CONCLUSIONS
-Across clinical trials, treatment with fingolimod 0.5 mg consistently reduced ARR rates compared with placebo and IFNβ-1a IM in patients with RRMS.
- Fingolimod 0.5 mg demonstrated consistent efficacy benefits over placebo and IFNβ-1a IM irrespective of time since onset of first symptom or duration of previous treatment, with the exception of patients in the IFNβ-1a IM subgroup treated previously for 1 year or less.
- The greatest improvements in ARR with fingolimod 0.5 mg compared with placebo and IFNβ-1a IM were seen in patients with disease duration of less than 3 years.
- These findings provide insight into the long-term outcomes of patients with relapsing forms of MS who are receiving DMTs, and suggest that starting fingolimod treatment early is likely to be particularly beneficial.

INTRODUCTION
- Higher annualized relapse rates (ARRs) early in the course of MS have been shown to correlate with poorer outcomes, including long-term disability.
- In phase 3 clinical trials, fingolimod significantly reduced ARRs in patients with relapsing-remitting multiple sclerosis (RRMS) compared with placebo (FREEDOMS and FREEDOMS II) and with interferon-β1a IM (TRANSFORMS).
- Pooling data from FREEDOMS, FREEDOMS II and TRANSFORMS provided a larger study population than was available from the individual studies for post hoc analyses of the efficacy of fingolimod in subgroups.

OBJECTIVES
- To report the effects of oral fingolimod treatment on ARRs in patients with RRMS according to duration of disease and duration of previous treatment with DMTs.

METHODS
Study design and participants
- Patients included in the pooled analyses had been randomized to receive oral fingolimod 0.5 mg or placebo once daily for 2 years (in FREEDOMS and FREEDOMS II) or to receive oral fingolimod 0.5 mg once daily or IFNβ-1a IM 30 µg once weekly for 1 year (in TRANSFORMS).
- In the three studies, patients (aged 18–55 years) had been diagnosed with RRMS in accordance with the 2005 revised McDonald criteria, had one or more confirmed relapses in the previous year or two or more in the previous 2 years, and had a score of 0–5.5 on the Expanded Disability Status Scale (EDSS).

Analyses
- Patient subgroups were defined according to:
  - Time since onset of first MS symptom (≤3 years versus >3 years before randomization).
  - Number of previous treatments received before randomization (0, ≤1, >1–3, >3 years before randomization).
- Subgroup analyses were performed on the intention-to-treat populations pooled from all three trials.

RESULTS
Study population
- In total, 2416 patients were included in the pooled analyses: 1212 in the fingolimod 0.5 mg group, 733 in the placebo group and 431 in the IFNβ-1a IM group. Table 1 presents patient disposition and study drug exposure.
  - Baseline demographics and disease characteristics were similar across treatment groups (Table 2).

Annualized relapse rates
- In patients with less than 3 years onset of first symptom, fingolimod 0.5 mg significantly reduced ARR by 69% (p<0.001) versus placebo and by 50% (p=0.002) versus IFNβ-1a IM (Figure 1).
- In patients with 3 or more years onset of first symptom, reductions in ARR with fingolimod 0.5 mg were 49% (p<0.001) versus placebo and 46% (p<0.001) versus IFNβ-1a IM.
- Fingolimod 0.5 mg significantly reduced ARR in patients with 0, ≤1–3, >1–3 and >3 years of treatment before randomization compared with placebo and IFNβ-1a IM, but not in patients in the IFNβ-1a IM group previously treated for 1 year or less (relative reduction: 35%, p=0.018).

p values are presented as mean (SD) unless otherwise noted.
All data are presented as mean (SD) unless otherwise noted. Values in these cells did not preclude receiving any drugs for the treatment of MS according to Ms Society case report forms.

References

Acknowledgments
The authors acknowledge Oxford PharmaLabs, Oxford, UK, for editorial support, which was funded by Novartis Pharmaceuticals Corporation. The final responsibility for the content lies with the authors.

This study was funded by Novartis Pharmaceuticals Corporation. (Poster presented at the 2015 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) | May 27–30, 2015 | Indianapolis, Indiana, USA.}

Figure 1. ARRs in patient subgroups defined by duration of disease and duration of previous treatment (intention-to-treat population).

Table 1. Patient disposition and study drug exposure (randomized population).

Table 2. Baseline demographics and patient characteristics (randomized population).

ARR ratio (95% CI)