Post-Marketing Study to Evaluate Pregnancy and Infant Outcomes in Women With Multiple Sclerosis Exposed to Ocrelizumab During 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

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 poliomyelitis]) at birth and throughout 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

- Financial support for this work has been provided by F. Hoffmann-La Roche Ltd, Basel, Switzerland
- No other conflicts of interest exist

TABLE 1. Description of study cohorts

<table>
<thead>
<tr>
<th>Study cohort</th>
<th>Number of pregnancies</th>
<th>Number of live births</th>
<th>Miscarriage rate</th>
<th>Preterm birth rate</th>
<th>Infections requiring hospitalization a</th>
<th>Small for gestational age</th>
<th>Fetal death/stillbirth</th>
<th>Preterm birth b</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCR-exposed cohort</td>
<td>705:2,115</td>
<td>540:1,620</td>
<td>0.09</td>
<td>0.16</td>
<td>0.04</td>
<td>0.07</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Comparator (900)</td>
<td>1,440:4,320</td>
<td>1,240:3,720</td>
<td>0.03</td>
<td>0.06</td>
<td>0.01</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>Primary comparison cohort</td>
<td>575:1,725</td>
<td>480:1,440</td>
<td>0.10</td>
<td>0.15</td>
<td>0.05</td>
<td>0.08</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

ACKNOWLEDGMENTS

- We would like to thank all patients, their families, and the investigators who participated in these trials. We would like to thank Optum DAPI and Optum for providing the data used in this study. We would like to thank all sponsors of the investigational product, including F. Hoffmann-La Roche Ltd, Basel, Switzerland

REFERENCES

4. FDA. OCREVUS™ (ocrelizumab). Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/761053Orig1s000Lbl.pdf
5. Data from Optum DAPI provided by Optum

RESULTS

- The study period will start from the first dispensing/prescription of OCR in the participating data sources (approved in the US in 2017 and in Denmark in 2018) Figure 3
- The number of OCR-exposed pregnancies and live births will be monitored yearly to inform the study size, and data extraction from the first data source is anticipated in Q1 2022, a minimum of 4 years after data accrual in the first data source
- The planned end date of study data is Q1 2023, following which, results will be prepared for dissemination to the MS community

Figure 1. Healthcare databases and registries included in the study

Figure 2. Study flow

Figure 3. Study timelines

CONCLUSIONS

- This study will complement the planned Ocrelizumab Pregnancy Registry (see Poster D51) and address current unmet needs of patients and investigators for evidence supporting effective contraception and counseling for patients and providers seeking conception while receiving Ocrelizumab

ACKNOWLEDGMENTS

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