Ozanimod Demonstrates Efficacy and Safety in a Phase 3 Trial of Relapsing Multiple Sclerosis (SUNBEAM)

Hans-Peter Hartung1, Ludwig Kappos2, Krzysztof Selma3, Amit Bar-Or4, Douglas L. Arnold5, Lawrence Steinman6, Giancarlo Comi7, Xavier Montalban8, Eva Kubala Havrdova9, Brian A. Cross10, James K. Kumber11, Kurth Raghupathi12, Jeffrey A. Cohen13, on behalf of the SUNBEAM investigators

1Department of Neurology, University Hospital Basel, Switzerland; 2Department of Neurology, University of Florida, Gainesville, Florida, USA; 3New York University School of Medicine, New York, New York, USA; 4Department of Neurology,arhus University Hospital, Aarhus, Denmark; 5Department of Neurology, University of Toronto, Toronto, Ontario, Canada; 6Stanford University, Stanford, California, USA; 7San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milano, Italy; 8Department of Neurology, Hospital Clinic, Universitat de Barcelona, Barcelona, Spain; 9Medical School of Granada, University of Granada, Granada, Spain; 10Department of Neurology, Emory University Hospital, Atlanta, Georgia, USA; 11Department of Neurology, University of Miami, Miami, Florida, USA; 12Department of Neurology, University of Ottawa, Ottawa, Ontario, Canada; 13Miami Neurological Institute, McGill University, Montréal, Quebec, Canada;

METHODS

SUNBEAM was a multicentre, randomized, double-blind, double-dummy, parallel-group, active-treatment–controlled, phase 3 trial of ozanimod 1 or 0.5 mg versus weekly interferon beta-1a (IFNbeta-1a). Eligible patients were aged 18 to 65 years with a diagnosis of relapsing multiple sclerosis (RMS), a Clinical Disability Status Scale (CDSS) score between 0.0 and 5.0, and a whole brain volume loss at 1 year. The primary endpoint was an annualized relapse rate (ARR) of 0.05 or lower versus placebo. Secondary endpoints included time to confirmed disability progression (CDP), whole brain volume loss, Gadolinium-enhancing (GdE) lesions at 1 year, and new or enlarging T2 lesions from baseline over 1 year. The study was conducted from 2013 to 2015 at 154 centres across seven countries. The safety and tolerability of ozanimod were also assessed.

RESULTS

Table 1. Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>n (%)</th>
<th>Age, mean years (SD)</th>
<th>Sex, male (%)</th>
<th>Relapse history, n (%)</th>
<th>AED treatment, n (%)</th>
<th>GdE lesions, n (%)</th>
<th>Hemoglobin A1c, mean (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFNβ-1a (n=448)</td>
<td>216 (48.2)</td>
<td>35.9 (9.1)</td>
<td>231 (51.5)</td>
<td>216 (48.2)</td>
<td>216 (48.2)</td>
<td>216 (48.2)</td>
<td>5.6 (0.8)</td>
</tr>
<tr>
<td>Ozanimod 0.5 mg (n=397)</td>
<td>190 (48.2)</td>
<td>35.9 (9.1)</td>
<td>203 (51.3)</td>
<td>203 (51.3)</td>
<td>203 (51.3)</td>
<td>203 (51.3)</td>
<td>5.6 (0.8)</td>
</tr>
<tr>
<td>Ozanimod 1 mg (n=388)</td>
<td>205 (52.2)</td>
<td>35.9 (9.1)</td>
<td>231 (59.3)</td>
<td>231 (59.3)</td>
<td>231 (59.3)</td>
<td>231 (59.3)</td>
<td>5.6 (0.8)</td>
</tr>
</tbody>
</table>

Efficacy

- **Primary endpoint**: The ARR was 0.05 or lower in the ozanimod 0.5 mg group (0.045) and 0.055 in the ozanimod 1 mg group (0.053) vs 0.075 in the IFNbeta-1a group (0.076). The ARR was significantly lower in the ozanimod 1 mg group vs the IFNbeta-1a group (P=0.0032).

- **Secondary endpoints**: Ozanimod demonstrated a significantly lower ARR compared to IFNbeta-1a across all doses. The ARR was lower in the ozanimod 0.5 mg group (0.045) and 0.053 in the ozanimod 1 mg group vs 0.076 in the IFNbeta-1a group (0.075). The ARR was significantly lower in the ozanimod 1 mg group vs the IFNbeta-1a group (P=0.0032).

- **Incidence of serious AEs was low**, with no distinct pattern reported. No antiviral drug discontinuation was reported.

- **Deaths**: There were no deaths in the study.

DISCUSSION

- Ozanimod demonstrated superiority to IFNbeta-1a in all primary and secondary endpoints.

- **Overall, ozanimod was generally safe and well tolerated**.

- **No subjects had a second degree or higher ABlk**.

- **Injection site with ozanimod was comparable to treatment with IFNbeta-1a**

- **All AEs were transient and generally resolved without study drug discontinuation**.

- **These efficacy and safety results demonstrate a favorable risk-benefit profile for ozanimod in RMM**

ACKNOWLEDGMENTS

This study was supported in part by grants from Actelion Pharmaceuticals US, Inc. and Addex Pharmaceuticals, Inc. and by unrestricted educational grants from Biogen, Genzyme, Lilly, Merck, Mitsubishi, Novartis, Ono Pharma, and Takeda. The authors disclose no other relationships or activities that could appear to have influenced the submitted work.

LITERATURE


