

SUPPLEMENTARY INFORMATION

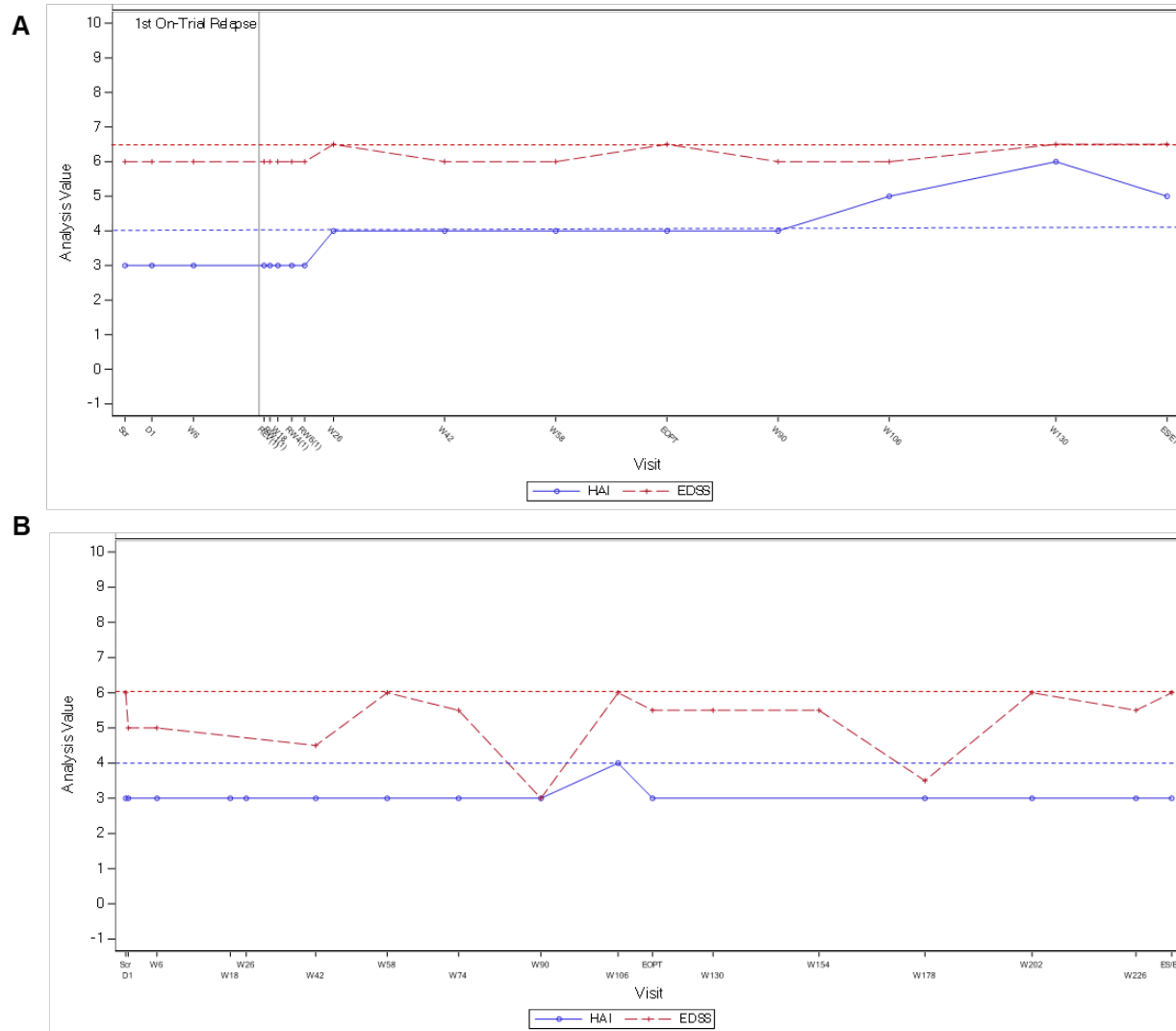
eAppendix

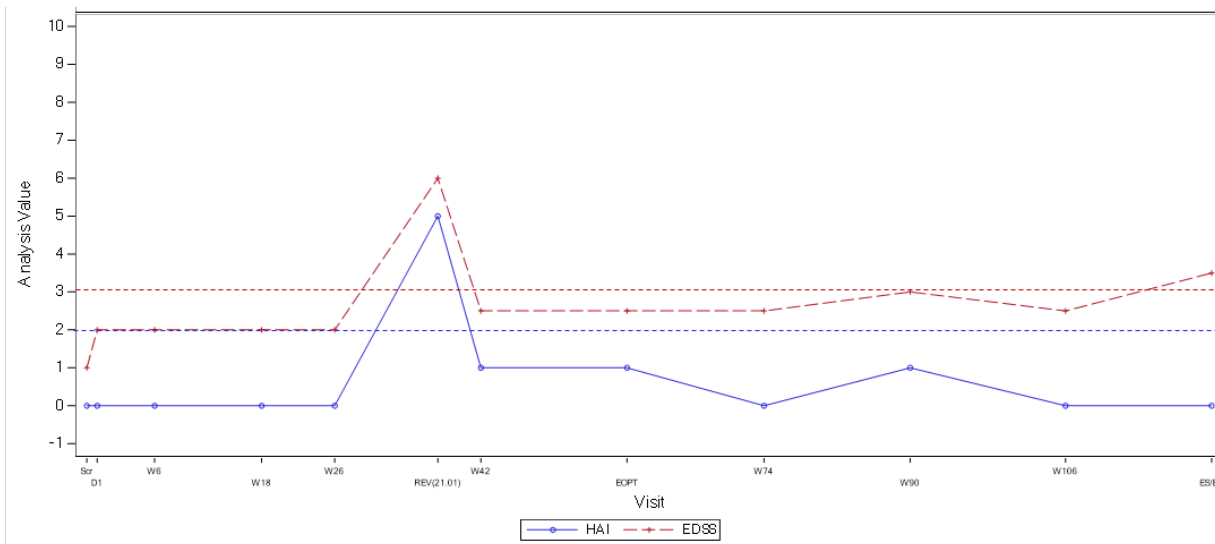
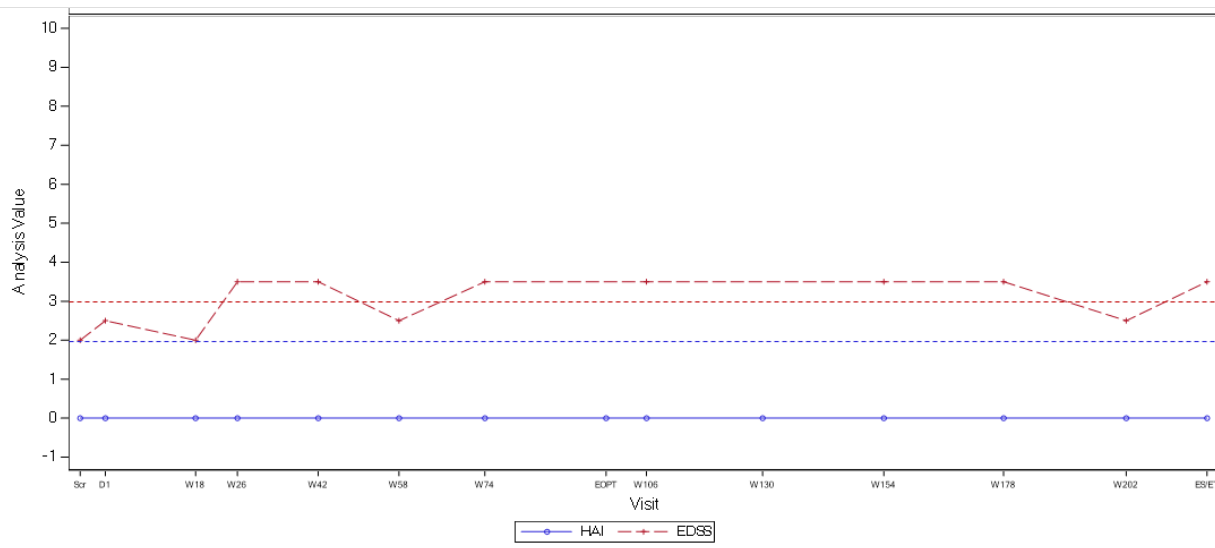
Meningococcal vaccination in patients who experience meningococcal infection:

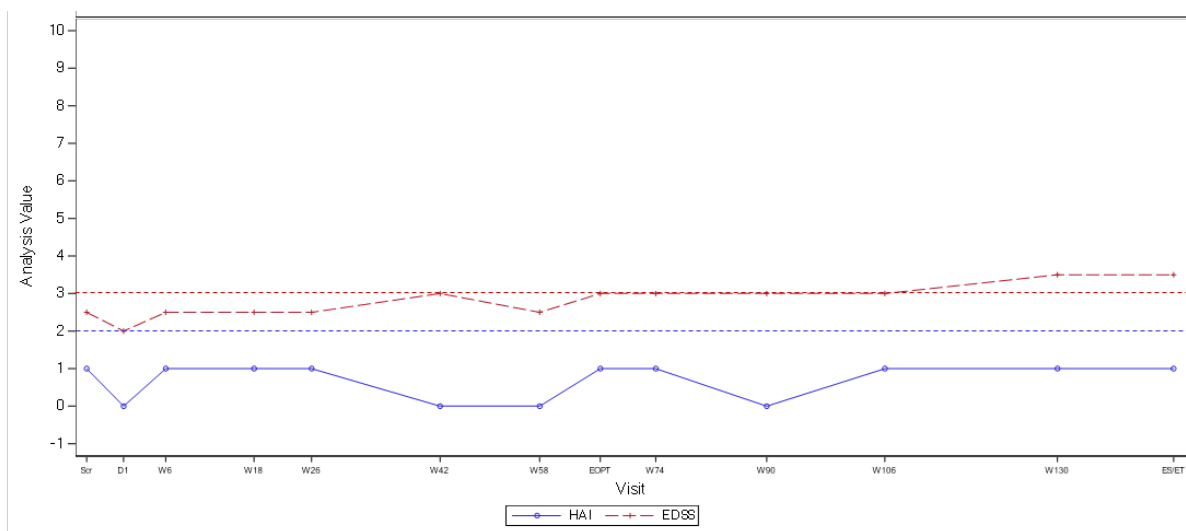
Patient 1 was vaccinated with meningococcal (groups A, C, Y, W) polysaccharide diphtheria toxoid conjugate vaccine approximately 2.5 years (day –930) before the first dose of ravulizumab. After ravulizumab initiation but prior to onset of the meningococcal infection, the patient further received 1 dose of meningococcal (groups A, C, Y, W) polysaccharide diphtheria toxoid conjugate vaccine (day 400) and 2 doses of meningococcal group B vaccine (days 266, 331). On day 483, the patient experienced meningococcal infection. The patient recovered from the infection and completed treatment in the trial, which included additional meningococcal vaccination.

Patient 2 was vaccinated with one dose of meningococcal groups A, C, Y, W, tetanus toxoid conjugate vaccine (day –38), and 2 doses of meningococcal group B vaccine (days –38 and –7) before starting ravulizumab. On day 22, the patient experienced meningococcal infection. The patient recovered from the infection but discontinued treatment during the primary treatment period.

eFigure 1 EDSS and HAI Over Time for Patients Who Experienced Clinically Important Worsening on EDSS at End of Study (n = 5)



C**D**

E

The red dashed line represents the score at which clinically important worsening in EDSS score would have been met for an individual patient, which was defined as an increase in EDSS score relative to baseline (D1) as follows: increase of ≥ 2.0 points if the baseline score was 0.0, ≥ 1.0 point if the baseline score was 1.0–5.0, or ≥ 0.5 if the baseline score was > 5.0 . EDSS scores ranged from 0 (no disability) to 10 (death).¹

The blue dashed line represents the score at which clinical worsening in HAI score would have been met for an individual patient, clinical worsening was defined as an increase of ≥ 2 points if the HAI baseline score was 0 or an increase of ≥ 1 point if the baseline score was > 0 . HAI scores range from 0 to 9, with higher scores indicating decreased independent ambulation.²

The following narratives are provided for the patients who had simultaneous increases in EDSS and HAI relative to baseline at any point:

The patient shown in **panel A** had moderate lymphedema starting at approximately week 14, which did not fully resolve by the end of study. At approximately the same time, the patient was seen for a relapse evaluation visit. The treating physician believed the patient met the protocol definition of a relapse consistent with partial transverse myelitis, although there was no increase in EDSS or HAI score observed over the course of the 6-week relapse evaluation period. This was not considered a relapse by the adjudication committee. Later, at about week 78, the patient developed a foot deformity, which had not resolved by the end of study. The EDSS ambulation score increased from 7 to 9 at the week 26, the end of PTP, the week 130, and the end of study visits. The Kurtzke Cerebellar FSS was 4x at the end of PTP and 3x at end of study (having been 3 at baseline), while others showed improvement.

The patient shown in **panel B** experienced an event of arthralgia (approximately week 105), which was ongoing at the end of study. At the week 106 visit, the EDSS ambulation score was 5 (having been 3 at baseline), and the pyramidal score was 2 (having been 0 at baseline). Cerebellar score was 1 (having been 0 at

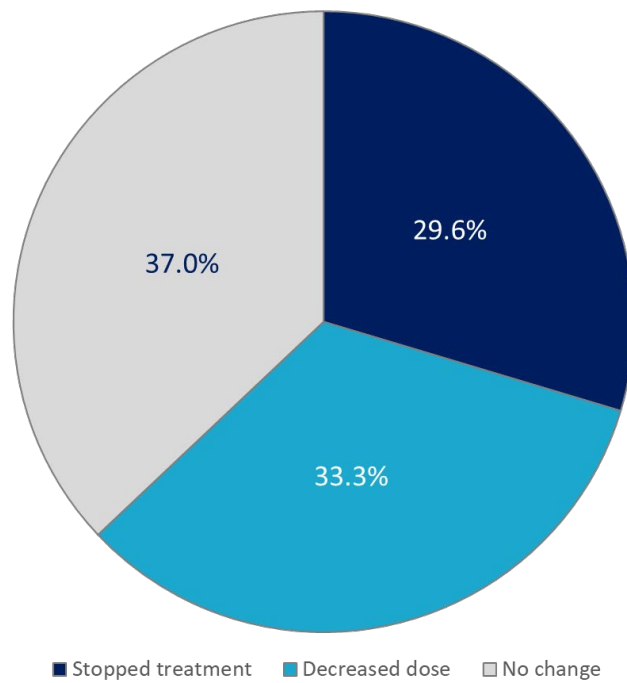
baseline); other Kurtzke FSS improved or remained the same at week 106. The treating physician did not consider this to represent a relapse, and it did not meet criteria for a case of interest, as defined in the protocol.

The patient shown in **panel C** experienced a serious event of spinal osteoarthritis at approximately week 37. At the relapse evaluation visit, the EDSS ambulation score was 6 and the pyramidal score was 3; both had been 0 at baseline. All other Kurtzke FSS either improved or remained the same. Neither the treating physician nor the adjudication committee considered this a relapse.

The patients shown in panels **D** and **E** did not experience simultaneous increases in EDSS and HAI relative to baseline at any point.

EDSS = Expanded Disability Status Scale; FSS = Functional Systems Score; EOPT = end of primary treatment period visit; ES/ET = date of completion/discontinuation/last assessment (or death); HAI = Hauser Ambulation Index; NMOSD = neuromyelitis optica spectrum disorder; PTP = primary treatment period; REV = relapse evaluation visit; RW = relapse follow-up week.

eFigure 2 Changes in IST Use Among Patients Taking an IST at Baseline (n = 27)^a



^aOne patient in the ravulizumab group reported as using IST at baseline in the PTP analysis³ was subsequently found to have stopped the IST before the first dose of ravulizumab.
IST = immunosuppressive therapy; PTP = primary treatment period.

eFigure References:

1. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-1452. doi: 10.1212/wnl.33.11.1444
2. Hauser SL, Dawson DM, Lerich JR, et al. Intensive immunosuppression in progressive multiple sclerosis. A randomized, three-arm study of high-dose intravenous cyclophosphamide, plasma exchange, and ACTH. *N Engl J Med*. 1983;308:173-180. doi: 10.1056/nejm198301273080401
3. Pittock SJ, Barnett M, Bennett JL, et al. Ravulizumab in aquaporin-4-positive neuromyelitis optica spectrum disorder. *Ann Neurol*. 2023;93(6):1053-1068. doi: <https://doi.org/10.1002/ana.26626>