Long-term efficacy of satralizumab in patients with NMOSD in the SAKura studies

Manuabu Araki, Benjamin Greenberg, Jeffrey L. Bennett, Jérôme de Seze, Ingo Kleiter, Lech Szczechowski, Edward Fox, Brian G. Weinshenker, H.-Christian von Büdingen, Daniela Stokmaier, Gaëlle Klingelschmitt, Kristina Weber, Cristina Costantino, Anthony Traboulsee, Takashi Yamamura

SAkuraSky, NCT02028884; SAKuraStar, NCT02073279

JSNT 2021: Thursday October 28 16:40 - 17:36 JST
Presentation # 10122
（様式4-B）申告すべきCOI状態がある場合

日本神経治療学会
COI開示

筆頭発表者名：荒木 学

■ 演題発表に関連し、開示すべきCOI関係にある企業などとして、

| ④ 講演料：lecture | 中外製薬 |

Medical writing assistance for this oral presentation was provided by ApotheCom and funded by Chugai Pharmaceutical Co., Ltd.

■ 本研究は各治験参加施設において、IRBの承認を得ている。
The current analyses used pooled data from the phase 3, randomized SAKura studies in NMOSD.

Relapse data across the combined double-blind and open-label extension (DB+OLE) periods of both studies were assessed, up to a CCOD of 7th June 2019.

Satralizumab significantly reduced patients’ risk of NMOSD relapse in the double-blind periods of both trials.1,2

SAKuraSky and SAKuraStar study design:1–3

<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>DB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OLE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Satralizumab 120 mg Q4W

Randomization
1:1 in SAKuraSky
2:1 in SAKuraStar

CEC-confirmed relapse

Placebo

Relapse data across the combined double-blind and open-label extension (DB+OLE) periods of both studies were assessed, up to a CCOD of 7th June 2019.

Satralizumab significantly reduced patients’ risk of NMOSD relapse in the double-blind periods of both trials.1,2

SAKuraSky double-blind period ended after the total number of PDRs reached 26 (CCOD: June 2018). For SAKuraStar, the double-blind period ended after 1.5 years (CCOD: October 2018). CCOD, clinical cut-off date; CEC, Clinical Endpoint Committee; DB, double-blind; LA, last administration; LO, last observation; OLE, open-label extension; PDR, protocol-defined relapse.

Time to first investigator-assessed protocol-defined relapse was the endpoint used for the current analysis

**Endpoint selection**

- In the SAkura study double-blind periods, **protocol-defined relapses (PDRs)** were assessed
  - PDRs had to meet certain criteria, and be confirmed by an independent CEC
- CEC adjudication was restricted to the double-blind periods, so the current analysis assessed **time to first investigator-assessed PDR in the combined DB+OLE period**
  - These were all relapses considered by the investigator to meet PDR criteria
  - In the double-blind period, 88% of investigator-assessed PDRs went on to be confirmed by the CEC

**Treatment exposure**

- The duration of patient exposure to satralizumab reached as high as **5+ years**

<table>
<thead>
<tr>
<th>Exposure, weeks</th>
<th>Double-blind period</th>
<th>DB+OLE period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=74)</td>
<td>Satralizumab (n=104)</td>
</tr>
<tr>
<td><strong>Median (range)</strong></td>
<td>54.6 (7–219)</td>
<td>96.1 (8–224)</td>
</tr>
</tbody>
</table>

CEC, Clinical Endpoint Committee; CRF, case-report form; DB, double-blind; ITT, intent to treat; OLE, open-label extension; PDR, protocol-defined relapse.
Patients randomized to satralizumab had a significant reduction in the risk of investigator-assessed PDR vs placebo.

Hazard ratio (95% CI) 0.49 (0.31–0.79)
Stratified P value (log-rank) 0.002

51% risk reduction

Between-group comparisons are based on patients original assigned treatment at randomization.

CI, confidence interval; DB, double-blind; ITT, intent to treat; OLE, open-label extension; PDR, protocol-defined relapse.
The reduction in relapse risk with satralizumab was more pronounced in AQP4-IgG seropositive patients.

AQP4-IgG+ patients (DB+OLE period)

- Hazard ratio (95% CI): 0.34 (0.19–0.62)
- Stratified P value (log-rank): <0.001
- 66% risk reduction

Between-group comparisons are based on patients original assigned treatment at randomization.

AQP4-IgG+, aquaporin-4 autoantibody seropositive; CI, confidence interval; DB, double-blind; ITT, intent to treat; OLE, open-label extension; PDR, protocol-defined relapse. The relapse data shown in the figure relate to investigator-assessed PDRs.
The annualized relapse rate decreased over time in patients randomized to satralizumab.

Annualized relapse rates are adjusted estimates from analysis based on the GEE Poisson regression model with repeated measurements using unstructured covariance matrix, adjusted by study identifier (SAkuraSky/SAkuraStar), AQP4 screening status (positive/negative) and year (1–4).

No patients randomized to satralizumab withdrew from the OLE due to a relapse.

CI, confidence interval; DB, double-blind; ITT, intent to treat; OLE, open-label extension; PDR, protocol-defined relapse; PY, patient years.

<table>
<thead>
<tr>
<th>Year</th>
<th>n</th>
<th>PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>105</td>
<td>102.0</td>
</tr>
<tr>
<td>Year 2</td>
<td>99</td>
<td>92.3</td>
</tr>
<tr>
<td>Year 3</td>
<td>86</td>
<td>69.2</td>
</tr>
<tr>
<td>Year 4</td>
<td>53</td>
<td>47.1</td>
</tr>
</tbody>
</table>
Across the DB+OLE periods of the SAkura studies, patients randomized to satralizumab had a significantly reduced risk of relapse vs placebo

- In the overall population, a 51% reduction in risk of investigator-assessed PDR was observed in patients originally randomized to satralizumab vs placebo
  - The risk reduction was more pronounced in AQP4-IgG seropositive patients (66% risk reduction)

- Annualized relapse rate decreased over a 4-year period in patients randomized to satralizumab

- No patients randomized to satralizumab withdrew from the OLE due to a relapse

- Investigator-assessed PDRs were evaluated for this analysis, as CEC adjudication was restricted to the double-blind period