Ocrelizumab in pregnancy and lactation

Overview

Pregnancy outcomes

- As of March 2022, 2,020 pregnancies had been reported in women with MS treated with OCR[1]
- Updated data, with newly reported cases including prospective outcomes, do not suggest an increased risk of adverse pregnancy or infant outcomes with ocrelizumab use, with or without *in utero* exposure, and remain in line with previous reports and expected epidemiological ranges[2,3]

MINORE study[4,5]

- MINORE (NCT04998812) will evaluate placental transfer of OCR and the corresponding pharmacodynamic effects in the infants of women with CIS or MS whose last dose of OCR was administered at any time ≤6 months before the LMP until the end of the first trimester

SOPRANINO study[6,7]

- SOPRANINO (NCT04998851) will evaluate the pharmacokinetics of OCR in the breast milk of lactating women with CIS or MS as well as the corresponding exposure and pharmacodynamic effects in the infant

Figure 1: Reported pregnancies in women with MS treated with OCR per year[1]

In the span of one year, reported pregnancies among women with MS treated with OCR rose from n=1,223 in the 2021 data cut (March 2021) to n=2,020 in the 2022 data cut (March 2022), marking an approximately 65% increase[1,8]

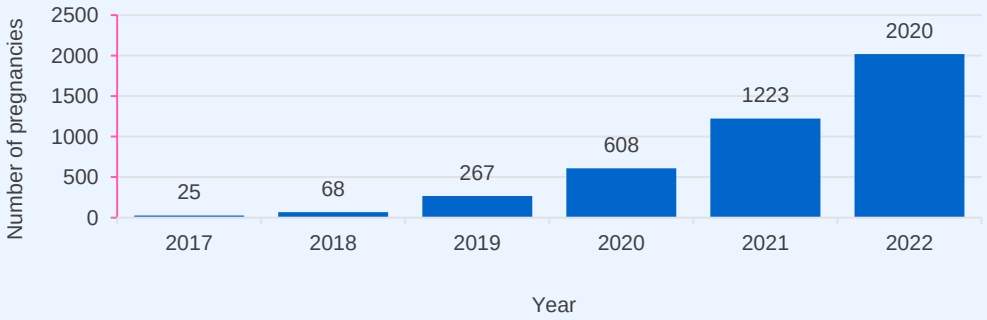

Table 1: Summary of pregnancy known outcomes by exposure category: Prospective and all*,[1]

- Across exposure categories, data were in line with expected epidemiological ranges[2,3]
- Of the 1,064 prospective and retrospective cases with known outcomes, 809 of those were live births with major congenital anomalies occurring in four full term pregnancies (0.5%) and four short term pregnancies (0.5%), all of which were in the exposed group[1]. There were two intrauterine foetal deaths with major congenital anomalies (1.2%) reported with unknown exposure[1]. These proportions and types of abnormality are consistent with epidemiological background (rate for children born in Europe with major congenital abnormalities is around 2–3% per year)[9].
  - Prospective cases were reported while ongoing, and their final outcomes were unknown at the time of the initial notification[1]
  - Retrospective (all) cases, are cases with known outcomes at the time of the initial notification[1]

	Prospective				All			
Exposure based on last OCR dose	**Not exposed *in utero* (n=314)**	**Exposed *in utero* (n=532)**	**Unknown timing of exposure (n=652)**	**Total cases (n=1,498)**	**Not exposed *in utero* (n=433)**	**Exposed *in utero* (n=705)**	**Unknown timing of exposure (n=882)**	**Total cases (n=2,020)**
Known outcomes, n (%)	163 (100.0)	286 (100.0)	147 (100.0)	596 (100.0)	278 (100.0)	443 (100.0)	343 (100.0)	1064 (100.0)
Live births, n (%)†	137 (84.0)	225 (78.7)	109 (74.1)	471 (79.0)	222 (79.9)	349 (78.8)	238 (69.4)	809 (76.0)
Full term (≥37 weeks) ‡	*87 (63.0)*	*137 (60.9)*	*45 (41.3)*	*269 (57.1)*	*140 (63.2)*	*189 (54.2)*	*74 (31.3)*	*403 (49.8)*
Pre-term (<37 weeks) ‡	*15 (10.9)*	*21 (9.3)*	*11 (10.1)*	*47 (10.0)*	*18 (8.2)*	*40 (11.5)*	*18 (7.6)*	*76 (9.4)*
Unknown Gwk‡	*35 (25.5)*	*67 (29.8)*	*53 (48.6)*	*155 (32.9)*	*64 (28.8)*	*120 (34.4)*	*146 (61.3)*	*330 (40.8)*
Live births with MCA§					-	*8 (2.2)*	*0 (0.0)*	*8 (1.0)*
Ectopic pregnancy, n (%)†	3 (1.8)	4 (1.4)	4 (2.7)	11 (1.8)	4 (1.4)	4 (0.9)	9 (2.6)	17 (1.7)
Therapeutic/elective abortion, n (%)†	6 (3.7)	33 (11.5)	7 (4.8)	46 (7.7)	13 (4.7)	44 (9.9)	15 (4.4)	72 (6.8)
Intrauterine foetal death n (%)†								
Spontaneous abortion (≤22 weeks)	17 (10.4)	23 (8.0)	27 (18.4)	67 (11.2)	38 (13.7)	41 (9.3)	79 (23.0)	158 (14.8)
Stillbirth (>22 weeks)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)	0 (0.0)	5 (1.1)	1 (0.3)	6 (0.6)

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Ongoing clinical trials: MINORE & SOPRANINO

MINORE[4,5]

- Enrolment of ~44 women between GWk 22–26, whose last OCR dose occurred at any time from 6 months before the LMP until the end of the first trimester
- **Primary endpoint:** Proportion of infants with B-cell levels below LLN at Week 6 of life
- **Key secondary endpoints:** serum OCR levels in umbilical cord blood, infant humoral immune responses to vaccinations
- More information is available at ClinicalTrials.gov

SOPRANINO[6,7]

- Enrolment of at least 20 women who delivered a term infant and made the decision to breastfeed whilst receiving OCR (inclusion from 2–24 weeks post-partum)
- **Co-primary endpoints:** Proportion of infants with B-cell levels below the LLN, measured 30 days after the mother's first postpartum OCR infusion; Estimated ADID over 60 days after the mother's first postpartum OCR infusion
- More information is available at ClinicalTrials.gov

Do you have patients with MS receiving OCR who are pregnant? Please remember to report the pregnancy accordingly:
If you are in the United States, your patients may be able to take part in a global registry of women with MS who are pregnant and either have or have not received ocrelizumab during or within 6 months before their pregnancy. Click here for information
Outside the United States: Please report any occurrence of pregnancy in women receiving OCR here

Footnotes

Table 1

**In utero* exposure based on timing of last OCR dose relative to LMP. †Percentages represent fractions of the total known outcomes of the respective exposure category (not exposed *in utero*, exposed *in utero* unknown exposure, total). ‡Percentages represent fractions of the total live births for the respective exposure category (not exposed *in utero*, exposed *in utero* unknown exposure, total). §The dash indicated that no cases were reported.

Abbreviations

ADID, average daily oral infant dose; CIS, clinically isolated syndrome; EUROCAT, European Surveillance of Congenital Anomalies; GWk, gestation week; LLN, lower limit of normal; LMP, last menstrual period; MCA, major congenital anomalies; OCR, ocrelizumab.

References

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4. ClinicalTrials.gov identifier: NCT04998812;
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