Prognostic Value of the MAGNIMS Score and its Application in Clinical Outcome Assessment of Disease Modifying Therapy in Patients with Relapsing Multiple Sclerosis: Results from the OPTIMUM Study of Ponesimod

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BACKGROUND

- For patients with multiple sclerosis (MS), clinicians need to understand the long-term prognosis after patients start a new disease-modifying therapy (DMT) to decide whether the treatment is working as intended
- Magnetic Resonance Imaging in MS (MAGNIMS) is a prognostic tool to facilitate the early identification of patients with relapsing MS who are suboptimally responsive or unresponsive to their existing DMT[1-3]
- MAGNIMS has good prognostic value in predicting long term disability progression in patients treated with various DMTs,[1-3]but it has yet to be used in patients receiving ponesimod

OBJECTIVE

- To assess the value of the MAGNIMS score at week 60 in assessing potential suboptimal treatment response and prognostic effect on disability status at week 108 in a large phase 3 clinical trial

METHODS

- Patients with relapsing MS randomized to either ponesimod 20 mg or teriflunomide 14 mg in the phase 3 OPTIMUM study[4] (ClinicalTrials.gov Identifier: NCT02425644) were classified according to MAGNIMS score[1] (**Table 1**) at week 60 (0, 1, or 2, with higher scores indicating worse clinical outcomes)
- Proportions of patients with different MAGNIMS scores in each treatment arm were compared
- The two treatment arms were pooled to increase the sample size and statistical power of the analysis
- Cox regression analysis was used to assess whether MAGNIMS score at week 60 could differentiate the risks of times to 12-and 24-week confirmed disability accumulation (CDA as defined in the OPTIMUM study[4]) at week 108

Table 1: MAGNIMS scoring criteria

MAGNIMS score	Number of new or enlarging T2 lesions over a pre-specified timeframe[a]	Number of relapses over a pre-specified timeframe[a]
0	0-2	0
2	0-2 or ≥3	1 0
2	≥0 or ≥3	≥2 1

[a]Studies used first 12–18 months of the treatment period
MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

RESULTS

- MAGNIMS score at week 60 was derived for 533 subjects in the ponesimod 20 mg arm and 528 subjects in the teriflunomide 14 mg arm, with the remaining subjects excluded due to missing T2 lesion data
- Demographics and baseline characteristics (**Table 2**)were similar between the treatment arms and similar tothe full analysis set
- Relative to teriflunomide, significantly more subjects in the ponesimod arm had a MAGNIMS score of 0 and significantly fewer had a MAGNIMS score of 2 (**Table 3**)
- Kaplan-Meier curves for both time to 12-week and 24-week CDA were clearly separated (log-rank *p*-value < 0.0001) among the MAGNIMS subgroups through 108 weeks (**Figures 1 and 2**)

Table 2: Demographic and baseline characteristics of subjects with a MAGNIMS score

Characteristic[a]	Ponesimod 20 mg (N = 533)	Teriflunomide 14 mg (N = 528)
Female	345 (64.7)	349 (66.1)
Mean age (SD), years	36.5 (8.76)	36.7 (8.74)
White race	518 (97.2)	516 (97.7)
Disease-modifying treatment received within 2 years prior to randomization	207 (38.8)	205 (38.8)
Baseline EDSS score, mean (SD)	2.55 (1.17)	2.54 (1.21)
Time since first symptom at randomization, mean (SD), years	7.43 (6.76)	7.60 (6.77)
Relapses in last year prior to study entry, mean (SD)	1.3 (0.62)	1.3 (0.65)
Multiple sclerosis subtype		
Relapsing-remitting	521 (97.8)	517 (98.0)
Secondary progressive	12 (2.2)	11 (2.0)
Presence of gadolinium-enhancing T1 lesions at baseline[b]	217 (40.7)	246 (46.6)
Volume of T2-weighted lesions, mean (SD), mm^3	8197.5 (10 298.76)	9632.3 (11 416.74)
Highly active disease[c]	185 (34.7)	185 (35.0)

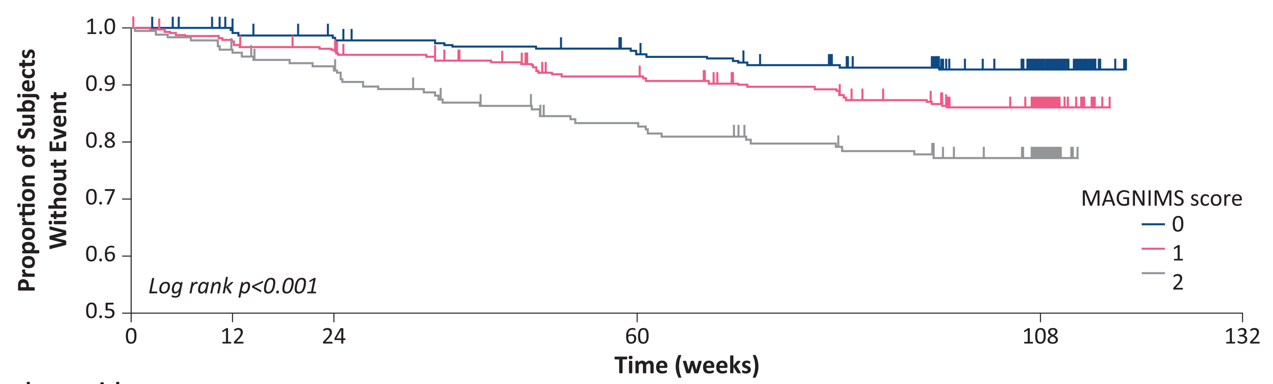
[a]Values are presented as numbers (%) unles otherwise stated.
[b]From the central reader.
[c]Two or more relapses within 1 year prior to study entry, a baseline Expanded Disability Status Scale score >2, and baseline magnetic resonance imaging or ≥1 gadolinium-enhancing T1 lesions; or any disease-modifying treatment received within 12 months prior to randomization and one or both of the following: (1) ≥1 relapses within 1 year prior to study entry and baseline magnetic resonance imaging showing ≥1 gadolinium-enhanced T1 lesions and/or ≥9 T2-weighted lesions or (2) a number of relapses within 1 year prior to study entry equal to or greater than the number of relapses between 2 years and 1 year prior to study entry, for patients with ≥1 relapses within the 2 years prior to study entry.
EDSS, Expanded Disability Status Scale; MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

Table 3: The proportion of subjects with each MAGNIMS score based on outcomes observed up to week 60, by treatment group[a]

MAGNIMS	Ponesimod 20 mg	Teriflunomide 14 mg	Odds ratio (95% CI)	P-value
0	304/533 (57.04%)	243/528 (46.02%)	1.56 (1.22–1.98)	<0.001
1	159/533 (29.83%)	177/528 (33.52%)	0.84 (0.65–1.09)	0.196
2	70/533 (13.13%)	108/528 (20.45%)	0.59 (0.42–0.82)	0.002

[a]Last observation carried forward was used for relapse data. For T2 data, subjects with missing assessment were excluded.
CI, confidence interval; MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

Figure 1. Time to 12-week CDA by MAGNIMS score (pooled)

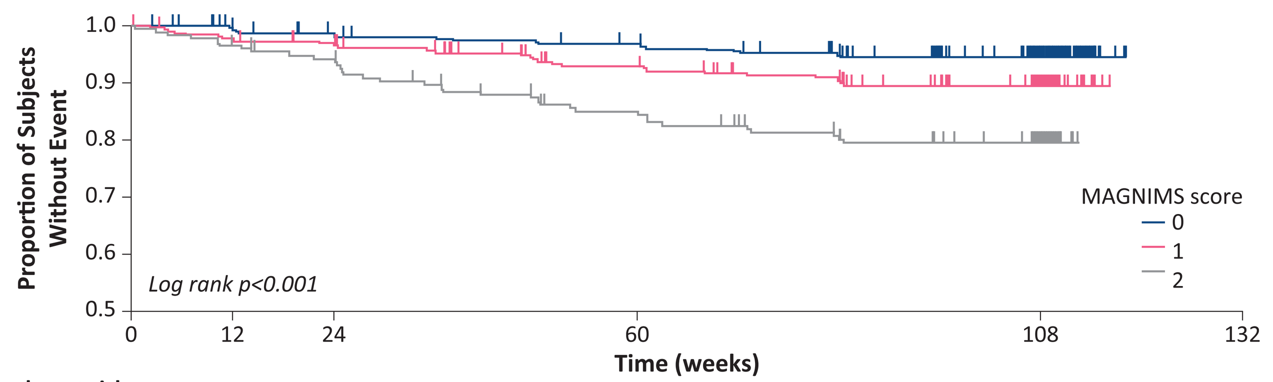


Number at risk

	0	12	24	60	108	132
0	547	539	527	508	372	0
1	336	326	320	293	200	0
2	178	170	163	139	90	0

CDA, confirmed disability accumulation; MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

Figure 2. Time to 24-week CDA by MAGNIMS score (pooled)



Number at risk

	0	12	24	60	108	132
0	547	538	527	514	377	0
1	336	327	322	297	205	0
2	178	171	165	142	91	0

CDA, confirmed disability accumulation; MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

- Hazard ratios comparing the risk of 12-week CDA between MAGNIMS score groups were broadly similar tothose comparing the risk of 24-week CDA between MAGNIMS score groups (**Table 4**)

Table 4: Risk of 12-week CDA and 24-week CDA at 108 weeks

Outcome	MAGNIMS score comparison	Hazard ratio (95% CI)	P-value
12-week CDA	1 vs 0	1.97 (1.28–3.03)	0.002
12-week CDA	2 vs 0	3.48 (2.23–5.42)	<0.001
12-week CDA	1 vs 0	1.99 (1.21–3.26)	0.007
12-week CDA	2 vs 0	4.14 (2.53–6.78)	<0.001

CDA, confirmed disability accumulation; CI, confidence interval; MAGNIMS, Magnetic Resonance Imaging in Multiple Sclerosis.

- Time to 12-week CDA and 24-week CDA at 108 weeks by MAGNIMS score were similar in the ponesimod 20 mg treatment arm and teriflunomide 14 mg treatment arm

CONCLUSIONS

- The results of this study demonstrate the potential of the MAGNIMS score to predict the long-term risk of worsening disability, helping clinicians identify patients with a suboptimal response to newly initiated DMTs prior to the availability of long-term disability data
- Treatment with ponesimod was found to result in significantly more patients than teriflunomide classified with a favorable MAGNIMS score of 0 at week 60
- Treatment with ponesimod also resulted in significantly fewer patients than teriflunomide classified with an unfavorable MAGNIMS score of 2 at week 60
- Further research providing longer-term follow-up data is needed to validate these findings, as the follow-up period was relatively short

References

1. Kunchok A et al. Prediction of on-treatment disability worsening in RRMS with the MAGNIMS score. *Mult Scler*. 2021;27(5):695-705.
2. Sormani MP et al. Predicting long-term disability outcomes in patients with MS treated with teriflunomide in TEMSO. *Neurol Neuroimmunol Neuroinflamm*. 2017;4(5):e379.
3. Sormani MP et al. MAGNIMS score predicts long-term clinical disease activity-free status and confirmed disability progression in patients treated with subcutaneous interferon beta-1a. *Mult Scler Relat Disord*. 2021;49:102790.
4. Kappos L et al. Ponesimod Compared With Teriflunomide in Patients With Relapsing Multiple Sclerosis in the Active-Comparator Phase 3 OPTIMUM Study: A Randomized Clinical Trial. *JAMA Neurol*. 2021;78(5):558-567.

Disclosures

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