Ocrelizumab in Pregnancy and Lactation

Overview

Pregnancy outcomes

- As of July 2023, 3253 pregnancies had been reported in women with MS treated with OCR[1]
- Pregnancy and outcome rates related to *in utero* exposure to OCR are presented below, in addition to epidemiological background rates in both MS and general populations

Summary of Pregnancy Outcomes by Exposure Category

- Reported pregnancies among women with MS treated with OCR rose from n=2020 (March 2022) to n=3253 (July 2023), marking an increase of approximately 62%[1,2]
- Most pregnancies resulted in live births (83.6%), and proportions were similar in the exposed and non-exposed groups[1]
- Among live births, 61.4% were full term and 8.5% were preterm[1]
  - Proportions were similar in the exposed and non-exposed groups
  - Gestational age was unknown in 30.2% of cases
- A higher proportion of elective terminations occurred in the exposed group (7.4%, vs 1.7% in the non-exposed group), but the overall cumulative (total cohort) proportion of elective abortions has decreased (5.1% in 2023 vs 11.5% in 2022 and 15.7% in 2021)[2]
- A smaller proportion of spontaneous abortions occurred in the exposed group (7.4%) compared with the non-exposed group (9.1%)[1]
- The overall rate of stillbirths remained low (<0.1%)[1]

Table 1. Summary of known pregnancy outcomes by exposure category:[a] Prospective cases[1b]

Number of MS pregnancies	Non-exposed (N=575)	Exposed (N=855)	Unknown (N=1016)	Total (N=2466)	Epidemiological rates	
Known outcomes	n=351	n=512	n=282	n=1145	MS background rate	General population background rate
Live births[b]	88.3%	84.2%	76.6%	83.6%	70.2–77.2[3]	70.2[3]
Full term (≥37 weeks)[c]	70.9%	65.7%	39.1%	61.4%	–	–
Preterm (<37 weeks)[c]	8.4%	9.5%	6.5%	8.5%	7.2–15.4[3–6]	6.5–10.4[3,4,6]
Unknown gestational age[c]	20.7%	24.8%	54.4%	30.2%	–	–
Ectopic pregnancy	0.9%	0.8%	2.5%	1.2%	0.6–1.3[3,4]	1.1–2.0[3,4]
Elective termination	1.7%	7.4%	5.0%	5.1%	10.7–18.1[3]	18.2[3]
Intrauterine fetal death[d]						
Spontaneous abortion, ≤22 weeks[d]	9.1%	7.4%	16.0%	10.0%	10.5–11.6[3–5]	10.0–20.0[3,4]
Stillbirth, >22 weeks[d]	–	0.2%	–	<0.1%	0.3–0.6[3,6]	0.2–0.7[3,6]

Dashes indicate that no cases were reported. [a]Exposure classification is based on OCR $t_{1/2}$=26 days (full elimination from the body is expected by approximately 4.5 months) and assuming no relevant placental transfer of IgG1 antibodies occurs prior to 12 weeks of gestation.[7,8b] *In utero* exposure based on timing of last OCR dose relative to the LMP. [c]Percentages represent fractions of the total live births for the respective exposure categories (not exposed in utero, exposed *in utero*, unknown exposure, total). [d]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total).

Major Congenital Anomalies

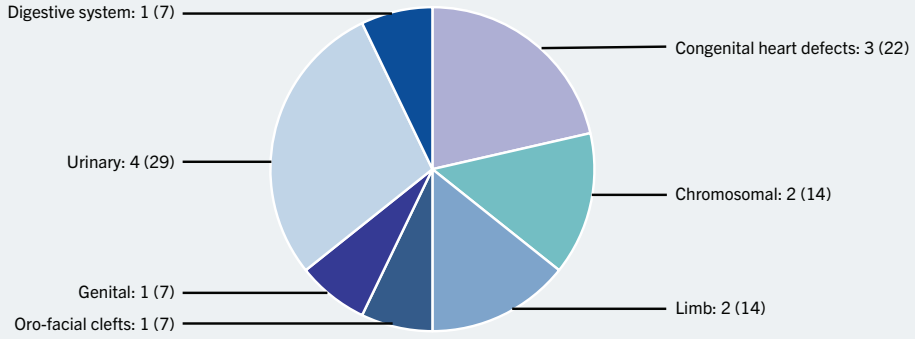
Table 2. Major congenital anomalies in pregnancies with known outcomes[1]

	Non-exposed	Exposed	Unknown exposure	Total
Live births	**N=310**	**N=431**	**N=216**	**N=957**
Live birth with MCA, n (%)[a]	4 (1.3)	7 (1.6)	1 (0.5)	12 (1.3)
Full term with MCA, n	3	4	1	8
Preterm with MCA, n[b]	1	3	–	4
Unknown GA with MCA, n[b]	–	–	–	–
Stillbirths >22 weeks	**N=0**	**N=1**	**N=0**	**N=1**
Stillbirth with MCA, n[b]	–	1	–	1
Live birth/stillbirth with MCA, n (%)[c]	4 (1.3)	8 (1.9)	1 (0.5)	13 (1.4)

[a]Percentages represent fractions of total live births for the respective exposure category. [b]Dashes indicate that no cases were reported. [c]Percentages represent fractions of the total stillbirths/live births for the respective exposure category.

- Proportions and types of MCAs are consistent with the epidemiological background.[3–6,9,10] It is estimated that around 2–4% of all children born every year will have an MCA[3–6,9]

Figure 1. Distribution of major congenital anomalies in pregnancies with known outcomes by EUROCAT[11] category, n (%)[1a]



[a]The number of major congenital anomalies prospectively reported is 14, as one live birth reported two MCAs.

Ongoing Clinical Trials: MINORE & SOPRANINO

MINORE[12,13]

- Enrollment of ~44 women at ≤GWk 30 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[13,14]

- 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

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; EUROCAT=European Surveillance of Congenital Anomalies; GA=gestational age; GWk=gestation week; IgG1=immunoglobulin G1; LLN=lower limit of normal; LMP=last menstrual period; MCA=major congenital anomalies; MS=multiple sclerosis; NCT=National Clinical Trials; no=number; OCR=ocrelizumab; $t_{1/2}$=half-life.

References:
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https://www.genentech-medinfo.com/our-products/neuroscience/ocrevus.html

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