P061

Pregnancy and Infant Outcomes in Women Receiving Ocrelizumab for the Treatment of Multiple Sclerosis: Analysis of the Largest Available Outcomes Database

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OBJECTIVE

To report on pregnancy and infant outcomes among women with MS exposed to ocrelizumab before or during pregnancy up to July 2023

CONCLUSIONS

- *In utero* exposure to ocrelizumab did not increase the risk of adverse pregnancy or infant outcomes compared with epidemiological background of both MS and general population[1–6]
- This is the largest dataset of pregnancy outcomes for an anti-CD20 therapy in MS[7]
- Reports of infant outcomes throughout the first year of life are very limited; continuous improvement of reporting by healthcare professionals remains a critical component to increase available evidence
- Pregnancy and infant outcomes are important to women with MS. Patients and data continue to be collected through post-marketing commitments (OCREVUS pregnancy registry)[8] and two prospective Phase IV studies examining infant B cell levels and ocrelizumab pharmacokinetics across the placenta (MINORE, MN42988) and breastmilk (SOPRANINO, MN42989)[9]

METHODS

Sources, Reporting Period and Type, and Definition of *In Utero* Exposure

Sources
- Reports from the Roche Global Safety Database: (1) interventional or non-interventional clinical studies, (2) spontaneous reports, (3) non-interventional programme, (4) published literature

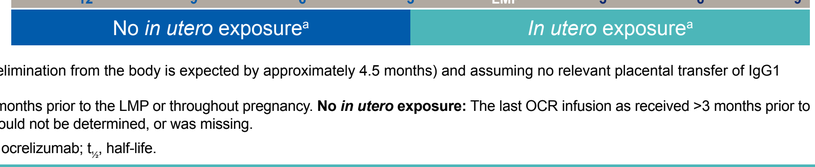
Reporting type
- **Prospective:** Final outcomes were unknown at initial notification
- **Retrospective:** Final outcomes were known at initial notification

Reporting period
- Cumulative pregnancies reported from

November 2008 to **12 July 2023**

Exposure

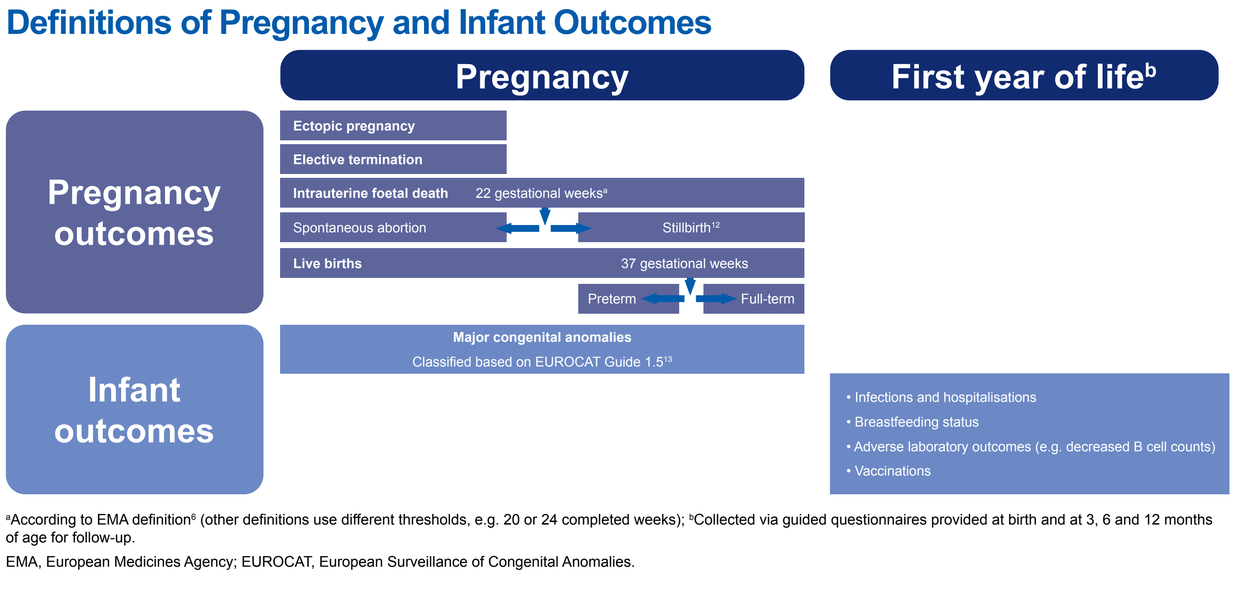
Timing of last OCR dose in relation to date of LMP (months)



[a]Exposure classification is based on OCR t½=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.[10,11]
***In utero* exposure:** The last OCR infusion was received ≤3 months prior to the LMP or throughout pregnancy. **No *in utero* exposure:** The last OCR infusion as received >3 months prior to the LMP. **Unknown exposure:** Where the exposure timing could not be determined, or was missing.

IgG1, immunoglobulin G1; LMP, last menstrual period; OCR, ocrelizumab; $t_{½}$, half-life.

Definitions of Pregnancy and Infant Outcomes

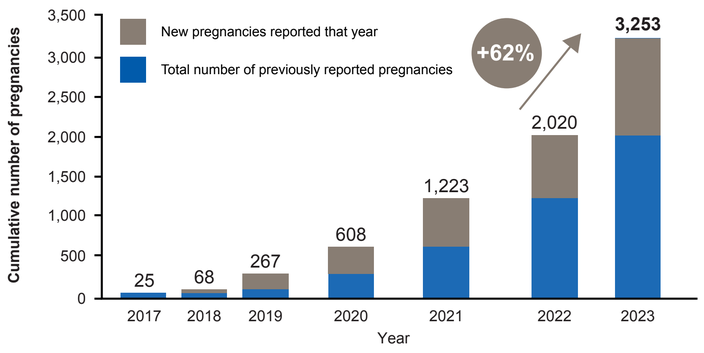


[a]According to EMA definition[6] (other definitions use different thresholds, e.g. 20 or 24 completed weeks); [b]Collected via guided questionnaires provided at birth and at 3, 6 and 12 months of age for follow-up.

EMA, European Medicines Agency; EUROCAT, European Surveillance of Congenital Anomalies.

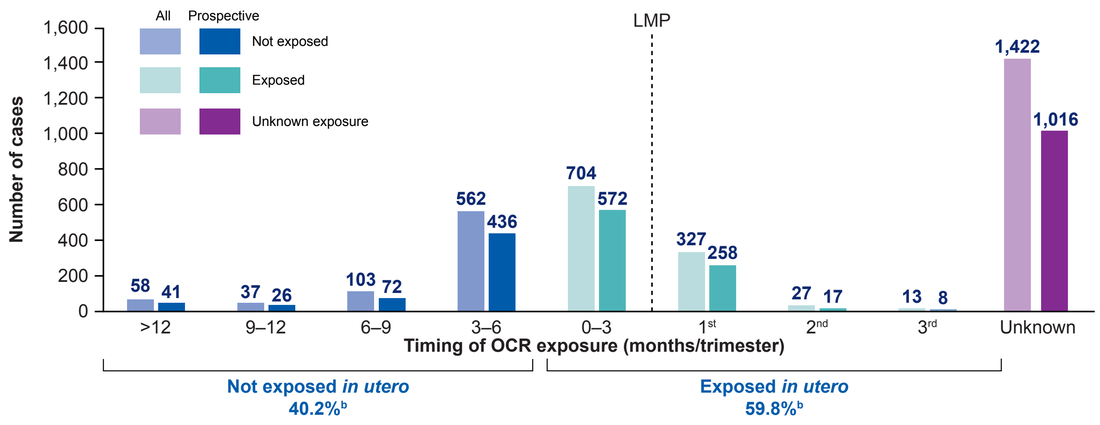
RESULTS

The cumulative number of pregnancies reported among women with MS treated with OCR continues to grow[7]



There was a 62% increase in the number of cases from 2022 to 2023

MS Pregnancies by *In Utero* Exposure:[a] All Cases and Prospective Cases



- **Median age at LMP (range) was 32.0 (16–60) years[c]**
- **Timing of last OCR dose in relation to LMP was known for 58% of all or prospective cases**
- **Where exposure was known, most cases were reported as exposed *in utero* and most exposed to the last OCR dose 0–3 months before LMP followed by 1st trimester of pregnancy**
- **For cases with no exposure *in utero*, most were reported in mothers exposed to the last OCR dose 3–6 months before LMP**

[a]Determined according to timing of last OCR dose in relation to date of LMP (months); exposure classification is based on OCR $t_{½}$=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; [b]Percentages represent fractions of prospective cases with known outcome and known timing of last OCR dose. [c]Cases with known age: n=2,676 (82.3%).

MS, multiple sclerosis; OCR, ocrelizumab.

IgG1, immunoglobulin G1; LMP, last menstrual period; OCR, ocrelizumab; $t_{½}$, half-life.

Pregnancy Outcomes by Exposure in Prospective Cases[a]

- **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)[7]
- **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** (<0.1%) remained low

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[b]	**88.3%**	**84.2%**	**76.6%**	**83.6%**	**70.2–77.2[1]**	**70.2[1]**
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[1–4]**	**6.5–10.4[1-2, 4]**
Unknown gestational age[c]	**20.7%**	**24.8%**	**54.4%**	**30.2%**	–	–
Ectopic pregnancy[b]	**0.9%**	**0.8%**	**2.5%**	**1.2%**	**0.6–1.3[1,2]**	**1.1–2.0[1,2]**
Elective termination[b]	**1.7%**	**7.4%**	**5.0%**	**5.1%**	**10.7–18.1[1]**	**18.2[1]**
Intrauterine foetal death[b]						
Spontaneous abortion, ≤22 weeks[b]	**9.1%**	**7.4%**	**16.0%**	**10.0%**	**10.5–11.6[1–3]**	**10.0–20.0[1,2]**
Stillbirth, >22 weeks[b]	–	**0.2%**	–	**<0.1%**	**0.3–0.6[1,4]**	**0.2–0.7[1,4]**

The dash indicates that no cases were reported; Please see Supplementary Materials for details on all cases, pregnancy outcomes by more granular timings of OCR exposure and listing of stillbirths.
[a]*In utero* exposure based on timing of last OCR dose relative to LMP; [b]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero,* unknown exposure, total); [c]Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero,* unknown exposure, total).
LMP, last menstrual cycle; MS, multiple sclerosis; OCR, ocrelizumab.

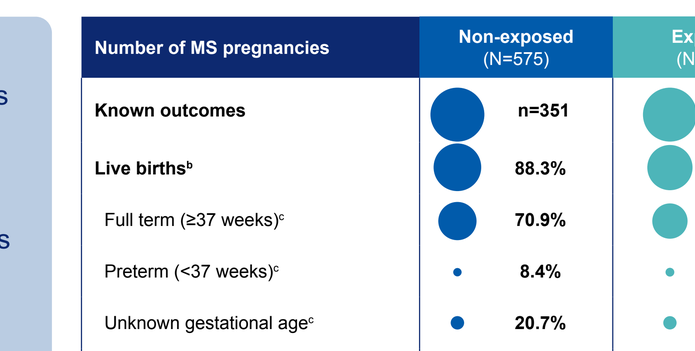
Major Congenital Anomalies in Pregnancies with Known Outcomes

Proportions and types are consistent with epidemiological background[1-6]

	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	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 (%)[b]	4 (1.3%)	8 (1.9%)	1 (0.5%)	13 (1.4%)

Around 2–4% of all children born every year will have a MCA[1–5]

Distribution of Major Congenital Anomalies by EUROCAT[13] Category, n (%)[c]



Please see Supplementary Materials for details on the listing of major congenital anomalies. The dash indicates that no cases were reported.
[a]Percentages represent fractions of total live births for the respective exposure category; [b]Percentages represent fractions of the total stillbirths/live births for the respective exposure category; [c]The number of major congenital anomalies prospectively reported is 14, as one live birth reported two MCAs; see Supplementary Materials for all cases.
EUROCAT, European Surveillance of Congenital Anomalies; GA, gestational age; MCA, major congenital anomaly.

Reports of Infant Outcomes Throughout the First Year of Life are Very Limited[a]

1,888 known pregnancy outcomes[b]

226 Infants with 1-year follow-up data

127 infants were exposed *in utero*
54 infants were not exposed *in utero*
45 infants had unknown exposure

80 infants were also exposed *in utero*
46 infants exposed via breastfeeding only

Infants with exposure via breastfeeding **126**

[a]For further details, see the Supplementary Materials. [b]Includes all known outcomes, either prospectively or retrospectively reported.

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