Patient-Reported Outcomes in Patients With Varying Clinical Disease Activity of Relapsing-Remitting Multiple Sclerosis in the DECIDE Study

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INTRODUCTION

- Physical disability progression (based on the Expanded Disability Status Scale [EDSS]) and relapses are common clinician-assessed outcomes in clinical trials of relapsing-remitting multiple sclerosis (RRMS) therapies.[1]
  - Limitations of the EDSS in the assessment of disability include: an emphasis on walking ability between scores of 4.0–7.0, potential for inter-rater inconsistency in neurological evaluation, and that its measurement of cognitive function is subjective and lacks sensitivity in the upper range[2,3]
  - Relapses in patients with MS can, but do not always, lead to confirmed disability progression (CDP).[4]
- Patient-reported outcomes (PROs), such as the 29-item Multiple Sclerosis Impact Scale (MSIS-29)[5] and the EuroQol 5-Dimensions (EQ-5D),[6] are important for assessing the impact of MS on patient functioning and daily activities from the patient's perspective.
- PROs may provide information on the impact of RRMS on patients beyond the outcomes typically used by physicians.

OBJECTIVES

- To evaluate PROs in patients with RRMS grouped according to clinical disease activity based on occurrence of 24-week CDP in the absence or presence of prior relapse in DECIDE.

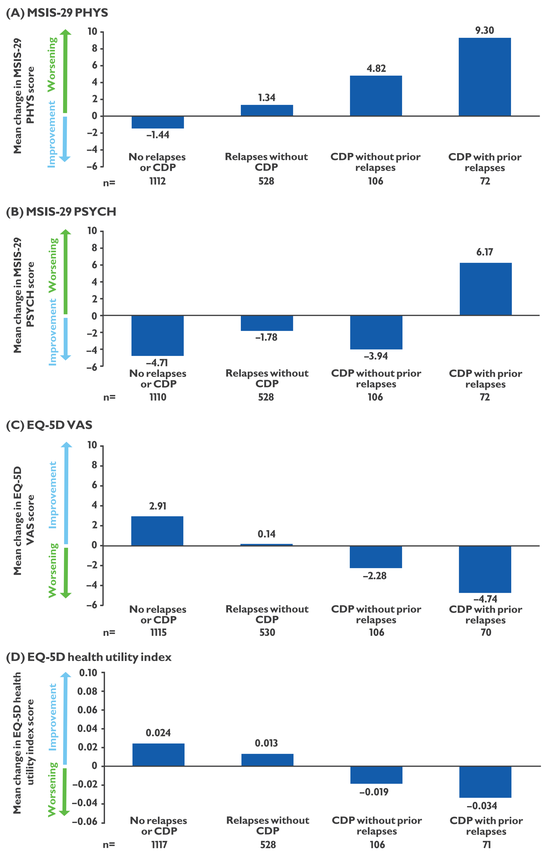
METHODS

- DECIDE was a randomized, double-blind, active-controlled study of daclizumab high-yield process (DAC HYP) 150 mg subcutaneous every 4 weeks vs. interferon (IFN) beta-1a 30 mcg intramuscular (IM) once weekly in patients with RRMS.[7]
- Twenty-four-week CDP was defined as an ≥1.0- or ≥1.5-point increase in EDSS score from a Baseline EDSS score ≥1.0 or 0.0, respectively, that was confirmed at 24 weeks.[7]
- In this post hoc analysis, patients from the intention-to-treat population were divided into 4 groups based on the occurrence and severity of clinical disease activity during DECIDE:
  - No relapses or CDP (least severe clinical disease activity)
  - Relapses without CDP
  - CDP without prior relapses
  - CDP with prior relapses (defined as onset of 24-week CDP within 90 days following the onset of relapse; most severe clinical disease activity).
- Mean change from Baseline at Week 96 was evaluated post hoc for the MSIS-29 physical (PHYS) and psychological (PSYCH) impact subscale scores, and the EQ-5D visual analog scale (VAS) and health utility index scores.
- For MSIS-29 PHYS and PSYCH scores, negative changes indicate improvement.[5]
- For EQ-5D VAS and EQ-5D health utility index scores, positive changes indicate improvement.[6]
- The percentage of patients with clinically meaningful worsening in MSIS-29 PHYS score (≥7.5-point worsening from Baseline[8]) was examined for each clinical disease activity group.
- Missing data for the MSIS-29 PHYS and PSYCH and the EQ-5D VAS and EQ-5D health utility index were imputed using a random effects model.
- Trend tests (based on an analysis of variance or frequency table) were conducted to assess the significance of the correlation between changes in PRO scores and the 4 disease activity groups.

RESULTS

- The majority of Baseline characteristics were similar between the 4 disease activity subgroups. Of note, the group of patients with CDP with prior relapses had a higher mean EDSS score at Baseline and had the fewest patients with gadolinium-enhancing (Gd^+) lesions present at Baseline (Table 1).
- When analyzed by treatment group at Week 96, more DAC HYP- than IM IFN beta-1a-treated patients were in the subgroup with no relapses or CDP (least severe clinical disease activity; Table 1).

Figure 1. Mean changes from Baseline in **(A)** MSIS-29 PHYS, **(B)** MSIS-29 PSYCH, **(C)** EQ-5D VAS, and **(D)** EQ-5D health utility index scores at Week 96 (overall population)



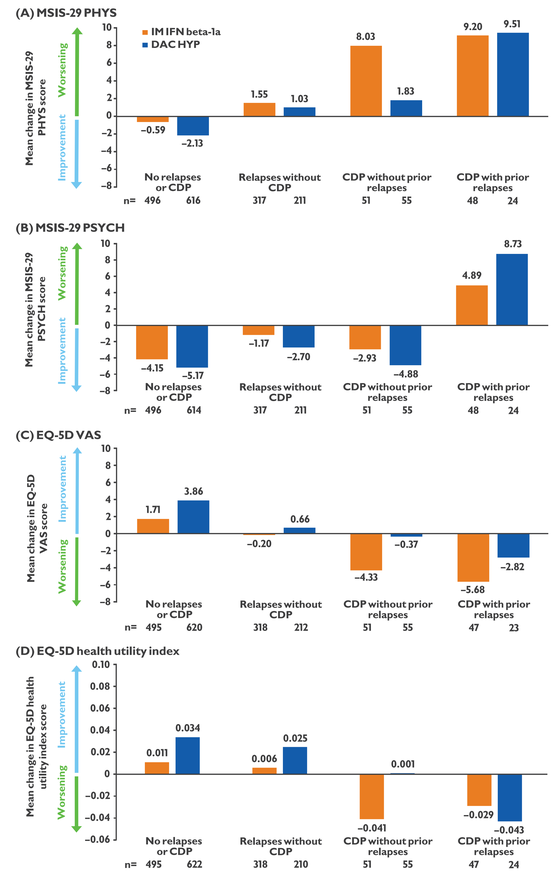
Missing data for the MSIS-29 PHYS and PSYCH and the EQ-5D VAS and EQ-5D health utility index were imputed using a random effects model. Patients who have not reached 24-week CDP and discontinued early were considered censored at their last EDSS assessment

Table 1. Demographics and baseline characteristics by clinical disease activity subgroup

Characteristic	No relapses or CDP			Relapses without CDP			CDP without prior relapses			CDP with prior relapses		
	IM IFN beta-1a n=504	DAC HYP n=627	Overall n=1131	IM IFN beta-1a n=319	DAC HYP n=212	Overall n=531	IM IFN beta-1a n=51	DAC HYP n=55	Overall n=106	IM IFN beta-1a n=48	DAC HYP n=25	Overall n=73
Mean (SD) age, y	36.9 (9.5)	35.9 (9.3)	36.3 (9.4)	34.4 (9.0)	36.1 (9.1)	35.1 (9.1)	39.3 (7.6)	42.4 (8.6)	40.9 (8.2)	38.0 (8.7)	40.4 (9.3)	38.8 (8.9)
Female, n (%)	348 (69.0)	420 (67.0)	768 (67.9)	211 (66.1)	149 (70.3)	360 (67.8)	36 (70.6)	37 (67.3)	73 (68.9)	32 (66.7)	19 (76.0)	51 (69.9)
Mean (SD) time since diagnosis, y	4.0 (4.6)	3.9 (4.8)	4.0 (4.7)	3.8 (4.2)	4.8 (5.2)	4.2 (4.7)	6.3 (7.2)	4.2 (4.8)	5.2 (6.1)	5.4 (4.8)	6.0 (6.2)	5.6 (5.3)
Mean (SD) no. of relapses within the previous year	1.5 (0.7)	1.5 (0.7)	1.5 (0.7)	1.7 (0.8)	1.7 (0.8)	1.7 (0.8)	1.5 (0.7)	1.5 (0.7)	1.5 (0.7)	1.8 (0.8)	1.6 (0.9)	1.7 (0.9)
Mean (SD) EDSS score	2.5 (1.2)	2.3 (1.1)	2.4 (1.2)	2.6 (1.2)	2.7 (1.2)	2.6 (1.2)	2.7 (1.5)	2.6 (1.5)	2.6 (1.5)	3.0 (1.3)	3.7 (1.3)	3.2 (1.3)
Mean (SD) no. of T2 lesions	49.7 (36.8)	48.1 (35.0)	48.8 (35.8)	53.1 (37.6)	50.9 (34.9)	52.3 (36.5)	66.8 (42.5)	49.0 (38.7)	57.8 (41.4)	49.7 (33.2)	60.4 (45.0)	53.3 (37.6)
Mean (SD) no. of Gd^+ lesions	1.9 (6.0)	1.7 (4.1)	1.8 (5.0)	2.9 (5.9)	3.1 (9.8)	3.0 (7.7)	2.4 (4.6)	1.1 (1.9)	1.8 (3.6)	1.8 (4.4)	1.2 (1.9)	1.6 (3.7)
Gd^+ lesions present at Baseline, n (%)	204 (40.5)	264 (42.1)	468 (41.4)	173 (54.2)	101 (47.6)	274 (51.6)	22 (43.1)	24 (43.6)	46 (43.4)	15 (31.3)	9 (36.0)	24 (32.9)

- For combined treatment groups, generally, mean PRO scores worsened as severity of disease activity increased (Figure 1A–D). Trend tests demonstrated that results for all PROs examined were highly correlated with the disease activity groups ($P<.01$ for all comparisons).
- DAC HYP-treated patients with no relapses or CDP showed mean improvement in PROs and DAC HYP-treated patients with CDP with prior relapses (most severe disease activity) showed mean worsening in PROs (Figure 2A–D).
- DAC HYP showed generally greater mean improvement or less mean worsening across most clinical disease activity subgroups when compared with IM IFN beta-1a, but between-treatment comparisons did not reach statistical significance (Figure 2A–D).
- For DAC HYP, trend tests demonstrate that results for the MSIS-29 PHYS and PSYCH ($P<.001$ for both) and the EQ-5D health utility index ($P=.023$) were significantly correlated with the disease activity groups, but not the EQ-5D VAS.
- For IM IFN beta-1a, trend tests demonstrate that results for the MSIS-29 PHYS and PSYCH and the EQ-5D VAS were significantly correlated with the disease activity groups ($P<.01$ for all), but not the EQ-5D health utility index.

Figure 2. Mean changes from Baseline in **(A)** MSIS-29 PHYS, **(B)** MSIS-29 PSYCH, **(C)** EQ-5D VAS, and **(D)** EQ-5D health utility index scores at Week 96 by treatment group



Missing data for the MSIS-29 PHYS and PSYCH and the EQ-5D VAS and EQ-5D health utility index were imputed using a random effects model. Patients who have not reached 24-week CDP and discontinued early were considered censored at their last EDSS assessment

- The percentage of patients with a clinically meaningful worsening in MSIS-29 PHYS score (≥7.5-point worsening from Baseline) increased as severity of clinical disease activity increased for individual and combined treatments (Table 2).

Table 2. Percentage of patients who had a clinically meaningful worsening in MSIS-29 PHYS score (≥7.5-point worsening from Baseline)

Disease activity group, % (n/N)	IM IFN beta-1a	DAC HYP	Overall
No relapses or CDP	14.5 (72/496)	11.9 (73/616)	13.0 (145/1112)
Relapses without CDP	24.6 (78/317)	24.2 (51/211)	24.4 (129/528)
CDP without prior relapses	41.2 (21/51)	36.4 (20/55)	38.7 (41/106)
CDP with prior relapses	45.8 (22/48)	45.8 (11/24)	45.8 (33/72)

CONCLUSIONS

- PROs are important tools in clinical trials that capture information on the impact of an MS treatment from the perspective of the patient, adding valuable data to that provided by clinical assessments.[5]
- Overall, MSIS-29 and EQ-5D outcomes generally worsened as severity of clinical disease activity increased.
- The MSIS-29 and EQ-5D detected improvements in patients with the least severe disease activity (no relapses or CDP), indicating that these PRO outcomes were sensitive to functional changes not detected by the clinical outcome measures.
- Compared with IM IFN beta-1a, DAC HYP showed a nonsignificant trend towards stronger benefits on PROs across most clinical disease activity groups, and more DAC HYP-treated patients were in the subgroup with the least severe clinical disease activity.
- Potential differences between disease activity subgroups should be explored in future research.
- These findings were consistent with clinical outcomes from DECIDE.[7]

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Disclosures

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