

Introduction and Purpose

Pregnancy is contraindicated under treatment with several disease-modifying therapies (DMTs) for multiple sclerosis (MS), including ponesimod, a sphingosine-1-phosphate receptor (S1P) modulator.¹ The management of pregnancies exposed to these DMTs can be challenging due to the paucity of data on fetal outcomes. In this report, we describe the clinical course and pregnancy outcome of a female patient with relapsing-remitting (RR) MS who became unexpectedly pregnant while on ponesimod therapy, discussing safety considerations and the relevance of pharmacovigilance reporting.

Materials and methods

Case report of a 30-year-old female patient with RRMS followed at our MS clinic at the Careggi University Hospital in Florence.

Case report

The patient was diagnosed with RRMS when she was 18 years old. She was previously treated with interferon and dimethyl-fumarate. The latter was discontinued due to recent clinical and radiological disease activity, manifesting as optic neuritis and occurrence of three new lesions on brain MRI, two of which were contrast-enhancing. She was then switched to ponesimod; her Expanded Disability Status Scale (EDSS) at that time was 1.0. Eight months into ponesimod therapy, the patient discovered an unplanned pregnancy, with an estimated exposure to the drug of roughly 10 days (Figure 1). The medication was immediately discontinued, and a pharmacovigilance report was submitted. The pregnancy proceeded uneventfully, except for placenta previa that required a planned cesarean section. After delivery, ponesimod was promptly reintroduced with dose titration; breastfeeding was avoided in accordance with current guidelines. No clinical or radiological disease reactivation was observed during or after the pregnancy. At the last follow-up 11 months after the delivery, the patient remained clinically stable (EDSS 1.0), and the newborn showed normal growth and development besides a low birth weight, with no congenital anomalies.

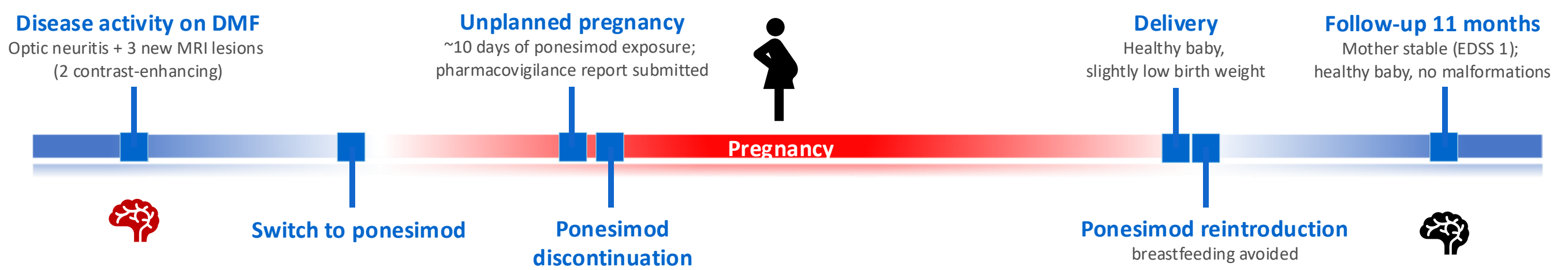


Figure 1: Timeline of the events related to an unplanned pregnancy occurring in a 30-year old female with RR-MS under ponesimod treatment. The drug was immediately discontinued and it was reintroduced shortly after the delivery. No clinical or radiological disease reactivations were observed, and the newborn did not show any congenital abnormalities, with normal growth and development up to the latest available follow-up.

Discussion and Conclusions

Ponesimod is contraindicated in pregnancy due to teratogenicity observed in preclinical animal studies.¹ However, real-world unexpected pregnancies may occur, and these could present a challenging management due to limited data in humans. Among 20 first-trimester exposed pregnancies reported in the pivotal trials, 6 live births without malformations, 8 elective terminations and 4 spontaneous abortions were described, with no increased signal for teratogenicity.² Ponesimod's short half-life (33 hours) and rapid reversibility of its effects may reduce the risk of teratogenicity if promptly withdrawn, and it could also affect the risk of rebound activity observed with other S1P modulators. In our patient, despite evidence of recent disease activity, ponesimod discontinuation within two weeks after conception and its early reintroduction postpartum were not associated with disease reactivation or rebound.

This report contributes to expanding the current knowledge on ponesimod use in unexpected pregnancies. In these events, reporting pregnancy outcomes is essential to support informed decision-making regarding pregnancy management. As data remain limited, pharmacovigilance reporting and enrolment in post-marketing registries are warranted. In this respect, The POEM (Pregnancy Outcomes Enhanced Monitoring) program is ongoing,³ aiming to collect long-term prospective data to better assess the reproductive safety of ponesimod.

References: 1. European Medicines Agency (EMA). Ponvory (ponesimod): EPAR - Summary of Product Characteristics. EMA website. Published 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/ponvory-epar-product-information_en.pdf

2. Rosas-Ballina, M., Wooller, A., Jones, R., Vaclavkova, A., & Havrdova, E. (2022, June). Fetal Exposure With Ponesimod Treatment Across Clinical Development Studies. In 2022 Annual Meeting of the Consortium of Multiple Sclerosis Centers. CMSC.

3. <https://catalogues.ema.europa.eu/node/3512/methodological-aspects>

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.