Effect of Daclizumab HYP vs. Intramuscular Interferon Beta-1a on No Evidence of Disease Activity in Patients With Relapsing-Remitting Multiple Sclerosis: Analysis of the DECIDE Study

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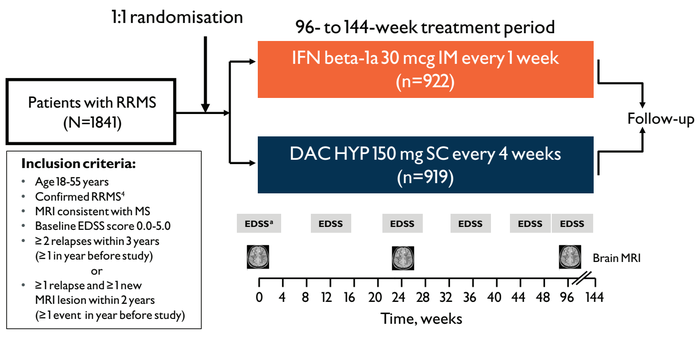
INTRODUCTION

- No evidence of disease activity (NEDA) is a composite endpoint that is increasingly studied in clinical trials of multiple sclerosis (MS) treatments. Both clinical and MRI (magnetic resonance imaging) measures of disease activity are used to define NEDA in a clinical trial setting.[1]
- Whether NEDA has utility or should be the goal of treatment in routine clinical practice has yet to be established, but its use is supported.[2]
- In the dose-finding Phase 2 SELECT study, daclizumab high-yield process (DAC HYP) treatment significantly increased the percentage of patients with relapsing-remitting MS (RRMS) who were disease activity free vs. placebo (39% vs. 11%, respectively; OR (odds ratio), 6.18; 95% CI, 3.71–10.32; P<.0001) after 52 weeks of treatment.[3]

OBJECTIVE

- To determine the percentage of patients with RRMS who achieved NEDA following ≥ 96 weeks of treatment with DAC HYP vs. intramuscular (IM) interferon (IFN) beta-1a in the Phase 3 DECIDE study.

Figure 1. DECIDE study design overview



EDSS = Expanded Disability Status Scale; SC = subcutaneous
[a]Also assessed at Weeks 60, 72, 84, 108, 120, 132 and 144

- All patients had a minimum of 2 and maximum of 3 years of treatment.
- The study ended when the last randomised patient completed 2 years of treatment.

DEFINITIONS

- Overall NEDA: completion of Week 96 with:
  - No clinical relapses
  - No 12-week confirmed disability progression
  - No new or enlarging T2 hyperintense lesions vs. Baseline
  - No gadolinium-enhancing (Gd+) lesions at Weeks 24 and 96
- Clinical NEDA: completion of Week 96 with:
  - No clinical relapses
  - No 12-week confirmed disability progression
- MRI NEDA: completion of Week 96 with:
  - No new or enlarging T2 hyperintense lesions and no Gd+ lesions at Weeks 24 and 96

METHODS

- *Primary analysis:* excluded patients with missing outcomes whose available outcomes satisfied NEDA criteria
- *Sensitivity analysis:* included patients with missing outcomes who would be considered NEDA if all available outcomes satisfied NEDA criteria

Statistical Analyses

- Logistic regression models were used to calculate ORs and P values for between-treatment comparisons.
- Models were adjusted for baseline relapse rate, baseline EDSS score (≤ 2.5, > 2.5), prior IFN beta use (yes, no) and baseline age (≤ 35, > 35 years).

Table 1. Demographics and baseline characteristics

Characteristic	IM IFN beta-1a n=922	DAC HYP n=919
Mean (SD) age, y	36.2 (9.3)	36.4 (9.4)
Female, n (%)	627 (68)	625 (68)
Mean (SD) duration of disease, y[a]	4.1 (4.7)	4.2 (5.0)
Mean (SD) no. of relapses within previous year	1.6 (0.8)	1.5 (0.7)
Mean (SD) EDSS score	2.5 (1.3)	2.5 (1.2)
Previous DMT, n (%)[b]	376 (41)	380 (41)
Prior IFN beta use, n (%)	311 (34)	308 (34)
Mean (SD) no. of Gd+ lesions	2.3 (5.9) n=909	2.0 (5.9) n=900
No. with any Gd+ lesion, n (%)	414 (45)	398 (43)
Mean (SD) no. of T2 hyperintense lesions	51.8 (37.4) n=908	49.2 (35.5) n=900

DMT = disease-modifying therapy
[a]Time since MS diagnosis
[b]Includes IFN beta, glatiramer acetate, natalizumab, mitoxantrone, azathioprine, fumaric acid, laquinimod, cyclophosphamide, mycophenolic acid, fingolimod, teriflunomide, methotrexate, alemtuzumab, cladribine, immunoglobulins, temsirolimus

Figure 2. Overall NEDA at 96 weeks

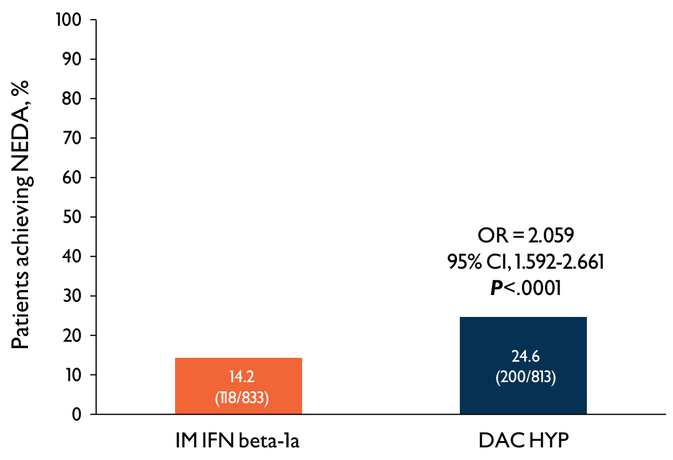


Figure 3. Clinical NEDA at 96 weeks

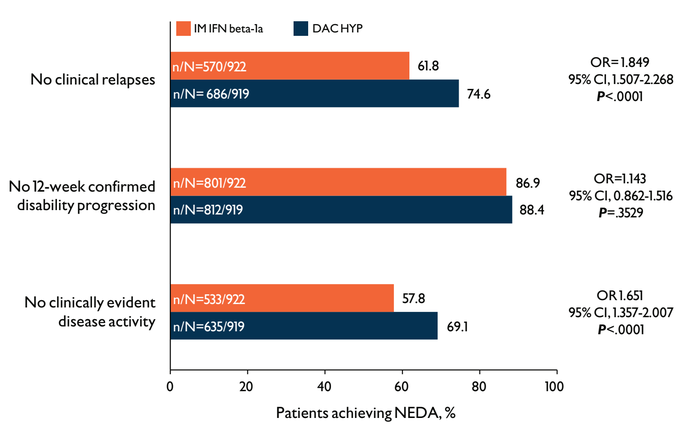


Figure 4. MRI NEDA at 96 weeks

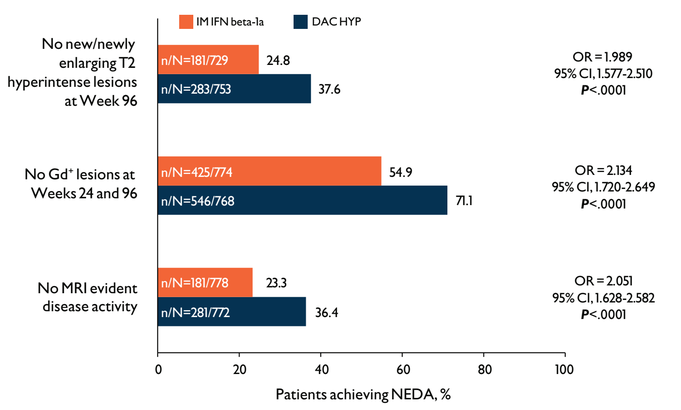
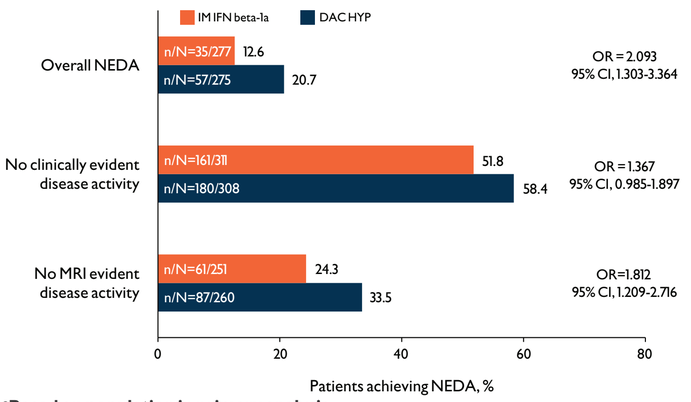


Table 2. Sensitivity analysis

	IM IFN beta-1a n=922	DAC HYP n=919	OR (95% CI) DAC HYP vs. IM IFN beta-1a
Overall NEDA	22.5% (207/922)	33.3% (306/919)	1.755 (1.423–2.165)
No clinically evident disease activity	57.8% (533/922)	69.1% (635/919)	1.651 (1.357–2.007)
No clinical relapses	61.8% (570/922)	74.6% (686/919)	1.849 (1.507–2.268)
No 12-week confirmed disability progression	86.9% (801/922)	88.4% (812/919)	1.143 (0.862–1.516)
No MRI evident disease activity	30.0% (256/853)	44.2% (389/880)	1.942 (1.583–2.382)
No new/enlarging T2 hyperintense lesions at Week 96	24.8% (181/729)	37.6% (283/753)	1.989 (1.577–2.510)
No Gd+ lesions at Weeks 24 and 96	59.1% (504/853)	74.7% (656/878)	2.119 (1.720–2.611)

Figure 5. Subgroup of patients with prior IFN beta therapy[a] at 96 weeks



[a]Based on population in primary analysis

CONCLUSIONS

- Treatment with DAC HYP for 96 weeks significantly increased the percentage of patients who achieved NEDA vs. those receiving IM IFN beta-1a (24.6% vs. 14.2%, respectively; P<.0001).
- In patients with prior IFN beta use, a greater percentage of DAC HYP-treated patients met overall NEDA criteria vs. the IM IFN beta-1a group at Week 96 (20.7% vs. 12.6%, respectively).
- Relative benefits on relapse rate, disability progression and brain MRI outcomes seen with DAC HYP translated into increases in the number of patients with NEDA in both the overall population and the subgroup analysed.
- NEDA is an emerging new concept for striving to halt all aspects of disease activity consistent with the growing zero tolerance for suboptimal treatment.

References

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Disclosures

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