Efficacy in Clinical and MRI Outcomes With Cladribine Tablets Treatment in Highly Active Relapsing Multiple Sclerosis (MAGNIFY-MS)

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CONCLUSIONS

Over 2 years, most patients treated with cladribine tablets remained relapse-free and stable on disability measures (EDSS, T25FW, and 9HPT)

Patients treated with cladribine tablets showed an early onset of action and sustained reduction in MRI lesion counts from Month 2 onwards

The benefit:risk profile of cladribine tablets remained unchanged over the study and was in line with observations made during the clinical development phase

INTRODUCTION

- MAGNIFY-MS (NCT03364036) was a phase IV study designed to increase understanding of the onset of action and sustained efficacy of cladribine tablets 3.5 mg/kg cumulative dose over 2 years in patients with highly active relapsing multiple sclerosis.
- Results from the 6-month magnetic resonance imaging (MRI) analysis (primary endpoint) were previously published.[1]

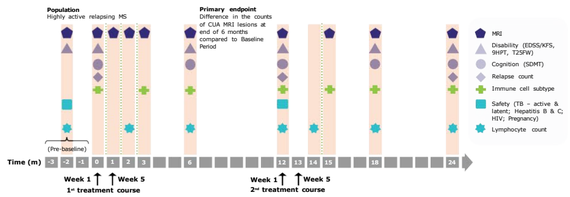
OBJECTIVES

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

METHODS

- Patients received cladribine tablets, with 2 weeks of active treatment per course (Week 1 and Week 5 of each year, **Figure 1**).
- Annualized relapse rate (ARR) was estimated from a Poisson regression model, using age and Expanded Disability Status Scale (EDSS) as covariates and relapse count as the dependent variable.
- EDSS, timed 25-foot walk (T25FW), and 9-hole peg test (9HPT) scores were recorded at Baseline and at Months 6, 12, 18, and 24.
- Concerning MRI, changes in lesion counts were compared exploratively between Baseline and post-Baseline visits (Months 1, 2, 3, 6, 12, 15, 18, and 24).
- Safety was analyzed descriptively.

Figure 1. Study Design



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

Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults).

RESULTS

- Baseline patient characteristics are shown in **Table 1**.

Table 1. Patient Baseline Characteristics

	Total (N=270)
Female, n (%)	180 (66.7)
Age in years, mean (±SD)	37.7 (±9.75)
Time since onset of MS in months, mean (±SD)	84.90 (±85.47)
Previous DMT use, n (%)	153 (56.7)
≥1 relapse within 12 months prior to Baseline, n (%)	267 (98.9)
Median number of relapses within 12 months prior to Baseline (IQR)	2 (1, 2)
EDSS ≤3 at Baseline, n (%)	204 (75.6)
Patients with MRI activity during Baseline Period, n (%)	
Patients with ≥1 annualized CUA lesion count	145 (53.7)
Patients with ≥1 mean T1 Gd+ lesion count	136 (50.4)
Patients with ≥1 annualized total active T2 lesion count	113 (41.9)

CUA, combined unique active; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium-enhancing; **IQR**, interquartile range; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **SD**, standard deviation

- During the treatment period, 83.0% (224/270) of patients did not have a qualifying relapse. Of those who had at least one qualifying relapse, most patients (37/46) had a single relapse.
- Qualifying relapse was treated with steroids in 13.3% of patients (36/270) and led to hospitalization in 1.9% of patients (5/270).
  - Mean (±SD) qualifying relapse count per patient was 0.2±0.57.
  - ARR (95% CI) was 0.11 (0.09, 0.15).
- Most patients showed disease stability in terms of T25FW or 9HPT (**Table 2**).

Table 2. Disability Status During Treatment Period

	Total (N=270)
No 6-month confirmed disability progression, n (%)	236 (87.4)
Unknown status	13 (4.8)
No 20% confirmed T25FW progression during treatment, n (%)	234 (86.7)
Unknown status	18 (6.7)
No 20% confirmed 9HPT progression during treatment, n (%)	247 (91.5)
Unknown status	15 (5.6)

9HPT, 9-hole peg test; **T25FW**, timed 25-foot walk

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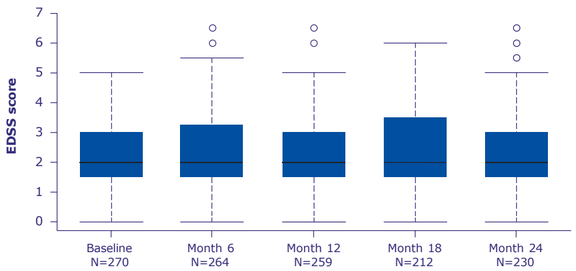
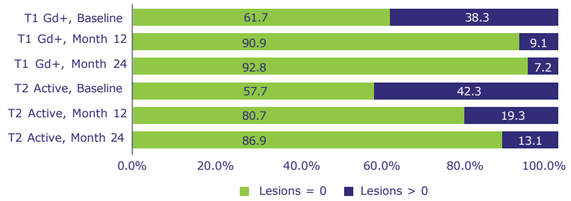
- EDSS score remained stable over time for most patients (median score of 2.0, **Figure 2**).
- The proportion of patients (N=217) free of combined unique active lesions increased from 47.0% at Baseline Period to 86.2% at the end of the study (Month 18–24).
- T1 gadolinium-enhancing and active T2 lesions were also reduced over time (**Figure 3**).
- Mean T1 Gd+ and annualized active T2 lesion counts were markedly reduced from Month 2 and sustained through Month 24.

Figure 2. EDSS Score Over Time



EDSS, Expanded Disability Status Scale

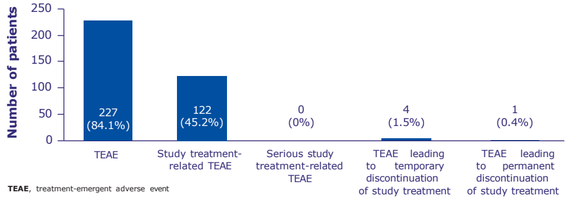
Figure 3. T1 Gd+ and T2 Active Lesions Over Time (%)



Gd+, gadolinium-enhancing

- Study treatment-related treatment-emergent adverse events were reported in 45.2% of patients (**Figure 4**).
- No serious study treatment-related adverse events were reported.
- Post-baseline lymphopenias were reported as either Grade 1 (12.2%); Grade 2 (42.2%); Grade 3 (24.4%); or Grade 4 (0.7%).
  - Lymphocyte counts remained within a normal range for 20.4% of patients.

Figure 4. Number (%) of Patients with Any TEAEs



TEAE, treatment-emergent adverse event

REFERENCE: 1. De Stefano, N, et al. *Neurol Neuroimmunol Neuroinflamm.* 2022;9(4):e1187.

DISCLOSURES: **NDS** is a consultant for Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva; has grants or grants pending from FISM and Novartis, is on the speakers' bureaux of Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva; and has received travel funds from the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva. **AA** has received honoraria or consulting fees from Bayer, Biogen, Celgene (BMS), the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Sanofi; and research support from Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Roche, and Sanofi. **FB** is supported by the NIHR Biomedical Research Centre at UCLH and is a consultant to Biogen, Combinostics, IXICO, the healthcare business of Merck KGaA, Darmstadt, Germany, and Roche. **AC** has received speakers'/board honoraria from Actelion (Janssen/J&J), Almirall, Bayer, Celgene (BMS), the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva, all for hospital research funds. 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She has received money for travel and speaker honoraria from Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Sanofi. **LL** has received honoraria for consulting services or speaking activities from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, and Roche; and research support from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, and Novartis. **XM** has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years with Alkhirla, Actelion (Janssen/J&J), Alexion, Biogen, Celgene (BMS), EMD Serono, Excemed, Immunic, Janssen, MedDay, the healthcare business of Merck KGaA, Darmstadt, Germany, Mylan, Nervgen, Novartis, Roche, Sandoz, Sanofi, Teva, TG Therapeutics, MSIF, and NMSS. **AP** has received honoraria from pharmaceutical companies. **KS** has received research support from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, and Novartis; speaking honoraria from, and/or served on an advisory role for, Amgen-Genzyme, Biogen, EMD Serono, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva; and remuneration for teaching activities from Academy, Medscape, and the Neurology Academy. **FS** has served on scientific advisory boards, been on the steering committees of clinical trials, served as a consultant, received support for congress participation, received speaker honoraria, or received research support for his laboratory from Biogen, Celgene (BMS), EMD Serono, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva. **HW** has received honoraria or consulting fees from Bayer, Biogen, Celgene (BMS), EMD Serono, Excemed, Immunic, Janssen, MedDay, the healthcare business of Merck KGaA, Darmstadt, Germany, Mylan, Nervgen, Novartis, Roche, Sandoz, Sanofi, Teva, TG Therapeutics, MSIF, and NMSS. **AF** has received honoraria from Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva, and research support from Novartis, Roche, and Sanofi. **HW** is member of scientific advisory boards/steering committees for Bayer, Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi, and Teva. 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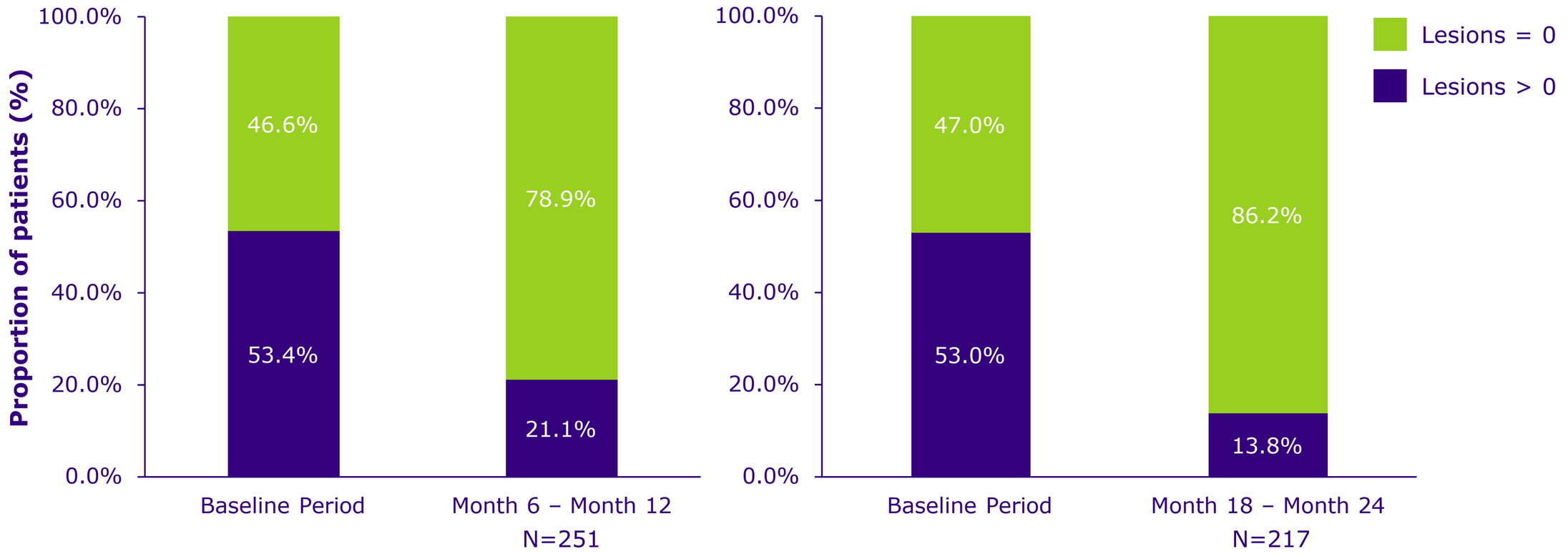
MAGNIFY-MS

Supplementary Figure 1. CUA Lesions Over Time (FAS)

- 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–Month 24).



CUA, combined unique active; **FAS**, full analysis set

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RESULTS

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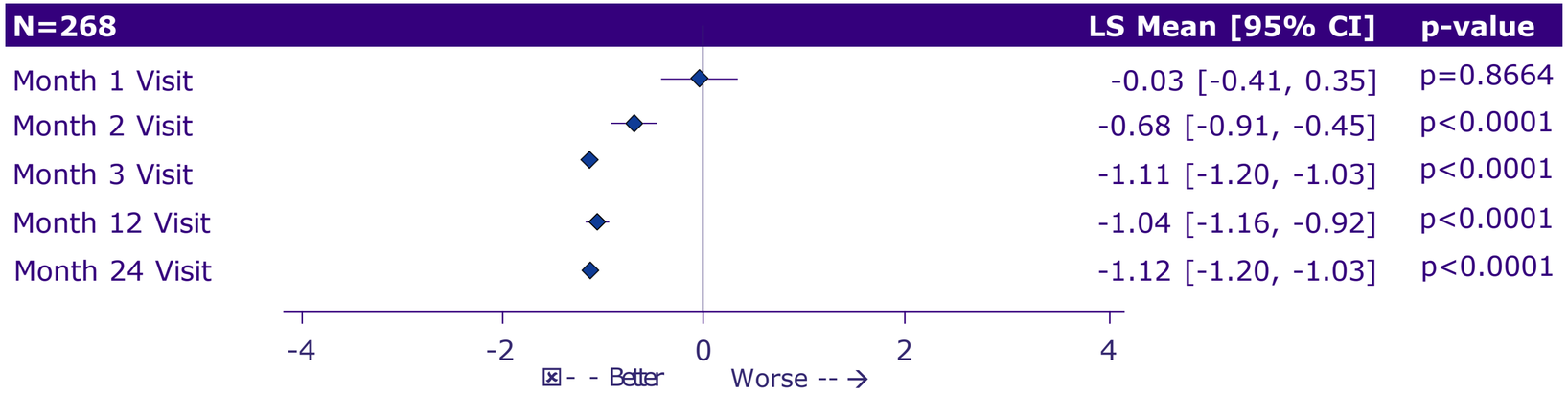
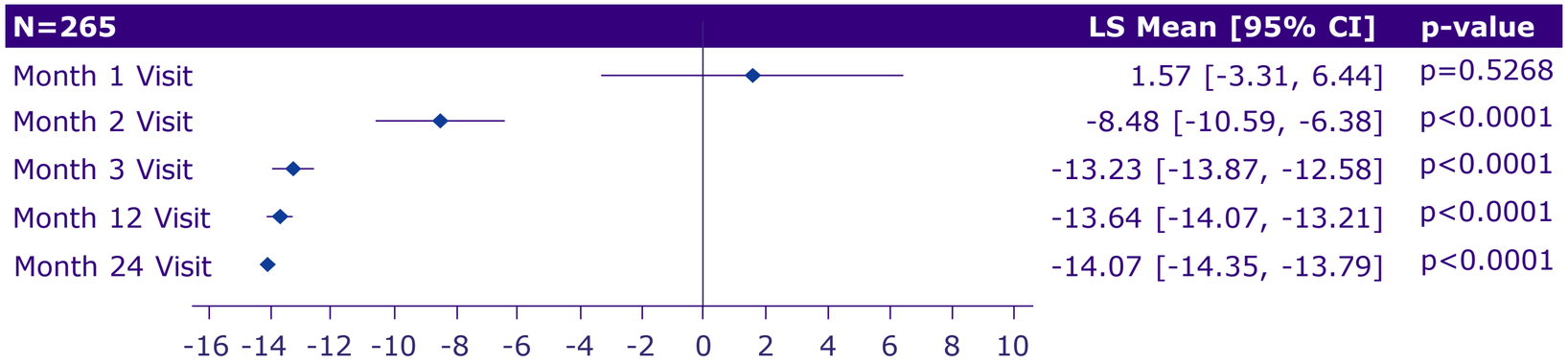
Supplementary Figure 2. T1 Gd+ and Annualized Active T2 Lesion Count: Change from Baseline Visit to Post-Baseline Visits (FAS)

- Mean T1 Gd+ and annualized active T2 lesion counts were markedly reduced from Month 2 and sustained through Month 24.

T1 Gd+ Lesions



Active T2 Lesions



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

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RESULTS

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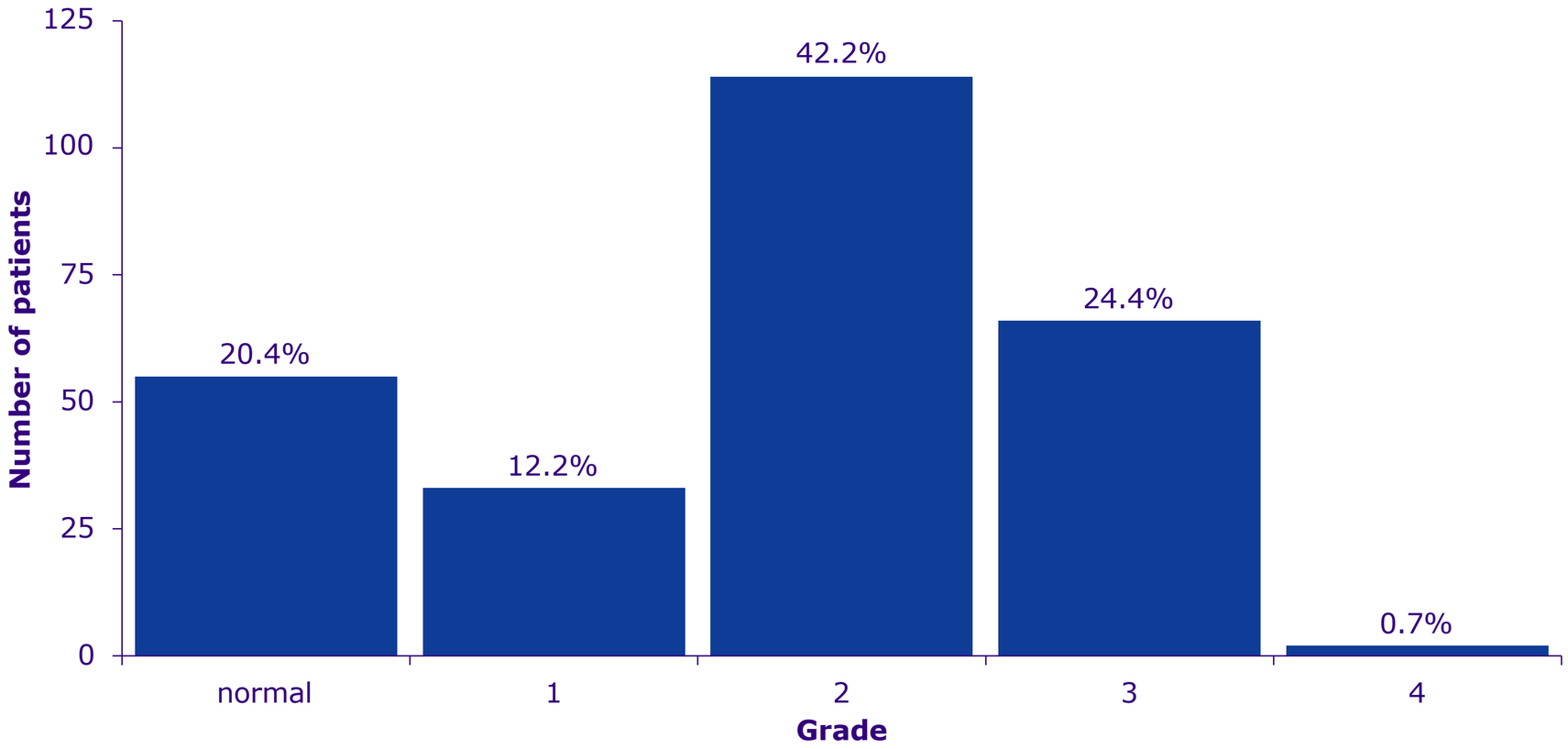
Supplementary Figure 3. Lymphocyte Counts – NCI-CTCAE Toxicity Grading – Highest Post-Baseline Grade (Safety Analysis Set)



NCI-CTCAE, National Cancer Institute – Common Terminology Criteria for Adverse Events

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RESULTS

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Supplementary Table 1. Safety Findings (Safety Analysis Set)

Number (%) of patients with:	Total (N=270)
Any TEAE	227 (84.1)
Mild	114 (42.2)
Moderate	103 (38.1)
Severe	10 (3.7)
Any study treatment-related TEAE*	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 treatment	1 (0.4)

*Worst severity per patient is reported.

TEAE, treatment-emergent adverse event

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