Phase 2 results of the RADIANCE trial: a randomized, double-blind, placebo-controlled trial of oral RPC1063 in relapsing multiple sclerosis

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Background: RPC1063 is an oral, selective sphingosine 1-phosphate 1 receptor modulator in clinical development for the treatment of relapsing multiple sclerosis (RMS).

Objectives: Demonstrate the superior efficacy of low (LD, 0.5 mg) and high (HD, 1.0 mg) dose RPC1063 vs. placebo (PBO), and characterize the safety of RPC1063 in patients with RMS.

Methods: RADIANCE is an international, combined Phase 2/3 trial. In the 24-week, Phase 2 portion, 258 patients were randomized (1:1:1) to PBO (n=88), LD (n=87) or HD (n=83). The primary endpoint was the cumulative number of total gadolinium-enhancing (GdE) lesions on MRI at Wks 12, 16, 20 and 24. Key secondary endpoints included number of GdE lesions at Wk 24, cumulative number of new/enlarging T2 lesions from Wks 12-24, and annualized relapse rate (ARR). Safety was assessed using vital signs, labs, ECG, Holter monitoring, PFT, OCT and adverse events (AEs). Patients were titrated to their assigned dose over one week to mitigate first dose heart rate effects.

Results: 98% of patients completed the trial. Cumulative total Wk 12-24 GdE lesions was reduced 86% in both RPC1063 arms vs. PBO (mean ± SD: PBO 11.1 ± 29.9, LD 1.5 ± 3.7, HD 1.5 ± 3.4, both p< 0.0001). Numbers of GdE lesions at Wk 24 were significantly reduced 91 and 94% (PBO 3.2 ± 9.8, LD 0.3 ± 0.9, HD 0.2 ± 0.6, both p< 0.0001) and cumulative Wks 12-24 new/enlarging T2 lesions 84 and 91% (PBO 9.0 ± 20.9, LD 1.4 ± 3.2, HD 0.8 ± 1.9, both p< 0.0001). A favorable trend in ARR reduction was observed vs. PBO (LD: 31%, p=0.27; HD: 53%, p=0.053).

The AE profiles were comparable between groups. The most common AEs in combined RPC1063 vs. PBO were nasopharyngitis (9.4 vs 13.6%), headache (4.7 vs 9.1%), and urinary tract infection (4.7 vs 2.3%). During the first 6 hours post first dose of RPC1063, maximum reductions in mean hourly heart rate were < 2 bpm from baseline and no patient had a minimum hourly heart rate < 45 bpm. No notable cardiac, pulmonary, ophthalmologic or malignancy AEs were observed. Transient alanine aminotransferase ≥3x upper limit of normal occurred in 3 patients (LD 2 (2.3%), HD 1 (1.2%)) that decreased with continued treatment.

Conclusions: Both doses of RPC1063 demonstrated large, significant and consistent reductions of all MRI measures of MS disease activity. The tolerability and safety results suggest a favorable risk-benefit profile of RPC1063 in the treatment of RMS. These results support the ongoing Phase 3 portion of the RADIANCE trial of RPC1063 vs. interferon beta-1a in RMS (NCT02047734).

Assigned speakers:
MD Amit Bar-Or , McGill University , Montreal , CA

Assigned in sessions:
13.09.2014, 08:30-10:00, Late breaking news, LB1, Late Breaking News (LB1.1-LB1.7), Auditorium