CO107

Indirect Treatment Comparison of Efgartigimod vs Immunoglobulins in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

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INTRODUCTION AND OBJECTIVES

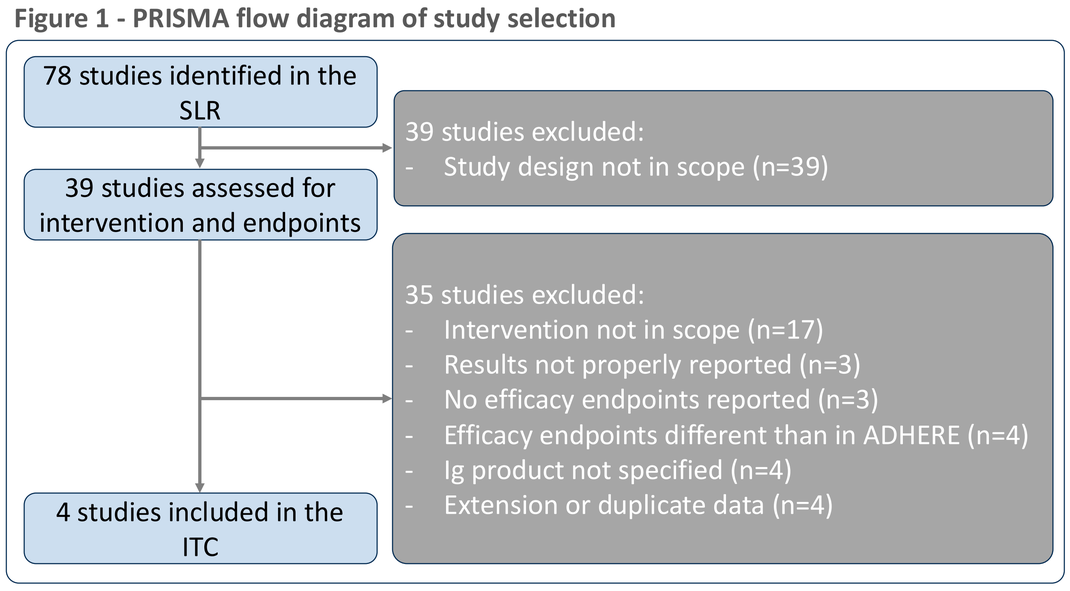
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a rare, serious autoimmune disease which causes demyelination and axonal damage of peripheral nerves.
- Intravenous (IV) and subcutaneous (SC) immunoglobulins (Ig) are established therapies for CIDP. Efgartigimod is the first and only FDA-approved neonatal Fc receptor (FcRn) blocker approved for the treatment of CIDP. The effectiveness of efgartigimod for the treatment of adults with CIDP was established in a two stage, multicenter study (ADHERE - NCT04281472)[1].
- Understanding the comparative efficacy of efgartigimod and Ig products would support decision-making in CIDP treatment. Since no direct comparative studies are available, we carried out an Indirect Treatment Comparison (ITC) to indirectly compare the efficacy of efgartigimod vs. EMA-authorised IVIg and SCIg products for CIDP.

METHODS

Selection of source data and ITC feasibility assessment

- All relevant efficacy data on efgartigimod and EMA-approved Ig products for CIDP were gathered via a systematic literature review (SLR).
- The studies identified in the SLR were evaluated through an ITC feasibility assessment to determine whether they were sufficiently comparable to the ADHERE trial for conducting an indirect comparison.
- The feasibility assessment included evaluation of study designs, patient characteristics, and efficacy endpoints.

Figure 1 - PRISMA flow diagram of study selection



Matching-Adjusted Indirect Comparison (MAIC) analysis

- The ITC used published aggregate data from the literature and individual patient data (IPD) from ADHERE. For each comparison, the ADHERE population was restricted to align with the inclusion criteria of the correspondent comparator study.
- MAICs were used to match ADHERE IPD with the baseline characteristics (prognostic factors and/or treatment effect modifiers) of each compared cohort. When applicable, the results of the single MAICs were meta-analysed.
- Based on the respective design, studies investigating IVIg[2,3] were compared vs. Stage A in ADHERE using an unanchored approach, while studies investigating SCIg products (IgPro20 and fSCIg)[4,5] were compared vs. Stage B in ADHERE using an anchored approach.

Table 1 – Comparisons included in the ITC analysis

Product	Study	Endpoint	n patients	Timepoint
IVIg	Mielke et al.[2]	Change in aINCAT	63 vs. 105	From BL to last visit up to 13 weeks
		Change in I-RODS	63 vs. 166	
		Change in MGS	63 vs. 202	
	PRIMA[3]	Time to aINCAT response	69 vs. 28	Over 12 weeks
IgPro20 0.2 g/kg (SCIg)	PATH[4]	Time to aINCAT deterioration	91 vs. 114	Over 25 weeks
		Change in aINCAT	91 vs. 113	From BL to last visit up to 25 weeks
		Change in I-RODS	90 vs. 114	
		Change in MGS (dominant)	91 vs. 114	
		Change in MGS (non-dominant)	91 vs. 114	
IgPro20 0.4 g/kg (SCIg)	PATH[4]	Time to aINCAT deterioration	91 vs. 115	Over 25 weeks
		Change in aINCAT	91 vs. 114	From BL to last visit up to 25 weeks
		Change in I-RODS	90 vs. 115	
		Change in MGS (dominant)	91 vs. 115	
		Change in MGS (non-dominant)	91 vs. 115	
fSCIg (SCIg)	ADVANCE-CIDP1[5]	Time to aINCAT deterioration	96 vs. 132	Over 32 weeks
		Change in aINCAT	96 vs. 132	From BL to last visit up to 32 weeks
		Change in I-RODS	95 vs. 132	
		Change in MRC	96 vs. 132	

RESULTS

Comparison versus IVIg

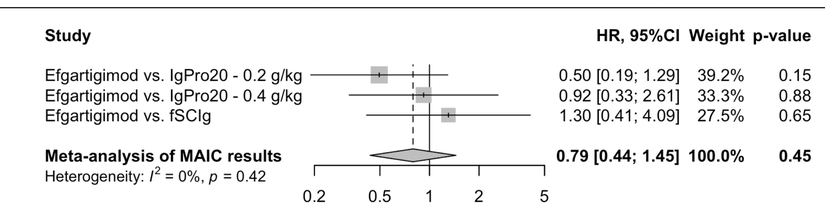
- Due to the poor overlap in baseline characteristics between the cohorts, the weighting process to match ADHERE to the studies investigating IVIg had limited success.
- The Effective Sample Size (ESS) was very low (from 2.3 to 4.7), indicating that inference is based on a very limited number of patients.
- As a result, the MAIC analyses comparing efgartigimod with IVIg did not allow for drawing meaningful conclusions.

Comparison versus SCIg products (IgPro20, fSCIg)

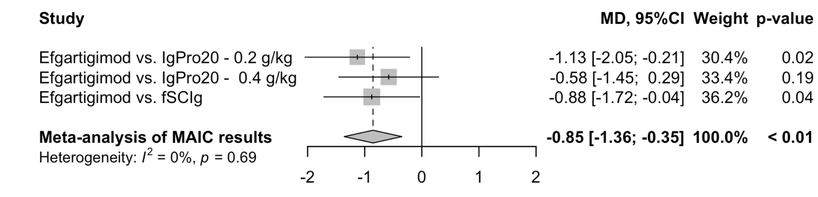
- In the analyses of efgartigimod vs. SCIg products, the weighting process was successful, and the ESS ranged from 46.6 to 84.0 patients, translating into robust results.
- Efgartigimod and SCIg products are associated with a similar time to adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) deterioration (HR: 0.79, 95% CI: [0.44, 1.45], p=0.45).
- The meta-analysis of the MAICs vs. IgPro20 (both doses) and fSCIg showed that efgartigimod is associated with significantly better results in change from baseline to the last visit in aINCAT (MD: -0.85, 95% CI: [-1.36, -0.35], p<0.01) and in Inflammatory Rasch-built Overall Disability Scale (I-RODS) (MD: 10.89 95% CI: [5.83, 15.95], p<0.01).
- The meta-analysis of the MAICs vs. low and high dose IgPro20 showed that efgartigimod is associated with significantly better results in change from baseline to the last visit in Mean Grip Strength (MGS) (MD: 9.71 95%CI: [1.99, 17.42], p=0.01 for dominant hand; MD: 8.79, 95%CI: [8.77, 15.80], p=0.01 for non-dominant hand).
- The MAIC analysis comparing the change from baseline to the last visit in the Medical Research Council (MRC) Sum Score showed that efgartigimod is associated with numerically better results than fSCIg (MD: 2.83, 95% CI: [-0.82, 6.47], p=0.13).

Table 2 – Results: time to aINCAT deterioration, change in aINCAT score, and change in I-RODS

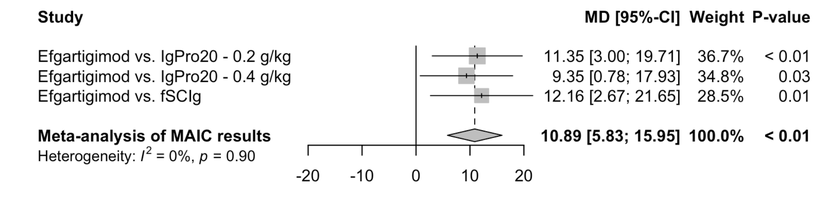
Time to aINCAT deterioration from Baseline



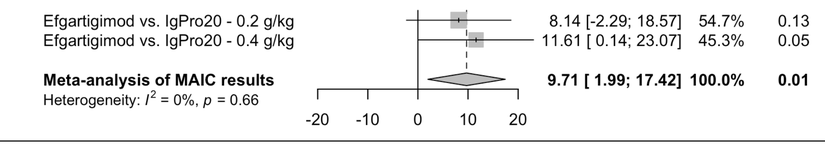
Change from Baseline in aINCAT



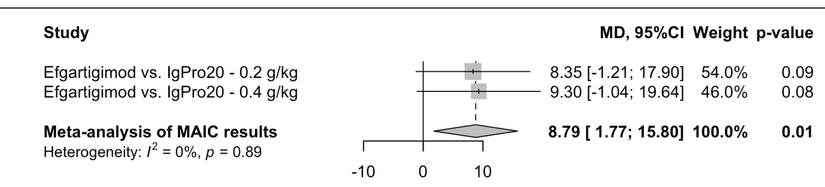
Change from Baseline in I-RODS



Change from Baseline in MGS, dominant hand



Change from Baseline in MGS, non-dominant hand



CONCLUSIONS

- This is the first study indirectly comparing the efficacy of efgartigimod and Ig products for treating CIDP patients.
- The findings indicate that efgartigimod might be associated with significantly better results than SCIg in terms of change in aINCAT, I-RODS and MGS score. Time to aINCAT deterioration and change in MRC Sum Score is similar between the compared treatments.
- This analysis is built on rigorous methods. However, limitations exist due to differences in the included populations that could not be fully adjusted for, as well as potential confounding factors that were not reported in the published studies and, therefore, were not included in the analysis.
- Notwithstanding these limitations, the analysis indicates that efgartigimod may be associated with greater efficacy than SCIg products for treating patients with CIDP.

ABBREVIATIONS:
aINCAT: adjusted Inflammatory Neuropathy Cause and Treatment; BL: Baseline; CI: Confidence Interval; CIDP: Chronic Inflammatory Demyelinating Polyneuropathy; CS: Corticosteroids; EMA: European Medicine Agency; ESS: Effective Sample Size; HR: Hazard Ratio; Ig: Immunoglobulin; IPD: Individual Patient Data; I-RODS: Inflammatory Rasch-built Overall Disability Scale; ITC: Indirect Treatment Comparison; IVIg: Intravenous Immunoglobulin; MAIC: Matching-Adjusted Indirect Treatment Comparison; MD: Mean Difference; MGS: Mean Grip Strength; MRC: Medical Research Council; SCIg: subcutaneous immunoglobulin; SLR: Systematic Literature Review.

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