Pregnancy and Infant Outcomes From an Ongoing Worldwide Surveillance Program of Cladribine Tablets: 5-year Pharmacovigilance Results From MAPLE-MS

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CONCLUSIONS

No cases of major congenital anomalies or stillbirth were reported in 180 pregnancies exposed to cladribine tablets between August 22, 2017 and May 12, 2022

It is necessary to counsel patients to prevent pregnancy and to use effective contraception during cladribine tablets intake and for at least 6 months after the last cladribine tablet intake in each treatment year

Robust conclusions cannot be made about the risks of adverse pregnancy outcomes with cladribine tablets, but no increase has been signaled thus far

INTRODUCTION

- Cladribine tablets are contraindicated during pregnancy. As a result, exposure is expected to be rare.
- A worldwide pregnancy surveillance program (MAPLE-MS) was set up to assess the effect of cladribine tablets exposure on pregnancy and infant outcomes.

OBJECTIVES

To present cumulative pregnancy exposure data and prevalence of pregnancy and infant outcomes in:

- Women with multiple sclerosis (MS) exposed to cladribine tablets at any time during pregnancy or within 6 months before pregnancy (**maternal cohort**).
- Pregnancies fathered by men with MS exposed to cladribine tablets within 6 months before partner pregnancy (**paternal cohort**).

Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults).

METHODS

- Between the date of approval of cladribine tablets (August 22, 2017) and the cut-off date (May 12, 2022), data on cladribine tablet exposure during pregnancy or within 6 months before pregnancy were captured in the sponsor's global safety database.
- Pregnancies were analyzed to assess:
  - Live birth
  - Spontaneous abortion
  - Stillbirth (or late fetal loss)
  - Elective termination
  - Ectopic pregnancy
  - Major congenital anomalies
- Data are presented by cohort, overall, and by case reporting type (retrospectively or prospectively reported).

RESULTS

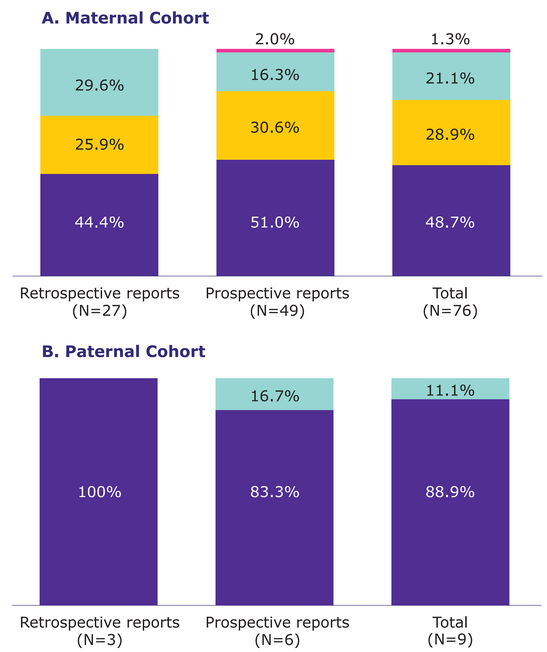
Table 1. Patient Characteristics

Characteristic	Maternal Cohort (N=76)	Paternal Cohort (N=9)
Mother's age at LMP, years (mean ± SD)	30.4 ± 6.2	35.0 ± 4.2
Gestational age at EOP, weeks (mean ± SD)	26.6 ± 15.1	35.0 ± 12.1
Gestational age group at EOP, n (%)		
<20 weeks	12 (37.5)	1 (14.3)
20–23 weeks	1 (3.1)	0 (0)
24–27 weeks	0 (0)	0 (0)
28–31 weeks	1 (3.1)	0 (0)
32–36 weeks	2 (6.3)	1 (14.3)
37–41 weeks	14 (43.8)	4 (57.1)
≥42 weeks	2 (6.3)	1 (14.3)
Unknown	44	2
Timing of exposure to cladribine tablets in relation to pregnancy, n (%)		
Before pregnancy	41 (53.9)	6 (66.7)
First trimester	20 (26.3)	NA
Only after first trimester	1 (1.3)	NA
Unknown	14 (18.4)	3 (33.3)

For continuous variables, unknown values are not included in the calculation of mean±SD.
EOP, end of pregnancy; **LMP**, last menstrual period; **NA**, not applicable; **SD**, standard deviation

- In the maternal cohort, 53.9% were exposed before pregnancy, 26.3% during first trimester, and 18.4% with unknown timing (**Table 1**). In the paternal cohort, 66.7% were exposed before pregnancy and 33.3% had unknown timing.
- Among women exposed to cladribine tablets, 48.7% had live births and 21.1% had spontaneous abortions (**Figure 1A**).
- In the maternal cohort, 180 pregnancies were reported; 76 (42.2%) with known outcomes (**Figure 1A**). In the paternal cohort, 22 pregnancies were reported; 9 (40.9%) with known outcomes (**Figure 1B**).
- There were no cases of major congenital anomalies or stillbirth reported in any cohort.

Figure 1. Prevalence of Known Pregnancy Outcomes Following Exposure to Cladribine Tablets



The denominator in the percent calculation (N) is the number of pregnancies with known outcome within the given cohort and stratum. In case of multifetal gestation, all associated fetuses/babies were counted separately.

Retrospective: Initial report was made after the pregnancy outcome had occurred.

Prospective: Initial report was made prior to the occurrence of the pregnancy outcome and therefore the pregnancy outcome was pending at the time of initial report.

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