Title: Pregnancy outcomes during the clinical development of cladribine in multiple sclerosis: an integrated analysis of safety for all exposed patients

Authors: A. Galazka[1], A. Nolting[2], S. Cook[3], T. Leist[4], G. Comi[5], X. Montalban[6], C. Hicking[2], F. Dangond[7]

[1]Merck, Aubonne, Switzerland. [2]Merck KGaA, Darmstadt, Germany. [3]Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ United States. [4]Division of Clinical Neuroimmunology, Thomas Jefferson University, Jefferson Medical College, Philadelphia, United States; [5]Department of Neurology and Institute of Experimental Neurology, Università Vita-Salute San Raffaele, Ospedale San Raffaele, Milan, Italy. [6]Hospital Universitari Vall d'Hebron, Barcelona, Spain. [7]EMD Serono, Inc., Billerica, MA USA.

Main Author:
Andrew Galazka
Merck, Aubonne, Switzerland

Background: During clinical trials of cladribine in patients with multiple sclerosis (MS), contraception was specified for men and women of child-bearing potential. Despite these precautions, pregnancies occurred during the clinical trial programme.

Objective: To report pregnancy outcomes from an integrated analysis of safety for patients exposed to cladribine during the clinical development programme in MS.

Methods: Pregnancy outcomes were recorded from an integrated analysis of safety of all exposed patients (cladribine n=1976, placebo n=802). Data on pregnancies recorded as adverse events were included from studies that involved treatment with parenteral cladribine or cladribine tablets.

Results: Overall, 64 pregnancies occurred among 57 women (44 pregnancies were in 38 women with exposure to cladribine; 20 in 19 women who received placebo). Eighteen (41%) pregnancies in the cladribine group and 9 (45%) in the placebo group resulted in live births. Among the pregnancies that did not lead to live births, 14 of those in the cladribine-treated group and 4 in the placebo group were terminated by induced abortion on the patient's decision; there were 9 spontaneous abortions in women treated with cladribine, and 5 in women who received placebo (which is consistent with epidemiological data on pregnancy outcomes), also, 3 medically indicated abortions were reported for 2 women treated with cladribine (2 due to ectopic pregnancy and 1 to choriocarcinoma) and 1 for a placebo recipient (Dandy-Walker congenital malformation with placental abruption). Female partners of 9 cladribine-treated males experienced 10 pregnancies, 9 of which resulted in live births (1 unknown outcome). Female partners of 2 placebo-treated males experienced 2 pregnancies (each outcome unknown).

Conclusion: In this limited population of pregnancies with potential exposure to cladribine, no congenital malformations were identified. Because of the potential for teratogenicity, further study is warranted to better understand any risks that might be associated with cladribine in pregnancy.

Disclosures: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

Author disclosures

AG is an employee of Merck, Aubonne, Switzerland, a division of Merck KGaA, Darmstadt, Germany.

AN is an employee of Merck KGaA, Darmstadt, Germany.

SC has received honoraria for lectures/consultations from Merck, Bayer HealthCare, Sanofi-Aventis, Neurology Reviews, Biogen Idec, Teva Pharmaceuticals, and Actinobac Biomed Inc.; has served on advisory boards for Bayer HealthCare, Merck, Actinobac Biomed, Teva Pharmaceuticals, and Biogen Idec; and received grant support from Bayer HealthCare.

TL has received consultancy fees or clinical research grants from Acorda, Bayer, Biogen, Daiichi, EMD Serono, Novartis, ONO, Pfizer, Teva Neuroscience.

GC has received consulting fees from Novartis, Teva Pharmaceutical Industries Ltd., Sanofi-Aventis, Merck, Receptos, Biogen Idec, Genentech-Roche, and Bayer Schering; lecture fees from Novartis, Teva Pharmaceutical Ind. Ltd., Sanofi-Aventis, Merck, Biogen Dompè, Bayer Schering, and Serono Symposia International Foundation; and trial grant support from Novartis, Teva Pharmaceutical Ind. Ltd., Sanofi-Aventis, Receptos, Biogen Idec, Genentech-Roche, Merck, Biogen Dompè, and Bayer Schering.

XM has received speaker honoraria and travel expenses for scientific meetings, steering committee member, and advisory board member of clinical trials for Bayer Schering Pharma, Biogen Idec, EMD Serono, Genentech, Genzyme, Novartis, Roche, Sanofi-Aventis, Teva Pharmaceuticals, and Almirall.

CH is an employee of Merck KGaA, Darmstadt, Germany.

FD is an employee of EMD Serono, Inc., Billerica, United States, a business of Merck KGaA, Darmstadt, Germany.