VERISMO: A Post-Marketing Safety Study to Determine the Incidence of All Malignancies and Breast Cancer in Patients With Multiple Sclerosis Treated With Ocrelizumab

D Wormser, J Evershed, G Ferreira, D Stokmaier, Q Wang, T Ziemssen
F Hoffmann-La Roche Ltd, Basel, Switzerland; Roche Products Ltd, Wehlyn Garden City, UK; Center of Clinical Neuroscience, Neurological Clinic, Carl Gustav Carus University Clinic, Dresden University of Technology, Dresden, Germany

BACKGROUND
Ocrelizumab is a recombinant, humanized, monoclonal antibody that selectively targets CD20+ B cells. Ocrelizumab has demonstrated superior efficacy to interferon (IFN) β-1a in patients with relapsing multiple sclerosis (RMS),1 and to placebo in patients with primary progressive multiple sclerosis (PPMS) in Phase III trials. — The proportions of patients with adverse events (AEs) or serious AEs (SAEs) were similar across the ocrelizumab, IFN β-1a, and placebo groups. — Pooled Phase III trial data from patients with RMS and PPMS indicated an imbalance in malignancies between the ocrelizumab and control arms. Ocrelizumab’s real-world safety profile in patients with multiple sclerosis (MS) newly exposed to ocrelizumab remains to be well-characterized.

OBJECTIVE
The primary objective of VERISIMO is to determine and characterize the incidence and mortality rates of all malignancies, including breast cancer, among patients with MS treated with ocrelizumab under routine clinical care.

METHODS
Study Design
— VERISIMO is a multi-center, multi-country, non-interventional, longitudinal post-marketing safety study on patients with MS who have newly treated with ocrelizumab or other MS disease-modifying therapies (DMTs).
— The study treatment and objectives of VERISIMO are provided in Tables 1 and 2.

Patient population
— Expected to enroll ≥10,000 patients (aged ≥18 years) with MS who were newly initiated treatment with ocrelizumab (≥30 days prior to study entry) or with another MS-approved DMT in the US and Germany.
— ≥4,000 patients exposed to other MS-approved DMTs (interferon β-1a, glatiramer acetate, cladribine, alemtuzumab, fingolimod, mitoxantrone, or natalizumab).

Primary objectives
— To determine the incidence rate of all malignancies and breast cancer following the first ocrelizumab treatment among patients with MS.
— To compare the observed incidence and mortality rates of all malignancies among patients treated with ocrelizumab and patients newly treated with approved MS DMTs other than ocrelizumab, as well as general populations.

Secondary objectives
— To determine the incidence rate of all malignancies and breast cancer following the first ocrelizumab treatment among patients with MS.
— To determine the time-to-event rate of all malignancies and breast cancer following the first ocrelizumab treatment among patients with MS.

Patient population
— Patients who received previous thrombolytic or chemotherapy treatment, or who are actively participating in other MS clinical trials will be excluded.

RESULTS
— The sample size and study duration will provide sufficient precision around the incidence rates to address the primary objective.
— The minimum detectable hazard ratio with 80% power will be 1.46 for the rate of all malignancies and 2.00 for the rate of female breast cancer.
— VERISIMO will integrate the results of CONFIDENCE in routine interim safety analyses and comparative long-term safety analyses.
— Comparative analyses will compare the rate of AEs in patients receiving ocrelizumab versus other DMTs, accounting for confounders.

CONCLUSION
— The VERISIMO post-marketing safety study will advance the understanding of the safety profile of ocrelizumab through the assessment of the potential risk of breast cancer and all malignancies in patients with MS newly exposed to ocrelizumab.

REFERENCES

DISCLOSURES
D Wormser is an employee and shareholder of F Hoffmann-La Roche Ltd. J Evershed is an employee of Roche Products Ltd. G Ferreira is an employee of F Hoffmann-La Roche Ltd. D Stokmaier and Q Wang are employees of F Hoffmann-La Roche Ltd. T Ziemssen has received grants and personal fees from F Hoffmann-La Roche Ltd. T Ziemssen has received grants and personal fees from Biogen, Novartis, Sanofi, and Takeda, and personal fees from Biogen, F Hoffmann-La Roche Ltd, and Merck.

Table 1. VERISIMO patient population

<table>
<thead>
<tr>
<th>Key data collected</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>End of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
<tr>
<td>Primary objectives</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
</tbody>
</table>

Table 2. VERISIMO study objectives

<table>
<thead>
<tr>
<th>Key data collected</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>End of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
<tr>
<td>Primary objectives</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
</tbody>
</table>

Table 3. VERISIMO data collection at different study time points

<table>
<thead>
<tr>
<th>Key data collected</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>End of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
<tr>
<td>Primary objectives</td>
<td>DMT (first-line vs. ocrelizumab treatment)</td>
<td>Other DMTs (first-line)</td>
<td>Ocrelizumab</td>
</tr>
</tbody>
</table>

Table 4. VERISIMO key study milestones

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Planned date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study start</td>
<td>Q3 2019</td>
</tr>
<tr>
<td>Data collection</td>
<td>Q3 2020 (in progress)</td>
</tr>
<tr>
<td>Final report of study results</td>
<td>Nov 2020 (at latest)</td>
</tr>
</tbody>
</table>