomal recessive red blood cell (RBC) disorders caused by a single point mutation in the β-gene.
• Multiple genotypes of the mutated β-gene may result in SCD, including homozygous inheritance, or heterozygous co-inheritance with other pathogenic variants of the β-gene.
• These point mutations result in the production of hemoglobin S, which polymerizes within RBCs under certain conditions, leading to the distortion of the RBC membrane and generation of dense and sickle RBCs.
• Pathologic RBCs contribute to microvascular occlusions, which present as acute painful episodes called vaso-occlusive episodes (VOE).
• In addition to VOEs, patients with SCD may experience severe chronic anemia, chronic pain, immune dysfunction, and progressive multi-organ damage.
• The current treatment strategy for patients with SCD includes hydroxyurea, along with newer treatments such as L-glutamine, crizanlizumab, and voxelotor.
• However, despite the availability of these treatments, considerable morbidity and mortality among patients with SCD still occur.
• Complement pathway activation occurs in patients with SCD at baseline, during acute pain crisis, and in delayed hemolytic transfusion reaction.
• Accumulating nonclinical data have suggested a multifocal role for complement dysregulation in the pathophysiology of SCD, including vaso-occlusion, hemolysis, inflammation, trombogenicity, endothelial activation, and end-organ damage.
• Crovalimab is a novel anti-complement C5 monoclonal antibody that allows for small-volume subcutaneous self-injection. Crovalimab demonstrated rapid, complete, and sustained complement inhibition and was efficacious and safe in three Phase 3 studies1,2 in patients with paroxysmal nocturnal hemoglobinuria, another complement-mediated disorder.

Methods

• CROSSWALK-c (NCT05075824) is a randomized, double-blind, placebo-controlled, Phase 2a study evaluating the efficacy, safety, pharmacokinetics, and pharmacodynamics of crovalimab as adjunct therapy in preventing VOEs in patients with SCD (Figure 1).

Figure 1: CROSSWALK-c study design

- Patients aged 12 to 55 years old and weighing ≥ 40 kg
- Confirmed diagnosis of HbSS or HbSβ
- 2 to 10 VOEs in the 12 months prior to randomization

Body weight

<table>
<thead>
<tr>
<th>Weight group</th>
<th>Week 1, Day 1: 1000 mg IV</th>
<th>Week 1, Day 2: 2450 mg SC</th>
<th>Weeks 2, 3, and 4: 340 mg SC QW</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.40 kg to &lt; 100 kg</td>
<td>Week 1, Day 1: 1000 mg IV</td>
<td>Week 1, Day 2: 2450 mg SC</td>
<td>Weeks 2, 3, and 4: 340 mg SC QW</td>
</tr>
<tr>
<td>2.00 kg</td>
<td>Week 1, Day 1: 1500 mg IV</td>
<td>Week 1, Day 2: 2450 mg SC</td>
<td>Weeks 2, 3, and 4: 340 mg SC QW</td>
</tr>
</tbody>
</table>

Inclusion and exclusion criteria

- Patients in both study arms will receive standard treatment for SCD as guided by the treating physician and/or institutional protocols.
- Adequate hepatic and renal function
- Patients with a confirmed diagnosis of HbSS or HbSβ
- 2 to 10 VOEs in the 12 months prior to randomization

Table 2: Efficacy endpoints in CROSSWALK-c

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Primary</th>
<th>Secondary</th>
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<tr>
<td>% reduced rate of medical facility VOE</td>
<td>% reduced rate of medical facility VOE</td>
<td>% reduced rate of medical facility VOE</td>
</tr>
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</table>

For additional information

Contact for more information about CROSSWALK-c, please visit https://clinicaltrials.gov/ct2/show/NCT05075824 or Contact: nicoche@roche.com (Study ID: BO2451)

References


Acknowledgements

- The investigators and clinical study sites.
- The study was sponsored by Genentech, Inc.

Disclosures

- Michael U. Callaghan, MD, is a consultant for Genentech, Inc.
- Kenneth I. Ataga, MD, is a consultant for Genentech, Inc. and has stock or stock options in Genentech, Inc.
- Thomas Perlatti is an employee of Genentech, Inc.
- Julia Ramos is an employee of Genentech, Inc.

For more information, please visit https://clinicaltrials.gov/ct2/show/NCT05075824

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