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Clinical Efficacy of Cladribine Tablets in Patients With Highly Active Relapsing Multiple Sclerosis: 36-Month Interim Results From the Extension Trial to the MAGNIFY-MS Study

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CONCLUSIONS

The Year 3 NEDA-3 rate of 81% (approximately two years after the final dose of cladribine tablets) demonstrates sustained efficacy

AE rates were low and mostly mild for both treatment-naïve and treatment-experienced patients; no new safety concerns were detected

INTRODUCTION

- MAGNIFY-MS (NTC03364046) demonstrated the efficacy and safety of cladribine tables in a modern/ contemporary multiple sclerosis (MS) cohort with highly active relapsing MS over 2 years[1]
- Patients who completed the parent study were eligible to enter a 2-year extension study, MAGNIFY-MS Extension (NCT04783935)

OBJECTIVES

To present the interim analysis from the MAGNIFY-MS Extension study (Year 3 after treatment initiation) with a focus on long-term clinical efficacy and safety

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METHODS

- Patients were treated with cladribine tablets (3.5 mg/kg cumulative dose over 2 years) in MAGNIFY-MS and were not to receive additional doses during the Extension (Years 3 and 4 after the first dose)
- The Year 3 visit period was defined as the time between the Month 24 and Month 36 visits
- Data captured during Year 3 of MAGNIFY-MS Extension were assessed for the following outcomes:

Rate of patients with no evidence of disease activity (NEDA-3)

Proportion of relapse-free patients

- NEDA-3 was defined as no qualifying relapses, no 6-month confirmed disability progression, and no new T1 gadolinium-enhancing (Gd+) and/or active T2 magnetic resonance imaging (MRI) lesions (estimated by Kaplan–Meier product limit estimate)
- For MRI outcomes, differences from Baseline of the MAGNIFY-MS parent study to all post-Baseline study visits were analyzed using a mixed-effects linear regression model
- Expanded Disability Status Scale (EDSS) scores and adverse events were also recorded
- Data were analyzed for all patients combined; subgroups included:
  - Treatment-naïve; and
  - Treatment-experienced

RESULTS

- A total of 219 out of 270 patients from the parent study (81.1%) entered the Extension phase and were included in the analysis: females, n=142 (64.8%); median age, 42.0 years; treatment-naïve, n=89 (40.6%)
- Patient characteristics in the Extension study were similar to those observed at Baseline in the MAGNIFY-MS parent study (see **supplementary Table 1**)
- NEDA-3 rates were consistently high during Year 3 for both treatment-naïve and treatment-experienced patients (**Table 1**)

During Year 3, the NEDA-3 rate was 80.56%, EDSS remained stable, and 90.4% of patients were relapse-free

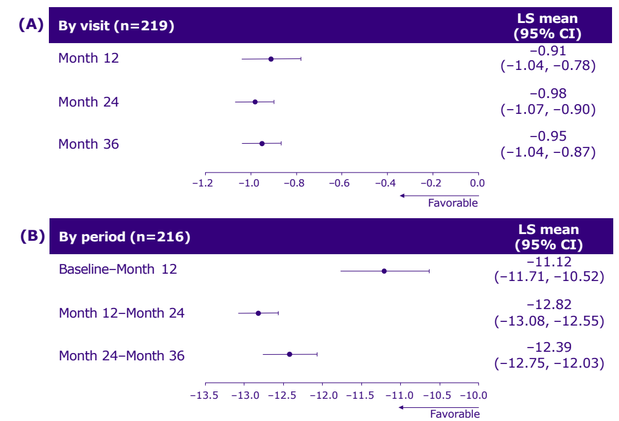
Table 1. Efficacy: NEDA-3 Rates During Year 3 Visit Period (Month 24–Month 36)

	Treatment-naïve		Treatment-experienced		All patients	
	Number of patients at risk/ censored	NEDA-3 rates, % (95% CI)	Number of patients at risk/ censored	NEDA-3 rates, % (95% CI)	Number of patients at risk/ censored	NEDA-3 rates, % (95% CI)
At 30 months[a]	84/1	95.48 (88.40, 98.28)	116/2	90.69 (84.19, 94.61)	200/3	92.65 (88.28, 95.43)
At 36 months[b]	63/14	85.99 (76.62, 91.80)	85/16	76.86 (68.41, 83.32)	148/30	80.56 (74.52, 85.31)

[a]30 months after treatment initiation, Month 6 of Year 3. [b]36 months after treatment initiation, Month 12 of Year 3
CI, confidence interval; **NEDA-3**, no evidence of disease activity

- T1 Gd+ counts (**Figure 1A**) and annualized active T2 lesion counts (**Figure 1B**) showed a clinically meaningful decrease from Baseline period to all subsequent periods, and to Month 24 and Month 36, respectively
- No new safety concerns were detected, in terms of rate, profile, or severity of adverse events (**Table 2**)

Figure 1. Full Analysis Set: Change from Baseline Visit/Period. (A). T1 Gd+ by Visit and (B). Annualized Active T2 Lesion Count by 12-Month Periods



The Baseline period was defined as the period between the screening and the Baseline MRI scan in MAGNIFY-MS study
CI, confidence interval; **Gd+**, gadolinium-enhancing; **LS**, least squares; **MRI**, magnetic resonance imaging

Table 2. Overview of Adverse Events During Year 3 Visit Period: Safety Analysis Set

Patients, n (%)	Treatment-naïve N=89 (100%)	Treatment-experienced N=130 (100%)	All patients N=219 (100%)
Any AE[a]	44 (49.4)	62 (47.7)	106 (48.4)
Mild	26 (29.2)	43 (33.1)	69 (31.5)
Moderate	17 (19.1)	15 (11.5)	32 (14.6)
Severe	1 (1.1)	3 (2.3)	4 (1.8)
Any serious AE	4 (4.5)	4 (3.1)	8 (3.7)
Most frequent non-serious AEs (by SOC and PT)[b], n (%)			
Infections and infestations	23 (25.8)	32 (24.6)	55 (25.1)
COVID-19[c]	9 (10.1)	19 (14.6)	28 (12.8)

[a]Worst severity per patient is reported. AEs reported during the Year 3 visit period. [b]Non-serious AEs by SOC and PT as determined by a frequency threshold of 5%. No serious AEs met the required 5% frequency threshold. [c]COVID-19 was the most common infection/infestation, followed by nasopharyngitis, influenza, pharyngitis, and sinusitis
AE, adverse event; **PT**, preferred term; **SOC**, system organ class

REFERENCE

1. De Stefano N, et al. *Neurol Neuroimmunol Neuroinflamm*. 2022;9(4):e1197.

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).

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