P423

Long-term Safety and Effectiveness of Fingolimod: 7 year Data from the LONGTERMS Study

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Background: LONGTERMS is an open-label, single-arm, long-term extension study of phase 2/3/3b fingolimod trials in relapsing MS, studying long-term safety and effectiveness of fingolimod.

Objective: Evaluate long-term safety and effectiveness in subpopulations of patients (pts) treated with fingolimod in phase 3/3b core/extension studies transitioning to LONGTERMS and estimate occurrence rate (OR) of serious infections in pts from LONGTERMS with sustained low absolute lymphocyte count (ALC).

Methods: Safety analysis was based on LONGTERMS cohort on continuous fingolimod 0.5mg (LC; n=1655, median exposure: 3.9y) previously enrolled in three phase 3 trials plus their extensions, and core cohort (CC; n=1212, exposure: 1.6y) pooled from core phase 3 trials. Incidence rate ratios (IRRs; IR for LC/CC) were reported for any AEs, SAEs and AEs of special interest. In a separate analysis, infections of pts from LONGTERMS cohort (N=3154) on continuous fingolimod 0.5mg and with sustained low ALC (< 0.4x109L for ≥60% records; [N=1084]) were summarized by fingolimod exposure (>/≤2y). OR ratio (OccRR; OccR for >2/≤2y) of serious infections was calculated. Effectiveness analysis included evaluation of relapse and disability outcomes in 980 pts from FREEDOMS/FREEDOMS II (pooled FREEDOMS; median exposure: 6.4y) and 732 from TRANSFORMS (exposure: 6.9y) who received ≥1 fingolimod dose in LONGTERMS. ARR (LS mean) and % of relapse free pts were assessed by treatment interval from fingolimod initiation up to data cut off. Kaplan-Meier (KM) estimates for pts not reaching EDSS score 4, 6, or 7 were evaluated. Data cut-off: Oct 2014.

Results: IRRs (95% CI) for AEs and SAEs were 0.74 (0.69-0.80) and 0.72 (0.58-0.89), respectively. IRRs for AEs of special interest were < 1 except for reports of lymphopenia presumably due to blinding of lymphocyte counts >0.2x109L in CC. OccRR (>2/≤2y; CI) of serious infections for pts with sustained low ALC was: 1.47 (0.75- 3.01). No increase of lymphopenia was reported in these pts. ARR remained low: M0-12 (pooled FREEDOMS, 0.16 and TRANSFORMS, 0.19) to M0-84 (0.10 and 0.12). Most pts remained relapse free (63% and 60%), and did not reach EDSS (KM estimates at Month (M) 60) ≥4 (76% and 78%), ≥6 (90% and 93%) and ≥7 (98% and 99%).

Conclusion: Long-term exposure of pts in this cohort did not raise new safety concerns and the overall low rate of serious infections was confirmed in pts with sustained low ALC. Clinical disease activity remained low for up for to 7y.