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**Abstract Title:** Employing Novel Indirect Treatment Comparison Methodologies to Differentiate the Efficacy of Ofatumumab and Other High Efficacy Therapies versus Orally Administered Disease Modifying Therapies for Relapsing Multiple Sclerosis

**Abstract Category:** Therapy - 42 - Others

**Preferred Presentation Type:** Oral or poster presentation

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### **Introduction:**

Emerging evidence challenges whether oral disease modifying therapies (DMTs) achieve similar efficacy to high efficacy therapies (HETs) in the treatment of relapsing multiple sclerosis (RMS). In the absence of head-to-head randomised controlled trial (RCT) data, indirect treatment comparisons (ITCs) can be used to estimate the relative efficacy between HETs and oral therapies.

### **Objectives/Aims:**

To differentiate HETs from oral therapies based on efficacy measures (annualised relapse rate (ARR), 3 and 6 month confirmed disease progression (3mCDP) (6mCDP)) using different ITC approaches.

### **Methods:**

Propensity score (PS) analyses were conducted to compare ofatumumab (OFA) to fingolimod (FIN) using inverse probability of treatment weighting (IPTW) to balance the trial populations for both therapies. The PS analyses used pooled individual patient-level data (IPD) from ASCLEPIOS I/II for OFA and from FREEDOMS I, II and TRANSFORMS for FIN. Unanchored simulated treatment comparisons (STCs) were conducted to compare OFA to each of the oral treatments by fitting a regression model for outcomes of interest. The STCs leveraged pooled IPD from ASCLEPIOS I/II and summary-level data (SLD) from individual phase 3 RCTs for cladribine (CLA), FIN and ozanimod (OZA). A network meta-analysis was also conducted to broadly compare the efficacy of DMTs for RMS, including HETs and oral therapies, using SLD from relevant RCTs.

### **Results:**

PS analyses demonstrated statistically significant superiority of OFA over FIN for reducing ARR (Rate Ratio 0.60, 95%CI 0.45-0.81) and delaying time to 3mCDP (HR 0.54, 95%CI 0.29-0.99), and numerical superiority over FIN for delaying time to 6mCDP (HR 0.59, 95%CI 0.31-1.12). Unanchored STCs demonstrated that OFA was (i) significantly superior to CLA, FIN, and OZA for reducing ARR, (ii) significantly superior to CLA, FIN and OZA for delaying 3mCDP and (iii) significantly superior to FIN and OZA for delaying 6mCDP; OFA was numerically superior to CLA for delaying 6mCDP. A network meta-

analysis (NMA) analysis also demonstrated that alemtuzumab, natalizumab, ocrelizumab and OFA were each at least numerically superior to CLA, FIN and OZA.

**Conclusion:**

Three different ITC approaches consistently found evidence supporting the separation of ofatumumab and other HETs (NMA only) from oral therapies based on their efficacy. Results of the present ITC analyses clearly support the therapeutic superiority of ofatumumab and other HETs over oral therapies with respect to reducing relapses and delaying disease progression.

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Dee Stoneman, Martin Merschhemk and Nicholas Adlard are employees of Novartis Pharma AG.

Robert Walker, Nicholas Riley and Morag Nelson are employees of Novartis Pharmaceuticals Australia.

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