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# Pregnancy Outcomes Following Exposure to Ofatumumab in Patients With MS: Results From the PRIM Study

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## CONCLUSIONS

- A total of 104 prospectively identified pregnancies in women with RMS exposed to ofatumumab with 30 known outcomes were reported from the Novartis Safety Database
- A total of 14 cases were reported retrospectively and outcomes were known in all these cases by the cut-off date
- No congenital anomalies or serious infections were reported in the live births
- Given the limited number of pregnancies identified so far and the number of pending outcomes, conclusions cannot be made on the generalizability of the current observations
- Novartis will continue to collect information on outcomes from women exposed to ofatumumab during pregnancy

A prospective observational registry on maternal and infant outcomes in women exposed to ofatumumab during pregnancy is currently active in the United States/Canada and Germany (NCT05634967)

- OTIS/MotherToBaby (US 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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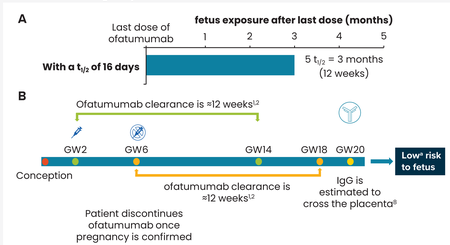
## INTRODUCTION

- Ofatumumab, a fully human anti-CD20 monoclonal antibody with a 20 mg subcutaneous monthly dosing regimen, is approved for the treatment of RMS in adults[1,2]
- The FDA and EMA labels of ofatumumab both state that women of childbearing potential should use effective contraception during treatment with ofatumumab and for 6 months after the last dose[1,2]
- Clinical data on the effect of ofatumumab 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 IgG during the first trimester is minimal and fetal IgG concentration starts to rise from the second trimester **(Figure 1)**[5,6]
  - Exposure to ofatumumab during gestation did not cause maternal toxicity in cynomolgus monkeys, and no adverse effects were observed on prenatal or postnatal development[7]

### Figure 1. Fetus exposure to ofatumumab based on terminal half-lives and IgG1 placental transfer characteristics




(A) Schema illustrating the elimination of ofatumumab. Average $t_{1/2}$ of ofatumumab: 16 days.
(B) Schema illustrating fetus exposure to ofatumumab.
[a]Low risk of a transplacental transfer of ofatumumab and B-cell depletion in fetus.

## OBJECTIVE

- To report the latest cumulative pregnancy outcomes data in women with MS exposed to ofatumumab during or in the 6 months prior to pregnancy

## METHODS

- The Novartis Global Safety Database includes cases from clinical trials and the post-marketing setting collected via the non-interventional **PR**egnancy outcomes **I**ntensive **M**onitoring (PRIM)
- Data on spontaneously reported pregnancies are collected using a set of targeted and structured checklists
- Pregnancy outcomes were analyzed in women with MS exposed to ofatumumab during pregnancy or up to 6 months prior to their last menstrual period (LMP; cut-off date: September 25, 2022)
  - Pregnancy and infant outcomes were collected up to a maximum of 1 year of the infant's age
  - The focus of the analysis was outcomes in **prospective cases** and 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 their nature

## PROSPECTIVE AND RETROSPECTIVE CASES

- **Prospective cases** are defined as cases for which, at the time of initial reporting (i.e., 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 normal or not specified)
- **Retrospective cases** are defined as cases for which, at the time of initial reporting (i.e., first receipt by Novartis), the pregnancy outcome has already occurred, or prenatal testing results were abnormal (regardless of whether the pregnancy outcome has occurred)

### Maternal and infant outcomes

**Pregnancy outcomes**
- Live births
- Stillbirths
- Induced terminations*
- Spontaneous abortions†

**Infant outcomes**
- Congenital malformation (major/minor/NOS)
- Chromosomal anomalies
- Infections requiring hospitalization
- Vaccination reaction
- Developmental delays

*Includes therapeutic and elective terminations, and ectopic pregnancy.
†Includes spontaneous abortions and abortion NOS.

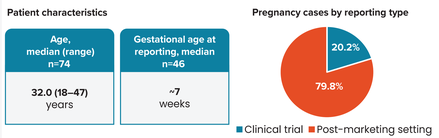
## RESULTS

## PROSPECTIVE CASES

### Patient characteristics and exposure to ofatumumab

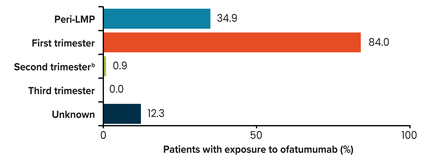
- **104 prospective pregnancies** with maternal exposure to ofatumumab were identified
  - Among these, most women were exposed to ofatumumab in the first trimester **(Figure 3)**

### Figure 2. Patient characteristics in prospective cases




n, pregnancy cases with available data

### Figure 3. Exposure to ofatumumab in prospective cases (fetus cohort; N=106)[a]

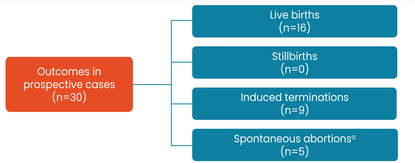



[a]The 104 prospective cases included a cohort of 106 fetuses (two pregnancies involving twins) and these are not mutually exclusive. The cases of exposure to ofatumumab were counted in more than one trimester and therefore should not be summed to 100%. The peri-LMP period for ofatumumab refers to the 180 days prior to the LMP. [b]case was lost to follow-up.

### Pregnancy outcomes

- As of the cut-off date, **30 outcomes were known in 104 prospective cases (Figure 4)**
- In the cohort of 106 fetuses (two pregnancies involving twins), 30 pregnancies were lost to follow-up (missing outcomes) and 46 were still ongoing (pending outcomes)

### Figure 4. Pregnancy outcomes in prospective cases




[a]Includes one blighted ovum and one abortion NOS. All spontaneous abortions were reported in the first trimester.

## INFANT OUTCOMES IN WOMEN WITH RMS EXPOSED TO OFATUMUMAB

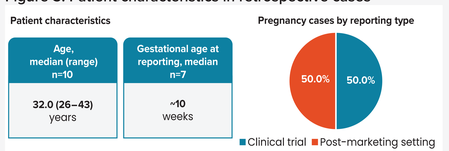
- In the 16 live births reported prospectively, there were:
  - No congenital anomalies
  - No serious infections
- PRIM is a non-interventional study, and no information on B-cell depletion or immunoglobulin/hematological abnormalities is expected to be collected as part of this study

## RETROSPECTIVE CASES

### Patient characteristics and exposure to ofatumumab

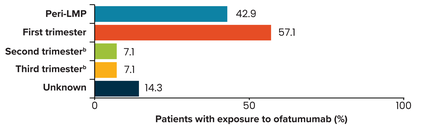
- **14 retrospective pregnancies** were reported in women with MS who were exposed to ofatumumab
  - Among these, most women were exposed to ofatumumab either in the first trimester or in the peri-LMP period **(Figure 6)**

### Figure 5. Patient characteristics in retrospective cases




n, pregnancy cases with available data

### Figure 6. Exposure to ofatumumab in retrospective cases (fetus cohort; N=14)[a]

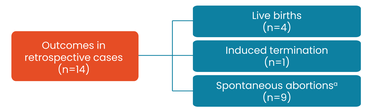



[a]The 14 retrospective cases included a cohort of 14 fetuses. The cases of exposure to ofatumumab were counted in more than one trimester and therefore should not be summed to 100%. The peri-LMP period for ofatumumab refers to the 180 days prior to the LMP. [b]The outcome was a live birth.

### Pregnancy outcomes

- As of the cut-off date, **14 outcomes were reported in 14 retrospective cases (Figure 7)**
- No congenital anomalies were reported in the four live births

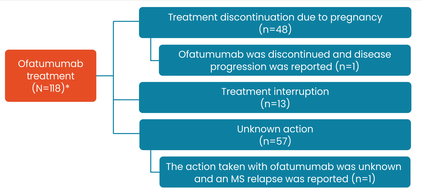
### Figure 7. Pregnancy outcomes in retrospective cases




[a]Includes one blighted ovum and one abortion NOS.

## OFATUMUMAB TREATMENT DISCONTINUATIONS/INTERRUPTIONS

### Figure 8. Ofatumumab treatment discontinuations/interruptions




*N=118: 104 prospective; 14 retrospective.

**ABBREVIATIONS:** CD, cluster of differentiation; EMA, European Medicines Agency; FDA, Food and Drug Administration; GW, gestational week; IgG, immunoglobulin G; LMP, last menstrual period; MS, multiple sclerosis; n, pregnancy cases with available data; NOS, not otherwise specified; PRIM, **PR**egnancy outcomes **I**ntensive **M**onitoring; RMS, relapsing multiple sclerosis; $t_{1/2}$, half-life.

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