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

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CONCLUSIONS

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

INTRODUCTION

- The early initiation of highly effective disease-modifying therapy is particularly important in patients with highly active relapsing multiple sclerosis (MS) to prevent worsening disability[1]
- Early results from the Phase IV MAGNIFY-MS study (NCT03364036) concerning 6-month magnetic resonance imaging (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

OBJECTIVES

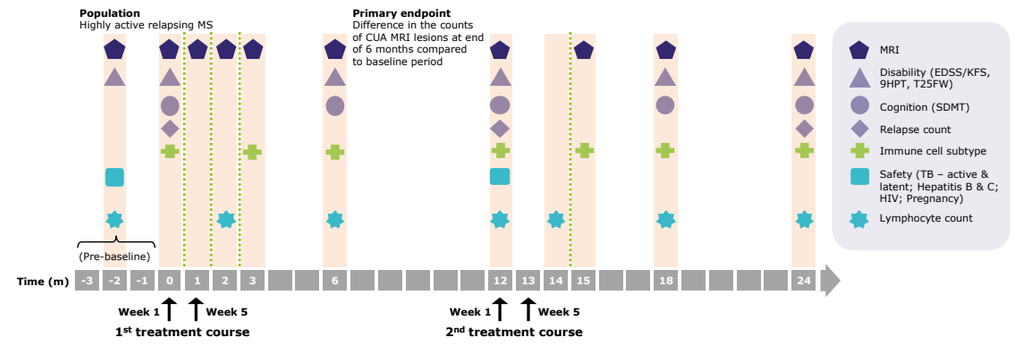
To report the 2-year MRI, clinical, and safety results from MAGNIFY-MS

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

METHODS

- Changes in combined unique active (CUA), T1 gadolinium enhancing (Gd+), and active T2 lesion counts were compared exploratively between baseline and post-baseline visits using a mixed-effects linear model for repeated measures annualised relapse rate (ARR) was estimated from a Poisson regression model
- The full analysis set (FAS) included all eligible patients (highly active relapsing MS patients aged ≥18 years with an Expanded Disability Status Score [EDSS] ≤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

Figure 1. 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; **m**, months; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis; **SDMT**, symbol digit modalities test; **T25FW**, timed 25-foot walk; **TB**, tuberculosis

RESULTS

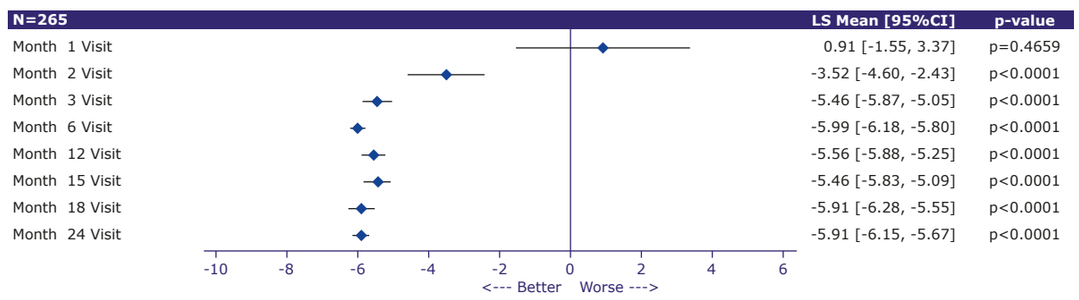
Table 1. Baseline Characteristics

	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 relapse within 12 months prior to Baseline, n (%)	267 (98.9)
EDSS ≤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 Baseline Period, n (%)	267 (98.9)
Patients with ≥1 lesion, n (%)	113 (41.9)

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

- A total of 270 patients were included in the FAS (**Table 1**). For patient disposition, see **Supplementary Figure 1**
- 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)

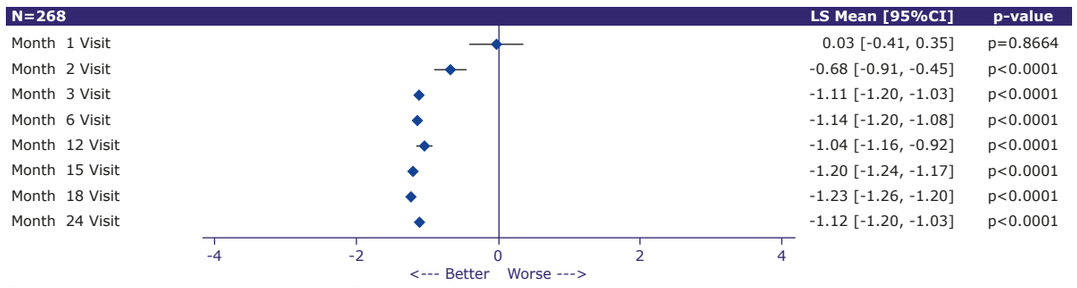
Figure 2. Annualised CUA Lesion Count – Change from Baseline Visit to Post-Baseline Visits: FAS



CI, confidence interval; **FAS**, full analysis set; **LS**, least square

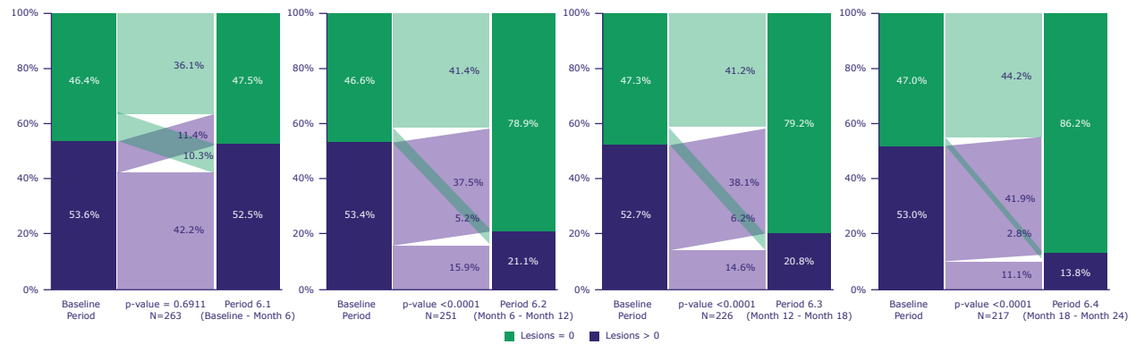
- Among patients with non-missing MRI data (N=265), significant reduction in the annualised CUA count was seen from Month 2 onwards (**Figure 2**)
  - The maximum mean change was reached at Month 6, and was maintained until Month 24
- Mean annualised T1 Gd+ (**Figure 3**) and active T2 lesion counts decreased in a similar manner (**Supplementary Figure 2**)

Figure 3. Annualised T1 Gd+ Lesion Count – Change from Baseline Visit to Post-Baseline Visits: FAS



CI, confidence interval; **FAS**, full analysis set; **LS**, least square

Figure 4. MRI Activity by 6 Month Periods – Cross-tabulation of Baseline and Post-Baseline Periods: FAS



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

- 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 (**Figure 4**)
- 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). Similar findings were apparent for the proportion of patients free of T1 Gd+ or active T2 lesions over this time frame (**Supplementary Figures 3 and 4**)

- Regarding safety, no serious adverse events (AE) potentially related to treatment were reported in the study. Study treatment-related treatment-emergent AEs were reported in 45.2% of patients, with 26.3% being mild, 17.4% moderate, and 1.5% severe (**Supplementary Table 1**)
- 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

SCAN HERE FOR ADDITIONAL CONTENT

REFERENCES
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.

DISCLOSURES
NDS is a consultant for Bayer, Biogen, Merck, Novartis, Roche, Sanofi, and Teva; has grants or grants pending from FISM and Novartis, is on the speakers' bureaus of Biogen, Merck, Novartis, Roche, Sanofi, and Teva; and has received travel funds from Merck, Novartis, Roche, Sanofi, and Teva. **AA** has received honoraria or consulting fees from Bayer, Biogen, Celgene (BMS), Merck, Novartis, Roche, and Sanofi; and research support from Bayer, Biogen, Merck, Roche, and Sanofi. **FB** is supported by the NIHR Biomedical Research Centre at UCLH and is a consultant to Biogen, Combinostics, IXICO, Merck, and Roche. **AC** has received speakers'/board honoraria from Actelion (Janssen/J&J), Almirall, Bayer, Biogen, Celgene (BMS), Merck, Novartis, Roche, Sanofi, and Teva, all for hospital research funds. He received research support from Biogen, Sanofi, and UCB, the European Union, and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience, and as topic editor for the Journal of International Medical Research. **TD** serves on scientific advisory boards for Bayer, Actelion (Janssen/J&J), Biogen, Celgene (BMS), GeNeuro, MedDay, Merck, Mitsubishi Pharma, Novartis, Roche, and Sanofi; has received funding for travel and/or speaker honoraria from Bayer, Biogen, Merck, Novartis, Roche, and Sanofi; and receives research support from Biogen, the European Union, Novartis, Roche, the Swiss MS Society, and the Swiss National Foundation. **SH** serves on advisory boards for Bayer, Biogen, Merck, Novartis, Roche, and Sanofi. She has received money for travel and speaker honoraria from Bayer, Biogen, Merck, Novartis, Roche, and Sanofi. **LL** has received honoraria for consulting services or speaking activities from Biogen, Merck, Novartis, and Roche; and research support from Biogen, Merck, 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 AbbVie, Actelion (Janssen/J&J), Alexion, Biogen, Celgene (BMS), EMD Serono Research & Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA), Roche, Immunic, Janssen Pharmaceuticals, MedDay, Merck, Mylan, Nervgen, Novartis, Sandoz, Sanofi, Teva, TG Therapeutics, Excemed, MSIF and NMSS. **AP** has received honoraria and operating grants from pharmaceutical companies. **KS** has received research support from Biogen, Merck, and Novartis; speaking honoraria from, and/or served in an advisory role for, Amgen-Gensenta, Biogen, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA), Merck, Novartis, Roche, Sanofi, and Teva; and remuneration for teaching activities from AcadeMe, 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 Research & Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA), Merck, Novartis, Roche, Sanofi, and Teva. **PV** has received honoraria or consulting fees from AB Science, Biogen, Celgene (BMS), Imcyse, Merck, 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, Merck, Novartis, Roche, Sanofi, and Teva. He received speaker honoraria and travel support from Bayer, Biogen, CSL Behring, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA), Fresenius Medical Care, Merck, Omniamed, Novartis, Sanofi, and Teva. He received compensation as a consultant from Biogen, Merck, Novartis, Omniamed, Roche, and Sanofi. He has received research support from Bayer, Biogen, Merck, Novartis, Sanofi, and Teva, as well as German Ministry for Education and Research (BMBF), German Research Foundation (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, Hertie Foundation, Merck, Novartis, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Münster, and RE Children's Foundation. **BK** and **AS** are employees of Merck Healthcare KGaA, Darmstadt, Germany. **LG** is an employee of EMD Serono Research and Development Institute, Inc., Billerica, MA, USA (an affiliate of Merck KGaA).

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