Early Onset of Action and Sustained Efficacy of MRI Outcomes During Cladribine Tablets Treatment in Highly Active Relapsing Multiple Sclerosis: Results of the 2-year MAGNIFY-MS Study

Nicola De Stefano[1], Anat Achiron[2], Frederik Barkhof[3,4], Andrew Chan[5], Tobias Derfuss[6], Suzanne Hodgkinson[7], Letizia Leocani[8], Xavier Montalban[9], Alexandre Prat[10], Klaus Schmierer[11,12], Finn Sellebjerg[13,14], Patrick Vermersch[15], Heinz Wiendl[16], Birgit Keller[17], Andrzej Smyk[17], Lidia Gardner[18]

[1]Department of Medicine, Surgery and Neuroscience, University of Siena, Siena, Italy; [2]Multiple Sclerosis Center, Sheba Academic Medical Center, Ramat Gan, Israel; [3]Department of Radiology, VU University Medical Center, Amsterdam, The Netherlands and [4]UCL Institute of Neurology, London, UK; [5]Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [6]Department of Neurology, University Hospital Basel, Basel, Switzerland; [7]Ingham Institute for Applied Medical Research, University of New South Wales Medicine, Sydney, NSW; Australia; [8]Experimental Neurophysiology Unit, Vita-Salute San Raffaele University, Milan, Italy; [9]Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitario Vall d'Hebron, Universitat Autonoma de Barcelona, Barcelona, Spain; [10]Department of Neurosciences, Université de Montréal, Montréal, QC, Canada; [11]The Blizard Institute, Centre for Neuroscience, Surgery & Trauma, Barts and The London School of Medicine & Dentistry, Queen Mary University of London, London, UK and [12]Clinical Board Medicine (Neuroscience), The Royal London Hospital, Barts Health NHS Trust, London, UK; [13]Danish MS Center, Department of Neurology, Copenhagen University Hospital - Rigshospitalet, Glostrup, Denmark and [14]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; [15]Univ. Lille, Inserm U1172 LilNCog, CHU Lille, FHU Precise, Lille, France; [16]Department of Neurology, Institute of Translational Neurology, University of Münster, Münster, Germany; [17]the healthcare business of Merck KGaA, Darmstadt, Germany; [18]EMD Serono, Billerica, MA, USA

Disclosures

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- The early initiation of highly effective disease-modifying therapy is particularly important in patients with highly active relapsing MS to prevent worsening disability[1]
- Early results from the Phase IV MAGNIFY-MS study (NCT03364036) concerning 6-month MRI findings (primary endpoint), were presented previously (ECTRIMS 2020) and highlighted the early onset of action of cladribine tablets[2,3]
- This presentation reports results at Month 24 of the study

1. He A, et al. *Lancet Neurol*. 2020;19:307–316. 2. De Stefano N, et al. *Mult Scler J*. 2020;26(S3):303. 3. De Stefano N, et al. *Neurol Neuroimmunol Neuroinflamm*. 2022;9(4):e1187.

MRI, magnetic resonance imaging; **MS**, multiple sclerosis

To report the 2-year MRI, clinical, and safety results from MAGNIFY-MS

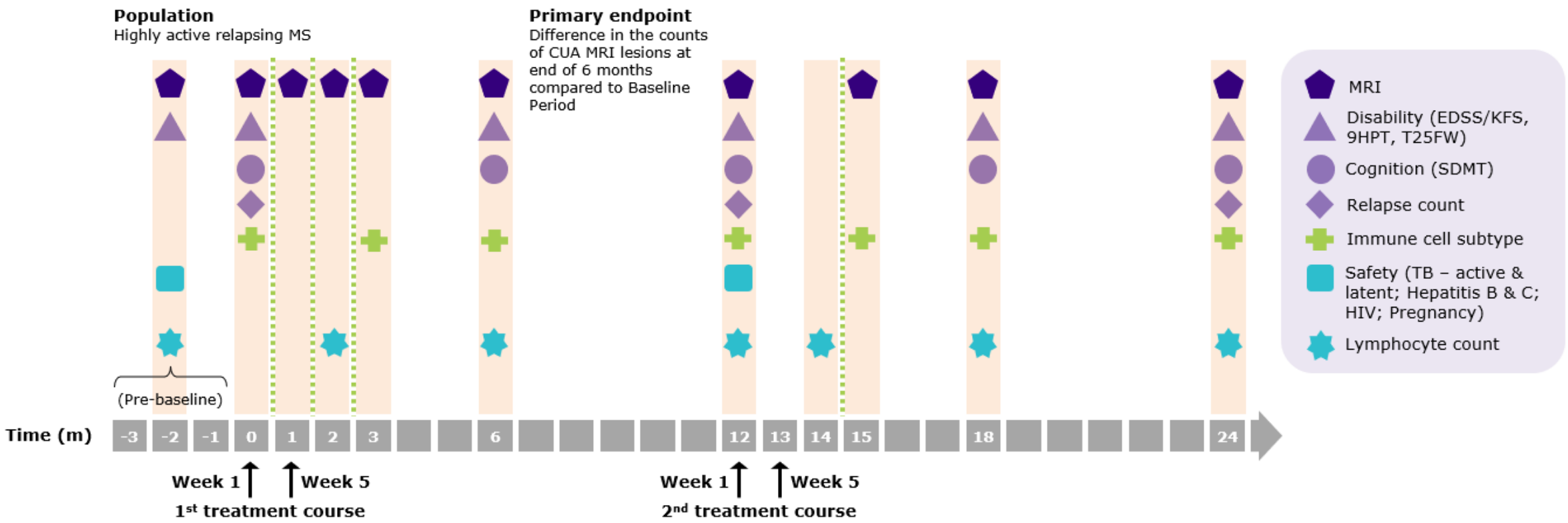
To determine the onset of action and maintenance of effect of cladribine tablets over 2 years

MRI, magnetic resonance imaging

- Changes in CUA, T1 Gd+, and active T2 lesion counts were compared exploratively between baseline and post-baseline visits using a mixed-effects linear model for repeated measures
- ARR was estimated from a Poisson regression model
- The full analysis set included all eligible patients (highly active relapsing MS patients aged ≥18 years with an EDSS score ≤5.0) treated with at least one dose of cladribine tablets
- The safety analysis set included all patients treated with at least one dose of cladribine tablets

ARR, annualized relapse rate; **CUA**, combined unique active; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium-enhancing; **MS**, multiple sclerosis

MAGNIFY-MS Study Design



9HPT, 9-hole peg test; **CUA**, combined unique active; **EDSS**, Expanded Disability Status Scale; **HIV**, human immunodeficiency virus; **KFS**, Kurtzke Functional System; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **SDMT**, symbol digit modalities test; **T25FW**, timed 25-foot walk; **TB**, tuberculosis

Patient Characteristics

	Total N=270
Female, n (%)	180 (66.7)
Age (Years), mean ± SD	37.7 ± 9.75
Time since onset of MS (Months), mean ± SD	84.90 ± 85.472
≥1 relapses within 12 months prior to Baseline, n (%)	267 (98.9)
EDSS score ≤3 at Baseline, n (%)	204 (75.6)
Previous DMT use, n (%)	153 (56.7)
Patients with CUA lesion count data during Baseline Period, n (%)	267 (98.9)
Patients with ≥1 lesion, n (%)	145 (53.7)
Patients with T1 Gd+ lesion count data during Baseline Period, n (%)	270 (100)
Patients with ≥1 lesion, n (%)	136 (50.4)
Patients with active T2 lesion count data during the Baseline Period, n (%)	267 (98.9)
Patients with ≥1 lesion, n (%)	113 (41.9)

A summary of patient disposition is shown in **Supplementary Figure 1**.

CUA, combined unique active; **DMT**, disease-modifying therapy; **Gd+**, gadolinium-enhancing; **MS**, multiple sclerosis; **SD**, standard deviation

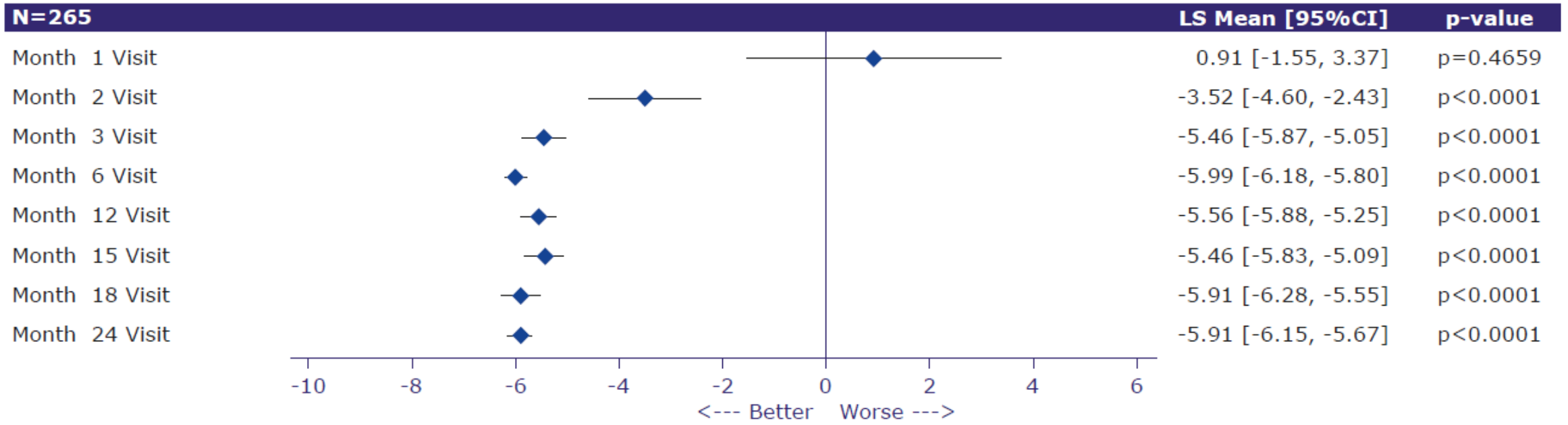
NfL Z-scores and MRI activity

- During the treatment period, 71.1% of patients did not have a qualifying relapse. At least 1 qualifying relapse was documented in 17% of patients; 11.9% had unknown relapse status
- The ARR for patients was 0.11 (95% confidence interval: 0.09, 0.15)
- EDSS remained stable over time for the majority of patients (median EDSS of 2.0)

ARR, annualized relapse rate; **EDSS**, Expanded Disability Status Scale

Annualized CUA Lesion Count – Change from Baseline Visit to Post-Baseline Visits: FAS

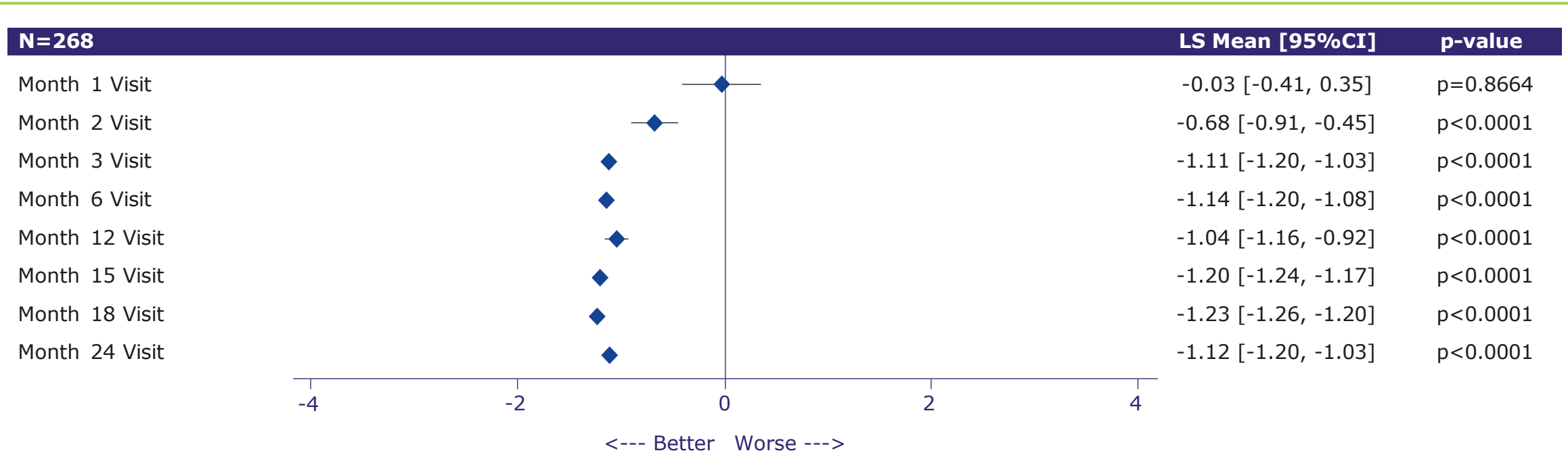
- Among patients with non-missing MRI data (N=265), significant reduction in the annualized CUA count was seen from Month 2 onwards
- The maximum mean change was reached at Month 6, and was maintained until Month 24



CI, confidence interval; **CUA**, combined unique active; **FAS**, full analysis set; **LS**, least square; **MRI**, magnetic resonance imaging

Annualized T1 Gd+ Lesion Count – Change from Baseline Visit to Post-Baseline Visits: FAS

- Mean annualized T1 Gd+ lesion counts decreased in a similar manner; see also **Supplementary Figure 2**

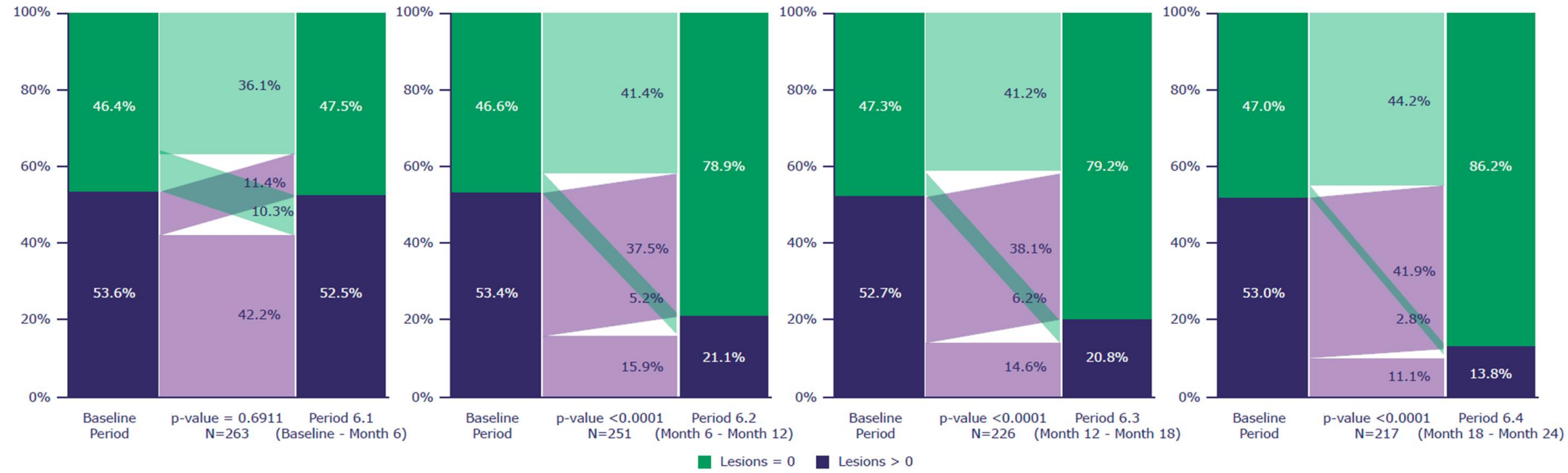


Findings for active T2 counts are shown in **Supplementary Figures 3 and 4**

CI, confidence interval; **FAS**, full analysis set; **Gd+**, gadolinium-enhancing; **LS**, least square

MRI Activity by 6 Month Periods – Cross-tabulation of Baseline and Post-Baseline Periods: FAS

- Significant reduction in MRI activity was observed starting at Month 2, and remained low, with 21.1% of patients with at least one lesion between Month 6 and 12 visits, 20.8% between Month 12 and 18 visits, and 13.8% between Month 18 and 24 visits
- The proportion of patients free of CUA lesions increased from 47.0% at baseline to 86.2% at the end of the study (Month 18 – 24)



Reduction in CUA lesion activity was reported in each of the analysed periods for patients with >0 lesions at baseline

CUA, combined unique active; **FAS**, full analysis set; **MRI**, magnetic resonance imaging

Safety

- No serious AEs potentially related to treatment were reported in the study
- Study treatment-related TEAEs were reported in 45.2% of patients, with 26.3% being mild, 17.4% moderate, and 1.5% severe
- Most post-baseline lymphopenias were Grade 1 (12.2%) or 2 (42.2%); 24.4% (66/270) of patients experienced Grade 3 and 0.7% (2/270) experienced Grade 4 lymphopenia

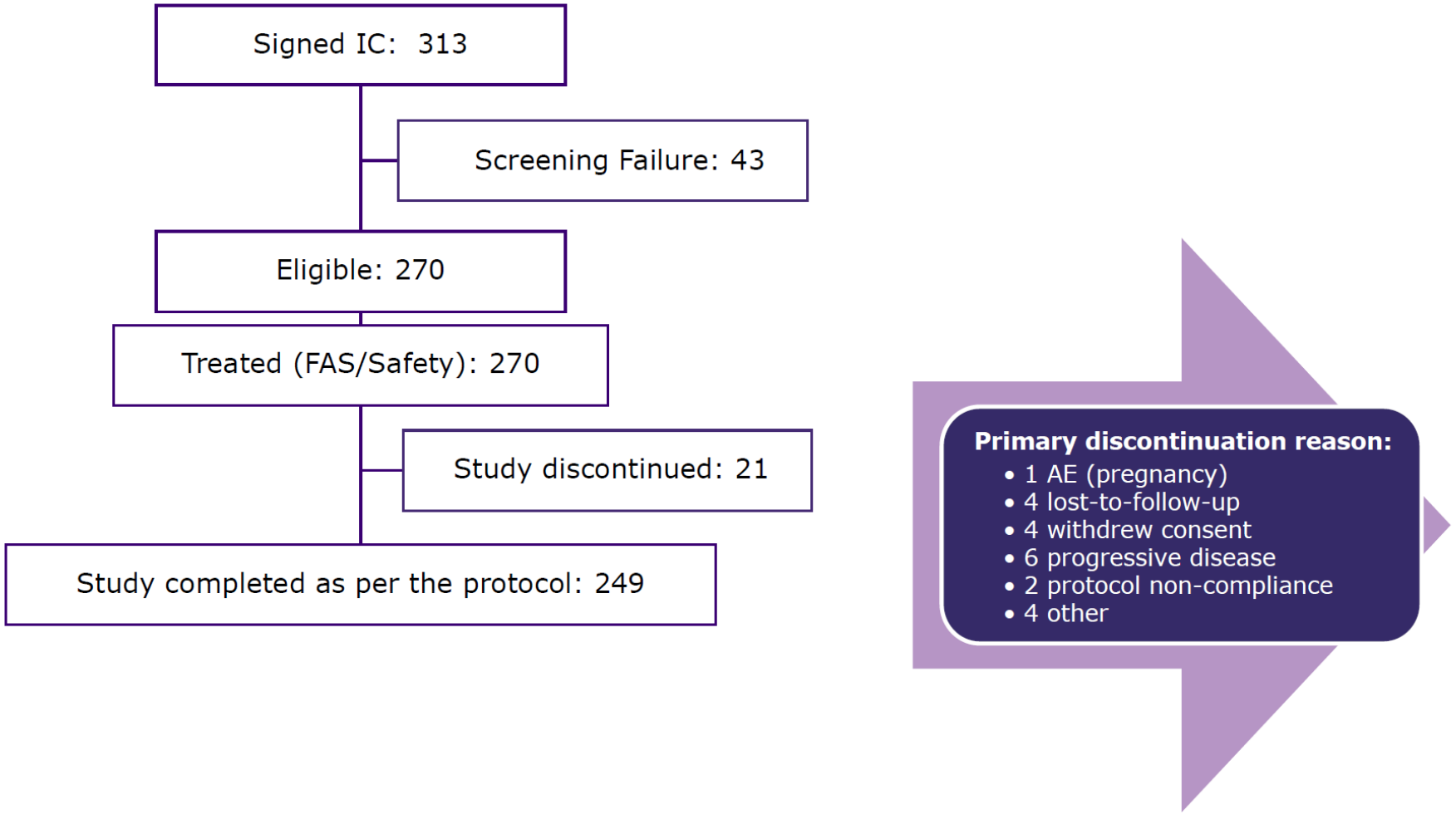
Safety findings are shown in **Supplementary Table 1**

AE, adverse event; **TEAE**, treatment-emergent adverse event

- Treatment with cladribine tablets shows an early onset of action from Month 2 onwards with a sustained reduction in MRI lesion counts (CUA, T1 Gd+, and active T2) up to the last evaluation at Month 24
- Over the 2 years, the benefit:risk profile of cladribine tablets remained unchanged and in line with observations made during the clinical development phase

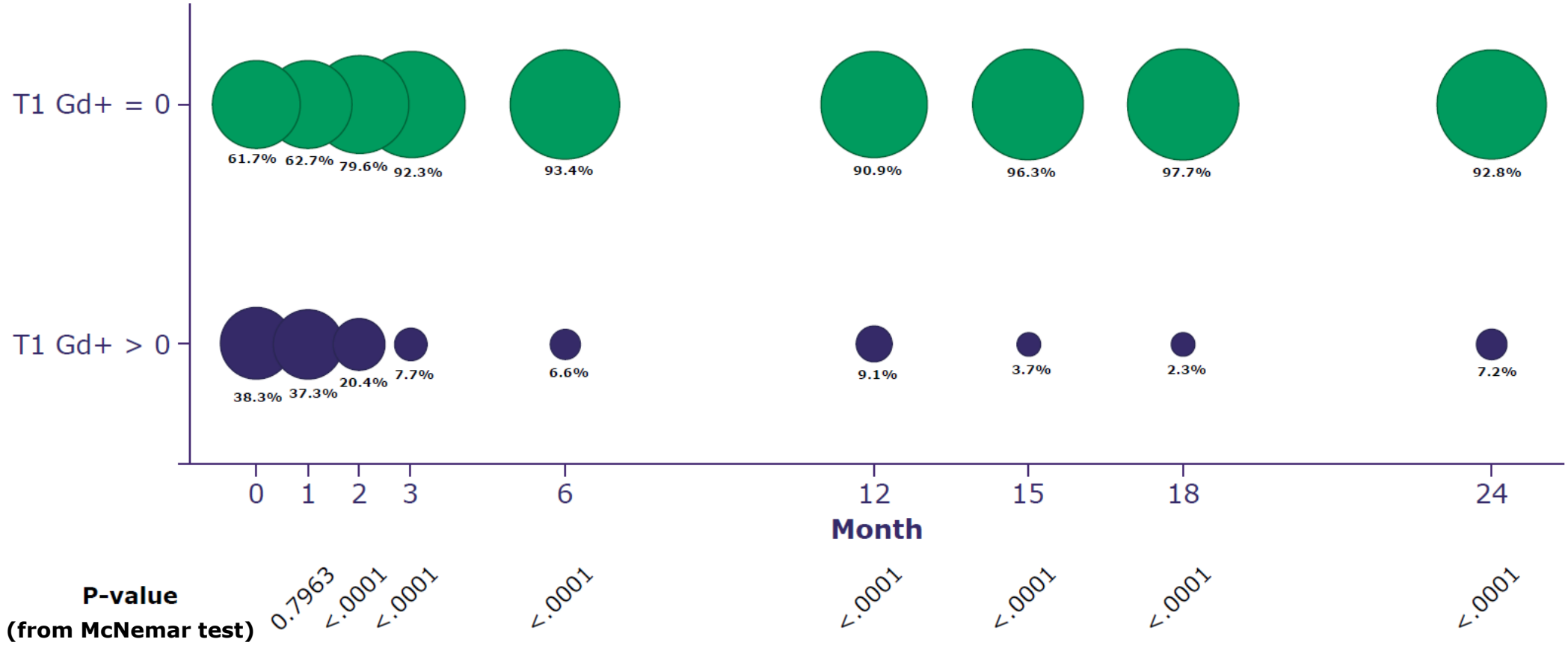
CUA, combined unique active; **Gd+**, gadolinium-enhancing

Supplementary Figure 1. Patient Disposition



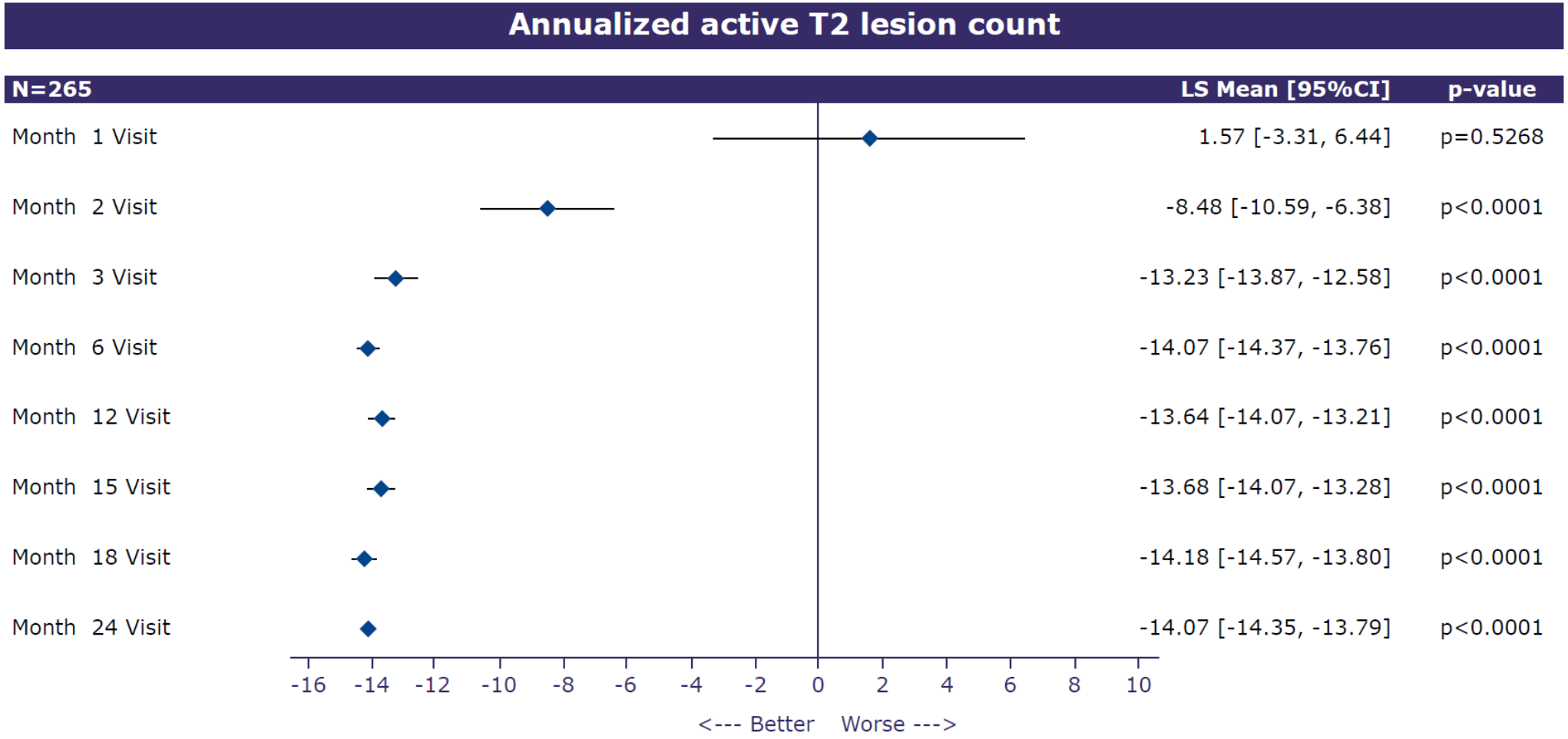
AE, adverse event; **FAS**, full analysis set; **IC**, informed consent

Supplementary Figure 2. T1 Gd+ Lesion Count – Activity by Visits: FAS



FAS, full analysis set; **Gd+**, gadolinium-enhancing

Supplementary Figure 3. Annualized T2 Lesion Count – Change from Baseline Visit to Post-Baseline Visits: FAS



CI, confidence interval; **FAS**, full analysis set; **Gd+**, gadolinium-enhancing; **LS**, least square

Supplementary Figure 4. Active T2 Lesion Count – Activity by Visits: FAS

FAS, full analysis set

Supplementary Table 1. Overview of Treatment-Emergent Adverse Events: Safety Analysis Set

Number of patients with:	Total N=270 n (%)
Any TEAE [a]	227 (84.1)
Mild	114 (42.2)
Moderate	103 (38.1)
Severe	10 (3.7)
Any study treatment-related TEAE [a]	122 (45.2)
Mild	71 (26.3)
Moderate	47 (17.4)
Severe	4 (1.5)
Any serious TEAE	14 (5.2)
Any study treatment-related serious TEAE	0 (0)
Any TEAE leading to temporary discontinuation of study treatment	4 (1.5)
Any TEAE leading to permanent discontinuation of study treat	1 (0.4)

[a]Worst severity per subject is reported.
The safety analysis set included all patients treated with at least one dose of cladribine tablets.

AE, adverse event; **TEAE**, treatment-emergent adverse event