Cutaneous Events in Daclizumab Beta-Treated Patients did not Impact Patient-Reported Outcomes in the DECIDE Study

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INTRODUCTION

- In DECIDE, the incidence of cutaneous adverse events (CAEs) was higher in the daclizumab beta (daclizumab beta)* group vs. the intramuscular (IM) interferon (IFN) beta-1a group (37% vs. 19%, respectively).[1]
- Most patients had CAEs that were mild or moderate in severity (daclizumab beta, 94%; IM IFN beta-1a, 98%); CAEs led to treatment discontinuation in 5% of daclizumab beta and <1% of IM IFN beta-1a patients.[1]
- Patient-reported outcomes (PROs) may capture the effects of CAEs on patients' daily activities and functioning.

OBJECTIVES

- Examine the impact of moderate/severe CAEs on PROs in patients with relapsing-remitting multiple sclerosis (RRMS) receiving daclizumab beta in DECIDE.

METHODS

- In DECIDE, patients received daclizumab beta 150 mg subcutaneous every 4 weeks (n=919) or IFN beta-1a 30 mcg IM once weekly (n=922) for ≥96 weeks, up to 144 weeks.[1]
- Patients completed the EuroQol 5-Dimensions 3-level version (EQ-5D; positive changes indicate improvement) and Multiple Sclerosis Impact Scale (MSIS-29; negative changes indicate improvement) at Baseline and every 24 weeks (Table 1).[2-4]
- In daclizumab beta patients with moderate/severe CAEs, scores on the EQ-5D, MSIS-29 physical (PHYS) and psychological (PSYCH) impact subscales and 5 MSIS-29 items were compared post hoc for the visits before (pre CAE), during and after (post CAE) the events.
- Mean changes in PRO scores from Baseline–Week 96 were compared between daclizumab beta patients without CAEs and daclizumab beta patients with moderate/severe CAEs.

RESULTS

- One hundred fifty-three of 919 daclizumab beta-treated patients experienced moderate/severe CAEs in DECIDE, 10 of whom did not have a PRO measurement post CAE.
  - Among 143 patients, 126 had moderate events only, 10 had severe events only and 7 had both.
  - For each PRO, mean changes from pre to during, during to post and pre to post CAE were small and not significant (Table 2).
- Mean increases (indicating improvement) in EQ-5D health utility index scores and mean decreases (indicating improvement) in MSIS-29 PHYS and PSYCH scores and the majority of MSIS-29 item scores from Baseline–Week 96 were similar among patients without CAEs and patients with moderate/severe CAEs. No significant differences were observed for the majority of comparisons (*P*>.05) except feeling mentally fatigued (*P*=.0244; Figure 1, Figure 2A).
- For the majority of MSIS-29 items, a similar percentage of patients without CAEs and patients with moderate/severe CAEs exhibited any improvement, no change or any worsening in score from Baseline–Week 96 (*P*>.05 for all comparisons based on chi-square test; *P*>.05 for all comparisons except feeling mentally fatigued [*P*=.0309] based on ordinal logistic regression; Figure 2B).those who did not (Figure 3A–D).

Table 1. PROs assessed in DECIDE

PRO	Format	Scoring
EQ-5D[2,4]	3 response options • No problems • Some problems • A lot of problems	Utility index scores range from –0.59 to 1.0 Positive changes indicate improvement
MSIS-29[3] 20-item PHYS 9-item PSYCH **Individual MSIS-29 items potentially affected by CAEs**[a] • Being stuck at home more than you would like to be • Cut down time spent on daily activities • Feeling mentally fatigued • Worries related to your MS • Feeling anxious or tense	5 response options • 1 = not at all • 2 = a little • 3 = moderately • 4 = quite a bit • 5 = extremely	Subscale scores range from 0 to 100[b] Negative changes indicate improvement

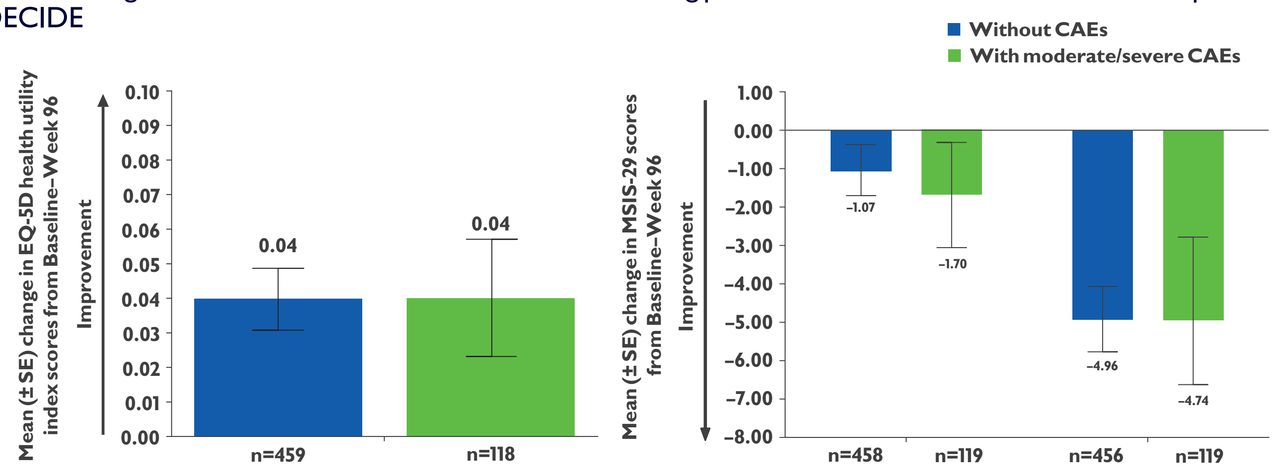
[a]Determined by investigators; [b]Individual items are summed and transformed to a 0 to 100 scale[3]

Table 2. Mean PRO scores and changes in PRO scores between pre, during and post moderate/severe CAE stages

Characteristic	Mean score			Mean change in score between CAE stages		
	Pre CAE n=143	During CAE n=87	Post CAE n=143	Pre CAE to during CAE[a]	During CAE to post CAE[a]	Pre CAE to post CAE[a]
EQ-5D health utility index	0.77	0.76	0.76	0	0.01	–0.01
MSIS-29 PHYS	22.02	20.42	22.12	–1.81	–0.02	0.10
MSIS-29 PSYCH	26.03	25.87	26.73	–0.99	–0.62	0.70
Individual MSIS-29 items potentially affected by CAEs						
Being stuck at home more than you would like to be	1.84	1.68	1.82	–0.14	0.05	–0.02
Cut down time spent on daily activities	1.88	1.81	1.88	–0.07	0.01	–0.01
Feeling mentally fatigued	2.17	2.24	2.23	0.01	–0.10	0.05
Worries related to your MS	2.11	2.06	2.04	–0.07	–0.07	–0.07
Feeling anxious or tense	2.04	2.08	2.15	–0.04	0.03	0.10

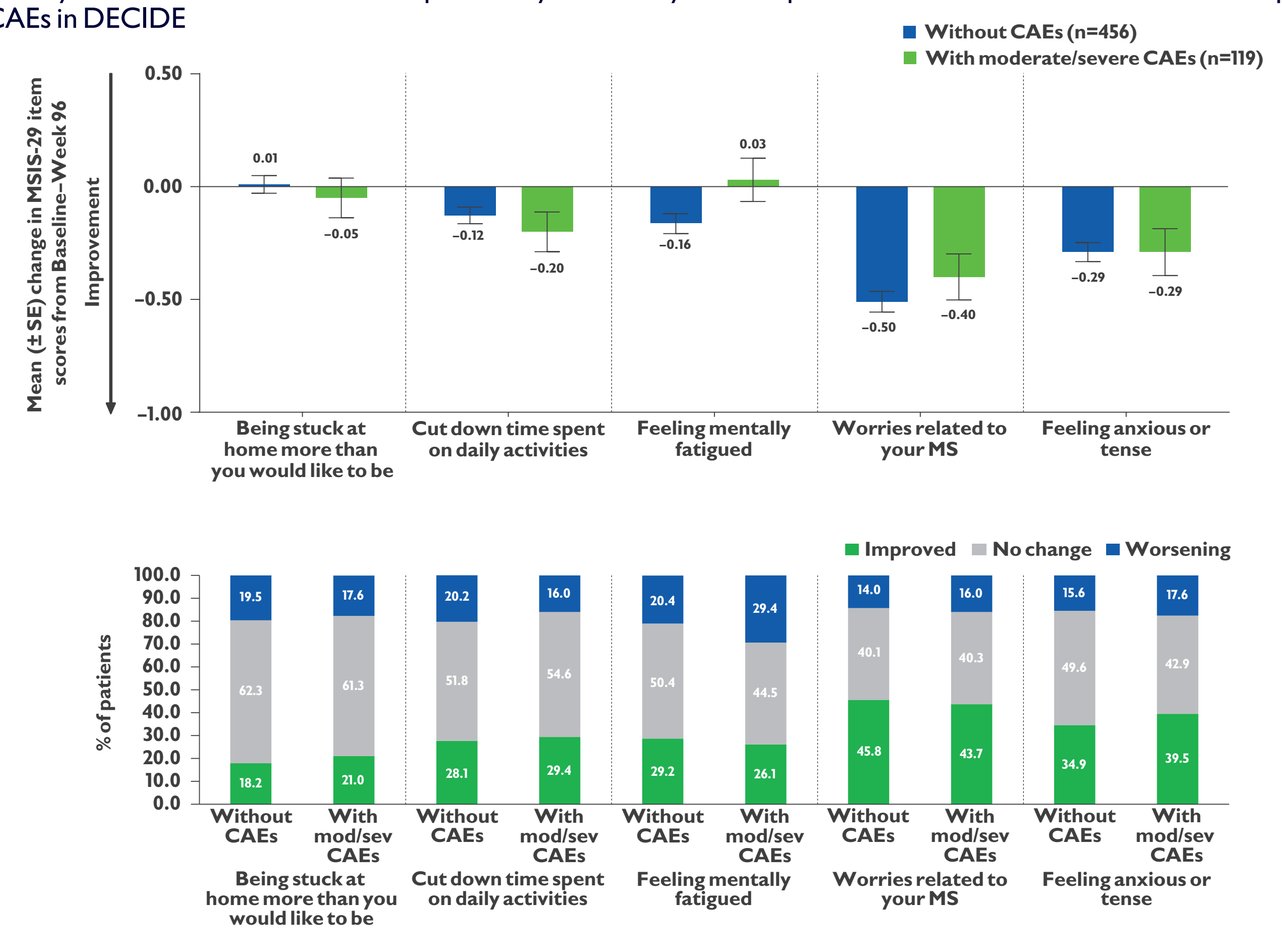
Analyses were limited to patients with moderate/severe CAEs and non-missing PRO measurements (n=143). For each event (events with exact starting date and ending date are counted only once), the pre-CAE measure is the measure right before the start date and the post-CAE measure is the measure right after the end date (or the last measurement after CAE starting date); average was used if there were multiple measurements during CAE. For patients with no event end date, the last PRO measurement was used. Among the 143 patients, 109 had a single event (moderate/severe CAE), with 26 not resolved; 34 patients had multiple events, with 12 having a mixture of resolved and non-resolved, 3 of the remaining 22 having all not resolved and 19 having all resolved. [a]Changes in mean PRO scores between CAE stages were not significant, as determined by paired *t* test (all *P*>.05)

Figure 1. Mean change in PRO scores from Baseline–Week 96 among patients with moderate/severe CAEs and patients without CAEs in DECIDE



Analysis includes patients with moderate/severe CAEs vs. patients without any CAEs; *P*>.05 for all comparisons as determined by analysis of covariance adjusting for Baseline score, Baseline Beck Depression Inventory (BDI) score, prior IFN beta use and Baseline age (≤35 vs. >35 years)

Figure 2. Analysis of individual MSIS-29 items potentially affected by CAEs in patients with moderate/severe CAEs and patients without CAEs in DECIDE



Mod = moderate; sev = severe ; Analysis includes patients with moderate/severe CAEs vs. patients without any CAEs ; [a]*P*>.05 for all comparisons except feeling mentally fatigued (*P*=.0244) as determined by analysis of covariance adjusting for Baseline score, Baseline BDI score, prior IFN beta use and Baseline age (≤35 vs. >35 years); [b]*P*>.05 for all comparisons based on chi-square test; *P*>.05 for all comparisons except feeling mentally fatigued (*P*=.0309) based on ordinal logistic regression adjusting for Baseline score, Baseline BDI score, prior IFN beta use and Baseline age (≤35 vs. >35 years)

CONCLUSIONS

- Moderate/severe CAEs observed during daclizumab beta treatment did not appear to affect overall patient-reported physical or psychological health or daily activities and functioning.
- The EQ-5D and MSIS-29 were not developed to detect the impact of CAEs on functioning and quality of life, though the majority of items deemed potentially pertinent to moderate/severe CAEs did not appear to be impacted by these events.
- The percentage of patients with improvement, no change or worsening from Baseline–Week 96 in the majority of MSIS-29 item scores potentially affected by moderate/severe CAEs was similar between patients without CAEs and those with moderate/severe CAEs, suggesting that moderate/severe CAEs may not have had a lasting impact on overall health status as reported by patients.

References 1. Krueger JG, *et al. Adv Ther*. 2016;33(7):1231-1245. 2. Rabin R, de Charro F. *Ann Med*. 2001;33(5):337-343. 3. Hobart J, *et al. Brain*. 2001;124(5):962-973. 4. Phillips G, *et al. Mult Scler Relat Disord*. 2016;6:66-72. **Disclosures** YL, KR, CW and GS: employees of and hold stock/stock options in Biogen; RG: former employee of and held stock/stock options in Biogen; W-SY: employee of Biogen at the time of the analysis; holds stock in Biogen; JT: postdoctoral fellow at Biogen; XY: employee of and holds stock/stock options in AbbVie Inc. **Acknowledgments** This study was sponsored by Biogen (Cambridge, MA, USA) and AbbVie Biotherapeutics Inc. (Redwood City, CA, USA). Writing and editorial support for the preparation of this poster was provided by Excel Scientific Solutions (Southport, CT, USA): funding was provided by Biogen and AbbVie Biotherapeutics Inc.

*Daclizumab beta, approved as ZINBRYTA®, has a different form and structure than an earlier form of daclizumab beta.