Poster DMT45

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Cumulative Pregnancy Outcomes in Patients With Multiple Sclerosis Following Maternal Exposure to Ofatumumab: Results From the Novartis Safety Database

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INTRODUCTION

- Ofatumumab (OMB), a fully human anti-CD20 monoclonal antibody with a 20-mg subcutaneous monthly dosing regimen, is approved for the treatment of relapsing multiple sclerosis in adults[1,2]
- The US Food and Drug Administration and European Medicines Agency labels of OMB state that women of childbearing potential should use effective contraception during treatment with OMB and for ≥6 months after the last dose[1,2]
- Clinical data on the effect of OMB treatment on pregnancy outcomes are currently limited
- Based on current knowledge:
  - Transient B-cell depletion and lymphopenia have been observed in infants whose mothers were exposed to other anti-CD20 antibodies during pregnancy[3,4]
  - The maternal-fetal transfer of immunoglobulin G (IgG) during the first trimester is minimal, and fetal IgG concentration starts to rise from the second trimester[5,6]
  - Exposure to OMB during gestation did not cause maternal toxicity in cynomolgus monkeys, and no adverse effects were observed on prenatal or postnatal development[7]

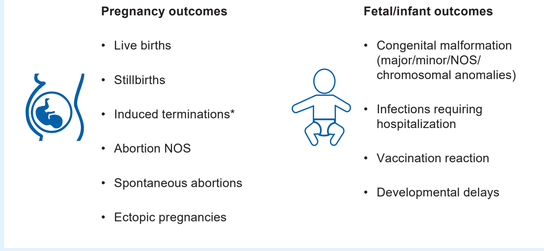
OBJECTIVE

- To report the latest cumulative pregnancy and infant outcomes data in women treated with OMB during or in the 6 months prior to pregnancy

METHODS

- The Novartis Global Safety Database includes cases from clinical trials and the postmarketing setting collected via the noninterventional **PR**egnancy outcomes **I**ntensive **M**onitoring (PRIM) study
- Data on spontaneously reported pregnancies are collected using a set of targeted and structured checklists
- Pregnancy outcomes were analyzed in women exposed to OMB during pregnancy or ≤6 months prior to their last menstrual period (LMP) (cutoff date: September 25, 2023)
  - Potential fetal exposure to OMB was categorized based on maternal injection(s) accounting for any injection from 6 months prior to LMP to the end of the pregnancy
- Pregnancy and infant outcomes were collected from the reporting of pregnancy up to a maximum of 1 year of the infant's age (**Figure 1**)
- This analysis was focused on outcomes in prospective cases with maternal exposure during pregnancy. Outcomes in retrospective cases are provided separately for completeness and are expected to be subject to an inherent reporting bias toward abnormal outcomes due to the retrospective nature
- **Prospective cases** are defined as cases for which, at the time of initial reporting (ie, first receipt by Novartis), the pregnancy outcome has not yet occurred or there is no report of an abnormal prenatal testing result (including cases where prenatal testing has not yet been performed or cases where prenatal testing has been performed but results were either not received yet by provider, normal, or not specified)
- **Retrospective cases** are defined as cases for which, at the time of initial reporting (ie, first receipt by Novartis), the pregnancy outcome has already occurred or prenatal testing results were abnormal (regardless of whether the pregnancy outcome has occurred)
- PRIM is a noninterventional study, and no information on B-cell depletion or immunoglobulin/hematological abnormalities is expected to be collected as part of this study

Figure 1. Pregnancy and Fetal/Infant Outcomes



NOS, not otherwise specified
*Includes therapeutic and elective terminations

RESULTS

Prospective Cases

Patient Characteristics and Exposure to OMB

- As of September 25, 2023, 279 prospective pregnancies with maternal exposure to OMB were identified
- Pregnancy cases by reporting type are summarized in **Figure 2** and maternal demographics are summarized in **Table 1**

Figure 2. Pregnancy Cases by Reporting Type

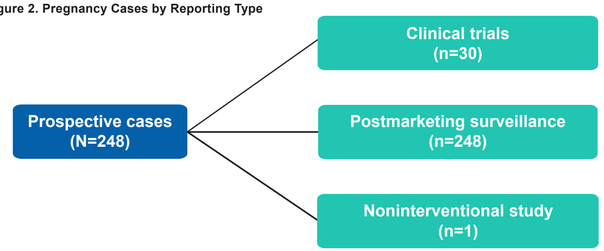


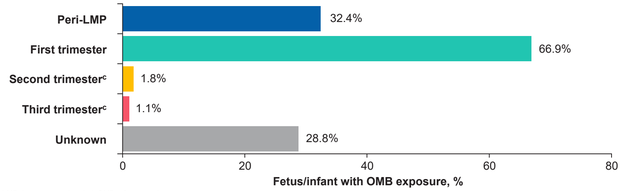
Table 1. Maternal Demographics

Demographics	
Maternal age at LMP, years, n (%)	161 (57.7)
Mean (SD)	31.4 (5.89)
Min, max	18, 44
Region, n (%)	279 (100)
North America	149 (53.4)
Western Europe	47 (16.8)
Asia and Oceania	44 (15.8)
Other	39 (14.0)
Gestational age at reporting, weeks, n (%)	93 (33.3)
Median	~7

LMP, last menstrual period

- Most fetuses/infants (n=188; 66.9%) were exposed to OMB during the first trimester; for 81 patients (28.8%), the exact timing of exposure was unknown (**Figure 3**)

Figure 3. Exposure to OMB[a] (Fetal/Infant Cohort[b]; N=281)



LMP, last menstrual period; OMB, ofatumumab
[a]Potential fetal exposure to OMB was categorized based on maternal injection(s) accounting for any injection from 6 months prior to LMP to end of pregnancy; [b]The 279 prospective pregnancy cases included a cohort of 281 fetuses/infants (2 pregnancies involving twins). Some pregnancies involved more than one trimester of exposure to ofatumumab and therefore are included in more than one category in the figure above. The peri-LMP period for ofatumumab refers to the 180 days prior to the LMP; [c]Cases exposed to ofatumumab in the second and third trimester either resulted in normal live births, or include pending outcomes, or were lost to follow-up

Pregnancy and Infant Outcomes

- As of September 25, 2023, among 279 prospective cases, there were 55 known pregnancy outcomes, 123 cases were ongoing at data lock point, and 101 cases were lost to follow-up
- Outcomes consisted of 29 live births, 12 induced terminations, 4 ectopic pregnancies, 11 spontaneous abortions, and 1 abortion (not otherwise specified) (**Figure 4**; **Table 2**)

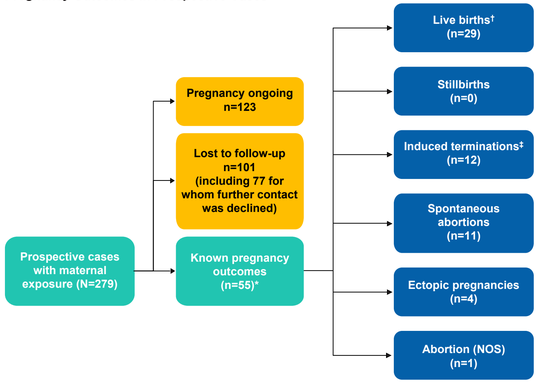
Table 2. Pregnancy Outcomes by Trimester of Exposure (Fetus Cohort With Maternal Exposure During Pregnancy)

	Live birth*	Induced termination†	Spontaneous abortion	Ectopic pregnancy	Abortion NOS	Total
Peri-LMP only	3	1	0	0	0	**4**
At least first trimester	20	10	10	2	1	**43**
Peri-LMP or first trimester	23	11	10	2	1	**47**
Overall‡	29	12	11	4	1	**57**

LMP, last menstrual period; NOS, not otherwise specified
*Includes 1 case of minor congenital malformation (hydronephrosis) and 1 set of twins; †Includes therapeutic and elective terminations with another set of twins; ‡Includes unknown trimester and other combinations of trimester

- In the 29 prospective live births, there were:
  - 28 full-term newborns including 1 set of twins
  - 1 premature newborn (34 weeks of gestation)
  - No major congenital anomalies or serious infections

Figure 4. Pregnancy Outcomes in Prospective Cases



NOS, not otherwise specified
*2 pregnancies involving twins; †Includes newborn with a minor congenital malformation (hydronephrosis) and 1 set of twins; ‡Includes therapeutic and elective terminations with another set of twins; 1 case of trisomy 18 and no reported abnormalities or reason for termination provided in the remaining 11 outcomes

Retrospective Cases

- As of September 25, 2023, 30 retrospective pregnancy cases were reported in women with MS who were exposed to OMB. One patient discontinued therapy with OMB due to delivery; no further details were provided
- Outcomes in the remaining 29 cases included 9 live births, 3 induced terminations, 16 spontaneous abortions, and 1 ectopic pregnancy
- No congenital anomalies were reported

KEY FINDINGS & CONCLUSIONS

- As of September 25, 2023, a total of 279 prospectively identified pregnancies in women exposed to ofatumumab (OMB), with 55 known pregnancy outcomes resulting in 57 fetuses/infants (2 pregnancies involving twins), were reported in the Novartis Global Safety Database
- No major congenital anomalies or serious infections were reported in the 29 prospective live births
- Given the limited data, conclusions cannot be made on the generalizability of the current observations
- Novartis will continue to collect information on outcomes from women exposed to OMB during pregnancy

- A prospective, observational registry on maternal and infant outcomes in women exposed to OMB during pregnancy is currently active in the United States/Canada and Germany (NCT05634967):
  - OTIS/MotherToBaby (United States and Canada): Please call 1-877-311-8972 or visit https://mothertobaby.org/join-study/
  - DMSKW (Germany): Please visit https://www.ms-und-kinderwunsch.de

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