Clinical Outcomes After Switching to Migalastat From Agalsidase alfa or Agalsidase beta in Patients With Fabry Disease: Post Hoc Analysis From ATTRACT


INTRODUCTION

- Fabry disease results from GLA gene variants that lead to functional deficiency of the α-Gal A enzyme and progressive accumulation of disease-causing substrates (e.g., globotriaosylceramide [Gb3]) in multiple organs, including kidney, heart, and blood vessels.
- Until recently, treatment options were limited to enzyme replacement therapy (ERT) with agalsidase alfa or agalsidase beta enzyme infusion every two weeks.
- Migalastat, a first-in-class pharmacologic chaperone, is approved in 38 countries, including the United States, for the treatment of patients aged 18 (United States and Canada) or 16 (other countries) years and older with Fabry disease and migalastat-amenable GLA variants.
- Migalastat acts by binding and stabilizing amenable α-Gal A variants in the endoplasmic reticulum, facilitating proper trafficking to lysosomes, where dissociation of migalastat allows α-Gal A to function properly to degrade accumulated substrates.
- Migalastat has demonstrated efficacy across multiple organs in ERT-naïve and ERT-experienced patients with Fabry disease and amenable GLA variants.

OBJECTIVE

- To evaluate, in this post hoc analysis, the clinical outcomes of patients who switched from agalsidase alfa or agalsidase beta to migalastat and patients who continued treatment with agalsidase alfa or agalsidase beta in the phase 3 ATTRACT clinical trial.

METHODS

Study Design

- ATTRACT (AT1001-012, NCT02128505) was a multicenter, randomized, open-label, active-controlled, phase 3 study to compare the efficacy and safety of 18 months of migalastat 150 mg every other day or ERT (agalsidase alfa 0.2 mg/kg or agalsidase beta 1.0 mg/kg every other week) in patients aged 16-74 years with a confirmed diagnosis of Fabry disease who were naive to ERT or received agalsidase alfa or agalsidase beta at the time of enrollment. During the 18-month randomized treatment period, because of the worldwide shortage of agalsidase beta, most patients were switched to migalastat. Subgroups were:
  - Patients who switched to migalastat from agalsidase beta
  - Patients who continued treatment with agalsidase alfa

RESULTS

<table>
<thead>
<tr>
<th>Treatment During 18-Month Randomized Treatment Period</th>
<th>Migalastat</th>
<th>Agalsidase alfa</th>
<th>Agalsidase beta</th>
<th>ERT</th>
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<tbody>
<tr>
<td>Mean (95% CI) annualized rates of change in eGFR</td>
<td>97.6±16.1</td>
<td>71.7 (6.8)</td>
<td>93.7 (5.6)</td>
<td>97.2 (8.1)</td>
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Analysis of efficacy endpoints, including eGFR and glomerular filtration rate, was done using the baseline value as the reference point for all time points. Safety data were reported for all patients who received ≥1 dose of migalastat or ERT during the 18-month randomized treatment period. Safety data were reported for all patients who received ≥1 dose of migalastat or ERT during the 18-month randomized treatment period. Safety data were reported for all patients who received ≥1 dose of migalastat or ERT during the 18-month randomized treatment period. Safety data were reported for all patients who received ≥1 dose of migalastat or ERT during the 18-month randomized treatment period.

Plasma Lyso-Gb

- Plasma Lyso-Gb, levels remained low and stable in patients who switched from ERT to migalastat.