DMT31

Cladribine Tablets After Treatment With Natalizumab (CLADRINA) Trial – Interim Analyses

Peter Sguigna,[1] Annette Okai,[2] Jeffrey Kaplan,[3] Kyle Blackburn,[1] Lauren Tardo,[1] Brooke Hayward,[4] Ursula Boschert,[5] Lori A. Lebson,[4] Julie Korich,[4] Navid Manouchehri,[1] Rehana Hussain,[1] Olaf Stuve[1,6]

[1]University of Texas Southwestern Medical Center, Dallas, TX, USA; [2]North Texas Institute of Neurology & Headache, Plano, TX, USA; [3]Kansas City Multiple Sclerosis and Headache Center, Overland Park, KS, USA; [4]EMD Serono, Rockland, MA, USA; [5]Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany; [6]VA North Texas Health Care System, Dallas VA Medical Center, Dallas, TX, USA

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CONCLUSIONS

No substantial new MS-related activity or AEs in the first 6 months of treatment have been reported thus far with cladribine tablets following switching from natalizumab

No increase in MS activity compared with baseline was reported, EDSS scores remained stable or decreased in 9 patients and increased in 7 patients, and a relapse in one patient on the day of treatment initiation is unlikely to be causally related to cladribine tablets

BACKGROUND

- Natalizumab is a recombinant humanized anti-VLA4 antibody indicated for the treatment of relapsing forms of MS, which inhibits the migration of lymphocytes from the peripheral blood into the CNS[1]
- Natalizumab is highly effective in reducing MS disease activity but is associated with complications such as:
  - Increased risk of developing PML[1]
  - Increased risk of MS disease reactivation and disease rebound following treatment cessation, peaking 4–7 months after treatment discontinuation[2]
- In order to prevent disease reactivation or rebound, induce prolonged disease remission, and decrease risk of PML following switches from natalizumab, data are needed around appropriate therapies (and timing) to follow natalizumab
- Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) preferentially reduce the levels of B and T lymphocytes within the peripheral blood,[3,4] and a retrospective study found minimal disease reactivation during treatment with cladribine tablets following a switch from natalizumab[5]

OBJECTIVE

- **The purpose of the CLADRINA study is to generate hypotheses regarding the safety, effectiveness, and immunological impact of cladribine tablets after switching from natalizumab in patients with RRMS or active SPMS. This poster summarizes selected interim data for the first 20 patients**

METHODS

- CLADRINA is an open-label, Phase 4 study in 40 participants with RRMS or active SPMS who meet the criteria for treatment with cladribine tablets as per the USPI
- Inclusion criteria include:
  - Age 18–60 years
  - EDSS score 0–5.5
  - ≥12 months of continuous natalizumab therapy
  - No relapses for 28 days
- Exclusion criteria include:
  - Previous cladribine tablet treatment
  - Natalizumab treatment failure
  - Diagnosis or suspicion of PML
  - Lymphocyte count outside of normal limits

Treatment

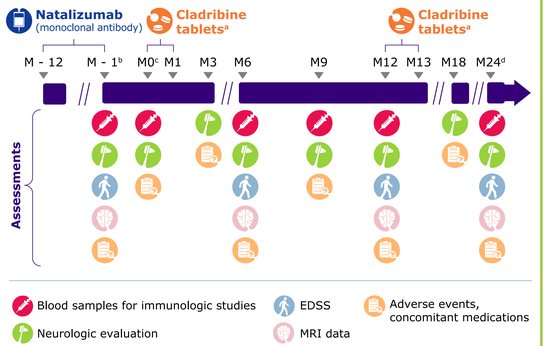
- All study participants will receive treatment with cladribine tablets 3.5 mg/kg cumulative dose over 2 years according to the approved USPI.[6] Initiation of treatment with cladribine tablets is recommended to occur at approximately 14 days after the last infusion of natalizumab, but a period of up to one month between natalizumab and cladribine tablets treatment is permitted

Study endpoints

- The primary endpoint is absolute and percent change from baseline to 6, 9, 12, and 24 months of selected biomarkers in blood:
  - CD3+ T lymphocytes
  - CD19+ B lymphocytes
  - CD11c+ DC subsets
  - NfL levels
- The secondary endpoints are annualized relapse rate and percent of patients experiencing a relapse over 12 and 24 months
- Exploratory measures include EDSS, MRI, and selected additional blood biomarkers
- Data available for this presentation include EDSS, MRI, relapses, and AEs to date; others will be presented in future communications

METHODS (cont.)

Study design



[a]Cladribine 10 mg tablets (3.5 mg/kg cumulative dose over two years) are administered per the USPI[6]; Year 2 treatment may be delayed up to six months to allow for lymphocyte recovery. [b]Screening. [c]Baseline (Day 1). [d]Follow-up can increase to up to 30 months depending on timing of Year 2 dose.

RESULTS

- 18 of 20 patients enrolled to date have completed 6 months of treatment

Baseline demographics and disease characteristics

Characteristic (N=20)	
Age, years, mean (SD)	42 (7.8)
Female sex, n (%)	13 (65)
Years since MS diagnosis, mean (SD)	5 (3.9)
JCV status, n (%)	
Positive (titer >0.40)	19 (95)
Intermediate (titer ≥0.20 to ≤0.40)	1 (5)
No. of relapses in prior 12 months	1
MRI activity in prior 12 months, n (%)	2 (10)
Total no. Gd+ T1 lesions in these pts	11
Total no. new T2 lesions in these pts	11

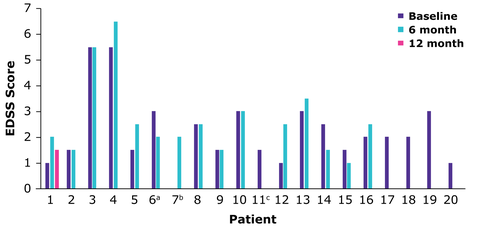
Mean (range) time between natalizumab and cladribine tablets treatment: 11.15 (3.00-23.00) days.

RESULTS (cont.)

Effectiveness

- There were no new MRI lesions after starting cladribine tablets
- No relapses were observed with the exception of one patient who had a clinical relapse associated with contrast-enhancing new lesions in the cervical spine on the day treatment was initiated
- Individual EDSS scores were available from baseline and 6 months for 16 out of 20 patients

Individual EDSS scores over time



[a]This patient had a relapse the day of cladribine tablet administration; [b]baseline score was 0; [c]6-month score was 0.

No study medication-related AEs have been reported

Characteristic (N=20)	
Any AE — no. of events	15
Any AE — no. of patients (%)	9 (45)
AE leading to discontinuation of trial agent — no. of patients (%)	0 (0)
Death — no. of patients (%)	0 (0)
Any serious AE — no. of patients (%)	0 (0)
Serious infections — no. of patients (%)	0 (0)
Specific AE — no. of patients (%)	
Somatic pain	2 (10)
COVID-19	2 (10)
Nausea	2 (10)
Nephrolithiasis	2 (10)
Accident[a]	1 (5)
Upper respiratory infection	1 (5)
Shortness of breath	1 (5)
Vomiting	1 (5)
Bromhidrosis	1 (5)
Hyporgasmia	1 (5)
Loss of appetite	1 (5)
Insomnia	1 (5)

[a]Accident was collar bone fracture.

Abbreviations: AE, adverse event; **CNS,** central nervous system; **COVID-19,** coronavirus disease 2019; **EDSS,** expanded disability status scale; **Gd+,** gadolinium-enhancing; **JCV,** John Cunningham virus; **MRI,** magnetic resonance imaging; **MS,** multiple sclerosis; **NfL,** neurofilament light chain; **PML,** progressive multifocal leukoencephalopathy; **pts,** patients; **RRMS,** relapsing-remitting multiple sclerosis; **SPMS,** secondary progressive multiple sclerosis; **USPI,** United States Prescribing Information.

References: 1. Shirani A and Stuve O. *Cold Spring Harb Perspect Med.* 2018;8:a029066. **2.** O'Connor PW, et al. *Neurology.* 2011;76:1858–1865. **3.** Comi G, et al. *Mult Scler Relat Disord.* 2019;29:168–174. **4.** Stuve O, et al. *Ther Adv Neurol Disord.* 2019;12:1–16. **5.** Möhn N, et al. *Ther Adv Neurol Disord.* 2019;12:1756286419887596. **6.** Mavenclad [package insert]. Rockland, MA; EMD Serono, Inc.; 2019.

Acknowledgments: The CLADRINA study (NCT04178005) is sponsored by EMD Serono, Rockland, MA, USA (CrossRef Funder ID: 10.13039/100004755), who reviewed and provided feedback on this poster. Writing and editorial support for the preparation of this poster was provided by Jenna Steere, PhD, and Delisa O'Brien of Ashfield MedComms (New York, NY, USA), an Ashfield Health company; funding was provided by the study sponsor. The authors had full control of the poster and provided their final approval of all content. This study was previously presented at ECTRIMS 2021 (13-15 October).

Disclosures: PS: has received research support from PSTP, CTM, PRC and served as an advisor to Genentech and Bristol Myers Squibb. **AO:** has received speaking and consulting fees from Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Rockland, MA, USA, Roche Genentech, Sanofi Genzyme; and received research support from Alexion, Biogen, Novartis, EMD Serono, Rockland, MA, USA, Roche Genentech, Sanofi Genzyme and TG therapeutics. **JK:** has received speaking fees from Alexion, Allergan, Amgen, Biogen, Biohaven, EMD Serono, Rockland, MA, USA, Horizon, Janssen, Lilly, Lundbeck, Mallinckrodt, Sanofi/Genzyme, and Teva, and participated in advisory boards for Genentech. **KB:** None. **LT:** None. **UB:** Employee of Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany. **BH, LAL, JK:** Employees of EMD Serono, Rockland, MA, USA. **NM:** None. **RH:** None. **OS:** Funded by a Merit Review grant (federal award document number [FAIN]BX005664-01) from the United States Department of Veterans Affairs, Biomedical Laboratory Research and Development, and receives grant support from EMD Serono, Rockland, MA, USA, Genzyme, and Exalys. He serves on the editorial board of *Therapeutic Advances in Neurological Disorders*, has served on data monitoring committees for Genentech-Roche, Pfizer, and TG Therapeutics without monetary compensation, and has advised EMD Serono, Rockland, MA, USA, Celgene, Genentech, TG Therapeutics, and Genzyme.

Prepared for the Consortium of Multiple Sclerosis Centers (CMSC) 2022 Annual Meeting - June 1-4; National Harbor, MD, USA