Lymphopenia Rates in CLARITY/CLARITY Extension are Unrelated to Disease Activity at Baseline

S. Cook\(^1\), G. Giovannoni\(^2\), P. Vermersch\(^3\), P. Soellberg-Saareinen\(^4\), B. Keller\(^5\), and J. Jack\(^6\)

\(^1\)Vanderbilt, The State University of New Jersey, New Jersey Medical School, Newark, NJ, USA; \(^2\)Queen Mary University of London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK; \(^3\)University of Helsinki, Department of Neurology, Helsinki, Finland; \(^4\)St. George's University of London, Department of Neurology, London, UK; \(^5\)Charité - Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany; \(^6\)Charité - Universitätsmedizin Berlin, Department of Neurology, Berlin, Germany.


text

INTRODUCTION

- In CLARITY, treatment with Cladribine Tablets showed strong efficacy in patients with relapsing multiple sclerosis (RMS) versus placebo over 2 years.\(^1\)
- In CLARITY Extension, Cladribine Tablets produced durable clinical benefits.\(^1\)
- There was no difference in clinical efficacy between treatment with Cladribine Tablets in CLARITY followed by placebo in CLARITY Extension, vs. treatment with Cladribine Tablets in CLARITY and CLARITY Extension. Patients with RMS and high disease activity (HDA) may be at higher risk of relapses and disability progression.\(^1\)
- In a post hoc analysis of CLARITY, patients with HDA had clinical and magnetic resonance imaging (MRI) response to Cladribine Tablets 10 mg/g cumulative dose over 2 years, referred to as Cladribine Tablets 3.5 mg/kg that were generally better than, or comparable with, the overall CLARITY population.\(^1\)
- Lymphopenia is an anticipated side effect of Cladribine treatment due to its pharmacological properties leading to selective depletion of lymphocytes, as observed in CLARITY and CLARITY Extension.\(^1\)
- While there does not appear to be a direct link between lymphocyte count reduction and clinical or MRI outcomes, it is relevant to investigate for HDA patients as more likely to experience lower lymphocyte counts.

OBJECTIVE

To determine the role of lymphopenia in patients with HDA in the CLARITY/CLARITY Extension studies in patients receiving Cladribine Tablets 3.5 mg/kg in CLARITY and other Cladribine Tablets 3.5 mg/kg in CLARITY Extension.

METHODS

- In this post hoc analysis, patients exposed to Cladribine Tablets 3.5 mg/kg in CLARITY or CLARITY Extension in Years 1 and 2 only are referred to as the CT 3.5 group (n = 665) and a subgroup of these patients who received further courses of Cladribine Tablets 3.5 mg/kg in Years 3 and 4 referred to as the CT 3.5 group (n = 196) (see Figure 1 for study design).

RESULTS

Lymphopenia based on adverse event reporting

- In the CT 3.5 group, the incidence rates of AESI lymphopenia were similar for the two HDA subgroups and the corresponding HDA and non-HDA subgroups (Table 1).
- In CT 3.5 Year 3 and Year 2, AESIs in 100-patient-years were similar in the HRA (n = 186) and HRA+DAT subgroups (11.50 and 13.09 respectively) and similarly compared between non-HDA groups (14.08 [n = 489] and 13.46 [n = 466]).
- In CT 7.0 at Year 4, rates were approximately double the CT 3.5 in Year 2, but different between HDA and non-HDA subgroups.
- There was a low rate of serious AESIs lymphopenia in the CT 3.5 HRA and non-HRA groups and no incidences in the CT 7.0 and non-HRA subgroups.
- For the CT 3.5 group, incidence of Grade 3 lymphopenia was similar or numerically lower in the HDA subgroup compared with non-HDA subgroups (Figure 3).
- In CT 7.0 at Year 4, Grade 3 lymphopenia incidence was lower in the HDA than the non-HDA subgroups.
- Overall, Grade 3 lymphopenia incidence was lower in CT 3.5 than Year 2 CT 7.0 at Year 4.
- Grade 4 lymphopenia incidence was low in all HDA and non-HDA subgroups.

Lymphopenia based on laboratory data

- Baseline mean absolute lymphocyte count (ALC) (±10%) in the overall CT 3.5 population was 1.92 ± 0.59.
- Mean ALC nadir (±10%) for HRA and HRA+DAT CT 3.5 patients at Year 2 were 0.73 and 0.72 respectively; mean ALC nadirs were 0.69 in both corresponding non-HDA subgroups (Table 2).

CONCLUSIONS

- There were no relevant differences between the HDA and non-HDA subgroups with regard to incidence of the AESI lymphopenia, ALC nadir, and time to ALC nadir.
- There were no relevant differences between the HRA and HRA+DAT subgroups with regard to incidence of the AESI lymphopenia and ALC nadir, suggesting that the conclusions of previously-treated patients did not change the risk and the severity of lymphopenia.
- It should be noted, however, that DAT patients represented only a small proportion of additional HDA patients.
- Patients who received CT 3.5 mg/kg had a lower incidence of AESI lymphopenia than patients who received CT 7.0.

REFERENCES


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DISCLOSURES

Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, and has received payment for travel reimbursement from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzyme Japan, and Novartis. Be is also a stockholder of Genzyme. Be is also a co-investigator of a study conducted under a license from the University of California, San Francisco, for the treatment of Behcet’s disease. Be received research funding from Takeda Pharmaceutical, and has received research support from the University of California, San Francisco for the treatment of Behcet’s disease. Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzyme Japan, and Novartis. Be is also a stockholder of Genzyme. Be is also a co-investigator of a study conducted under a license from the University of California, San Francisco, for the treatment of Behcet’s disease. Be received research funding from Takeda Pharmaceutical, and has received research support from the University of California, San Francisco for the treatment of Behcet’s disease. Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzyme Japan, and Novartis. Be is also a stockholder of Genzyme. Be is also a co-investigator of a study conducted under a license from the University of California, San Francisco, for the treatment of Behcet’s disease. Be received research funding from Takeda Pharmaceutical, and has received research support from the University of California, San Francisco for the treatment of Behcet’s disease. Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzyme Japan, and Novartis. Be is also a stockholder of Genzyme. Be is also a co-investigator of a study conducted under a license from the University of California, San Francisco, for the treatment of Behcet’s disease. Be received research funding from Takeda Pharmaceutical, and has received research support from the University of California, San Francisco for the treatment of Behcet’s disease. Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzyme Japan, and Novartis. Be is also a stockholder of Genzyme. Be is also a co-investigator of a study conducted under a license from the University of California, San Francisco, for the treatment of Behcet’s disease. Be received research funding from Takeda Pharmaceutical, and has received research support from the University of California, San Francisco for the treatment of Behcet’s disease. Be is named inventor for multiple claims relating to Bevacizumab, Sanoit Co., Ltd and Nippon Roche. Be has received consulting and research support from Biogen, Biogen Japan and Teva Pharmaceutical. Be has received travel reimbursement from Biogen and Teva Pharmaceutical, has received honorarium from Teva Pharmaceuticals, Biogen, Biogen Japan, Genzyme, Genzy...