Reduction in CUA MRI Lesions in the First 6 Months after Cladribine Tablets Treatment for Highly Active Relapsing Multiple Sclerosis: MAGNIFY-MS Subgroup Analysis

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CONCLUSIONS

Treatment with cladribine tablets demonstrated an early onset of action with respect to CUA lesion count, irrespective of patients' baseline relapse activity or prior DMT history.

Reduction in mean CUA count was observed starting from the end of the first month of treatment. This reduction increased with time during the observation period, extending to the end of Month 6.

CUA, combined unique active; **DMT**, disease-modifying therapy

INTRODUCTION

- The CLARITY trial showed that outcomes in cladribine tablet-treated patients were superior to placebo with regard to number and relative reduction of MRI lesions over 96 weeks.
- MAGNIFY-MS aims to determine the onset of action of cladribine tablets (3.5 mg/kg cumulative dose over 2 years) in patients with highly active relapsing MS†.
- Interim results from the MAGNIFY-MS study indicate that cladribine tablets show an early onset of action on MRI lesions, significantly reducing CUA lesion counts between the end of Month 1 and the end of Month 6 after initiating treatment, with a reduction that increased with time.[1]

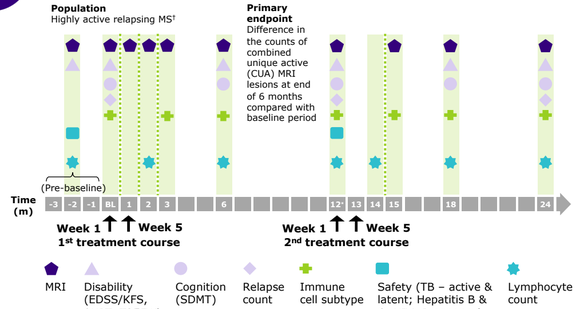
†As defined by: one relapse in the previous year and at least one T1 Gd+ lesion, or 9 or more T2 lesions, while on therapy with other DMTs, or two or more relapses in the previous year, whether on DMT treatment or not.
CUA, combined unique active; **DMT**, disease-modifying therapy; **Gd+**, gadolinium enhancing; **MRI**, magnetic resonance imaging; **MS**, multiple sclerosis

OBJECTIVES

To report the onset of action of cladribine tablets 3.5 mg/kg over 2 years, in patients with highly active relapsing MS by observing changes in counts of CUA lesions during the first 6 months of MAGNIFY-MS according to patient subgroups.

CUA, combined unique active; **MS**, multiple sclerosis

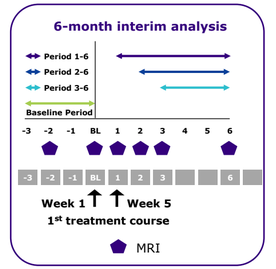
METHODS



*Second treatment course may be delayed for some patients, according to the lymphocyte count. †As defined by: one relapse in the previous year and at least one T1 Gd+ lesion, or 9 or more T2 lesions, while on therapy with other DMTs, or two or more relapses in the previous year, whether on DMT treatment or not.

- MAGNIFY-MS is an ongoing Phase IV, open-label, single-arm, multicenter, 2-year study.
- Patients with highly active relapsing MS† received cladribine tablets, with 2 weeks active treatment per course (Week 1 and Week 5 of each year).

- **270 patients** treated (12 withdrawals during year 1).
- Subgroups included: **HRA*/non-HRA, treatment, naïve/prior DMT treatment**, and **CUA lesion count > 0 at baseline**.
- MRI scans for all subgroups were performed during the baseline period and at Months 1, 2, 3, and 6†.
- Differences in CUA lesion count between post-baseline periods (**Period 1, Months 1–6; Period 2, Months 2–6;** and **Period 3, Months 3–6**) were compared with the baseline period.
- CUA lesion count was standardized to period length and number of MRIs in a period.
- Mixed effects linear model used to account for within- pooled center correlation and adjusted for CUA lesion count during the baseline period, age, and baseline EDSS (> 3, ≤ 3 [reference]).

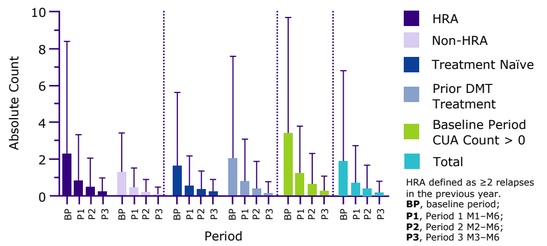


*HRA defined as ≥2 relapses in the previous year.
†Baseline period defined as the time between screening and study baseline.

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

RESULTS

Figure 1. Standardized CUA Lesion Counts (Mean ± SD)



HRA defined as ≥2 relapses in the previous year.
BP, baseline period; **P1**, Period 1 M1–M6; **P2**, Period 2 M2–M6; **P3**, Period 3 M3–M6

Table 1. Change from Baseline Period in Standardized CUA Lesion Count: HRA and Non-HRA Subgroups

	Period	Patients, n (%)	Least Squares Mean Estimate†	95% Confidence Interval	*P* value
HRA* (n=164)	Period 1 (Month 1–6)	152 (92.7)	-1.446	[-1.6978, -1.1935]	< 0.0001
	Period 2 (Month 2–6)	152 (92.7)	-1.801	[-1.9903, -1.6123]	< 0.0001
	Period 3 (Month 3–6)	147 (89.6)	-2.018	[-2.1330, -1.9022]	< 0.0001
Non-HRA (n=106)	Period 1 (Month 1–6)	100 (94.3)	-0.827	[-1.0019, -0.6522]	< 0.0001
	Period 2 (Month 2–6)	100 (94.3)	-1.057	[-1.1627, -0.9517]	< 0.0001
	Period 3 (Month 3–6)	99 (93.4)	-1.201	[-1.2676, -1.1340]	< 0.0001

*HRA defined as ≥2 relapses in the previous year.

- Standardized CUA lesion counts were **significantly reduced in all 3 Periods** across both HRA and non-HRA groups.

Table 2. Change from Baseline Period in Standardized CUA Lesion Count: Treatment Naïve and Prior DMT Treatment Subgroups

	Period	Patients, n (%)	Least Squares Mean Estimate†	95% Confidence Interval	*P* value
Treatment Naive (n=117)	Period 1 (Month 1–6)	107 (91.5)	-1.092	[-1.2350, -0.9500]	< 0.0001
	Period 2 (Month 2–6)	108 (92.3)	-1.316	[-1.4215, -1.2105]	< 0.0001
	Period 3 (Month 3–6)	108 (92.3)	-1.460	[-1.5759, -1.3443]	< 0.0001
Prior DMT Treatment (n=153)	Period 1 (Month 1–6)	145 (94.8)	-1.269	[-1.4852, -1.0535]	< 0.0001
	Period 2 (Month 2–6)	144 (94.1)	-1.637	[-1.8323, -1.4427]	< 0.0001
	Period 3 (Month 3–6)	138 (90.2)	-1.876	[-1.9816, -1.7696]	< 0.0001

- Standardized CUA lesion counts were **significantly reduced in all 3 Periods** across both treatment naïve and prior DMT treatment groups.

Table 3. Change from Baseline Period in Standardized CUA Lesion Count: Baseline Period CUA Lesion Count > 0

	Period	Patients, n (%)	Least Squares Mean Estimate†	95% Confidence Interval	*P* value
Baseline Period CUA Count > 0 (n=141)	Period 1 (Month 1–6)	140 (99.3)	-2.253	[-2.4970, -2.0080]	< 0.0001
	Period 2 (Month 2–6)	141 (100)	-2.790	[-3.0011, -2.5790]	< 0.0001
	Period 3 (Month 3–6)	137 (97.2)	-3.132	[-3.2702, -2.9933]	< 0.0001

- Standardized CUA lesion counts were **significantly reduced in all 3 Periods** among those with a baseline CUA lesion count > 0.

†Least Squares Means fitting a mixed effects linear model, adjusted for the baseline count, age (years), EDSS score at baseline (> 3 vs. ≤ 3 [reference]), and within-pooled center correlation.
CUA, combined unique active; **DMT**, disease modifying therapy; **EDSS**, Expanded Disability Status Scale; **HRA**, high relapse activity

1. De Stefano N, et al. *Mult Scler.* 2020;26(S3):303

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This study was sponsored by Merck KGaA, Darmstadt, Germany.

RESULTS

Patient Characteristics

	HRA* (n=164)	Non-HRA (n=106)	Treatment naïve (n=117)	Prior DMT treatment (n=153)	Baseline Period CUA count > 0 (n=141)	Total (n=270)
Female, n (%)	107 (65.2)	73 (68.9)	76 (65.0)	104 (68.0)	97 (68.8)	180 (66.7)
Age (years), mean ± SD	37.6 ± 9.8	37.8 ± 9.8	37.6 ± 10.1	37.8 ± 9.5	35.3 ± 9.0	37.7 ± 9.8
Time since onset of MS (months), mean ± SD	75.4 ± 84.3	99.6 ± 85.5	44.1 ± 55.1	116.1 ± 91.4	74.2 ± 76.1	84.9 ± 85.5
Time since first relapse (months), mean ± SD	42.1 ± 67.5	73.8 ± 76.3	18.9 ± 33.7	81.3 ± 82.1	46.5 ± 60.1	54.4 ± 72.6
Median number of relapses within 12 months prior to baseline	2.00	1.00	2.00	1.00	2.00	2.00
Median EDSS at baseline	2.25	2.00	2.00	2.00	2.00	2.00

* HRA defined as ≥2 relapses in the previous year.
CUA, combined unique active; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **HRA**, high relapse activity; **MS**, multiple sclerosis; **SD**, standard deviation

RESULTS

Tables 1-3. Change from Baseline Period in Standardized CUA Lesion Count

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Standardized CUA lesion counts were **significantly reduced in all 3 Periods** across both HRA and non-HRA groups.
Standardized CUA lesion counts were **significantly reduced in all 3 Periods** across both treatment naïve and prior DMT treatment groups.
Standardized CUA lesion counts were **significantly reduced in all 3 Periods** among those with a baseline CUA lesion count > 0.

***HRA defined as ≥2 relapses in the previous year.** †Least Squares Means fitting a mixed effects linear model, adjusted for the baseline count, age (years), EDSS score at baseline (> 3 vs. ≤ 3 [reference]), and within-pooled center correlation.
CUA, combined unique active; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **HRA**, high relapse activity

RESULTS

Change from Baseline Period in T1 Gd+ Lesion Count

	Visit	Patients, n (%)	Least Squares Mean Estimate†	95% Confidence Interval	*P* value
HRA* (n=164)	Month 1	154 (93.9)	-0.144	[-0.8821, 0.5942]	0.7003
	Month 2		-1.021	[-1.4149, -0.6273]	**< 0.0001**
	Month 3		-1.563	[-1.7077, -1.4178]	**< 0.0001**
	Month 6		-1.748	[-1.8382, -1.6580]	**< 0.0001**
Non-HRA (n=106)	Month 1	104 (98.1)	0.022	[-0.4901, 0.5335]	0.9331
	Month 2		-0.617	[-0.8747, -0.3601]	**< 0.0001**
	Month 3		-1.038	[-1.1163, -0.9600]	**< 0.0001**
	Month 6		-1.010	[-1.0898, -0.9295]	**< 0.0001**
Treatment Naïve (n=117)	Month 1	109 (93.2)	-0.127	[-0.7754, 0.5205]	0.6968
	Month 2		-0.725	[-1.0033, -0.4461]	**< 0.0001**
	Month 3		-1.092	[-1.2206, -0.9628]	**< 0.0001**
	Month 6		-1.191	[-1.3099, -1.0713]	**< 0.0001**
Prior DMT Treatment (n=153)	Month 1	149 (97.4)	-0.036	[-0.7425, 0.6711]	0.9206
	Month 2		-0.955	[-1.3567, -0.5526]	**< 0.0001**
	Month 3		-1.569	[-1.6828, -1.4545]	**< 0.0001**
	Month 6		-1.638	[-1.7100, -1.5669]	**< 0.0001**
Baseline Period CUA Count > 0 (n=141)	Month 1	141 (100)	-0.257	[-1.0993, 0.5853]	0.5471
	Month 2		-1.598	[-2.0413, -1.1547]	**< 0.0001**
	Month 3		-2.488	[-2.6359, -2.3396]	**< 0.0001**
	Month 6		-2.633	[-2.7483, -2.5175]	**< 0.0001**

T1 Gd+ lesion counts were significantly decreased from Month 2 onwards.

***HRA defined as ≥2 relapses in the previous year.** †Least Squares Means fitting a mixed effects linear model, adjusted for the baseline count, age (years), EDSS score at baseline (> 3 vs. ≤ 3 [reference]), and within-pooled center correlation.
CUA, combined unique active; **DMT**, disease-modifying therapy; **EDSS**, Expanded Disability Status Scale; **Gd+**, gadolinium enhancing; **HRA**, high relapse activity; **MRI**, magnetic resonance imaging