Prasinezumab in early-stage Parkinson's disease: Additional data from the PADOVA study

Tania Nikolcheva,[1] *Gennaro Pagano,*[2,3] *Judith Anzures-Cabrera,*[4] *Tanya Simuni,*[5] *Kenneth Marek,*[6] *Nicola Pavese,*[7] *Klaus Seppi,*[8] *Fabrizio Stocchi,*[9] *Ronald B. Postuma,*[10] *Nathalie Pross,*[1] *Annabelle Monnet,*[11] *Geoffrey A. Kerchner,*[2] *Patrik Brundin,*[2] *and Azad Bonni;*[2] *for the PADOVA Investigators and Prasinezumab Study Group*

17–21 March | AD/PD 2026

Affiliations

1. Product Development Neurology, F. Hoffmann-La Roche Ltd, Basel, Switzerland
2. Roche Pharma Research and Early Development (pRED), Neuroscience and Rare Diseases Discovery and Translational Area, Roche Innovation Center, F. Hoffmann-La Roche Ltd, Basel, Switzerland
3. University of Exeter Medical School, London, UK
4. Roche Products Ltd, Welwyn Garden City, UK
5. Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
6. Institute for Neurodegenerative Disorders, New Haven, CT, USA
7. Clinical Ageing Research Unit, Newcastle University, Newcastle upon Tyne, UK
8. Department of Neurology, Medical University Innsbruck, Innsbruck, Austria
9. Department of Neurology, University San Raffaele Roma and the Institute for Research and Medical Care, IRCSS San Raffaele Pisana, Rome, Italy
10. Department of Neurology, McGill University and Montreal Neurological Institute, Montreal, QC, Canada
11. Product Development Data Science, F. Hoffmann-La Roche Ltd, Basel, Switzerland

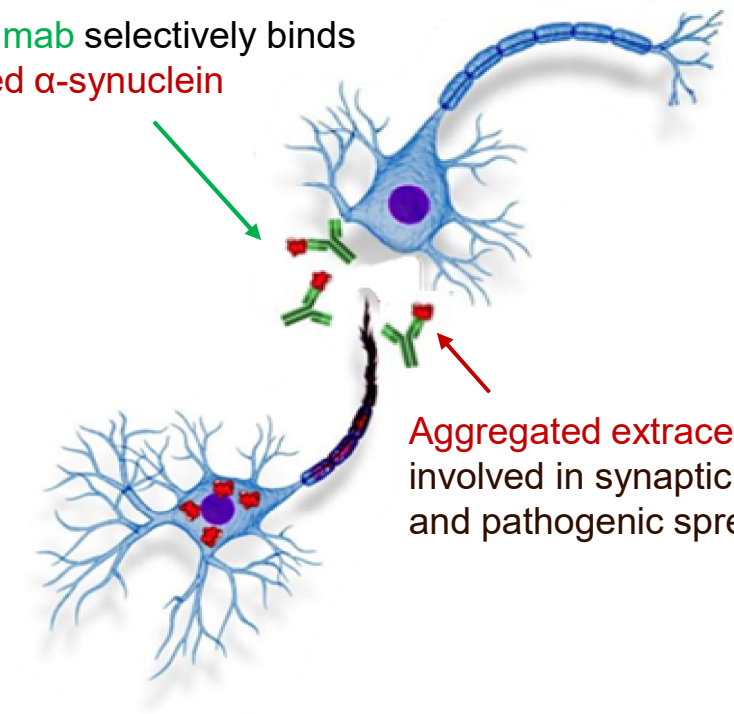
Disclosures

- **Tania Nikolcheva, Gennaro Pagano, Judith Anzures-Cabrera, Nathalie Pross, Annabelle Monnet, Geoffrey A. Kerchner, Patrik Brundin and Azad Bonni:** Full-time employees and own shares of F. Hoffmann-La Roche Ltd
- **Tanya Simuni:** Consultant for AcureX, Adamas, AskBio, Amneal, Blue Rock Therapeutics, Critical Path for Parkinson's Consortium (CPP), Denali, Michael J Fox Foundation, Neuroderm, Sanofi, Sinopia, Roche, Takeda and Vanqua Bio. Served advisory boards for AcureX, Adamas, AskBio, Denali, and Roche, and as a member of the scientific advisory board of Neuroderm, Sanofi and UCB. Received research funding from Amneal, Biogen, Neuroderm, Prevail, Roche, and UCB and is an investigator for NINDS, MJFF, Parkinson's Foundation
- **Kenneth Marek:** Consultant for the Michael J Fox Foundation, Mitro, Roche, BMS, GAIN, Calico, Sanofi, Teva, Biohaven, BMS, Merck, GEHC, Lilly, ABLi, and Prothena. Stock in Mitro, Biohaven, ABLi
- **Nicola Pavese:** Member of advisory boards for Hoffmann-La Roche, Bial, AbbVie, Teva, Biohaven, Teitur Trophics. Has received honoraria from Medtronic, Bial, Britannia, AbbVie, GE Healthcare, Boston Scientific and has received grants from Independent Research Fund Denmark, Danish Parkinson's disease Association, Parkinson's UK, Center of Excellence in Neurodegeneration (CoEN) network award, GE Healthcare Grant, Multiple System Atrophy Trust, Weston Brain Institute, EU Joint Program Neurodegenerative Disease Research (JPND), EU Horizon 2020 research, The Michael J. Fox Foundation, F. Hoffmann-La Roche, Medtronic, Symbyx
- **Klaus Seppi:** Recipient of grants from the FWF Austrian Science Fund, the Michael J. Fox Foundation, International Parkinson and Movement Disorder Society, AOP Orphan Pharmaceuticals AG, and EU (all to the institution). He has received payment for consultations from Ono Pharma UK, Lundbeck, and Ever Pharma and payment for lectures from Teva, UCB, AOP Orphan Pharmaceuticals AG, Roche, Grünenthal, Stada, Licher Pharma, Biogen, Bial, and AbbVie. He has also received payment for participation in advisory boards from Bial, Stada, and AbbVie, and honoraria from the International Parkinson and Movement Disorders Society
- **Fabrizio Stocchi:** Consultant for AbbVie, Bial Pharma, Biogen, F. Hoffmann-La Roche Ltd., H. Lundbeck A S, Mitsubishi Tanabe Pharma America, Inc., Sunovion Pharmaceuticals, Inc., Teva Pharmaceutical Industries, Zambon, and Britannia, and is supported by a grant from the Italian Ministry of Health (Ricerca Corrente)
- **Ronald B. Postuma:** Consultant for Biogen, Clinilabs, Curasen, Eisai, Inc., F. Hoffmann-La Roche Ltd., Merck, Takeda California, Inc., and Vaxxinity

Prasinezumab is a humanised IgG1 monoclonal antibody that selectively binds aggregated α-synuclein[1,2]

Prasinezumab's proposed mode of action for the treatment of Parkinson's disease[1]

Prasinezumab selectively binds aggregated α-synuclein



Aggregated extracellular α-synuclein involved in synaptic loss and pathogenic spread

Proposed effects:

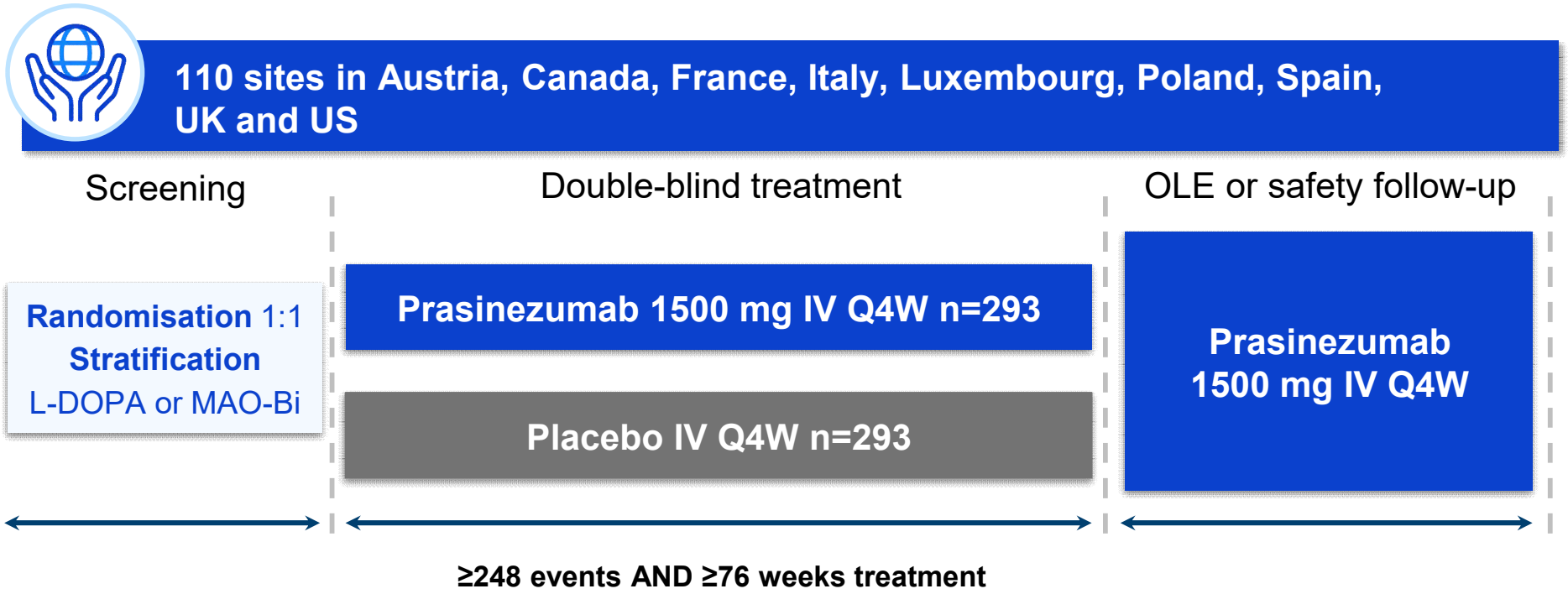
- Reducing neuronal toxicity
- Preventing cell-to-cell transfer of pathogenic α-synuclein aggregates
- Slowing disease progression

IgG, immunoglobulin.

1. Angot E, et al. *Lancet Neurol*. 2010; 9(11):1128–38; 2. Vekrellis K & Stefanis L. *Expert Opin Ther Targets*. 2012;16(4):421–32.

PADOVA assessed prasinezumab effect on top of symptomatic therapy

Global Phase IIb study in early-stage Parkinson's disease with a novel time-to-event approach



Key inclusion criteria

Early-stage PD

- MDS criteria incl. DaT-SPECT deficit
- 3 months to 3 years from diagnosis
- H&Y Stage I/II
- MDS-UPDRS Part IV = 0

Stable symptomatic therapy

- L-DOPA or MAO-Bi
- Stable dose for 3 months

Primary endpoint

Time to confirmed motor progression (MDS-UPDRS Part III *OFF**)

The mentioned compounds and their use are investigational and have not yet received regulatory approval in any country.
*Practically defined OFF-medication state (≥12 hours since the last dose of L-DOPA).
DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; H&Y, Hoehn & Yahr; IV, intravenous; L-DOPA, levodopa; MAO-Bi, monoamine oxidase type B inhibitor; MDS, Movement Disorder Society; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; OLE, open-label extension; PD, Parkinson's disease; Q4W, every 4 weeks.
ClinicalTrials.gov. NCT04777331. PADOVA Phase II clinical trial. Available at: https://clinicaltrials.gov/ct2/show/NCT04777331 (last accessed 29 January 2026).

Baseline characteristics well balanced across arms

Population consistent with early-stage PD; ~74% of participants on L-DOPA

Key baseline demographic and disease characteristics		Placebo n=293	Prasinezumab n=293	All N=586
Age (yr)	mean (SD)	64.4 (7.5)	64.0 (7.2)	64.2 (7.3)
Sex, male	n (%)	189 (64.5)	183 (62.5)	372 (63.5)
Time from diagnosis (months)	mean (SD)	18.4 (9.0)	18.8 (9.5)	18.6 (9.2)
Hoehn & Yahr stage	n (%)			
1		40 (13.7)	38 (13.0)	78 (13.3)
2		250 (85.3)	251 (85.7)	501 (85.5)‡
MDS-UPDRS Part II	mean (SD)	5.1 (4.1)	4.9 (3.5)	5.0 (3.8)
MDS-UPDRS Part III *OFF**	mean (SD)	24.6 (10.8)	24.3 (9.9)	24.5 (10.4)
MDS-UPDRS Part III†	mean (SD)	19.5 (9.8)	19.0 (8.9)	19.2 (9.4)
MDS-UPDRS Part IV = 0	n (%)	283 (96.6)	282 (96.2)	565 (96.4)
MoCA	mean (SD)	26.4 (2.7)	26.6 (2.9)	26.5 (2.8)
SE-ADL completely independent	n (%)	288 (98.3)	285 (97.3)	573 (97.8)
Striatal binding ratio: putamen ipsilateral	mean (SD)	0.87 (0.3)	0.88 (0.3)	0.87 (0.3)
Stratification factor	n (%)			
L-DOPA		217 (74.1)	218 (74.4)	435 (74.2)
MAO-Bi		76 (25.9)	75 (25.6)	151 (25.8)

*Practically defined *OFF*-medication state (≥12 hours since the last dose of L-DOPA); †Refers to the L-DOPA population; ‡7 patients were randomised with Hoen & Yahr Stage 3 in PADOVA (3 in the placebo group and 4 in the prasinezumab group).
L-DOPA, levodopa; MAO-Bi, monoamine oxidase type B inhibitor; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; PD, Parkinson's disease; SD, standard deviation; SE-ADL, Schwab and England Activities of Daily Living scale; yr, year.

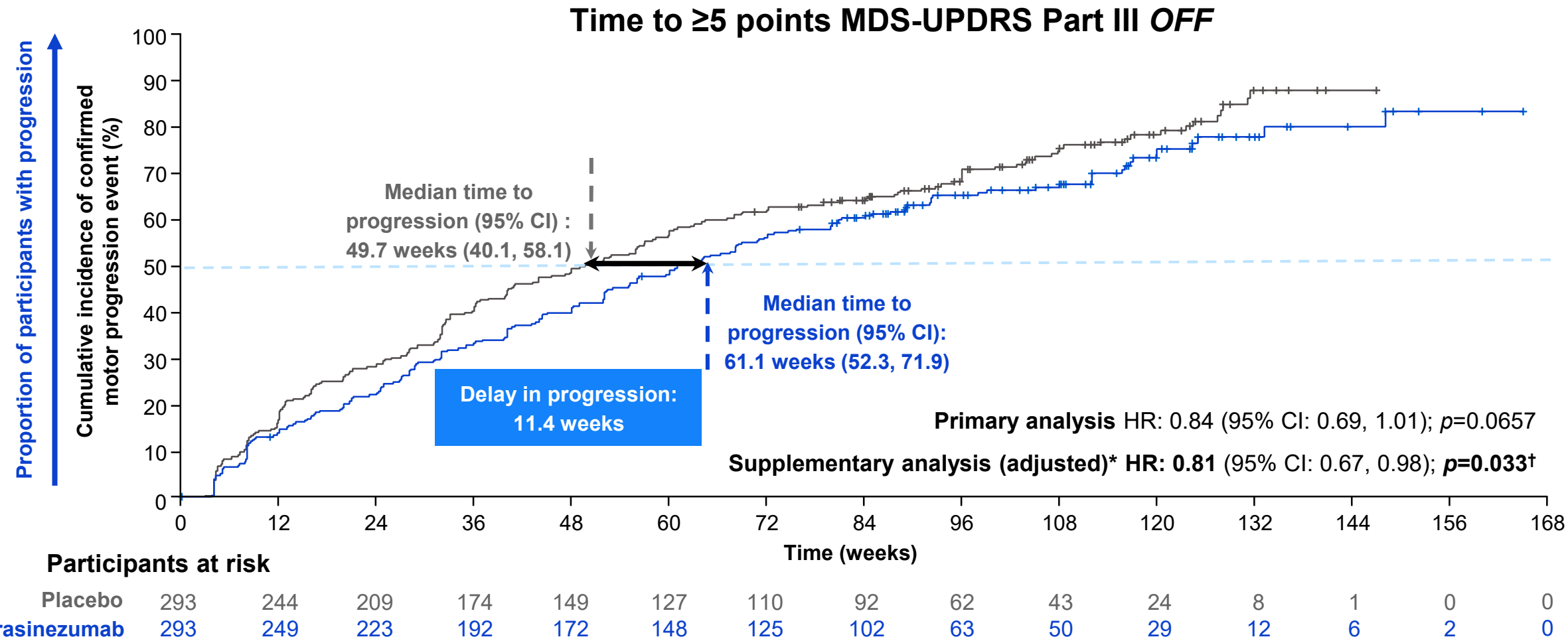
Prasinezumab continues to show favourable safety & tolerability

- Strong safety profile and extensive patient exposure
  - Prasinezumab has demonstrated a favourable safety and tolerability profile across over 900 Parkinson's disease study participants, with more than 500 treated for 2.5 to 5 years
- PADOVA safety summary
  - IRRs comparable between groups (11% prasinezumab vs 12.8% placebo); no serious IRRs
  - Three deaths: two in placebo, one in prasinezumab arm; deemed unrelated to study drug
  - SAEs and AEs Grade 3–5 were similar in incidence between prasinezumab and placebo
  - Two AEs leading to study drug discontinuation in prasinezumab and three in placebo arm
- High transition and retention rate in OLEs
  - ~750 participants currently in PASADENA & PADOVA OLEs

AE, adverse event; IRR, infusion-related reaction; OLE, open-label extension; SAE, serious adverse event.

Prasinezumab showed a trend towards delaying motor progression

Signal of efficacy on top of effective symptomatic therapy



Participants at risk

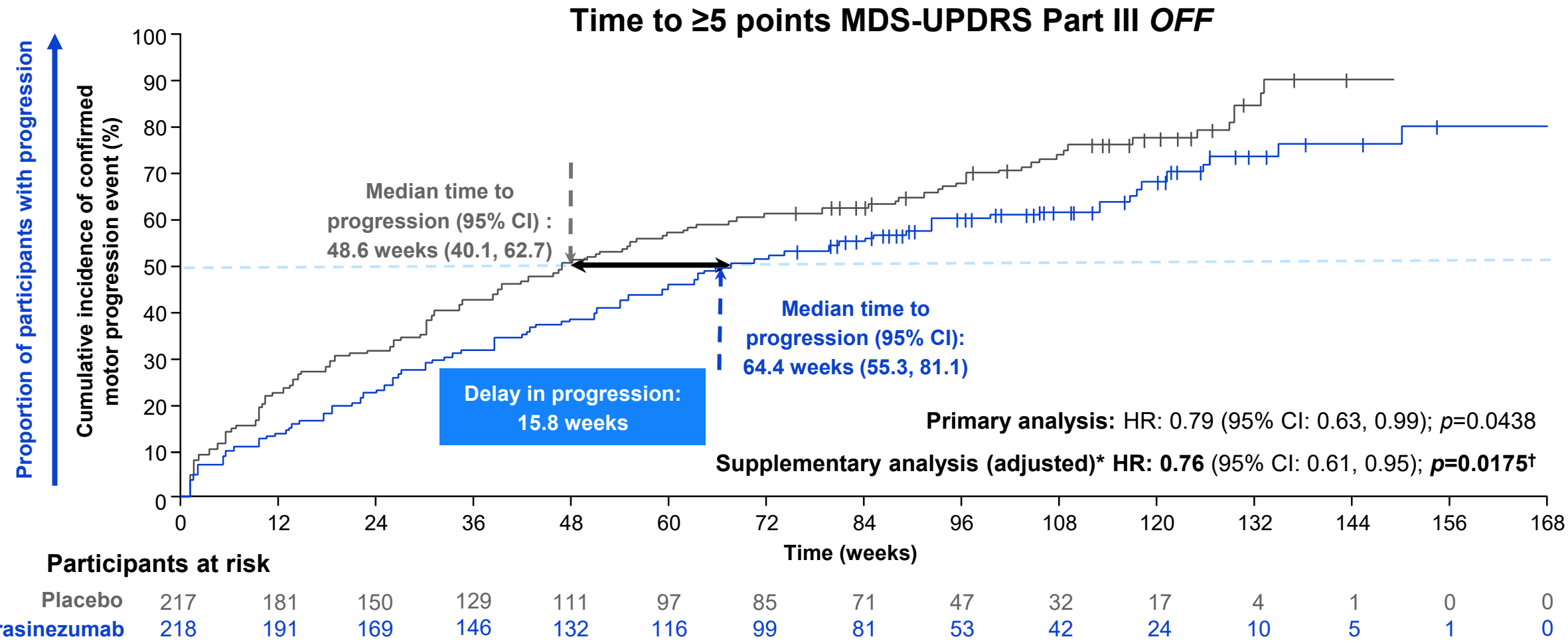
Placebo	293	244	209	174	149	127	110	92	62	43	24	8	1	0	0
Prasinezumab	293	249	223	192	172	148	125	102	63	50	29	12	6	2	0

Participants received prasinezumab 1500 mg or placebo Q4W. *Covariates used for adjustment: H&Y stage (1 vs ≥2), DaT-SPECT putamen ipsilateral, age (<60 vs ≥60), sex (male vs female), BL MDS-UPDRS Part III. The intercurrent events of treatment discontinuation and LEDD increase prior to event are handled with the treatment policy strategy; †For descriptive purposes, nominal p-values are displayed.

BL, baseline; CI, confidence interval; DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; H&Y, Hoehn and Yahr; HR, hazard ratio; LEDD, levodopa equivalent daily dose; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; Q4W, every four weeks.

Prasinezumab showed a trend towards delaying motor progression

Signal of efficacy more pronounced in pre-specified L-DOPA subgroup (~74% of total study population)



Participants at risk

Placebo	217	181	150	129	111	97	85	71	47	32	17	4	1	0	0
Prasinezumab	218	191	169	146	132	116	99	81	53	42	24	10	5	1	0

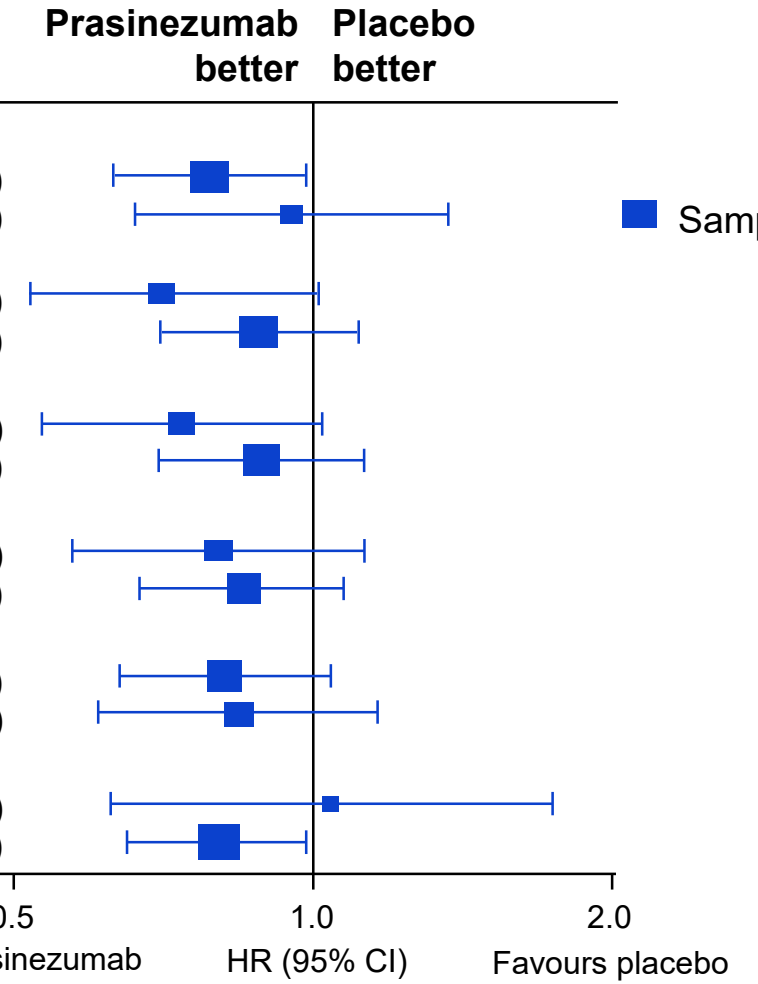
Participants received prasinezumab 1500 mg or placebo Q4W. *Covariates used for adjustment: H&Y stage (1 vs ≥2), DaT-SPECT putamen ipsilateral, age (<60 vs ≥60), sex (male vs female), BL MDS-UPDRS Part III. The intercurrent events of treatment discontinuation and LEDD increase prior to event are handled with the treatment policy strategy; †For descriptive purposes, nominal p-values are displayed.

BL, baseline; CI, confidence interval; DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; H&Y, Hoehn and Yahr; HR, hazard ratio; L-DOPA, levodopa; LEDD, levodopa equivalent daily dose; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; Q4W, every four weeks.

Consistent trends in favour of prasinezumab in prespecified subgroups

Signal of efficacy on top of effective symptomatics across majority of subgroups

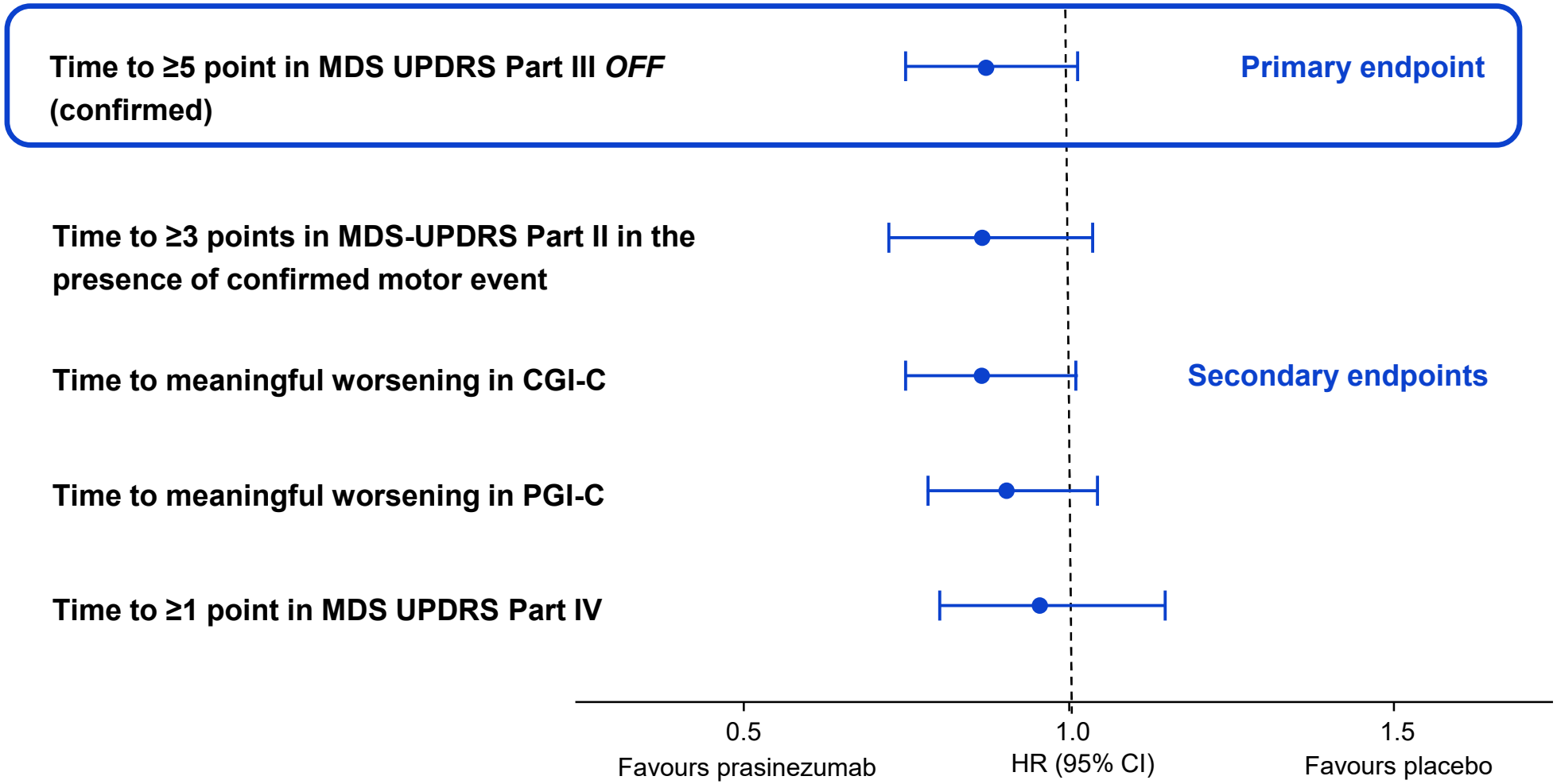
Baseline risk factors	Total n	HR	95% CI
PD medication at baseline*			
L-DOPA	435	0.79	(0.63, 0.99)
MAO-Bi	151	0.96	(0.67, 1.39)
Age at baseline			
<60 years	171	0.71	(0.50, 1.02)
≥60 years	415	0.89	(0.71, 1.12)
Age at diagnosis			
<60 years	200	0.74	(0.54, 1.03)
≥60 years	386	0.89	(0.70, 1.13)
Time since diagnosis at baseline			
≤12 months	193	0.80	(0.57, 1.12)
>12 months	393	0.85	(0.67, 1.07)
Sex			
Male	372	0.82	(0.65, 1.05)
Female	214	0.85	(0.61, 1.17)
H&Y stage at baseline			
1	78	1.05	(0.63, 1.76)
2	508	0.81	(0.65, 0.99)



*Stratification factor.
CI, confidence interval; H&Y, Hoehn & Yahr; HR, hazard ratio; L-DOPA, levodopa; MAO-Bi, monoamine oxidase type B inhibitor; PD, Parkinson's disease.

Consistent trends in favour of prasinezumab across TTE endpoints

Clinical signals extend beyond motor signs



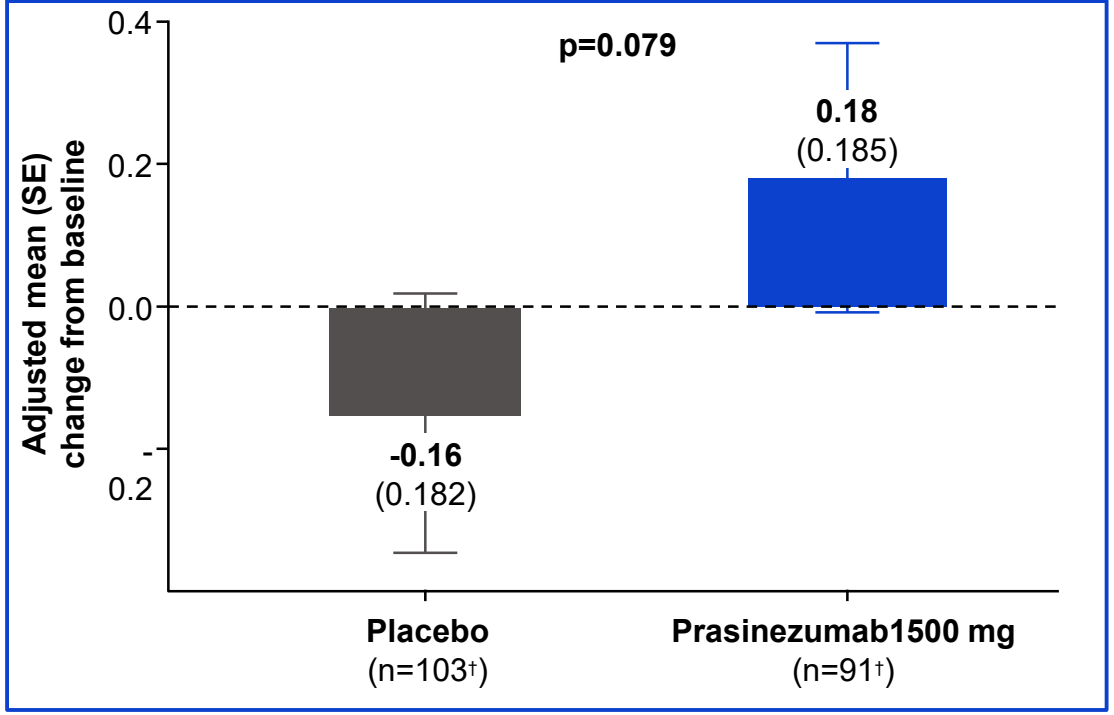
Participants received prasinezumab 1500 mg or placebo Q4W.

CGI-C, Clinical Global Impression of Change; CI, confidence interval; HR, hazard ratio; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; PGI-C, Patient Global Impression of Change; Q4W, every four weeks; TTE, time-to-event.

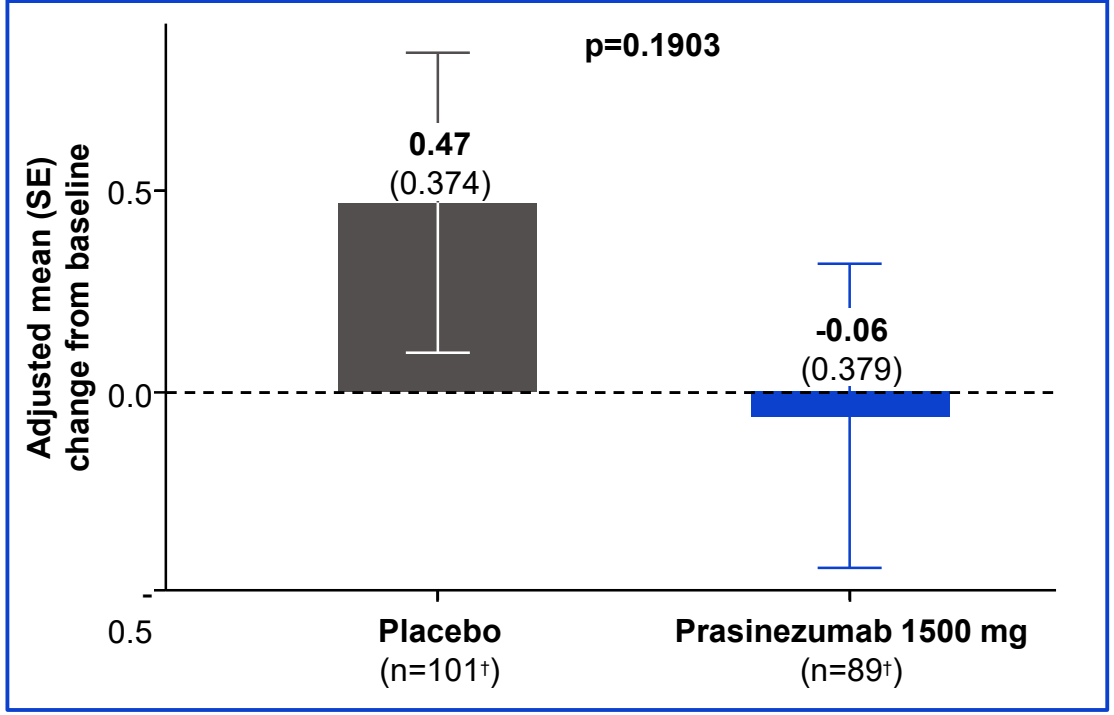
First biomarker evidence of prasinezumab impacting disease pathology

Prasinezumab associated with stabilisation of neuromelanin and reduced iron accumulation in key brain regions

Neuromelanin MRI at Week 76
Substantia nigra pars compacta intensity



Iron (R2*) MRI at Week 76
Substantia nigra pars compacta (average)



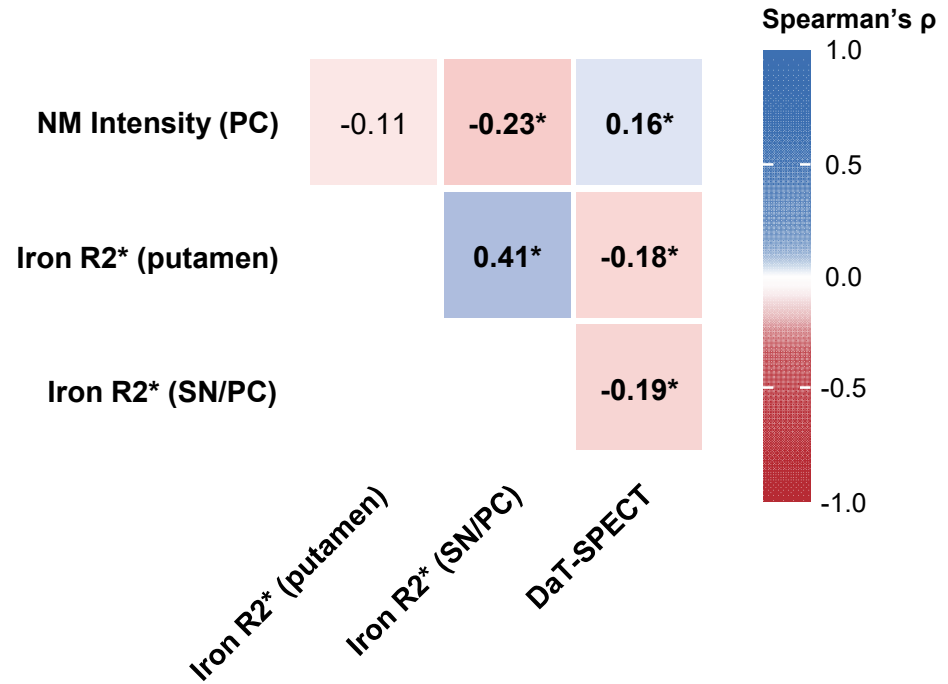
Error bars represent SE; p-values are nominal.

*R2 MRI sequence used for imaging; †Data generated in sites that had access to MRI sequence.
MRI, magnetic resonance imaging; SE, standard error.

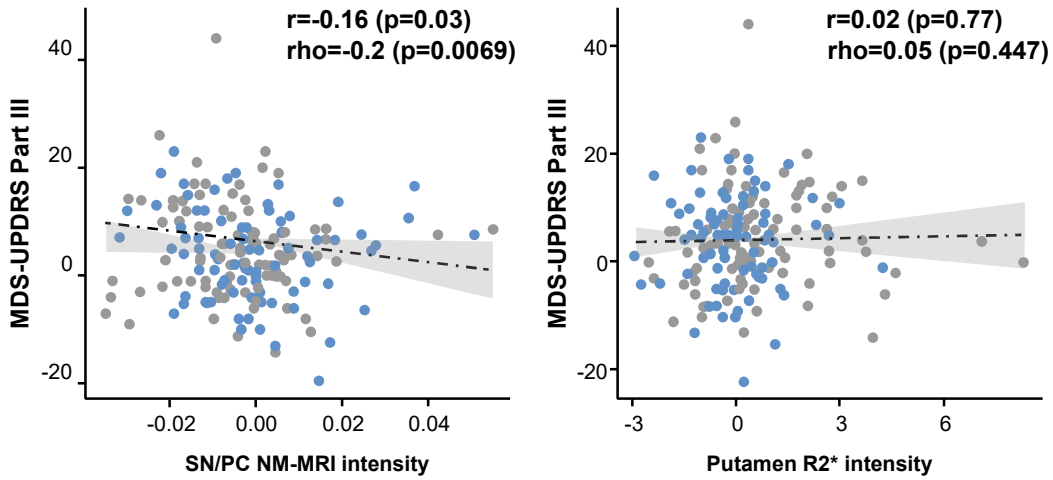
Biomarker evidence suggests impact on underlying disease pathology

Imaging biomarkers show biological convergence of common pathways and potential link to clinical changes

Biological convergence of imaging biomarker results at baseline (NM ↔ Iron ↔ DaT-SPECT)



Longitudinal NM MRI changes correlate with MDS-UPDRS III



- Individuals with slowed decrease of NM-MRI also progressed slower on MDS-UPDRS III
- Cross-sectionally, these correlations were not observed

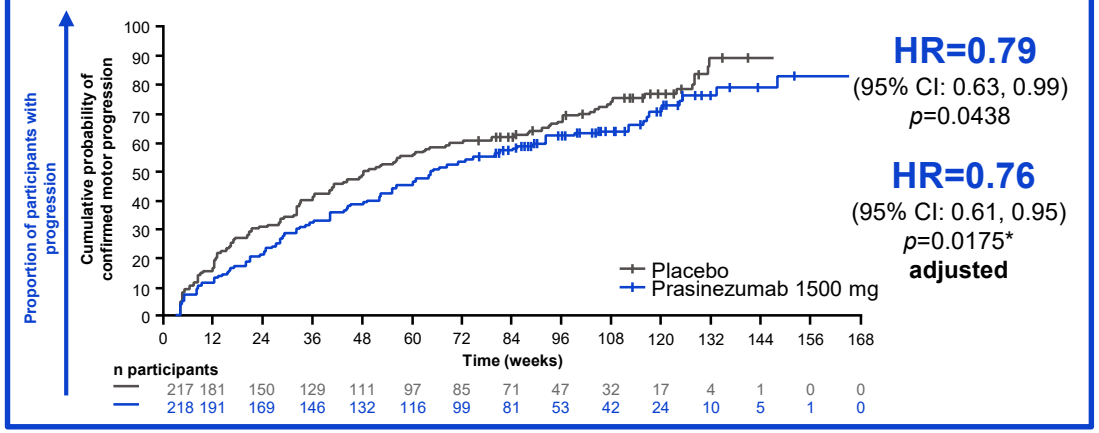
Prasinezumab's Impact on Neuromelanin- and Iron-sensitive MRI Biomarkers in Parkinson's Disease: Findings From the PADOVA Phase IIb Study
Kustermann T, et al. **Poster Hall, 17–19 Mar**

*p<0.05 (Spearman rank correlation).
DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; NM, neuromelanin; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MRI, magnetic resonance imaging; PD, Parkinson's disease; r, Pearson correlation; rho, Spearman rank correlation; SN/PC, substantia nigra pars compacta.

Treatment effect more pronounced in the prespecified L-DOPA subgroup

Time to confirmed motor event (MDS-UPDRS Part III *OFF*)

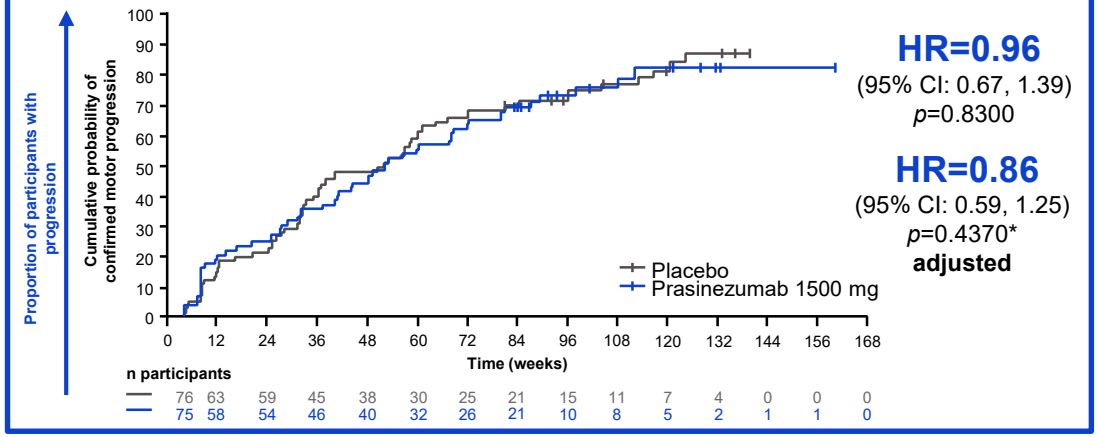
L-DOPA



HR=0.79
(95% CI: 0.63, 0.99)
p=0.0438

HR=0.76
(95% CI: 0.61, 0.95)
p=0.0175*
adjusted

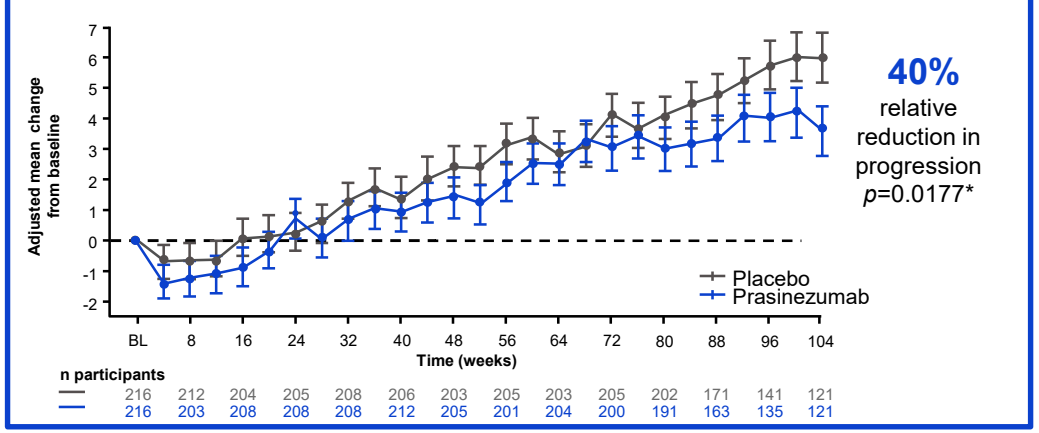
MAO-Bi



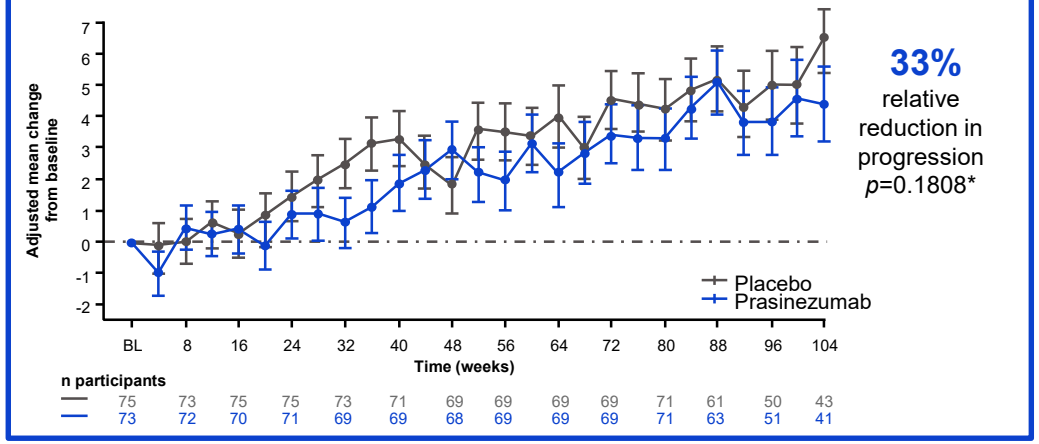
HR=0.96
(95% CI: 0.67, 1.39)
p=0.8300

HR=0.86
(95% CI: 0.59, 1.25)
p=0.4370*
adjusted

Change from Baseline to Week 104 MDS-UPDRS Part III *OFF*



40%
relative reduction in progression
p=0.0177*



33%
relative reduction in progression
p=0.1808*

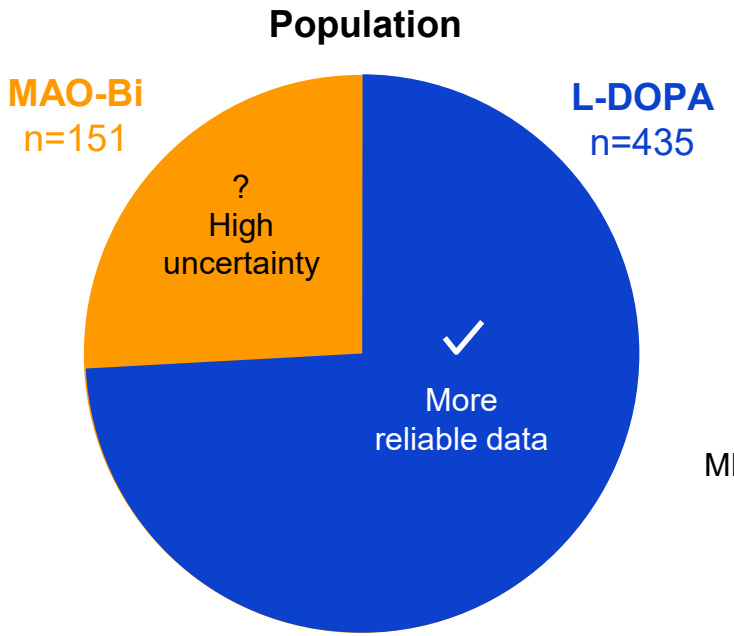
Covariates used for adjustment: H&Y stage (1 vs ≥2), DaT-SPECT putamen ipsilateral, age (<60 vs ≥60), sex (male vs female), BL MDS-UPDRS Part III. The intercurrent events of treatment discontinuation and LEDD increase prior to event are handled with the treatment policy strategy. *For descriptive purposes, nominal p-values are displayed.

BL, baseline; CI, confidence interval; DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; H&Y, Hoehn & Yahr; HR, hazard ratio; L-DOPA, levodopa; LEDD, levodopa equivalent daily dose; MAO-Bi, monoamine oxidase type B inhibitor; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale.

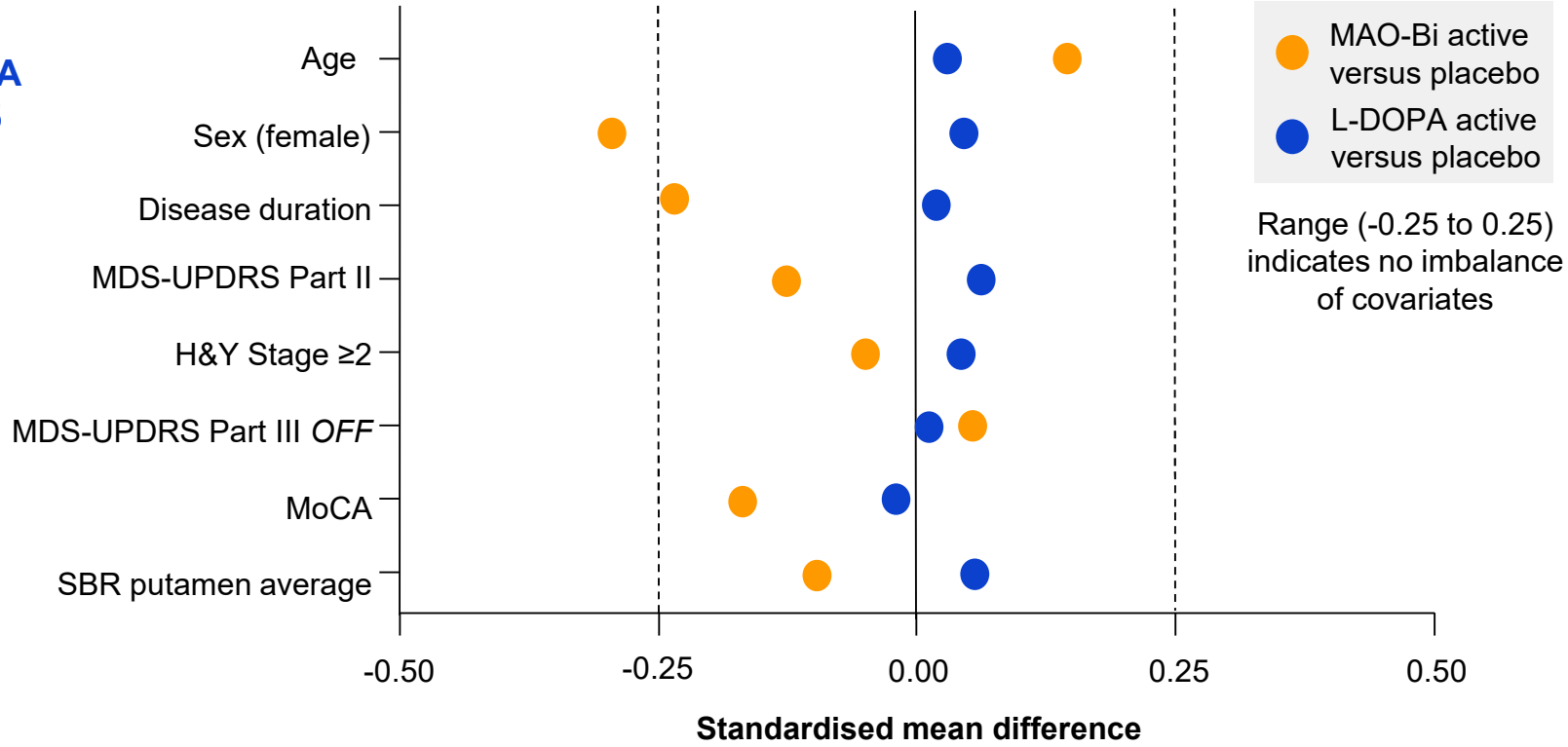
Subgroup outcomes impacted by sample size and baseline balance

L-DOPA cohort provides robust signal; MAO-Bi data limited by sample size

Sample size constraints



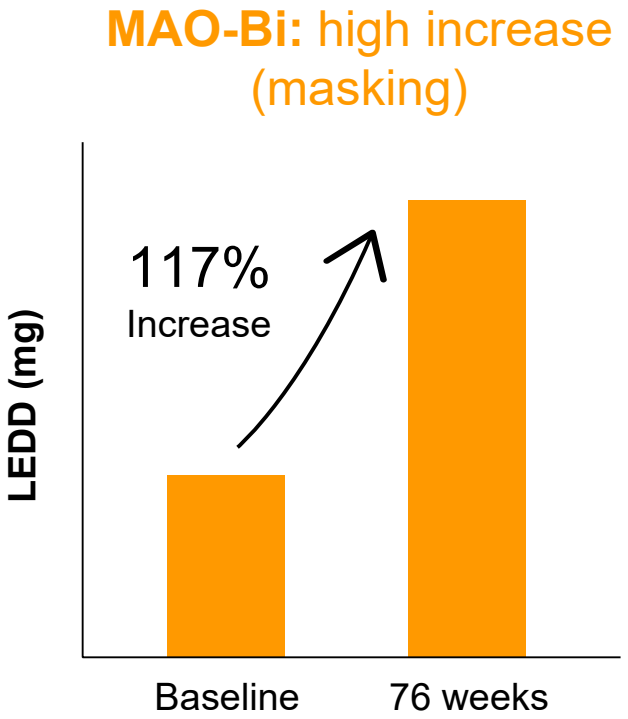
Baseline imbalances

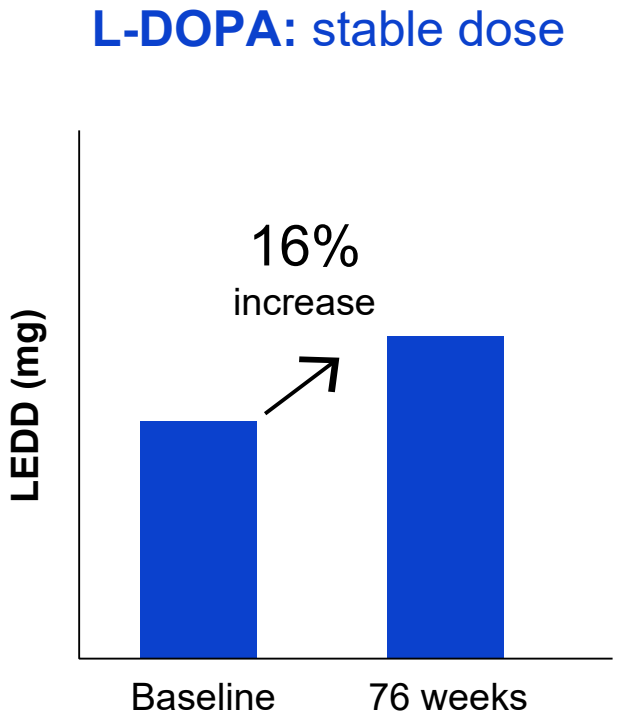


H&Y, Hoehn and Yahr; L-DOPA, levodopa; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MAO-Bi, monoamine oxidase type B inhibitor; MoCA, Montreal Cognitive Assessment; SBR, specific binding ratio.

Large increase in background therapy masked effect in MAO-Bi subgroup

Symptomatic treatment adjustments likely confounded the efficacy signal in this subgroup



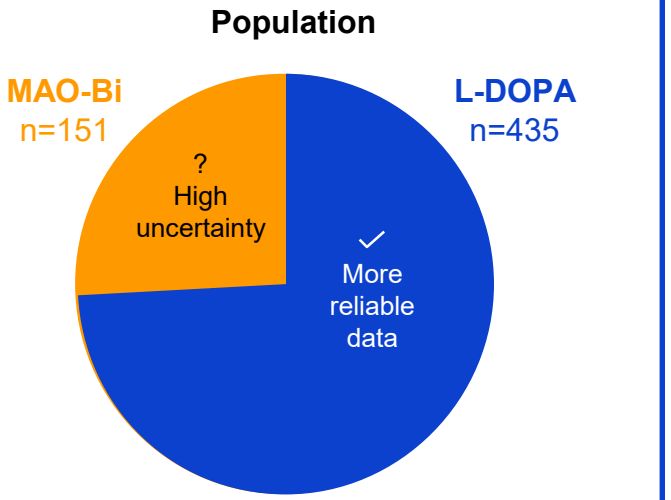


L-DOPA, levodopa; LEDD, levodopa equivalent daily dose; MAO-Bi, monoamine oxidase type B inhibitor.

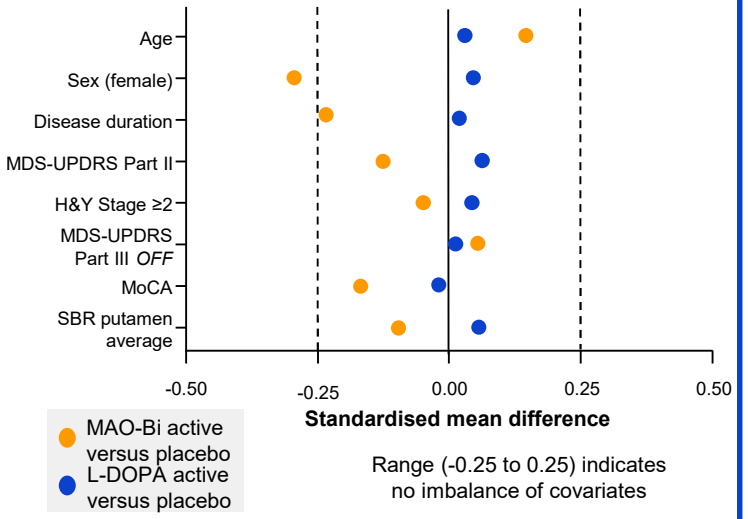
L-DOPA subgroup provides reliable signal of efficacy

Methodological reasons likely contributed to lower treatment effect in MAO-Bi subgroup

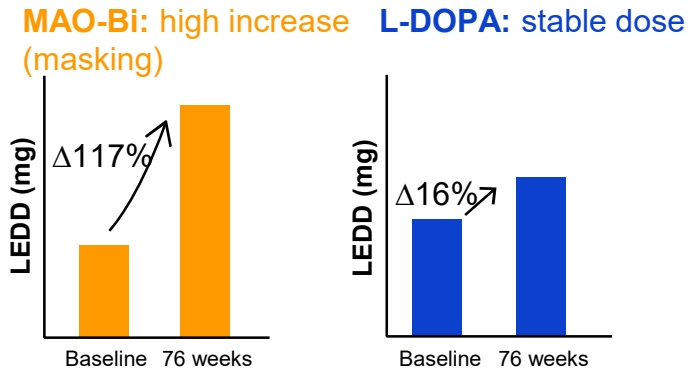
Sample size constraints



Baseline imbalances



Symptomatic masking



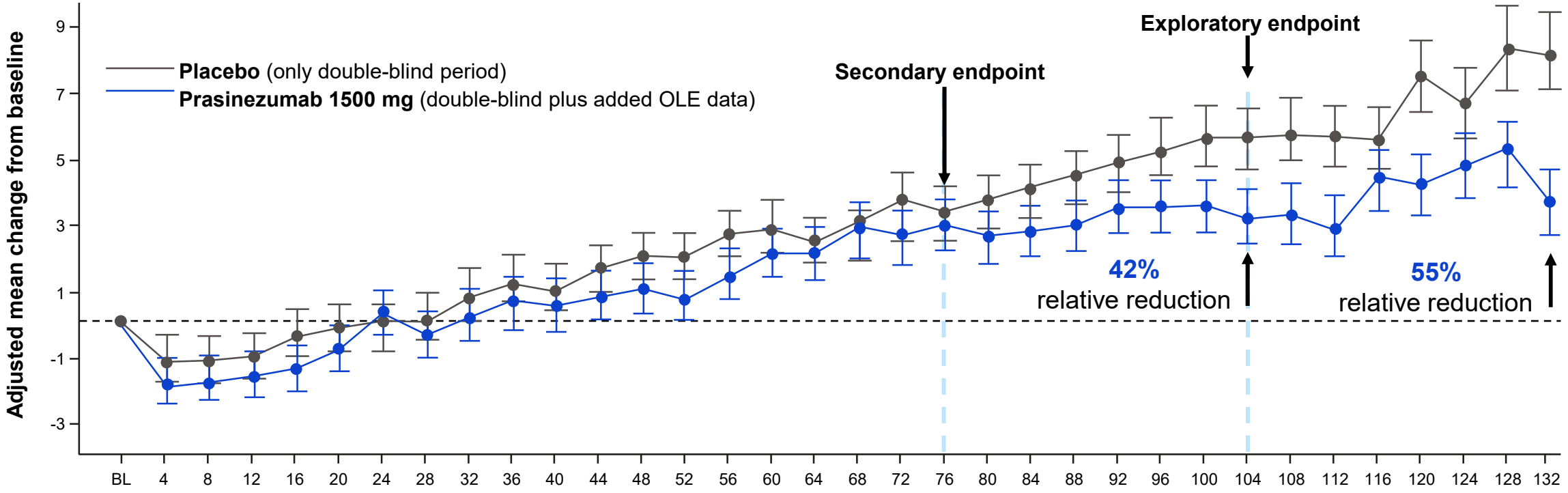
Potential treatment effect masked

Reliable treatment effect

H&Y, Hoehn and Yahr; L-DOPA, levodopa; LEDD, levodopa equivalent daily dose; MAO-Bi, monoamine oxidase type B inhibitor; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment; SBR, specific binding ratio.

Persistent reduction of motor progression: 6-month OLE

Consistently stronger signal in L-DOPA subgroup over 2.5 years; mirrors PASADENA results



Participants at risk

Placebo	216	208	212	204	204	208	205	208	208	209	206	208	203	209	205	206	203	199	205	196	202	188	171	153	141	134	121	112	98	87	74	64	52	38
Prasinezumab	216	212	203	209	208	208	208	209	208	204	212	207	205	203	201	203	204	201	200	197	191	188	165	157	152	145	144	129	127	114	88	82	76	59

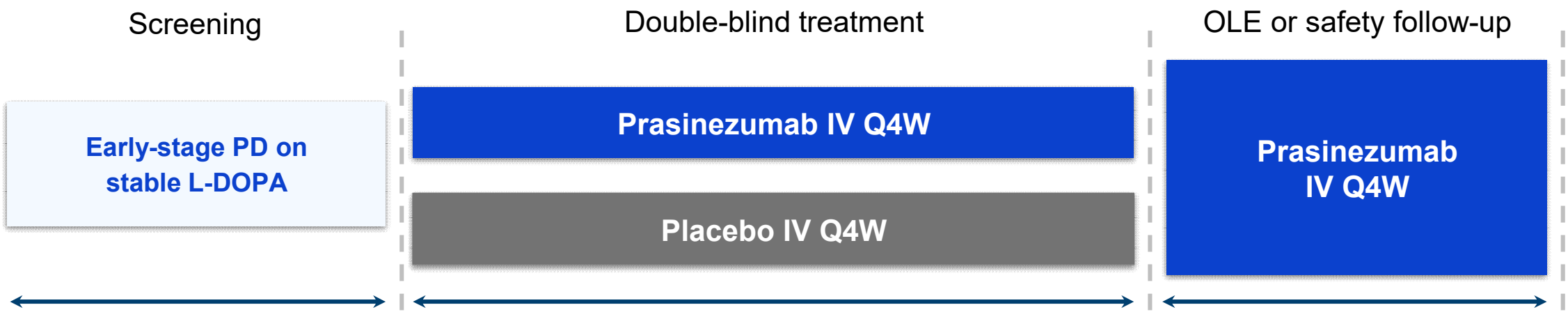
Modeling PD Progression To Quantify Long-Term Treatment Effects
Ribba B, et al.
Thurs 19 Mar, 15:35 PM, Hall A3

Sustained Effect of Prasinezumab on Parkinson's Disease Motor Progression in the Open-label Extension of the PASADENA Trial 5-year Update
Gullotta F, et al. **Poster Hall, 17–19 Mar**

Covariates used for adjustment in MMRM model: medication at baseline (MAO-Bi vs L-DOPA), H&Y stage (1 vs ≥2), DaT-SPECT putamen ipsilateral, age (<60 vs ≥60), sex (male vs female), MDS-UPDRS Part III.
BL, baseline; DaT-SPECT, dopamine transporter imaging with single-photon emission computed tomography; H&Y, Hoehn & Yahr; L-DOPA, levodopa; MAO-Bi, monoamine oxidase type B inhibitor; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; MMRM, Mixed Model for Repeated Measures; OLE, open-label extension.

PARAISO builds on learnings from the PADOVA trial

Global Phase III study will randomise ~900 participants across 18 locations

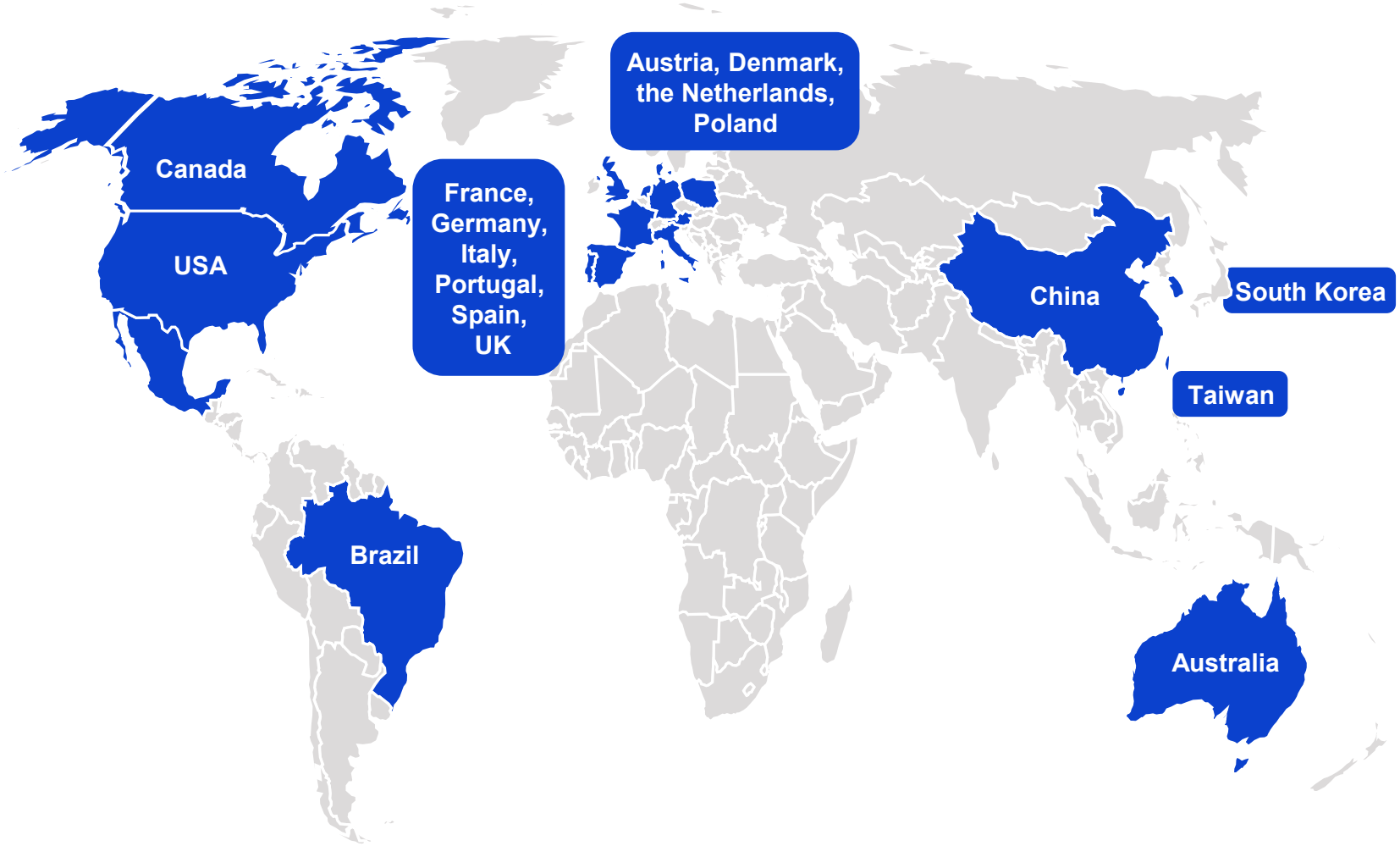


Primary endpoint Time to confirmed motor progression (MDS-UPDRS Part III *OFF**)

The mentioned compounds and their use are investigational and have not yet received regulatory approval in any country.
*Practically defined OFF-medication state (≥12 hours since the last dose of L-DOPA).
IV, intravenous; L-DOPA, levodopa; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; OLE, open-label extension; PD, Parkinson's disease; Q4W, every 4 weeks.
ClinicalTrials.gov. NCT07174310. PARAISO Phase III clinical trial. Available at: https://clinicaltrials.gov/study/NCT07174310 (last accessed 29 January 2026).

PARAISO: global study now recruiting

Global Phase III study will randomise ~900 participants across 18 locations



ClinicalTrials.gov. NCT07174310. PARAISO Phase III clinical trial. Available at: https://clinicaltrials.gov/study/NCT07174310 (last accessed 29 January 2026).

Summary

Prasinezumab demonstrates potential to delay Parkinson's progression

- Delayed motor progression on top of effective symptomatic therapy
- First biomarker evidence of impact underlying disease pathology
- Clinical signal maintained through 6-month open-label extension
- Favourable safety and tolerability profile confirmed

Phase III PARAISO trial underway, optimised by PADOVA insights

Acknowledgements

We thank all the study participants and their families, and investigators and site staff, for their time and commitment to the prasinezumab clinical development programme

https://go.roche.link/bcjhx4