Ocrelizumab in pregnancy and lactation

Overview

Pregnancy outcomes

- As of July 2023, 3,253 pregnancies had been reported in women with MS treated with OCR[1]
- This is the largest dataset of pregnancy outcomes for an anti-CD20 therapy in MS[1,2]
- *In utero* exposure to OCR did not increase the risk of adverse pregnancy or infant outcomes compared with epidemiological background of both MS and general populations[3–8]

MINORE study[9,10]

- MINORE (NCT04998812) is an ongoing study evaluating 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[10,11]

- SOPRANINO (NCT04998851) is an ongoing study evaluating 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]

Reported pregnancies among women with MS treated with OCR rose from n=2,020 (March 2022), to n=3,253 (July 2023), marking an increase of approximately 62%[1,2]

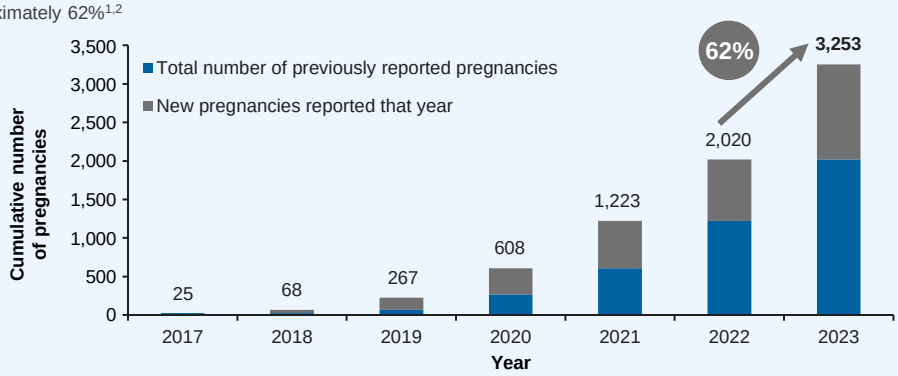

Table 1: Summary of known pregnancy outcomes by exposure category:* Prospective cases†,[1]

- **Most pregnancies resulted in live births** (83.6%), and proportions were similar in the exposed and non-exposed groups
- **Most live births were full term** (61.4%), and a smaller proportion were preterm (8.5%)
  - 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**, but the overall cumulative proportion of elective abortions is decreasing (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%)
- The overall **rate of stillbirths remained low** (<0.1%)

Number of MS pregnancies	Non-exposed (N=575)	Exposed (N=855)	Unknown (N=1,016)	Total (N=2,446)	Epidemiological rates	
					MS background rate	General population background rate
Known outcomes	n=351	n=512	n=282	n=1,145		
Live births†	88.3%	84.2%	76.6%	83.6%	70.2–77.2[3]	70.2[3]
Full term (≥37 weeks)§	70.9%	65.7%	39.1%	61.4%	–	–
Preterm (<37 weeks)§	8.4%	9.5%	6.5%	8.5%	7.2–15.4[3-6]	6.5–10.4[3,4,6]
Unknown gestational age§	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 foetal death‡						
Spontaneous abortion, ≤22 weeks‡	9.1%	7.4%	16.0%	10.0%	10.5–11.6[3-5]	10.0–20.0[3,4]
Stillbirth, >22 weeks‡	–	0.2%	–	<0.1%	0.3–0.6[3,6]	0.2–0.7[3,6]

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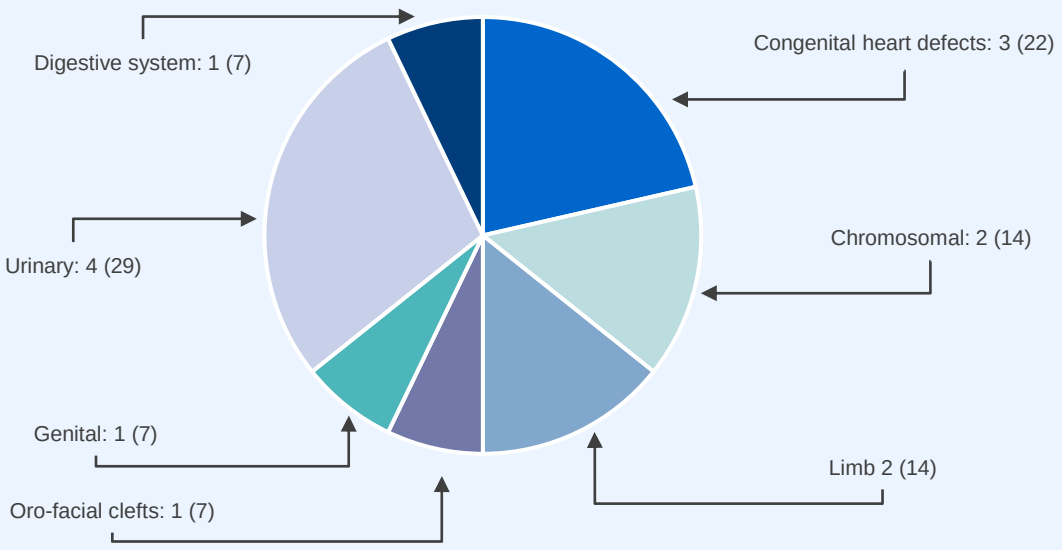
Table 2: Major congenital anomalies in pregnancies with known outcomes[1]

Proportions and types of MCAs are consistent with epidemiological background.[3–8] It is estimated that around 2–4% of all children born every year will have an MCA[3–7]

	Non-exposed	Exposed	Unknown exposure	Total
Live births	**N=310**	**N=431**	**N=216**	**N=957**
Live birth with MCA, n (%)*	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†	1	3	–	4
Unknown GA with MCA, n†	–	–	–	–
Stillbirths >22 weeks	**N=0**	**N=1**	**N=0**	**N=1**
Stillbirth with MCA, n†	–	1	–	1
Live birth/stillbirth with MCA, n (%)‡	4 (1.3%)	8 (1.9%)	1 (0.5%)	13 (1.4%)

Figure 2: Distribution of major congenital anomalies by EUROCAT[12] category, n (%)*,[1]



Ongoing clinical trials: MINORE & SOPRANINO

MINORE[9,10]

- Enrolment 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[10,11]

- 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 postpartum)
- **Co-primary endpoints:** Proportion of infants with B-cell levels below 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:
Please report any occurrence of pregnancy in women receiving OCR via our MedInfo portal here

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Footnotes

Table 1

The dash indicates that no cases were reported.

*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;[13,14]

†*In utero* exposure based on timing of last OCR dose relative to the LMP;

‡Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total);

§Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total).

Table 2

*Percentages represent fractions of total live births for the respective exposure category;

†The dash indicates that no cases were reported;

‡Percentages represent fractions of the total stillbirths/live births for the respective exposure category.

Figure 2

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

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

1. Hellwig K, et al. Presented at ECTRIMS-ACTRIMS 2023 (Poster P061);
2. Oreja-Guevara C, et al. Presented at ECTRIMS 2022 (Presentation O038);
3. Andersen JB, et al. *Eur J Neurol* 2022;30:162–71;
4. Khan E, et al. *J Neuroimmunol* 2023;383:578178;
5. Lopez-Leon S, et al. *J Neurol* 2020;267:2721–31;
6. MacDonald SC, et al. *Am J Epidemiol* 2019;188:57–66;
7. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep* 2008;57:1–5;
8. European Medicines Agency (EMA). Guideline on the Exposure to Medicinal Products During Pregnancy: Need for Post-Authorisation data. November 2005. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-exposure-medicinal-products-during-pregnancy-need-post-authorisation-data_en.pdf. Accessed 13 November, 2023;
9. ClinicalTrials.gov identifier: NCT04998812. Accessed 13 November, 2023;
10. Bove R, et al. *MSARD* 2022;64:103963;
11. ClinicalTrials.gov identifier: NCT04998851. Accessed 13 November, 2023;
12. European Surveillance of Congenital Anomalies (EUROCAT) Guide 1.5. Available from: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/data-collection/guidelines-for-data-registration_en. Accessed 13 November 2023;
13. Palmeira P, et al. *Clin Dev Immunol* 2012;2012:985646;
14. Simister NE. *Vaccine* 2003;21:3365–69.