B cells, T cells and inflammatory CSF biomarkers in primary progressive MS and relapsing MS in the OBOE (Ocrelizumab Biomarker Outcome Evaluation) trial

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Disclosures

A Bar-Or has served on scientific advisory boards for Biogen, F. Hoffmann-La Roche Ltd, Genentech, Inc., GlaxoSmithKline, Guthy-Jackson/GGF, MedImmune, Merck, EMD Serono, Mitsubishi Tanabe, Ono, Receptos and Sanofi Genzyme and has received research support from Biogen, Novartis and Sanofi Genzyme.

JL Bennett has served on scientific advisory boards and performed consulting services for EMD Serono, Frequency Therapeutics, Clene Nanomedicine, Viela Bio and Alexion and has received research support from Mallinckrodt.

HC von Büdingen is an employee of F. Hoffmann-La Roche Ltd.

R Carruthers is a site investigator for studies funded by F. Hoffman-La Roche Ltd, Novartis, MedImmune and EMD Serono and receives research support from Teva Innovation Canada, Roche Canada and Vancouver Coastal Health Research Institute. R. Carruthers has received honoraria from F. Hoffmann-La Roche Ltd, EMD Serono, Sanofi, Biogen, Novartis and Teva.

K Edwards has received research/grant support from Biogen, Sanofi Genzyme, Genentech, Inc., F. Hoffmann-La Roche Ltd and Novartis.

R Fallis has nothing to disclose.

JM Gelfand has received consulting fees from Biogen and Alexion and research support from Genentech, Inc.

PS Giacomini has served on scientific advisory boards for Actelion, Allergan, Bayer, Biogen Idec, Celgene, EMD Serono, F. Hoffmann-La Roche Ltd, Sanofi Genzyme, Novartis, Pendopharm and Teva and has received research grants from Biogen and Teva Neuroscience.

B Greenberg has received consulting fees from Alexion, EMD Serono and Novartis. He has received grant funding from the NIH, NMSS, Transverse Myelitis Association, Guthy-Jackson Foundation, PCORI, Chugai, MedImmune and MedDay. He is an unpaid board member of the Transverse Myelitis Association.

D Hafler has, in the past 10 years, consulted for the following companies: Bayer Pharmaceuticals, Biohaven Pharmaceuticals, Bristol Myers Squibb, Compass Therapeutics, Eisai Pharmaceuticals, EMD Serono, Genentech, Inc., Juno Therapeutics, McKinsey & Co, MedImmune, AstraZeneca, Mylan Pharmaceuticals, Neurophage Pharmaceuticals, NKT Therapeutics, Novartis, Proclara Biosciences, Questcor, Roche, Sage Therapeutics, Sanofi Genzyme, Toray Industries and Versant Ventures. Dr Hafler's work was generously supported by grants from the National Institutes of Health (U19 AI089992, R25 NS079193, P01 AI073748, U24 AI11867, R01 AI22220, UM 1HG009390, P01 AI039671, P50 CA121974, R01 CA227473) and the National Multiple Sclerosis Society (CA 1061-A-18, RG-1802-30153). Dr Hafler is also supported by grants from the National Institute of Neurological Disorders and Stroke and the Nancy Taylor Foundation for Chronic Diseases. In addition, Dr Hafler has received funding for his laboratory from Bristol Myers Squibb, Genentech, Inc., Novartis, Questcor, Sanofi Genzyme and Race to Erase MS.

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Disclosures (cont.)

E Longbrake has received honoraria for consulting from Genentech, Inc., Genzyme, Biogen, Teva, EMD Serono and Celgene.

C Ionete has served on scientific advisory boards for EMD Serono and Sanofi Genzyme and has received research support from F. Hoffmann-La Roche Ltd, Genentech, Inc., Biogen and Sanofi Genzyme.

U Kaunzner has nothing to disclose.

C Lock has served on scientific advisory boards or as a speaker for Biogen, Sanofi Genzyme, EMD Serono and Bristol Myers Squibb and has done consulting for InterX Inc and Diagnose Early.

B Musch is an employee of Genentech, Inc. and a shareholder of F. Hoffmann-La Roche Ltd.

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J Pei is an employee of Genentech, Inc. and a shareholder of F. Hoffmann-La Roche Ltd.

F Piehl has received research grants from Biogen, Genzyme, Merck KGaA and Novartis and fees for serving as Chair of DMC in clinical trials for Parexel.

MS Weber receives research support from the Deutsche Forschungsgemeinschaft (DFG; WE 3547/5-1), Novartis, Teva, Biogen Idec, F. Hoffmann-La Roche Ltd, Merck and the ProFutura Program of the Universitätsmedizin Göttingen; serves as an editor for *PLoS One*; and has received travel funding and/or speaker honoraria from Biogen Idec, Merck Serono, Novartis, F. Hoffmann-La Roche Ltd, Teva, Bayer and Genzyme.

T Ziemssen has received consulting and/or speaking fees from Almirall, Bayer, Biogen, Merck, Novartis, F. Hoffmann-La Roche Ltd, Sanofi and Teva and has received grant/research support from Biogen, Novartis, Sanofi and Teva.

A Herman is an employee of Genentech, Inc. and a shareholder of F. Hoffmann-La Roche Ltd.

C Harp is an employee of Genentech, Inc. and a shareholder of F. Hoffmann-La Roche Ltd.

AH Cross has, in the past year, received fees or honoraria for consulting from Biogen, Celgene, EMD Serono, F. Hoffmann-La Roche Ltd, Genentech, Inc. and Novartis and received fees for serving on scientific advisory boards and reviewing grants for the Conrad N. Hilton Foundation and Race to Erase MS.

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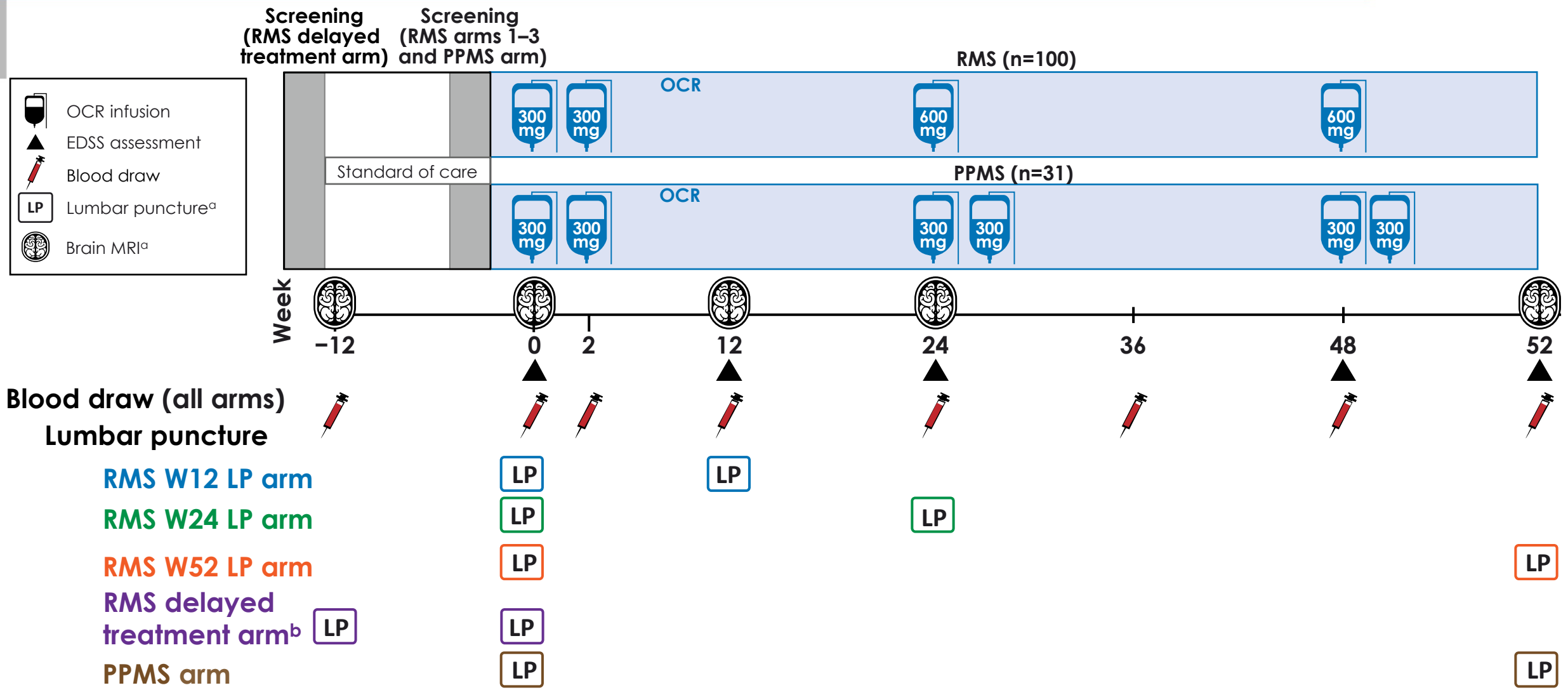
OBOE: A hypothesis-generating study designed to examine multiple biomarkers of neurodegeneration and inflammation as well as markers of B-cell mechanisms in MS



[a]Collection of CSF should precede the brain MRI, and both of these assessments should occur up to 5 days (preferably 1–2 days) before OCR administration;
[b]Delayed treatment arm will serve as a biomarker control, with both lumbar punctures occurring 12 weeks apart and before the first dose of OCR.
CSF, cerebrospinal fluid; EDSS, Expanded Disability Status Scale; LP, lumbar puncture; OCR, ocrelizumab; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; W, Week.

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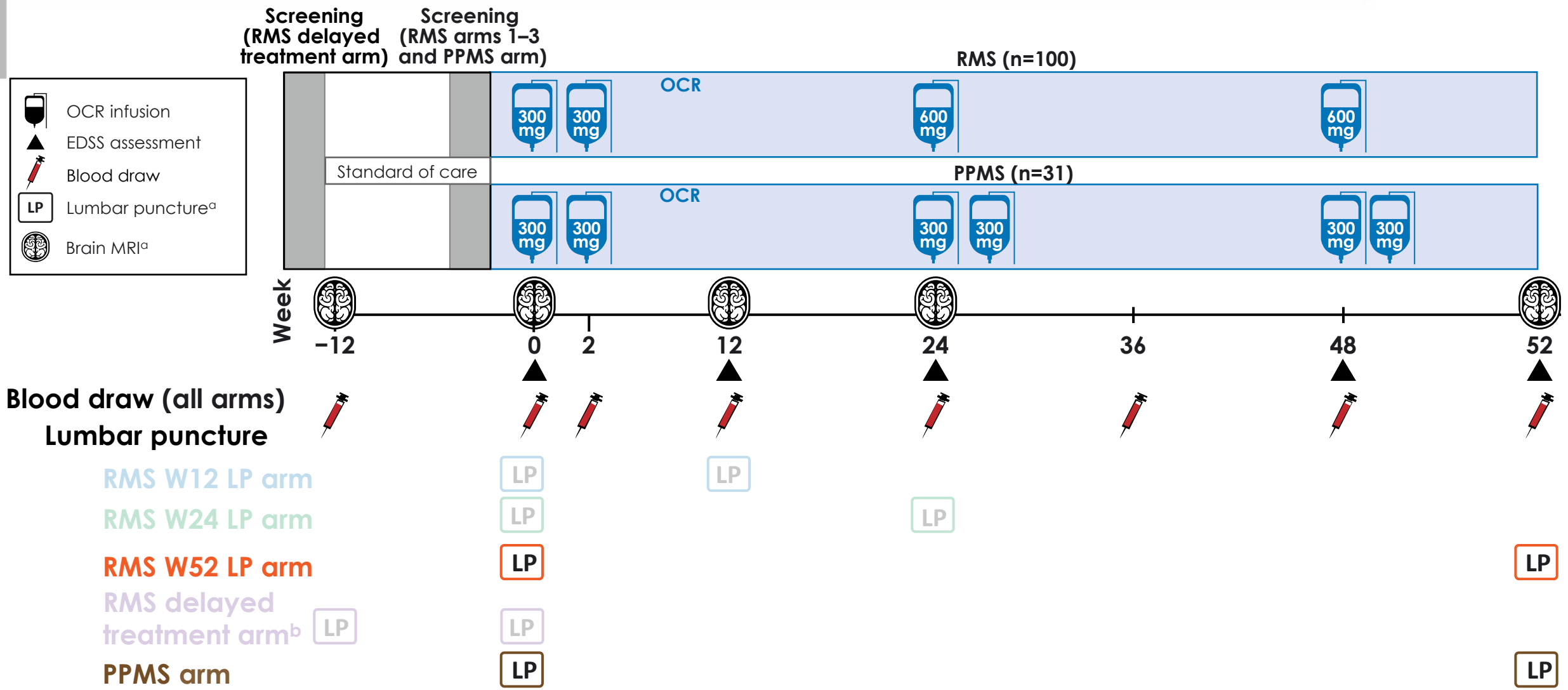

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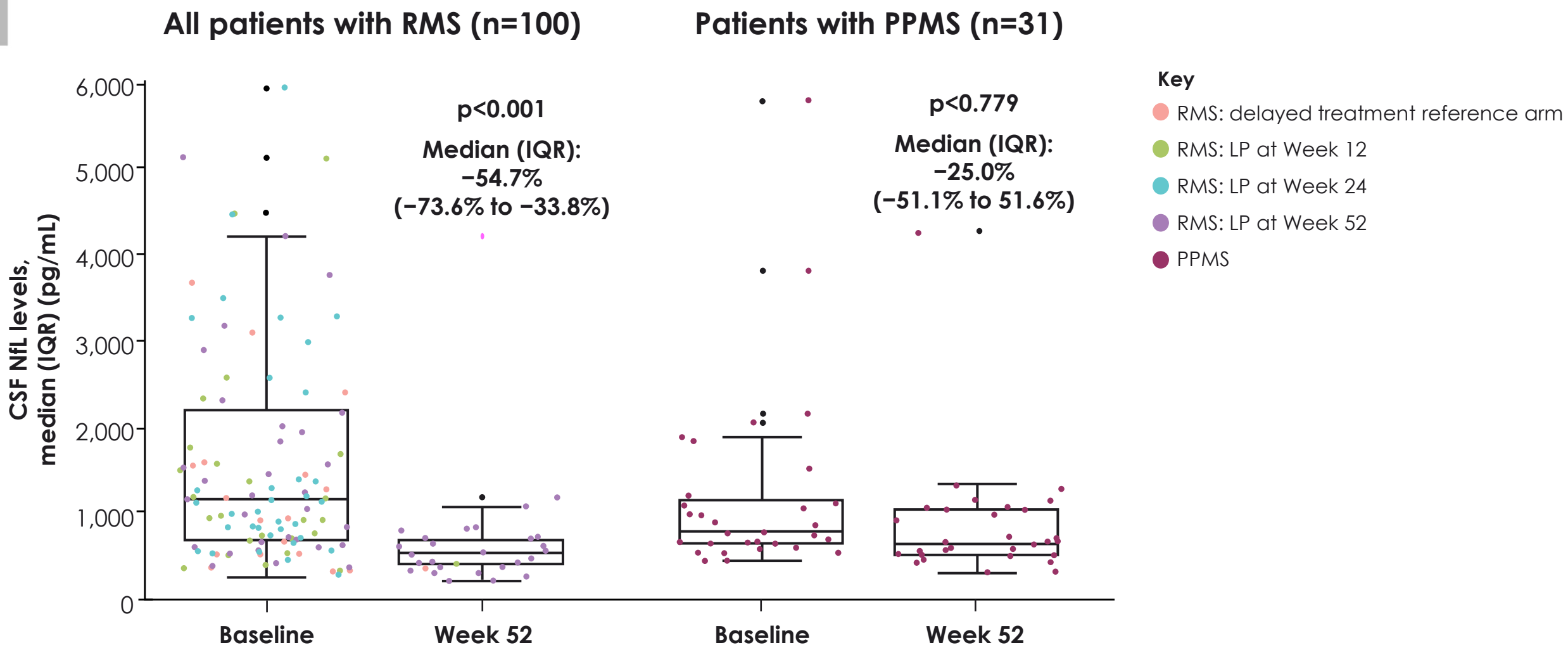
Baseline CSF B-cell, T-cell and inflammatory marker levels were similar in patients with RMS and those with PPMS, while NfL levels were higher in the RMS group relative to PPMS

Marker	Pooled RMS (n=100)	PPMS (n=31)
Mean age, mean (SD), years	**36.6 (10.4)**	**44.9 (7.4)**
Female, %	**68.0**	**48.4**
Time since first MS symptom, mean (SD), years	**3.8 (6.8)**	**1.6 (2.3)**
Previously treated, n (%) **Treatment naïve,** n (%)	**41 (41.0)** **59 (59.0)**	**8 (25.8)** **23 (74.2)**
CSF NfL, median (IQR), pg/mL	**1,226.4 (701.5–2,564.3)** (n=97)	**741.0 (606.9–1,166.0)** (n=31)
CSF CD19⁺ B cells, median (IQR), cells/µL	**0.05 (0.01–0.13)** (n=80)	**0.05 (0.01–0.10)** (n=17)
CSF CD3⁺ T cells, median (IQR), cells/µL	**2.1 (0.9–4.3)** (n=81)	**3.18 (1.3–7.0)** (n=21)
CSF CXCL13, median (IQR), pg/mL	**9.9 (3.9–27.4)** (n=85)	**3.9 (3.9–9.7)** (n=28)
CSF CCL19, median (IQR), pg/mL	**47.0 (31.7–67.5)** (n=87)	**58.9 (36.4–68.2)** (n=29)

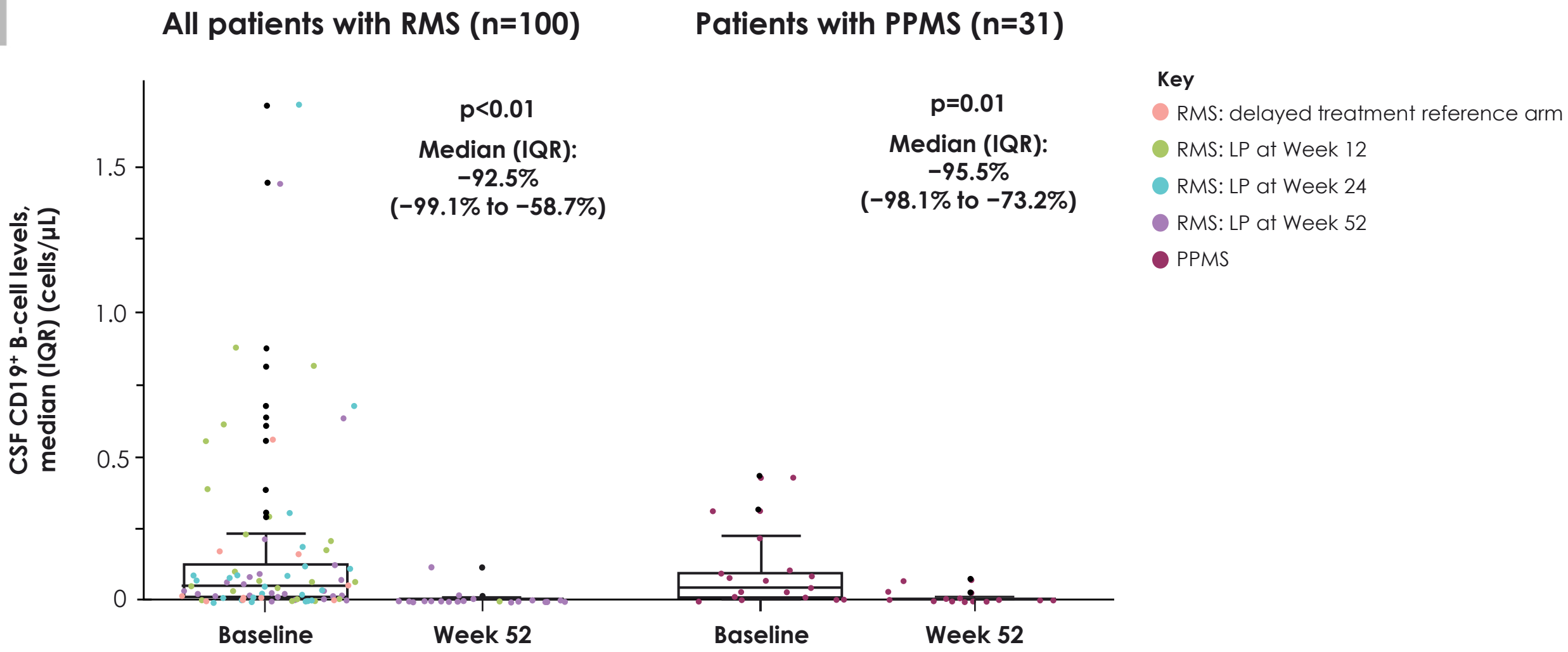
CSF, cerebrospinal fluid; IQR, interquartile range; MS, multiple sclerosis; NfL, neurofilament light chain; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis.

CSF NfL levels in ocrelizumab-treated patients with RMS and those with PPMS



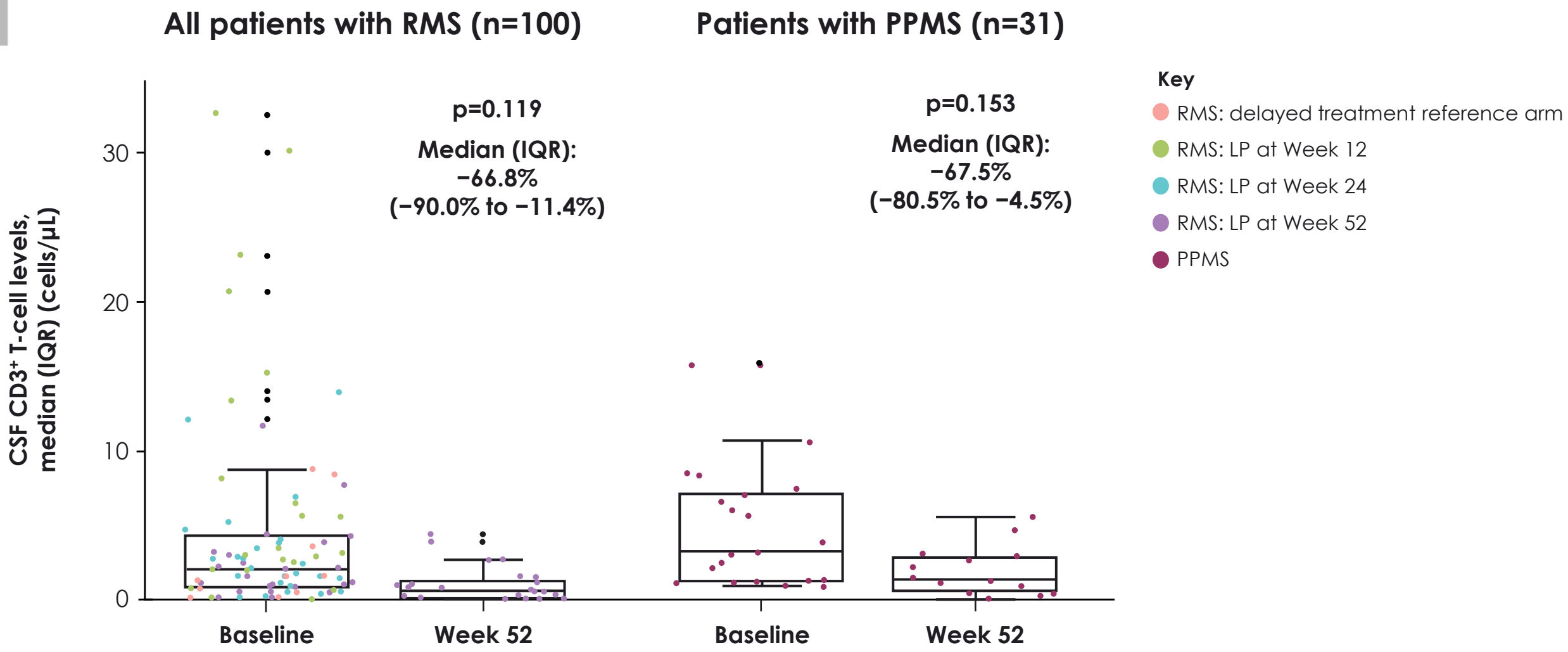
Median % change from baseline, Wilcoxon p value % change from baseline. Black dots represent outliers. CSF, cerebrospinal fluid; IQR, interquartile range; LP, lumbar puncture; NfL, neurofilament light chain; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis.

CSF CD19+ B-cell levels in ocrelizumab-treated patients with RMS and those with PPMS



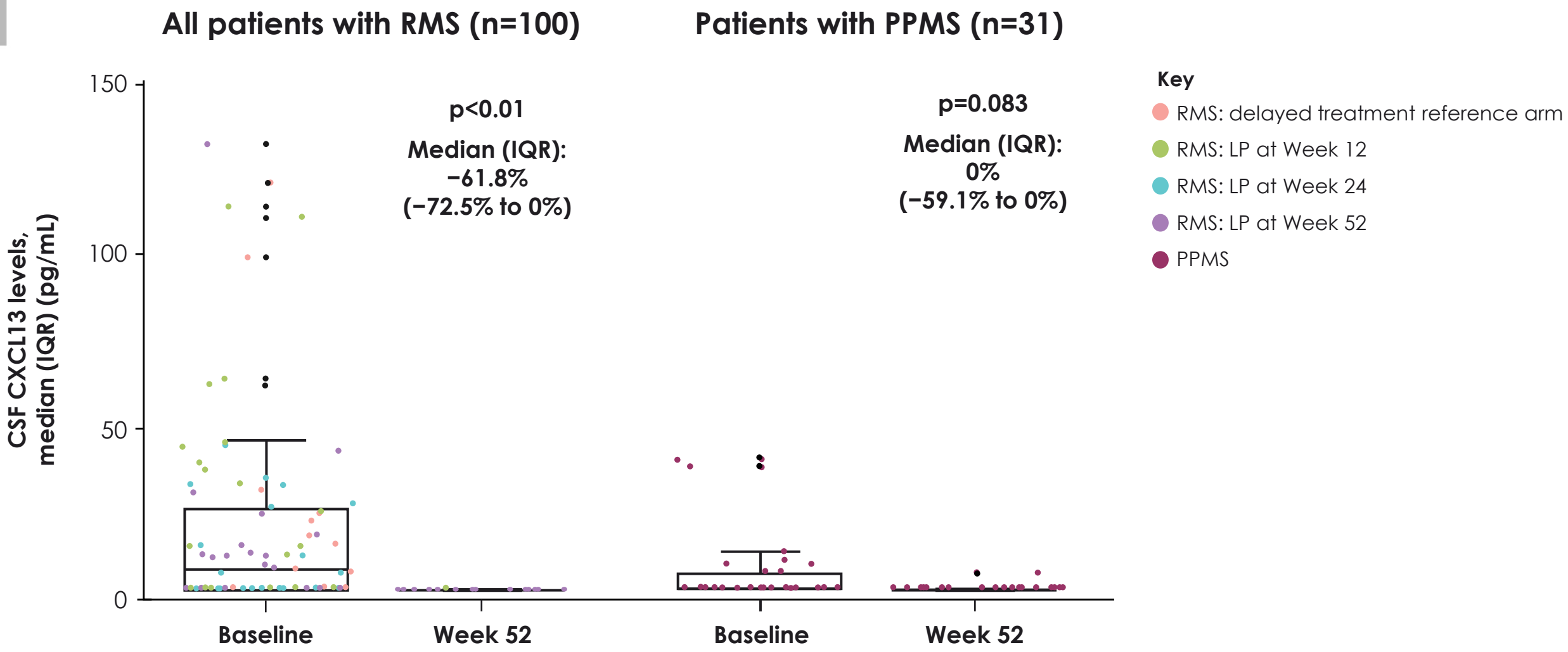
Median % change from baseline, Wilcoxon p value % change from baseline. Black dots represent outliers. CSF, cerebrospinal fluid; IQR, interquartile range; LP, lumbar puncture; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis.

CSF CD3+ T-cell levels in ocrelizumab-treated patients with RMS and those with PPMS



Median % change from baseline, Wilcoxon p value % change from baseline. Black dots represent outliers. CSF, cerebrospinal fluid; IQR, interquartile range; LP, lumbar puncture; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis.

CSF CXCL13 levels in ocrelizumab-treated patients with RMS and those with PPMS



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Conclusions

- Baseline CSF B-cell, T-cell and inflammatory marker levels were similar in patients with PPMS and those with RMS, while NfL levels were higher in the RMS group relative to PPMS
- CSF B-cell, T-cell and CXCL13 levels were reduced following ocrelizumab treatment in patients with PPMS and those with RMS

CSF, cerebrospinal fluid; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis.

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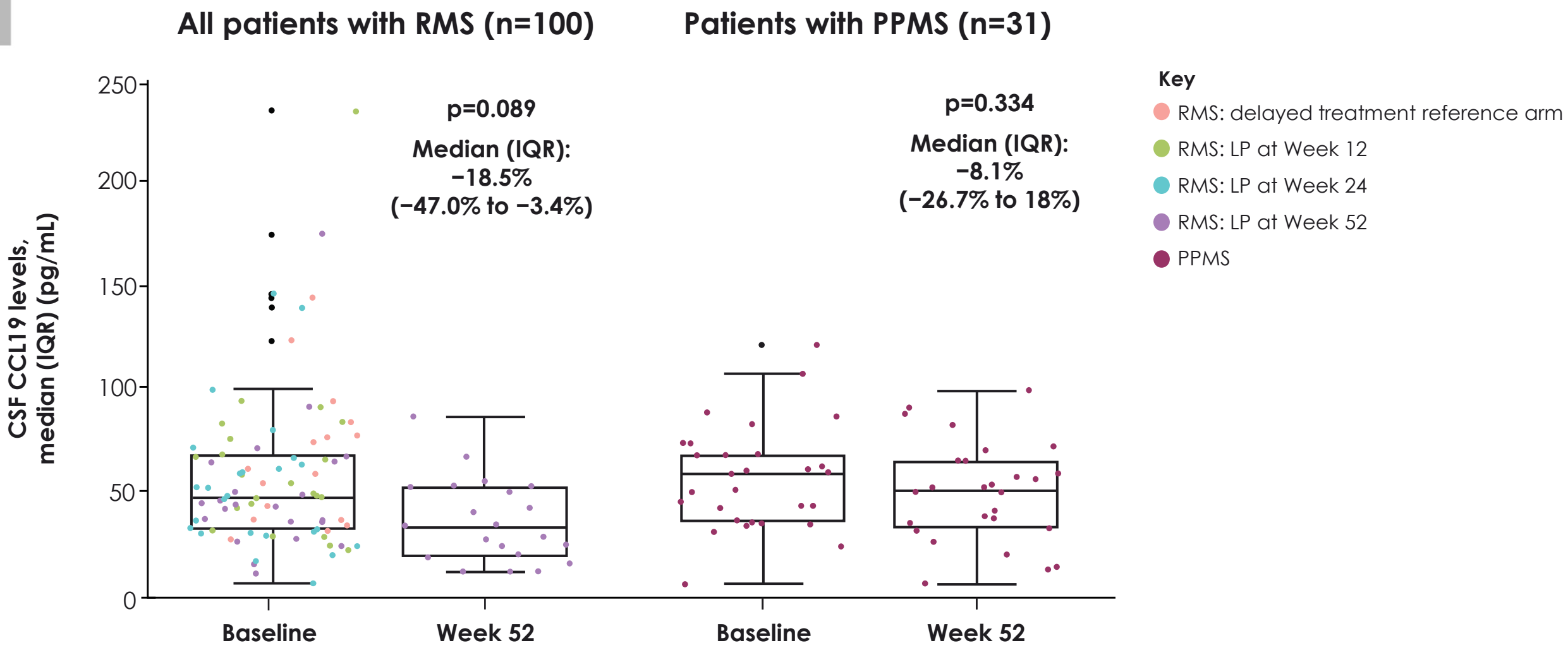
Backup

CSF CCL19 levels in ocrelizumab-treated patients with RMS and those with PPMS



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