OVERVIEW

The Swiss-based company AB2 Bio is conducting a clinical study in North America (U.S.A. and Canada), and recruiting patients in several regions. The aim of this Phase III study is to assess the efficacy and safety of Tadekinig alfa in patients with monogenic, interleukin-18 driven autoinflammation caused by NLRC4-MAS mutation or XIAP deficiency.

Tadekinig alfa is the drug name for a recombinant human interleukin-18 binding protein (r-hIL-18BP) which is administered by subcutaneous injections of 2 mg/kg every two days.

THERAPY UNDER STUDY

Monogenic disorders caused by NLRC4-MAS mutation and XIAP deficiency are generally associated with high levels of interleukin-18 (IL-18). We believe that treatment with Tadekinig alfa can inhibit the pro-inflammatory cascade triggered by IL-18, and may help to manage the severe symptoms of the disease such as primary hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS). This hypothesis is supported by the successful treatment of a patient carrying a mutation of the NLRC4 gene with Tadekinig alfa (Journal of Allergy and Clinical Immunology, 2017, 139, 1698-1701) and other preclinical and clinical research.

STUDY APPROACH

The NLRC4/XIAP Phase III Study is a multicenter, double-blind, placebo-controlled, randomized withdrawal trial to evaluate safety and efficacy of Tadekinig alfa:

<table>
<thead>
<tr>
<th>Study phase</th>
<th>Time</th>
<th>Study drug</th>
<th>Standard-of-care (SOC)</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>Week 1 Day 1</td>
<td>Tadekinig alfa 2 mg/kg s.c. every 2 days ± 5 h</td>
<td>SOC tapering per SOC treatment over 26 days</td>
<td>- Primary efficacy</td>
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<tr>
<td>Single-Arm Open Label (SAOL)</td>
<td>18 weeks</td>
<td>- Tadekinig alfa</td>
<td></td>
<td>- Secondary efficacy</td>
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<tr>
<td>Randomized withdrawal (RW)</td>
<td>Week 16 Day 126</td>
<td>- Placebo</td>
<td></td>
<td>- Safety</td>
</tr>
<tr>
<td>EOS</td>
<td>Week 26 Day 182</td>
<td></td>
<td>To assess the safety and local tolerability of Tadekinig alfa over the entire duration of the study</td>
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</tbody>
</table>

* Responders (i.e., patients not flaring at end of SAOL) are randomized into RW phase

Eligibility for this study will be determined in an initial screening visit.

The study has an overall duration of approximately 26 weeks: An 18-week single-arm, open-label (SAOL) phase, during which Tadekinig alfa will be administered in addition to the standard-of-care treatment used to control flares, immediately followed by an 8-week randomized-withdrawal (RW) phase to evaluate efficacy and safety. All patients who completed the SAOL phase without experiencing a flare at the end of SAOL will be enrolled in the RW phase, where they will be randomized to either Tadekinig alfa or placebo (IMP).

All study-related treatments and assessments are performed by one of the qualified study centers listed overleaf. Patients will visit the study center for the initial screening and baseline measurements, then for weekly or monthly assessments. For patients released from hospital, the IMP can be administered at the study center or by a home-care nurse at the patient’s home. These services are offered as part of the study.
PATIENTS ELIGIBLE FOR TREATMENT

Key inclusion criteria for this study are:

- Patients ≤ 17 years of age
- Patients with genetic diagnosis of NLRC4-MAS mutation or XIAP deficiency (caused by BIRC4 gene mutation)
- A history of ongoing inflammation with ferritin ≥ 500 ng/mL OR persistent C-reactive protein (CRP) elevation ≥ 2 times the upper limit of normal (ULN), AND

For more information about inclusion/ exclusion criteria, please go to ClinicalTrials.gov (NCT03113760).

HOW TO ENROLL PATIENTS

Treating physicians: Please contact our Contract Research Organization to clarify the details of enrollment:

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6005 Hidden Valley Road, Suite 170
Carlsbad, CA 92011
Maggie Bloomberg Sr. Project Manager Phone: 760 658 5913 or Maggie.Bloomberg@precisionformedicine.com
Laurie McPherson Clinical Team Lead Phone: 760 557 1612 or Laurie.McPherson@precisionformedicine.com
Study website: www.ab2bioresearch.com

LEAD PRINCIPAL INVESTIGATOR

Edward M. Behrens, MD
Chief, Division of Rheumatology, The Children's Hospital of Philadelphia
Joseph Lee Hollander Chair in Pediatric Rheumatology
Assistant Professor of Pediatrics, Perelman School of Medicine at The University of Pennsylvania

QUALIFIED STUDY CENTERS AND INVESTIGATORS

United States:
Boston Children's Hospital, Boston, MA, Dr. Fatma Dedeoglu
Children's Hospital of Philadelphia, Philadelphia, PA, Dr. Edward Behrens (Lead Principal Investigator)
Children's Healthcare of Atlanta, Atlanta, GA, Dr. Sharmuganathan Chandrakasan
Cincinnati Children's Hospital Medical Center, Cincinnati, OH, Dr. Rebecca Marsh
Rady Children's Hospital, San Diego, CA, Dr. Harold Hoffman
Shand's Children's Hospital, Gainesville, FL, Dr. Akaluck Thatayatikom
Texas Children's Hospital, Houston, TX, Dr. Lisa Forbes Satter
UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, Dr. Scott Canna

Canada:
CHU Sainte-Justine, Montreal, Dr. Julie Barsalou / Dr. Fabien Touzot
The Hospital for Sick Children (SickKids), Toronto, Dr. Ronald Laxer

SPONSOR

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