Pregnancy and Infant Outcomes in Women with Multiple Sclerosis Receiving Ocrelizumab: Analysis of Approximately 4,000 Pregnancies to Date

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See our other pregnancy-related presentations at ECTRIMS: MINORE (P087), SOPRANINO (O039) and peripartum disease activity (P591 & P1240)

OBJECTIVE

To report on pregnancy and infant outcomes among women with MS exposed to ocrelizumab before or during pregnancy up to 28 March 2024

KEY TAKEAWAYS

***In utero exposure* to ocrelizumab is not associated with an increased risk of adverse pregnancy or infant outcomes:** most pregnancies resulted in live births that were full term, with other outcomes similar among exposed and non-exposed pregnancies

The **frequency of MCAs was within the range** reported for other MS cohorts and for the general population[1-7]

This is the **largest dataset of reported pregnancies for an anti-CD20 therapy in MS**,[8] complimenting data from two prospective Phase IV studies examining infant B-cell levels and ocrelizumab pharmacokinetics across the placenta (MINORE, NCT04998812),[9] and breastmilk (SOPRANINO, NCT04998851)[10]

INTRODUCTION

- As of March 2024, >350,000 people with MS had initiated OCR treatment globally, amounting to >1 million patient years[11]
- Women with MS of childbearing potential[12] and the number of those exposed to OCR before, during and after pregnancy is increasing[8]
- OCR labelling advises the use of contraception during treatment and for 6–12 months after the last infusion;[13] however, pregnancies may occur during this interval

METHODS

Sources, Reporting Type and Period, Exposure

Sources

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

Reporting type

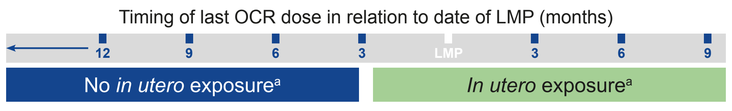
- **Prospective:** Final outcomes were unknown at initial notification
- **Retrospective:** Final outcomes were known at initial notification

Reporting period

- Cumulative pregnancies reported from

5 November 2008 to **28 March 2024**

Exposure



[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.[14–17] *In utero* exposure: The last OCR infusion was received ≤3 months prior to the LMP or during pregnancy. No *in utero* exposure: The last OCR infusion was received >3 months prior to the LMP. Unknown exposure: Where the exposure timing could not be exactly determined or was missing.

Definitions of Pregnancy and Infant Outcomes

Pregnancy outcomes[11]

Pregnancy

- **Ectopic pregnancy**
- **Elective termination**
- **Intrauterine foetal death** — 22 gestational weeks[a]
- Spontaneous abortion ↔ Stillbirth[18]
- **Live births** — 37 gestational weeks
  - Preterm ↔ Full-term

Infant outcomes

First year of life[b]

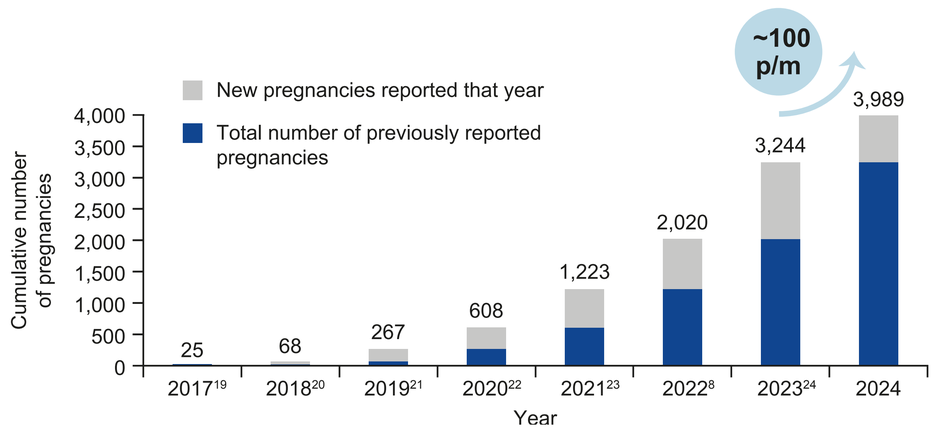
Major congenital anomalies
Classified based on EUROCAT Guide 1.5 into major, minor and not determinable[2]

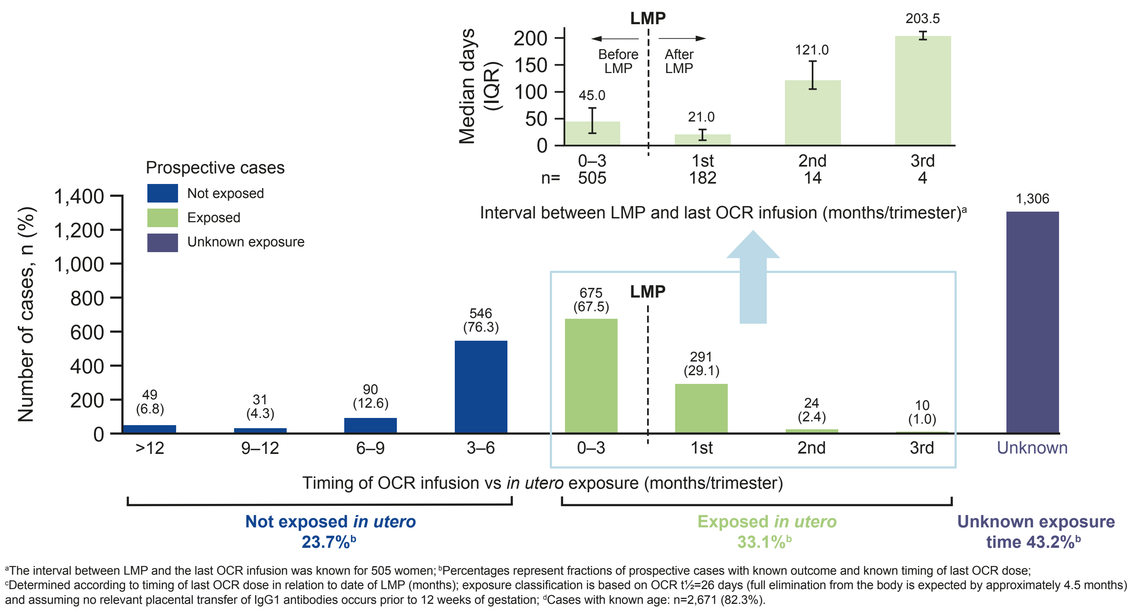
- Adverse laboratory outcomes (e.g. B-cell counts)
- Vaccinations
- Infections and other adverse events

[a]According to EMA definition[1] (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. Additional information available in Supplementary Material.

RESULTS

The Cumulative Number of Pregnancies Reported Among Women with MS Treated with OCR Continues to Grow[19] with an Increase of ~100 New Pregnancy Cases per Month from 2023 to 2024





- Most prospectively reported cases were considered *in utero*[c] exposed, of which the majority had the last OCR dose 0-3 months before the LMP (median: 45 days), followed by 1st trimester of pregnancy (median: 21 days)
- For prospective cases, median age was 32.0 (Q1–Q3: 29–35) years[d]

[a]The interval between LMP and the last OCR infusion was known for 505 women; [b]Percentages represent fractions of prospective cases with known outcome and known timing of last OCR dose; [c]Determined according to timing of last OCR dose in relation to date of LMP (months); 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; [d]Cases with known age: n=2,671 (82.3%).

Exposure to OCR by Different Administration Timings was Not Associated with an Increased Risk of Adverse Pregnancy or Infant Outcomes

- In prospectively reported cases, exposure to OCR[a] was not associated with an increased risk of adverse pregnancy or infant outcomes compared with the epidemiological background of both MS and general populations[1, 3–7]
- Most pregnancies resulted in live births (84.4%) that were full term (61.4%), and a smaller portion were preterm (8.0%)
  - Proportions were similar in the exposed and non-exposed groups
  - Gestational age was unknown in 30.7% of live births
- A higher proportion of elective terminations occurred in the exposed group, but the overall cumulative proportion of elective abortions is decreasing (4.7% in 2024 vs 7.4% in 2023 and 11.5% in 2022)[8]
- The overall rate of stillbirths (0.2%) remained low

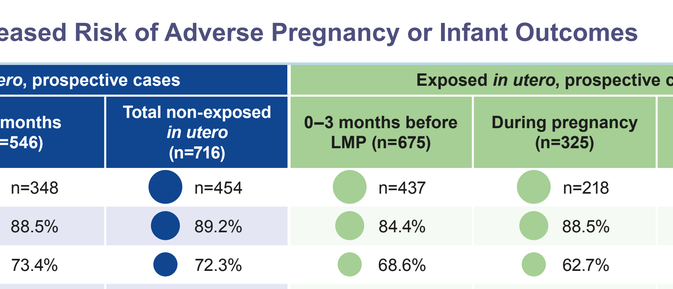
Exposure based on last OCR dose	Non-exposed *in utero*, prospective cases			Exposed *in utero*, prospective cases			Total prospective cases (n=3,022)[b]	Epidemiological rates	
Number of MS pregnancies	**>6 months (n=170)**	**3–6 months (n=546)**	**Total non-exposed *in utero* (n=716)**	**0–3 months before LMP (n=675)**	**During pregnancy (n=325)**	**Total exposed *in utero* (n=1,000)**		**MS background rate**	**General population background rate**
Known outcomes	n=106	n=348	n=454	n=437	n=218	n=655	n=1,502	-	-
Live births[c]	91.5%	88.5%	89.2%	84.4%	88.5%	85.8%	84.4%	70.2–77.2[4]	70.2[4]
Full term (≥37 weeks)[d]	69.1%	73.4%	72.3%	68.6%	62.7%	66.5%	61.4%	-	-
Preterm (<37 weeks)[d]	7.2%	8.4%	8.1%	9.2%	7.3%	8.5%	8.0%	7.2–15.4[4–7]	6.5–10.4[4–7]
Unknown gestational week[d]	23.7%	18.2%	19.5%	22.2%	30.1%	24.9%	30.7%	-	-
Live births with MCA[d]	-	1.9%	1.5%	1.6%	2.1%	1.8%	1.3%	2.2–4.0[4,6,7]	2.7–4.0[4,7]
Ectopic pregnancy[c]	-	0.9%	0.7%	0.9%	-	0.6%	0.9%	0.6–1.3[4,5]	1.1–2.0[4,5]
Elective termination	-	2.3%	1.8%	5.9%	6.9%	6.3%	4.7%	10.7–18.1[4]	18.2[4]
Intrauterine/foetal death[c]									
Spontaneous abortion (≤22 weeks)	8.5%	8.3%	8.4%	8.0%	4.6%	6.9%	9.8%	10.5–11.6[4–6]	10.0–20.0[4,5]
Stillbirth (>22 weeks)	-	-	-	0.7%	-	0.5%	0.2%	0.3–0.6[4,7]	0.2–0.7[4,7]
Live births/stillbirths with MCA[e]	-	1.9%	1.5%	1.9%	2.1%	1.9%	1.4%	2.2–4.0[4,6,7]	2.7–4.0[4,7]

Data as of 28 March 2024. Dash indicates a data value of 0.
[a]*In utero* exposure based on timing of last OCR dose relative to the LMP; [b]Total includes cases of unknown exposure; [c]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total); [d]Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total); [e]Percentages represent fractions of total live births and stillbirths.
Additional data available in Supplementary Material.

The Rates of MCAs Were Similar in Exposed and Non-Exposed Groups, and Were in Line with Epidemiologic Background Rates[1,3-7]

	Number of pregnancies with MCAs		Relative risk (95% CI)[c]
	Roche database prospective cases (n=1,271)[a]	EUROCAT (n=3,677,470)[b]	
LB with MCAs			
All (n=1,268)	17 (1.3%)		0.64 (0.40 to 1.03)
Exposed *in utero* (n=562)	10 (1.8%)	75,756[d]	0.86 (0.47 to 1.60)
Not exposed *in utero* (n=405)	6 (1.5%)		0.72 (0.33 to 1.59)
LB and SB with MCAs[e]			
All (n=1,271)	18 (1.4%)		0.53 (0.34 to 0.84)
Exposed *in utero* (n=565)	11 (1.9%)	97,755[f]	0.73 (0.41 to 1.32)
Not exposed *in utero* (n=405)	6 (1.5%)		0.56 (0.25 to 1.23)

Distribution of MCAs by EUROCAT[2] Category, n (%)[g] for Prospectively Reported Live and Stillbirths



575 Infants with up to 1-year follow-up

- **256 (44.5%)** exposed *in utero*
- **143 (24.9%)** not exposed *in utero*
- **51 (8.9%)** infants exposed via breastfeeding only
- **125 (21.7%)** unknown exposure

42 (26.6%) breastfed infants were also exposed *in utero*

158 Infants with exposure via breastfeeding

- Infant outcomes remain limited due to incomplete reports (up to 95.6% missing information)
- HCP reporting remains essential to increase available evidence

[a]Prospectively reported pregnancy outcomes with following outcomes: Live births/stillbirths/intrauterine or foetal deaths of unknown gestational age; [b]Number of pregnancies with following outcomes: Live births + foetal deaths + TOPFA reported between 2017 and 2022 (period from year of regulatory approval of OCR to last available data in the EUROCAT database);[25] [c]Relative risk (with associated 95% CI) was calculated for rates of MCAs reported in the Roche database of prospective cases versus the EUROCAT database; [d]Number of anomalies reported in live births; [e]No prospective intrauterine/foetal death cases with unknown gestational age were reported; [f]Number of total anomalies (reported in live births + foetal deaths + TOPFA); [g]The number of prospectively reported live and stillbirths with at least one MCA was 18; two live births reported two MCAs each, totalling 20 MCAs.
Additional data available in Supplementary Material.

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DISCLOSURES

R Dobson received research support from Multiple Sclerosis Society UK, Horne Family Foundation, Barts Charity, Merck, Biogen and Celgene; consultancy fees from F. Hoffmann-La Roche Ltd, Novartis, Sandoz and Biogen (all payments made are institutional and used to support research/educational activities); honoraria for lectures, speaking etc. from Biogen, F. Hoffmann-La Roche Ltd, Sanofi-Genzyme, Merck, Novartis, Janssen and Teva Pharmaceuticals; support for attending meetings and/or travel from Novartis, Biogen and Janssen (all payments made are institutional and used to support research/educational activities); and is part of the Association of British Neurologists MS Advisory Group and NHS England Clinical Reference Group. **S Vukusic** received grants and research support from Biogen, Novartis, Merck-Serono, F. Hoffmann-La Roche Ltd and Sanofi-Genzyme; consultancy fees from F. Hoffmann-La Roche Ltd, Biogen, Bristol Myers Squibb/ Celgene, Janssen, Novartis, Merck-Serono, Sandoz, Sanofi-Genzyme and Teva Pharmaceuticals; and payment/honoraria for lectures, speaking etc. from F. Hoffmann-La Roche Ltd, Biogen, Bristol Myers Squibb/Celgene, Novartis, Merck-Serono, Sandoz, Sanofi-Genzyme and Teva Pharmaceuticals. **R Bove** received consultancy fees from Alexion, EMD Serono, Horizon, Janssen, TG Therapeutics and Sanofi; and is funded by the National Multiple Sclerosis Society Harry Weaver Award, National Institutes of Health and Department of Defense, as well as Biogen, Eli Lilly, F. Hoffmann-La Roche Ltd and Novartis. **K Hellwig** received grant/contract support, consultancy fees, honoraria and/or compensation from the Federal Innovationsfonds, National MS Society in Germany, Almirall, Bayer, Biogen, Sanofi, Teva Pharmaceuticals, Bristol Myers Squibb/Celgene, Janssen, Hexal, F. Hoffmann-La Roche Ltd, Novartis and Merck. **KM Krysko** received grants from MS Canada; a contract for a study site from Roche; speaking or consultancy fees from Biogen, EMD Serono, Novartis and F. Hoffmann-La Roche Ltd; and served as an advisory board member for Biogen, EMD Serono, Novartis and F. Hoffmann-La Roche Ltd; and a scientific advisory committee member for Bristol Myers Squibb. **C Pietrasanta** received consultancy fees from F. Hoffmann-La Roche Ltd. **T McElrath** received research support from the National Institutes of Health and NX Prenatal Inc.; compensation for service on the scientific advisory boards of Mirvie Inc., F. Hoffmann-La Roche Ltd and Momenta Pharmaceuticals, Inc.; and consultancy fees from F. Hoffmann-La Roche Ltd and Comanche Biopharma. **G Ferreira** is a consultant for F. Hoffmann-La Roche Ltd. **L Craveiro**, **D Goncalves Pereira Alves**, **D Zecevic**, **C-J Lin** and **N Pasquarelli** are employees of and shareholders of F. Hoffmann-La Roche Ltd. **C Oreja-Guevara** received speaker and consultation fees from Alexion, Amgen, Biogen Idec, Bristol Myers Squibb, Horizon, Janssen, Merck, Novartis, F. Hoffmann-La Roche Ltd, Sanofi-Genzyme, Sandoz, Viatris, Neuraxpharm and Teva Pharmaceuticals.

ABBREVIATIONS

CD20, cluster of differentiation 20; **EMA**, European Medicines Agency; **EUROCAT**, European Surveillance of Congenital Anomalies; **HCP**, healthcare professional; **IFD**, intrauterine/foetal deaths of unknown gestational age; **IgG1**, immunoglobulin G1; **IQR**, interquartile range; **LB**, live births; **LMP**, last menstrual period; **MCA**, major congenital anomaly; **MS**, multiple sclerosis; **OCR**, ocrelizumab; **p/m**, per month; **Q**, quarter; **SB**, stillbirth; **t½**, half-life; **TOPFA**, termination of pregnancy for foetal anomaly.

ACKNOWLEDGEMENTS

We would like to thank all mothers and babies as well as their families and the investigators participating in this study. This study is sponsored by F. Hoffmann-La Roche Ltd. Writing and editorial assistance was provided by Nucleus Global and funded by F. Hoffmann-La Roche Ltd.

Presented at the 40th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); 18–20 September 2024; Copenhagen, Denmark.