Relapse-Associated Worsening and Progression Independent of Relapse Activity in Patients With Relapsing Multiple Sclerosis in the Phase III OPERA I and OPERA II Studies

L Kappos,1 JS Wolinsky,2 G Giovannoni,3 DL Arnold,4 Q Wang,5 C Bernacchioni,6 F Modest,7 M Manfrini,8 S Belachew,9 SL Hauser9
1University Hospital Basel, Basel, Basel, Switzerland; 2McGovern Medical School, The University of Texas Health Science Center at UTHealth, Houston, TX, USA; 3Queen Mary University of London, London, UK; 4McGill University, Montreal, QC, Canada; 5Neurology Research, Montreuil, QC, Canada; 6# Hoffmann-La Roche Ltd, Basel, Switzerland; 7University of California, San Francisco, San Francisco, CA, USA

INTRODUCTION AND PURPOSE

The term disability ‘progression’ should be reserved for patients in the progression phases of multiple sclerosis (MS), when the accumulation of disability occurs independent of relapse activity.

A recent study using a modified Expanded Disability Status Scale (EDSS) reference to the first fixed baseline assessment defined confirmed progression independent of relapse activity (PIRA) and suggested an increased risk of disability progression in patients with relapsing MS treated with a highly effective disease-modifying therapy (DMT).

In a recent non-inferiority study of the relapse-free phase of 2 placebo-controlled randomised clinical trials (OPERA I and OPERA II) assessing IFN β-1a and OCR for relapsing forms of MS (US vs rest of world) and study ID.

METHODS

Study Population

Time to first event of confirmed disability progression (CDP), composite RAW and composite PIRA were assessed in the post-hoc intention-to-treat (ITT) population of OPERA I and OPERA II double-blind analyses.

Analyses

Composite CDP

Composite CDP was defined as a disability increase measured by EDSS (increase of ≥1.0 if baseline EDSS ≤5.5, or ≥0.5 if baseline EDSS >5.5) or ≥20% increase in T25FW or ≥20% increase in 9HPT.

Composite RAW

In OPERA I and OPERA II, patients were defined as a disability increase from fixed baseline assessment occurring 30 days after the onset of a protocol-defined relapse and measured by EDSS (increase of ≥1.0 if baseline EDSS ≤5.5, or ≥0.5 if baseline EDSS >5.5) or ≥20% increase in T25FW or ≥20% increase in 9HPT.

Composite PIRA

Composite PIRA was defined as a disability increase from the original study baseline assessment where the disability increase was measured by an increase in EDSS score (≥1.0 if baseline EDSS ≤5.5, or ≥0.5 if baseline EDSS >5.5) or ≥20% increase in T25FW or ≥20% increase in 9HPT.

RESULTS

Baseline Demographics and Disease Characteristics

Table 1 shows the summary statistics of baseline characteristics in the OPERA I and OPERA II populations.

DISCLOSURES

PIRA and RAW as a Proportion of Overall Composite CDP

The proportion of overall first events of confirmed disability progression (CDP) comprised to composite RAW events in patients with RAW events measured by both 8% (3/41) (PIRA+CDP=74/943) and 8% (3/41) (PIRA+CDP=74/943) in (Figure 2). (Table 3) Figure 3.

In both treatment groups, the majority of patients experiencing composite CDP and composite RAW events appeared to be mostly non-protocol-defined relapse activity. Moreover, only 4% of patients with 12-week composite CDP events experienced both RAW and RAW events (Figure 2). (Table 4)

CONCLUSIONS

A considerable proportion of overall accumulation in disability in a typical RMS population is independent of relapse activity.

Table 3. Summary analyses of composite PIRA

Table 4. Summary analyses of composite RAW

For Table 1, please scan here

Table 2. Summary of composite CDP, composite RAW and composite PIRA by component (OPERA I and OPERA II pooled ITT population)

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Figure 1. Schematic representations of composite RAW and composite PIRA definitions

Figure 2. Relative contributions of composite RAW and composite PIRA vs overall composite CDP in respective treatment groups (OPERA I and OPERA II pooled ITT population)

Figure 3. Proportions of patients with all respective combinations of protocol-defined relapse, 12-week confirmed CDP, 12-week confirmed RAW and composite CDP (OPERA I and OPERA II pooled ITT population) -See animation

For Table 2, please scan here

Figure 1. Relative contributions of composite RAW and composite PIRA vs overall composite CDP in respective treatment groups (OPERA I and OPERA II pooled ITT population)

Figure 2. Proportions of patients with all respective combinations of protocol-defined relapse, 12-week confirmed CDP, 12-week confirmed RAW and composite CDP (OPERA I and OPERA II pooled ITT population) -See animation

For Table 3, please scan here

Table 2. Summary of composite CDP, composite RAW and composite PIRA by component (OPERA I and OPERA II pooled ITT population)

Table 3. Summary analyses of composite PIRA

Table 4. Summary analyses of composite RAW

For Table 1, please scan here

Table 1 shows the summary statistics of baseline characteristics in the OPERA I and OPERA II populations.

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