# Efficacy of Daclizumab HYP vs. Intramuscular Interferon Beta-1a on Disability Progression Across Patient Demographic and Disease Activity Subgroups in DECIDE

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## INTRODUCTION

- Daclizumab high-yield process (DAC HYP) is a humanised monoclonal antibody that reversibly modulates interleukin 2 signalling, which specifically reduces pro-inflammatory activated T cells and results in expansion of immunoregulatory CD56$^{bright}$ natural killer cells.[1,2]
- In DECIDE, treatment with DAC HYP 150 mg subcutaneous once every 4 weeks vs. interferon (IFN) beta-1a 30 mcg intramuscular (IM) once weekly reduced the risk of 24-week confirmed disability progression by 27% (*P*=.033) in patients with relapsing-remitting multiple sclerosis (MS).[3]
- Full safety data from DECIDE have previously been described.[4]

## OBJECTIVES

- To evaluate the effects of DAC HYP vs. IM IFN beta-1a on 24-week confirmed disability progression in patient subgroups based on baseline patient characteristics from DECIDE.

## METHODS

- Twenty-four–week confirmed disability progression was a tertiary endpoint in DECIDE.
  - Disability progression was defined as 24-week confirmed increase in Expanded Disability Status Scale (EDSS) score of ≥1.0 point from a baseline score of ≥1.0 or ≥1.5 points from a baseline score of 0.
  - Disability progression by EDSS score was analysed by a Cox proportional hazards model adjusted for baseline EDSS score (continuous variable), prior IFN beta use (yes, no) and baseline age (≤35, >35 years; excluding covariates defining the subgroup).
- Pre-specified subgroups were analysed based on demographics and baseline disease characteristics as described in Table 1.

**Table 1.** Baseline patient subgroups[a]

| Subgroup, n (%) | IM IFN beta-1a n=922 | DAC HYP n=919 | Total n=1841 |
|---|---|---|---|
| **Demographic subgroups** | | | |
| Age, y | | | |
| ≤35 | 449 (49) | 451 (49) | 900 (49) |
| >35 | 473 (51) | 468 (51) | 941 (51) |
| Sex | | | |
| Female | 627 (68) | 625 (68) | 1252 (68) |
| Male | 295 (32) | 294 (32) | 589 (32) |
| **MS baseline disease characteristic subgroups** | | | |
| Disease duration from time of diagnosis, y | | | |
| <3 | 484 (52) | 491 (53) | 975 (53) |
| ≥3 to <10 | 312 (34) | 293 (32) | 605 (33) |
| ≥10 | 126 (14) | 135 (15) | 261 (14) |
| No. of relapses in previous 12 months | | | |
| ≤1 | 476 (52) | 513 (56) | 989 (54) |
| >1 | 446 (48) | 406 (44) | 852 (46) |
| EDSS score | | | |
| <3.5 | 631 (68) | 659 (72) | 1290 (70) |
| ≥3.5 | 291 (32) | 260 (28) | 551 (30) |
| Gd$^+$ lesions | | | |
| Present | 414 (45) | 398 (43) | 812 (44) |
| Absent | 495 (54) | 502 (55) | 997 (54) |
| T2 hyperintense lesion volume | | | |
| < Median | 439 (48) | 465 (51) | 904 (49) |
| ≥ Median | 469 (51) | 435 (47) | 904 (49) |
| Any prior IFN beta use[b] | | | |
| Yes | 311 (34) | 308 (34) | 619 (34) |
| No | 611 (66) | 611 (66) | 1222 (66) |
| Any prior MS treatment (excluding steroids) | | | |
| Yes | 376 (41) | 380 (41) | 756 (41) |
| No | 546 (59) | 539 (59) | 1085 (59) |
| Disease activity at Baseline | | | |
| High[c] | 204 (22) | 184 (20) | 388 (21) |
| Low | 713 (77) | 723 (79) | 1436 (78) |

Gd$^+$ = gadolinium-enhancing; MRI = magnetic resonance imaging
[a]All groups pre-specified in the statistical analysis plan
[b]Includes IFN beta, IFN beta-1a and IFN beta-1b
[c]At least 2 relapses in the year before randomisation and ≥1 Gd$^+$ lesion at baseline MRI

## RESULTS

- Patient baseline characteristics were similar in both treatment groups. (Table 2)

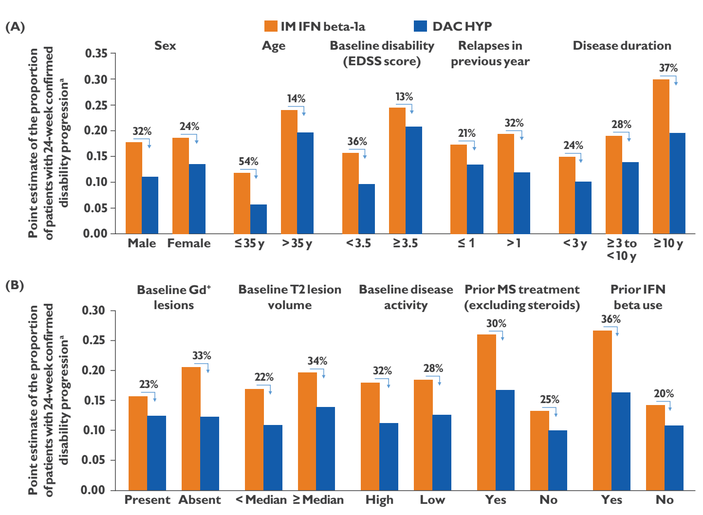
### Efficacy

- Point estimates of reductions in the risk of 24-week confirmed disability progression across all subgroups defined by baseline patient demographics and disease characteristics indicate consistent trends favouring DAC HYP over IM IFN beta-1a. (Figure 1A and 1B)
- Across all subgroups, hazard ratios tended to favour treatment with DAC HYP vs. IM IFN beta-1a. (Figure 2)

**Table 2.** Baseline patient demographics and disease characteristics

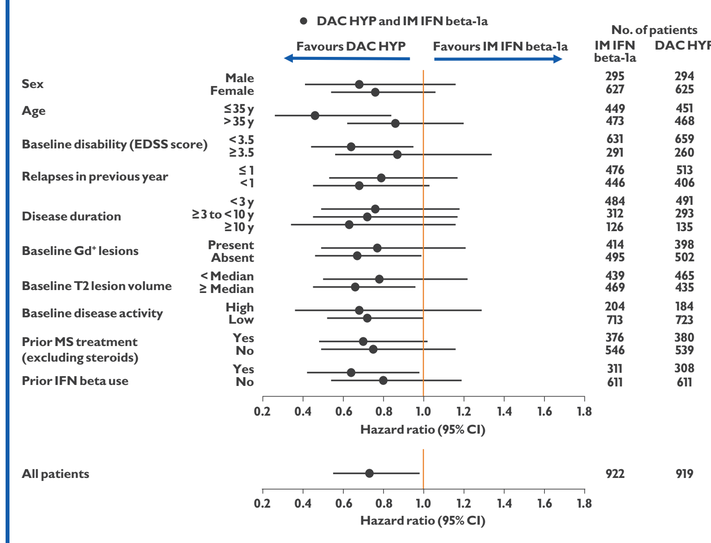
| Characteristic | IM IFN beta-1a n=922 | DAC HYP n=919 | Total n=1841 |
|---|---|---|---|
| **Demographic characteristics** | | | |
| Mean (SD) age, y | 36.2 (9.3) | 36.4 (9.4) | 36.3 (9.3) |
| Female, n (%) | 627 (68) | 625 (68) | 1252 (68) |
| White, n (%) | 828 (90) | 823 (90) | 1651 (90) |
| **MS disease characteristics** | | | |
| Mean (median) time since MS diagnosis, y | 4.1 (2.0) | 4.2 (2.0) | 4.2 (2.0) |
| Mean (SD) no. of relapses in previous year | 1.6 (0.8) | 1.5 (0.7) | 1.6 (0.7) |
| Mean (SD) no. of relapses in previous 3 years | 2.7 (1.3) | 2.7 (1.2) | 2.7 (1.3) |
| Mean (SD) baseline EDSS score | 2.5 (1.3) | 2.5 (1.2) | 2.5 (1.2) |
| MRI brain lesions | | | |
| Mean (SD) no. of Gd$^+$ lesions | 2.3 (5.9) | 2.0 (5.9) | 2.1 (5.9) |
| Mean (SD) no. of T2 hyperintense lesions | 51.8 (37.4) | 49.2 (35.5) | 50.5 (36.5) |
| Median (range) T2 hyperintense lesion volume, mm$^3$ | 5878.5 (9–99,205) | 5117.5 (0–128,481) | 5439.5 (0–128,481) |
| Mean (SD) no. of T1 hypointense lesions | 33.9 (34.5) | 31.8 (33.9) | 32.9 (34.2) |
| Median T1 hypointense lesion volume, mm$^3$ | 1325.0 | 1216.0 | 1256.0 |

**Figure 1.** DAC HYP treatment effect compared with IM IFN beta-1a on 24-week confirmed disability progression (baseline demographics and disease characteristics)




Among patients with ≥1 tentative progression, the probability of confirmation for those with a missing EDSS assessment to confirm progression was estimated via logistic model adjusted for treatment group, baseline EDSS score (continuous variable), change in EDSS score from Baseline to the tentative progression and presence (or absence) of a relapse within the last 29 days of the tentative progression. For patients with multiple tentative progressions, the confirmed (if patient had a confirmed progression) or the last (if patient did not have any tentative progressions confirmed) tentative progression record was retained. The multiple imputation via this logistic regression model was conducted 50 times. The Cox proportional hazards model as specified in the Methods was conducted on each one of the 50 datasets. Finally, the hazard ratio, SE of this estimate and the *P* values were combined using Rubin's rule.[5] [a]Analyses were exploratory and statistical significance was not assessed.

**Figure 2.** Forest plot for 24-week confirmed disability progression for DAC HYP vs. IM IFN beta-1a by baseline demographics and disease characteristic subgroups




Hazard ratios based on Cox proportional hazards model, adjusted for the following covariates (excluding covariates defining the subgroup): baseline EDSS score (continuous variable), prior IFN beta use (yes, no) and baseline age (≤35, >35 years).

## CONCLUSIONS

- Overall, treatment with DAC HYP resulted in a 27% reduction (hazard ratio, 0.73; 95% CI, 0.55–0.98; P=.033) in 24-week confirmed disability progression, a tertiary outcome in DECIDE.
- Point estimates of the risk of disability progression show trends favouring DAC HYP over IM IFN beta-1a across all pre-specified subgroups. Numerical differences in risk reduction were noted for age, baseline EDSS score, baseline Gd+ lesions, T2 lesion burden and prior IFN beta use, though CIs showed substantial overlap for all subgroup comparisons.
- The numerically larger effect of DAC HYP compared with IM IFN beta-1a in reducing 24-week confirmed disability progression in patients who had previously received IFN beta may reflect in part the inclusion of patients who had previously experienced disease activity while on IFN beta.
- As interpretation of these analyses is exploratory, further analyses of functional and patient-reported measures of physical disability may be useful to better assess treatment effects in subgroups.

### References

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