#1063: Long-term Efficacy of Siponimod Treatment for up to 5 Years in Patients with Secondary Progressive Multiple Sclerosis: Analysis of the EXPAND Extension Study

Authors

L. Kappos[1], G. Giovannoni[2], R. Gold[3], R. J. Fox[4], P. Vermersch[5], R. H.B. Benedict[6], A. Bar-or[7], N. Rouyrre[8], D. Piani-Meier[8], S. Ritter[9], A. Kilaru[8], F. Dahlke[8], G. Karlsson[8], B. A.C. Cree[10]; [1]Neurologic Clinic and Policlinic, Departments of Medicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital and University of Basel, Basel/Switzerland, [2]Blizard Institute, Barts and The London School of Medicine and DentistrQueen Mary University of London, London/United Kingdom, [3]Department of Neurology, St Josef-Hospital/Ruhr-University Bochum, Bochum/Germany, [4]Mellen Center for Treatment and Research in Multiple Sclerosis, Neurological Institute, Cleveland Clinic, Cleveland, Ohio/USA, [5]Univ. Lille, INSERMU995, CHU Lille, FHU Imminent, F-59000 Lille/France, [6]Department of Neurology, University at Buffalo, Buffalo, New York/USA, [7]Center for Neuroinflammation and Experimental Therapeutics and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania/USA, [8]Novartis Pharma AG, Basel/Switzerland, [9]Novartis Pharmaceuticals Corporation, East Hanover, New Jersey/USA, [10]Department of Neurology, UCSF Weill Institute for Neurosciences, University of California San Francisco, San Francisco, California/USA

Type

Abstract

Topic

MS and related disorders

Category

ePoster or Oral

Background and aims

In the EXPAND-Core study, siponimod significantly reduced 3-/6-month (m) confirmed disability progression (3mCDP/6mCDP) and cognitive decline in secondary progressive multiple sclerosis (SPMS) patients. We assessed long-term efficacy of siponimod on disability, cognitive processing speed (CPS) and relapses in SPMS patients from the Core and Extension parts of the EXPAND study.

Methods

This analysis included patients who received >=1 dose of randomised treatment (siponimod 2mg/placebo; 36m Extension data cut-off [April 2019]; total study duration =<5 years). Efficacy analyses included time-to-3mCDP/time-to-6mCDP, time-to-6m confirmed meaningful worsening in CPS (6mCW; >=4 points in SDMT) and annualised relapse rate (ARR) for the continuous (CSG: siponimod in Core/Extension) and switch groups (PSG: placebo in Core/switched to siponimod in Extension).

Results

Of the 1224 (74% of 1651 randomised) patients entering the Extension, 878 (72%) were ongoing. Patients in CSG versus PSG were less likely to experience 3mCDP (p=0.0064) and 6mCDP (p=0.0048). Time-to-6mCDP was prolonged by 54% for the 25th percentile and risk for 6mCDP reduced by 22% in CSG versus PSG; median time-to-6mCDP not reached for CSG. Decline in CPS on SDMT was delayed (p=0.0014) and risk for 6mCW reduced by 23% in CSG versus PSG (**Table**). ARR was reduced by 52% in CSG versus PSG (p<0.0001); the effect was similar for relapses without complete recovery, requiring steroids/hospitalisations.

Parameter	Continuous siponimod group (N=1099)	Placebo-siponimod group (N=546)	p-value	Relative risk reduction %, HR (95% CI)	Delay in time-to-event %
	KM estimate*				
Time-to-6mCDP on EDSS* % of patients without event up to Month 48	58.65 (55.34; 61.96)	52.40 (47.58; 57.21)	0.0048[a]	22%, 0.78 (0.66; 0.92)	-
Time to 6mCDP on EDSS for the 25th percentile Months	21.0	13.6	-	-	54%
Time-to-6mCW on SDMT* % of patients without event up to Month 48	68.28 (65.16; 71.39)	58.45 (53.67; 63.24)	0.0014[a]	23%, 0.77 (0.65; 0.92)	-
Time-to-6mCW on SDMT for the 25th percentile Months	29.6	18.3	-	-	62%

*KM estimates relate to the end day of the interval. The Greenwood formula is used for the CIs of the KM estimates. The numbers provided in parentheses are CI values. CIs are point-wise rather than simultaneous intervals; [a]Using a log-rank test stratified by treatment group

3mCDP, 3-month confirmed disability progression; 6mCDP, 6-month confirmed disability progression; 6mCW, 6-month confirmed worsening; CI, confidence interval; CPS, cognitive processing speed; EDSS, Expanded Disability Status Scale; HR, hazard ratio; KM, Kaplan–Meier; SDMT, Symbol Digit Modalities Test

Table. Efficacy results

Conclusion

Benefits on disability, cognitive processing speed and relapses of CSG over PSG gained during the controlled period are sustained for up to 5 years, demonstrating the sustained treatment effect and advantage of early treatment initiation with siponimod in patients with SPMS.

Disclosure

This study was funded by Novartis Pharma AG, Basel, Switzerland. A detailed disclosure from each author will be included in the oral/poster presentation.

Abstract also submitted to AAN 2020; acceptance pending.

Affirmations

Authors agreement: I confirm, that all authors mentioned in the author block of this abstract have been informed about, and agreed to this submission. (I confirm)

Originality: This abstract contains new and original information, not published elsewhere prior to 23 May 2020. (I confirm)