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No Increase in Malignancy Risk with Cladribine Tablets in Patients with Relapsing Multiple Sclerosis

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, New Jersey, United States of America
[4]Jefferson University, Comprehensive MS Center, Philadelphia, Pennsylvania, United States of America
[5]Epartment of Neurology and Institute of Experimental Neurology, Università Vita-salute San Raffaele, Ospedale San Raffaele, Milan, Italy
[6]Division of Neurology, St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada
[7]Emd Serono Research & Development Institute Inc., Billerica, Massachusetts, United States of America

Background: An independent meta-analysis determined that malignancy risk was not increased with cladribine tablets (CT) compared with other DMDs in patients with RMS. An unusually low rate was observed in the placebo (pbo) group.1 lymphocyte reductions occur following annual courses of CT, but are transient relative to the sustained clinical efficacy characteristic of selective immune reconstitution therapy. Data from additional trials/registry with CT3.5 mg/kg (CT3.5) (up to 8 years of follow up) are now available. The objective was assessment of malignancy risk with CT3.5 monotherapy and pbo 3 phase iii trials and the premiere registry, and comparison with a global malignancy database.
Methods: CT3.5: N=923, 3433 patient-years' [PY] total exposure time. PBO: N=641, 2026PY. An independent, blinded adjudication committee reviewed case reports of malignancies. Standardized incidence ratios (SIR) for malignancies were calculated in relation to the globocan reference population (excluding non-melanoma skin cancers [nMScs]) and a danish reference population for nMSc rates.
Results: CT3.5 incidence per 100PY of confirmed malignancy was 0.293 (95%CI 0.158–0.544); PBO was 0.148 (95%CI 0.048–0.460), the 95% CI (-0.166–0.414) of the risk difference included 0. Analysis of sir showed that CT3.5 malignancy rate was almost identical (0.97, 95%CI 0.44–1.85) to the globocan population. PBO sir was numerically lower (0.48, 95% CI 0.14–1.53). No cases of haematological, lymphoproliferative or virus-induced cancers occurred. No clustering of specific tumour types occurred; incidence of skin cancer was not increased with CT3.5 versus PBO. The incidence of malignancies with CT3.5 was constant without increase over time.
Conclusions: Analysis of malignancy rates in a cohort of patients with up to 8 years of follow up confirms the conclusions of the earlier meta-analysis; the incidence of malignancies with CT3.5 is similar to that in a matched reference population.