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Long-term Efficacy of Siponimod Treatment for up to 5 Years in Patients with SPMS: Analysis of the EXPAND Extension Study

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Disclosures

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Gavin Giovannoni is a steering committee member on the daclizumab trials for AbbVie, the BG12 and daclizumab trials for Biogen, the fingolimod and siponimod trials for Novartis, the laquinimod trials for Teva and the ocrelizumab trials for Roche. He has also received consultancy fees for advisory board meetings for oral cladribine trials for Merck KGaA, Genzyme-Sanofi, and in relation to DSMB activities for Synthon BV, as well as honoraria for speaking at the Physicians' Summit and several medical education meetings. He is also the Co-Chief Editor of Multiple Sclerosis and Related Disorders (Elsevier).

Ralf Gold has received compensation for serving as a consultant or speaker from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience, and he or the institution he works for has received research support from Bayer HealthCare, Biogen Idec, Merck Serono, Novartis and Teva Neuroscience; he has also received honoraria as a Journal Editor from SAGE and Thieme Verlag.

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Objective and Endpoints

Objective

- To assess the long-term efficacy of siponimod in patients with SPMS from the core and extension parts of the EXPAND Phase 3 study

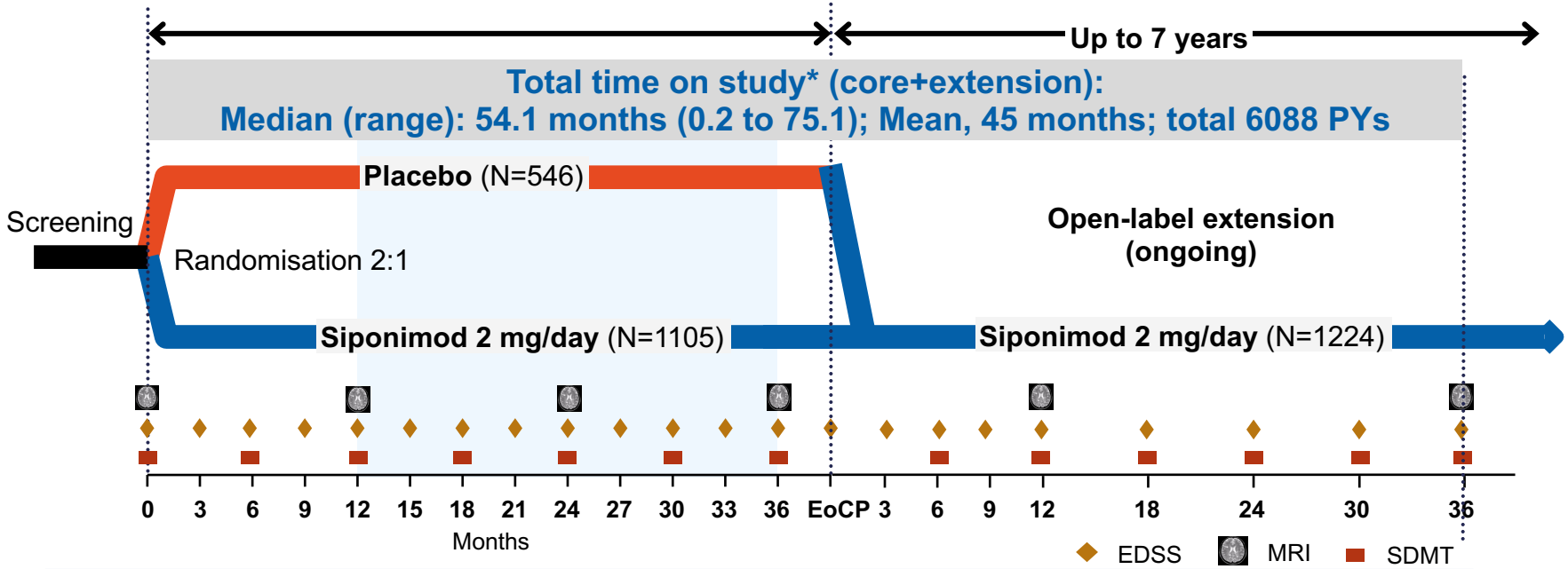
Endpoints

- Time-to-6mCDP based on EDSS score
- Time-to-6mCW[a] in cognitive processing speed (CPS) based on SDMT score
- ARR

[a]Time-to-6m confirmed meaningful worsening of ≥4 points from baseline in SDMT score.

3m/6mCDP, 3-month or 6-month confirmed disability progression; 6mCW, 6-month confirmed worsening; AEs, adverse events; ARR, annualized relapse rate; CPS, cognitive processing speed; EDSS, Expanded Disability Status Scale; SAEs, serious adverse events; SDMT, Symbol Digit Modalities Test; SPMS, secondary progressive multiple sclerosis

Study Design: EXPAND Core+Extension

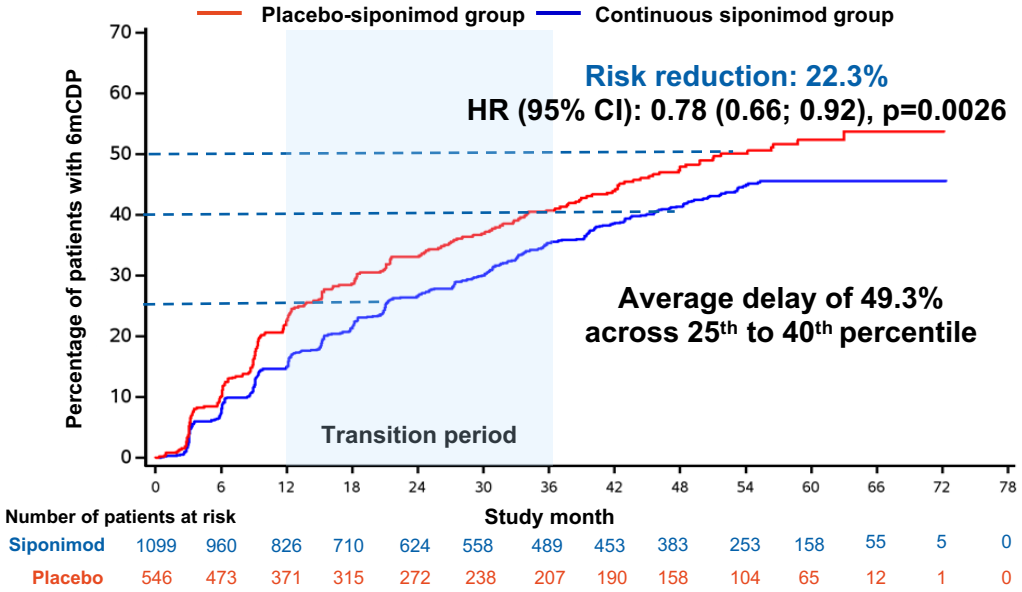


Overall, 74.1% of randomized patients entered the extension; of those, 72.2% were ongoing in the continuous siponimod group and 71.4% in the placebo-siponimod group

***Extension data cut-off: April 2019 (Month 36 visit of extension]; total study duration (core+extension): ≤5 years**

EDSS, Expanded Disability Status Scale; EoCP, end of core part; PYs, patient years; SDMT, Symbol Digit Modalities Test; SPMS, secondary progressive MS

Effect of Siponimod on 6-month Confirmed Disability Progression and Time to Disability Progression

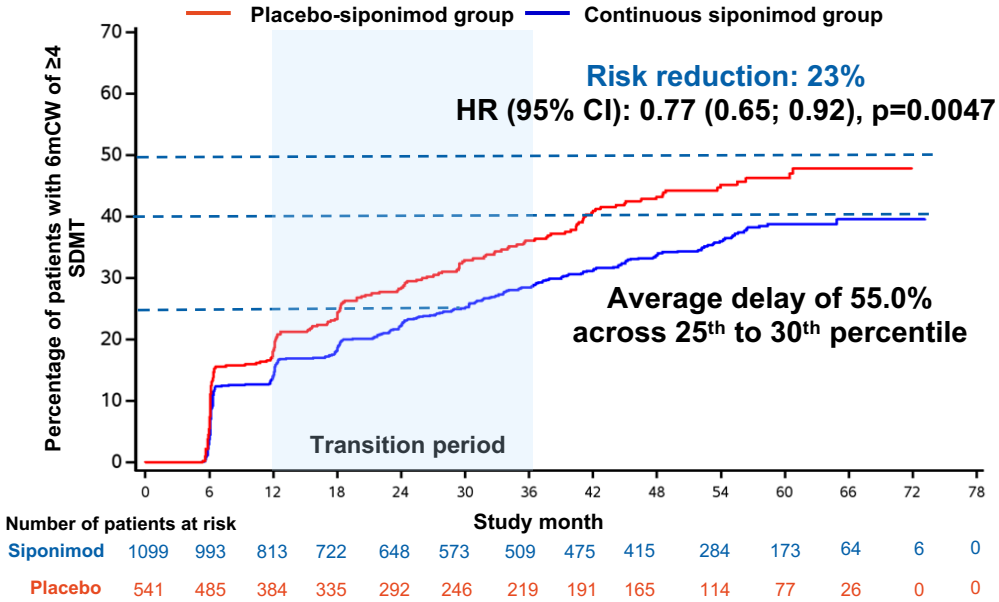


Percentile (months)	Placebo-siponimod (N=546)	Continuous siponimod (N=1099)	Delay (%)
25th	13.6	21.0	54%
30th	18.4	29.8	62%
40th	33.9	44.9	32%
Median	51.7	nr	

- **The risk of 6mCDP was reduced by 22.3% in the continuous siponimod group**
- **Time to 6mCDP was prolonged by 49%**

6mCDP, 6-month confirmed disability progression; CI, confidence interval; EDSS, Expanded Disability Status Scale; HR, hazard ratio; KM, Kaplan Meier

Effect of Siponimod on 6-month Confirmed Clinically Meaningful Worsening in Cognitive Processing Speed

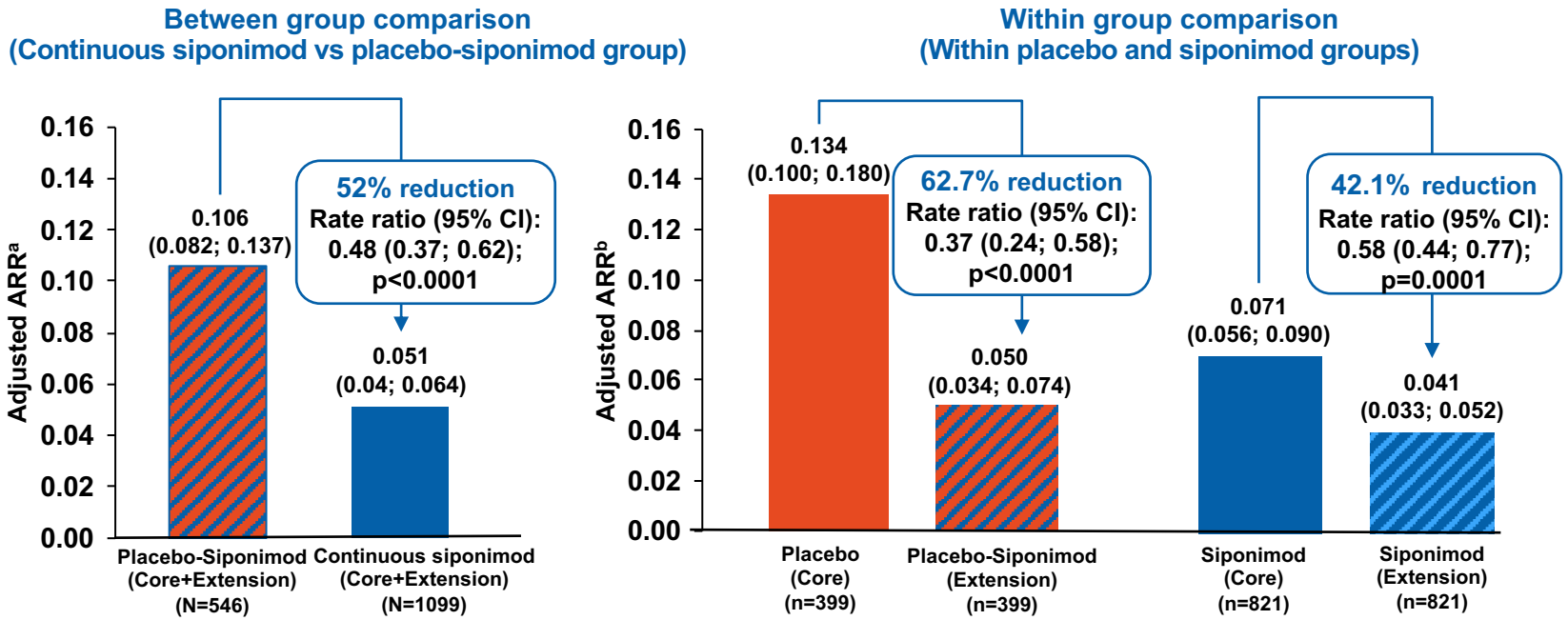


Percentile (months)	Placebo-siponimod (N=546)	Continuous siponimod (N=1099)	Delay (%)
25th	18.3	29.6	62%
30th	26.4	39.0	48%
40th	41.3	n.r.	

- The risk of 6mCW in CPS was reduced by 23% in the continuous siponimod group
- Time to 6mCW was prolonged by 55%

6mCW, 6-month confirmed worsening; CI, confidence interval; CPS, cognitive processing speed; HR, hazard ratio; KM, Kaplan Meier; n.r, not reached; SDMT, Symbol Digit Modalities Test

Siponimod effect on Annualized Relapse Rate (ARR)



Overall ARR was lower in the continuous siponimod versus switch group
After switching to siponimod ARR was similarly reduced as in the siponimod group

[a]Negative binomial regression model adjusted for the core part treatment group; [b]Poisson regression model adjusted for treatment period (core part, extension part); Both also adjusted for country, baseline EDSS, SPMS group (with/without superimposed relapses; baseline definition), and baseline number of T1 Gd+ lesions categories
ARR, annualized relapse rate; EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; SPMS, secondary progressive multiple sclerosis

Conclusions

- The treatment benefit of siponimod observed in the core study was sustained with long-term treatment for up to 5 years
  - Delay by approximately 50% in time to disability progression and meaningful worsening in cognitive processing speed
- Sustained differences favoring patients on continuous siponimod treatment versus patients who switched later to siponimod from placebo highlight the benefit of earlier treatment initiation
- These sustained effects, together with the long-term safety profile of siponimod which was consistent with the core study (data not shown) support the value of this compound for the treatment of active SPMS

CPS, cognitive processing speed