MODELLING THE LONG-TERM EFFECTIVENESS OF INEBILIZUMAB IN THE CURRENT TREATMENT LANDSCAPE IN NMOSD

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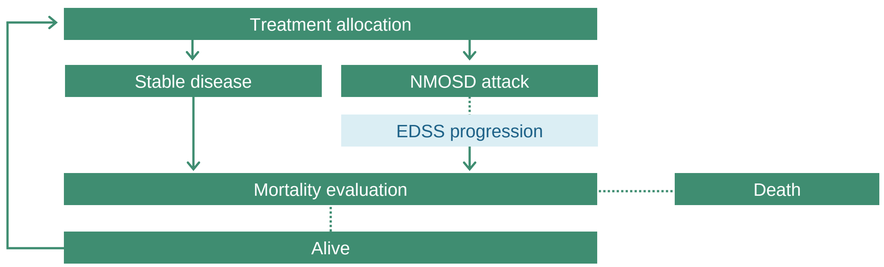
Introduction

- Neuromyelitis Optica Spectrum Disorder (NMOSD) is a chronic, antibody (Ab)-mediated inflammatory disorder of the central nervous system (CNS). NMOSD is characterized by recurrent attacks, permanent neurological damage and cumulative disability impacting the health-related quality of life (HRQoL).
- Due to the chronic nature of NMOSD, understanding the long-term relative effectiveness of immunotherapies is vital. We developed a model simulating long-term outcomes to evaluate the effects of inebilizumab compared with eculizumab, satralizumab and rituximab in patients with aquaporin 4 (AQP4) positive NMOSD.

Methods

- A Markov model was developed (see figure 1) with cycles of one month. In each cycle, patients have a treatment-specific risk of experiencing an NMOSD attack. An attack may lead to permanent progression in the Expanded Disability Status Scale (EDSS) score, a method for quantifying the worsening of disability in NMOSD. The scale ranges from 0 to 10, with 0 being full function and 10 being death.
- Data on time to first committee-adjudicated attack (CAA) from the open-label period (OLP) from the N-MOmentum trial (1,2) with inebilizumab were used to extrapolate the risk of an attack and simulate the annualized relapse rate beyond the study period (base case). A sensitivity analysis using a MAIC based on time to first investigator-adjudicated attack (IAA) from relevant trials was included.
- Anchored matching adjusted indirect comparisons (MAIC) were applied to estimate the relative effects of inebilizumab vs comparators based on data from the randomized period for inebilizumab and from the relevant clinical trials for eculizumab (3) and satralizumab (4). As no randomized controlled trial suitable for conducting an anchored MAIC of inebilizumab and rituximab existed at the time of the analysis, we estimated the relative efficacy of the two by comparing individual patient-level data (IPD) for patients treated with inebilizumab from the N-MOmentum trial with published IPD data from four studies on rituximab using an unanchored MAIC (5,6,7,8).
- Treatment discontinuation was based on trial discontinuation rates converted to annual rates (5.3%, 9.6%, 5.3% and 10.5% for inebilizumab, eculizumab, satralizumab and rituximab, respectively). Following discontinuation, patients remain off treatment to capture the effect of only first-line treatment. Patients who discontinued treatment were assumed to receive placebo for the remaining model time horizon. The model simulated NMOSD-related mortality based on disease progression.
- SF-36v2 measurements from the N-MOmentum trial were mapped to health utility values using the Rowen algorithm (9). Each EDSS category was ascribed a utility value (EDSS 0-1 = 0.8418 and EDSS 8-9 = 0.3926). If patients experienced an NMOSD attack, a utility decrement of -0.199 was applied (for one model cycle).

Figure 1. Model structure



Results

- The relative risk for NMOSD attacks of inebilizumab vs eculizumab, satralizumab and rituximab were estimated to be 3.947, 0.666 and 0.741, respectively.
- Over a lifelong time horizon (75 years), treatment with inebilizumab resulted in a life expectancy of 22.09 life years compared to 16.67 with eculizumab, 21.44 with satralizumab and 15.63 with rituximab, corresponding to 12.57, 8.69, 11.86 and 7.87 quality-adjusted life years (QALYs) for inebilizumab, eculizumab, satralizumab and rituximab, respectively. Results from the base case (CAA) are presented in table 1.

Figure 2. Mean EDSS following treatment initiation

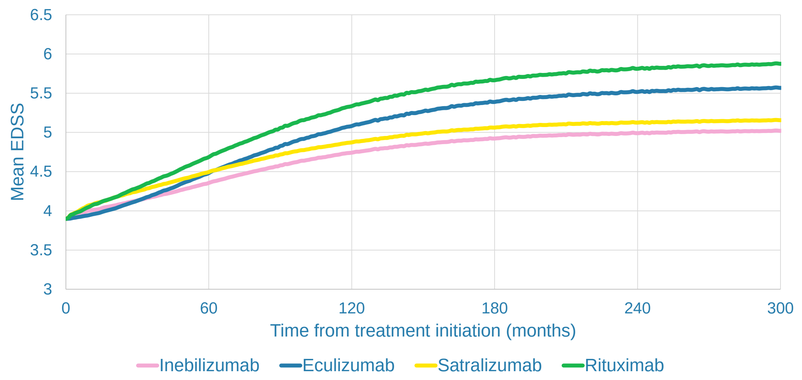


Table 1. Results from the CAA base case analysis and the IAA sensitivity analysis

Analysis		Relative risk	95% confidence intervals	Life years	Δ vs inebilizumab	QALYs	Δ vs inebilizumab
Inebilizumab	CAA	-	-	22.09	-	12.57	-
Eculizumab	CAA	3.947	0.972, 14.706	16.67	-5.42	8.69	-3.88
Satralizumab	CAA	0.666	0.284, 1.563	21.44	-0.65	11.86	-0.71
Rituximab	CAA	0.741	0.585, 0.937	15.63	-6.46	7.87	-4.70
Inebilizumab	IAA	-	-	21.90	-	12.55	-
Eculizumab	IAA	1.507	0.700, 3.245	16.02	-5.88	8.23	-4.32
Satralizumab	IAA	0.489	0.188, 1.277	20.79	-1.11	11.34	-1.21
Rituximab	IAA	0.839	0.655, 1.076	15.26	-6.64	7.69	-4.86

Sensitivity analysis

- The sensitivity analysis using a MAIC based on time to first IAA from relevant trials largely confirmed the initial findings as the relative risk of inebilizumab vs eculizumab, satralizumab and rituximab was 1.507, 0.489 and 0.839, respectively. Results from the IAA sensitivity analysis are presented in table 1.

Conclusions

- The results suggest that treatment with inebilizumab is associated with an increase in life expectancy and QALYs compared to eculizumab, satralizumab and rituximab. Relative efficacy and discontinuation were the key drivers of the results.
- The IAA sensitivity analysis using a MAIC based on time to first investigator-adjudicated attack from relevant trials largely confirmed the beneficial effect of inebilizumab demonstrated in the base case.

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Disclosures

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K Patterson, F Sorio-Vilela, D Cimbora and N Rampal are employees of Horizon and own stock

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