Design of a Multi-Source Post-Marketing Study to Evaluate Pregnancy and Infant Outcomes in Women With Multiple Sclerosis Who Were Exposed to Ocrelizumab During, or Within 6 Months Before, Pregnancy

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**BACKGROUND**
- Ocrelizumab (OCR) is a recombinant, humanized, monoclonal immunoglobulin G1 antibody that selectively targets CD20+ B cells.
- Immunoglobulins such as OCR do not cross the placenta during the first trimester of pregnancy, but transfer of OCR can occur thereafter.
- The safety profile of OCR has been investigated in multiple clinical trials and although the use of effective contraception was mandatory, 25 pregnancies have been reported in women with multiple sclerosis (MS) receiving OCR during these trials up to the end of January 2017; in 14 of these 25 pregnancies, the fetuses were considered to have been exposed to OCR.
- The small number of pregnancies and pregnancy outcomes* that have been reported from clinical trials means the safety profile of OCR in pregnancy and fetal outcomes has yet to be established.
- Therefore, and as part of post-marketing activities, this study has been designed to provide a greater degree of information to patients and clinicians.
- OCR has an average terminal half-life of 26 days* and based on the estimated elimination rates after the last administration, the current European and FDA label information states: "Women of childbearing potential should use contraception while receiving ocrelizumab and for 12 months after the last infusion of ocrelizumab" and "You should use birth control (contraception) during treatment with ocrelizumab and for 6 months after your last infusion of ocrelizumab*, respectively.

**OBJECTIVE**
- To assess the pregnancy and infant safety of OCR after maternal use in the 6 months before or during pregnancy in the setting of routine healthcare.

**METHODS**
- To characterize pregnancy and infant outcomes of women with MS exposed to OCR during the 6 months before the estimated date of conception or at any time during pregnancy, including:
  - The frequency of selected adverse pregnancy outcomes (e.g. spontaneous abortions, stillbirths, elective abortions, preterm births, C-sections, and urinary and other infections).
  - The frequency of selected adverse fetal/neonatal/infant outcomes (e.g. major congenital malformations, small for gestational age, adverse effects on immune system development [adverse effects on immune system development include hospitalization due to infectious diseases, cancer, and vaccine-preventable diseases and vaccine-associated polyneuromyelitis]) at birth and through at least the first year of life of infants.
- This study will compare the frequency of each safety event of interest between OCR-exposed pregnant women with MS and two comparison cohorts.

**Study Design**
- The study will be conducted in existing population-based healthcare databases and registries (Figure 1).
- The study cohorts will include (Table 1 and Figure 2):
  - OCR-exposed pregnancies in women with MS.
  - Pregnancies not exposed to OCR in women with MS.
  - Pregnancies not exposed to OCR in women without MS.

**DISCLOSURES**
- AV Margulis, EB Andrews, S Hernandez-Diaz, M Magargr, E Rivero-Ferrer, S Bader-Weder, J Evershed, M Garas, Q Wang, D Wormser are employees of RTI Health Solutions a business unit of RTI International. RTI Health Solutions performed the study design, data collection, data analysis, and manuscript preparation. This study was sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland, a company in the Roche Group and the results will be presented during the 70th Academy of Neurology (AAN) Annual Meeting, April 2018.2018; Los Angeles, CA, USA. The study was funded by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance for this presentation was provided by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

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**Table 1. Description of study cohorts**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Description</th>
<th>Recruitment Details</th>
<th>Enrollment Details</th>
<th>Exclusion Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCR-exposed cohort</td>
<td>Women with MS who were exposed to OCR during the 6 months before the estimated date of conception or at any time during pregnancy</td>
<td>Ocrelizumab (OCR) is a recombinant, humanized, monoclonal immunoglobulin G1 antibody that selectively targets CD20+ B cells.</td>
<td>12 months after the last infusion of OCR</td>
<td>None</td>
</tr>
<tr>
<td>Primary comparison cohort</td>
<td>Pregnancies not exposed to OCR in women with MS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary comparison cohort</td>
<td>Pregnancies not exposed to OCR in women without MS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**REFERENCES**
- F. Hoffmann-La Roche Ltd, Basel, Switzerland. Writing and editorial assistance for this presentation was provided by F. Hoffmann-La Roche Ltd, Basel, Switzerland. Presented at the 70th Academy of Neurology (AAN) Annual Meeting, April 2018; Los Angeles, CA, USA.