Ocrelizumab in Pregnancy and Lactation

Overview

Pregnancy outcomes[1]

- As of March 2021, 1223 pregnancies had been reported in women with MS treated with OCR, an increase of approximately 100% relative to the previous data cut (n=608; March 2020)[1,2]
- Updated data do not suggest an increased risk of adverse pregnancy outcomes with ocrelizumab use, with or without *in utero* exposure, and remain in line with previous reports and expected epidemiological ranges[3,4]

MINORE study[5,6]

- 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[7,8]

- 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

Summary of Pregnancy Outcomes by Exposure Category[1a]

- Across exposure categories, data were in line with expected epidemiological ranges[3,4]
- Five stillbirths (0.8%) were reported, of which three presented with comorbidities as potential confounders. All were retrospectively reported cases and no increase in rate was observed since the 2020 data cut[2]
- Seven major congenital anomalies (1.6%) were reported, of which four were potentially confounded by risk factors

Exposure based on last OCR dose	Not exposed *in utero* (n=307)			Exposed *in utero* (n=414)			Unknown timing of exposure (n=502)	Total cases (n=1223)
Outcome, n (%)[b]	<6 months (n=69)	<3–6 months (n=238)	Total not exposed *in utero* (n=307)	0–3 months (n=265)	During pregnancy (n=142)	Total exposed *in utero*[c] (n=414)		
Known outcomes	45 (100.0)	134 (100.0)	179 (100.0)	158 (100.0)	75 (100.0)	236 (100.0)	189 (100.0)	604 (100.0)
Live births[d]	29 (64.4)	98 (73.1)	127 (70.9)	114 (72.2)	56 (74.7)	171 (72.5)	129 (68.3)	427 (70.7)
Full term (≥37 weeks)	21 (72.4)	54 (55.1)	75 (59.1)	65 (57.0)	28 (50.0)	94 (55.0)	33 (25.6)	202 (47.3)
Pre-term (<37 weeks)	2 (6.9)	11 (11.2)	13 (10.2)	18 (15.8)	8 (14.3)	26 (15.2)	8 (6.2)	47 (11.0)
Unknown Gwk	6 (20.7)	33 (33.7)	39 (30.7)	31 (27.2)	20 (35.7)	51 (29.8)	88 (68.2)	178 (41.7)
Live births with MCA	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	4 (7.1)	5 (2.9)	2 (1.6)	7 (1.6)
Ectopic pregnancy	4 (8.9)	2 (1.5)	6 (3.4)	1 (0.6)	1 (1.3)	2 (0.8)	5 (2.6)	13 (2.2)
Therapeutic/elective abortion	1 (2.2)	11 (8.2)	12 (6.7)	23 (14.6)	7 (9.3)	30 (12.7)	12 (6.3)	54 (8.9)
Spontaneous abortion (≤22 weeks)	11 (24.4)	23 (17.2)	34 (19.0)	17 (10.8)	10 (13.3)	29 (12.3)	42 (22.2)	105 (17.4)
Stillbirth (>22 weeks)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.9)	1 (1.3)	4 (1.7)	1 (0.5)	5 (0.8)

[a]An embryo/fetus was considered to have exposure to OCR *in utero* if the last infusion occurred within 3 months of conception, during pregnancy, or *in utero* with timing unknown. [b]Proportions of live births, ectopic pregnancies, therapeutic/elective abortions, spontaneous abortions, and stillbirths were calculated using known outcomes of the respective exposure category as the denominator. [c]Total exposed *in utero* includes seven *in utero* exposure cases for which exact timing of exposure could not be determined. [d]Proportions of live birth gestational age and anomalies were calculated using live births in the respective exposure category as the denominator.

MINORE[5,6]

- Enrollment 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[7,8]

- Enrollment of at least 20 women who delivered a term infant and made the decision to breastfeed while receiving OCR (inclusion from 2–24 weeks postpartum)
- **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:
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. For information, visit https://www.ocrevuspregnancyregistry.com/.

The Prescribing Information is the primary source of information on the known and potential risks associated with ocrelizumab.

Abbreviations:
ADID=average daily oral infant dose; CIS=clinically isolated syndrome; GWk=gestational week; LLN=lower limit of normal; LMP=last menstrual period; MCA=major congenital anomalies; OCR=ocrelizumab.

References:
1. Dobson R, et al. Presented at: ECTRIMS 2021. October 13–15, 2021. Virtual. Presentation P641. 2. Bove R, et al. Presented at: ECTRIMS 2020. September 9–12, 2020. Virtual. Presentation P1132. 3. Lopez-Leon S, et al. *J Neurol.* 2020;267:2721–2731. 4. Centers for Disease Control and Prevention. *MMWR Morb Mortal Wkly Rep.* 2008;57:1–5. 5. ClinicalTrials.gov identifier: NCT04998812. Updated November 11, 2021. https://clinicaltrials.gov/ct2/show/NCT04998812 6. Hellwig K, et al. Presented at: ECTRIMS 2021. October 13–15, 2021. Virtual. Poster P655. 7. ClinicalTrials.gov identifier: NCT04998851. Updated October 28, 2021. https://clinicaltrials.gov/ct2/show/NCT04998851 8. Bove R, et al. Presented at: ECTRIMS 2021. October 13–15, 2021. Virtual. Poster P686.

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