

# Digital Health Technology Detects Group Differences in Practically-Defined OFF-L-DOPA State: Results of PADOVA PH IIb Study of PRASINEZUMAB



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## What does this mean for the Parkinson's community?

- Prasinezumab is a monoclonal antibody that binds extracellular alpha-synuclein and aims to slow down the relentless progression of PD.
- The present post-hoc results indicate that the probability of detecting treatment effects may be increased when DHT data are collected in the practically-defined OFF L-DOPA state, as is standardly done for the in clinic MDS-UPDRS Part III examination. This hypothesis requires confirmation in a prospective study.

## Objectives

To report motor progression in the PADOVA trial—a study of prasinezumab in early-stage Parkinson's disease.

Progression was captured via the Roche PD Mobile Application, a Digital Health Technology (DHT) tool, in participants maintained on stable MAO-Bi or L-DOPA monotherapy<sup>1</sup>.

## Methodology

- 586 participants (74% L-DOPA; 26% MAO-Bi) received monthly doses of prasinezumab (n = 293) or placebo (n = 293) until ≥ 248 primary events occurred and all completed ≥ 76 study weeks [Table 1].

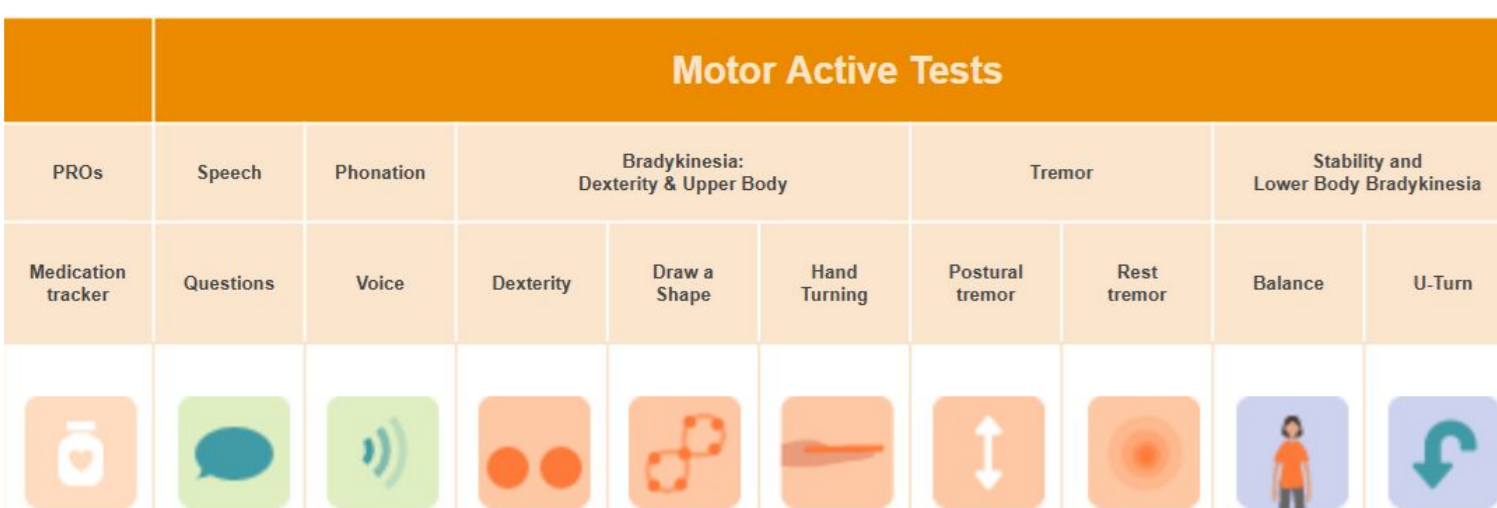
**Table 1. Baseline characteristics of PADOVA MAO-Bi, L-DOPA subgroups, and full analysis set (FAS) with digital data.**

If not otherwise indicated, means (SDs) are shown.

Variable	MAO-Bi	L-DOPA	FAS
n	136	387	523
Age (y)	62.7 (6.6)	64.9 (7.5)	64.4 (7.3)
Gender (% M)	65.4%	62.5%	63.3%
H&Y stage = 1	22.1%	11.3%	14.2%
H&Y stage >=2	77.9%	88.6%	85.8%
MDS-UPDRS part III (OFF)	22.8(10.3)	25.0 (10.4)	24.4 (10.4)
MDS-UPDRS part III (ON)	NA	19.1 (9.5)	19.1 (9.5)

- Participants performed daily active motor tasks on provisioned study smartphones at home, and input when they last took medication [Figure 1].

**Figure 1. Roche PD Mobile Application.**



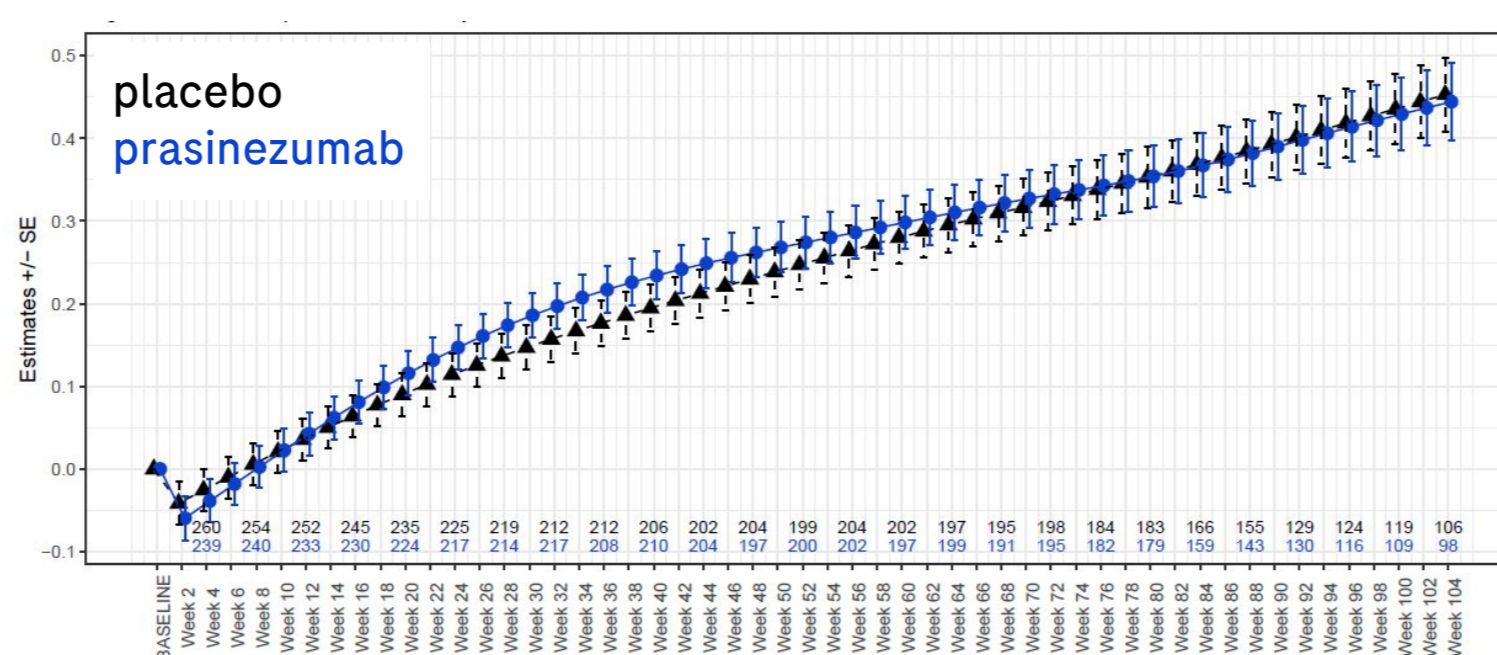
- DHT outcome measures included summary global motor ('Simple Sum') and Bradykinesia scores, as well as individual 'features' for each active task.
- Pre-specified** measures (cf. Table 2) were analyzed as 2-week aggregates in the FAS.
- All analyses used generalized additive mixed models (GAMMs) or mixed models for repeated measures (MMRMs) tested for effects of prasinezumab on changes from baseline to 72 and 104 weeks in treatment policy, covarying baseline value, symptomatic medication at randomization, and baseline Hoehn and Yahr stage, contralateral putaminal DaT-SPECT ratio, age group (< 60 years vs. ≥ 60 years) and sex.
- Since PwPD typically take L-DOPA several times daily, all data were assumed to be collected in a practically-defined ON state (i.e. 1-10h post intake); unexpectedly, PwPD on L-DOPA monotherapy collected 40% of at-home data in practically-defined OFF state.
- Therefore, **post-hoc analyses** also examined all scores in the L-DOPA population, split by practically-defined ON/OFF states (requiring 8-week aggregates).

## Results: pre-specified analyses in Full Analysis Set (FAS)

- Analyses of the **prespecified features** showed no robust group differences in progression (all p>.05) [Table 2] [Figure 2]. Similar results were found in the MAO-Bi and L-DOPA subgroups.

**Figure 2. No group difference in Bradykinesia Score progression in FAS.**

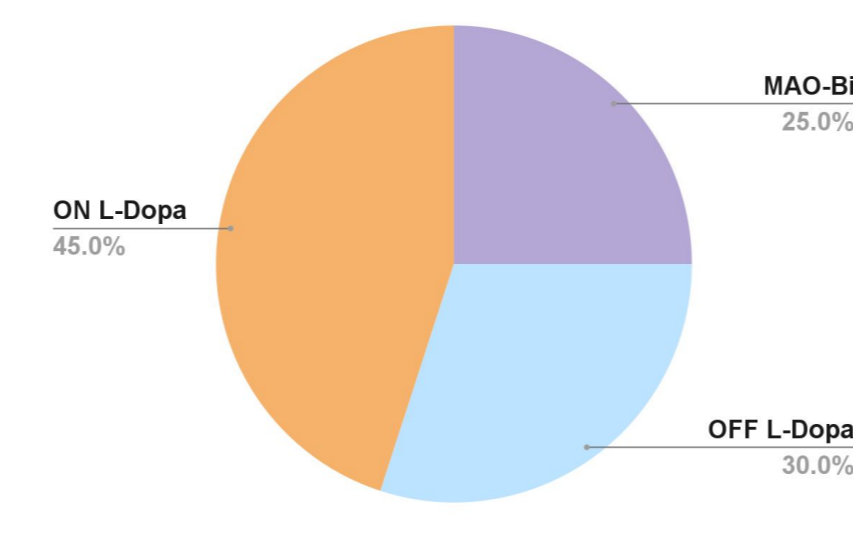
GAMM-estimated mean change from baseline to week 104 (standard error bars) are shown. Bottom: sample sizes, per group and time point



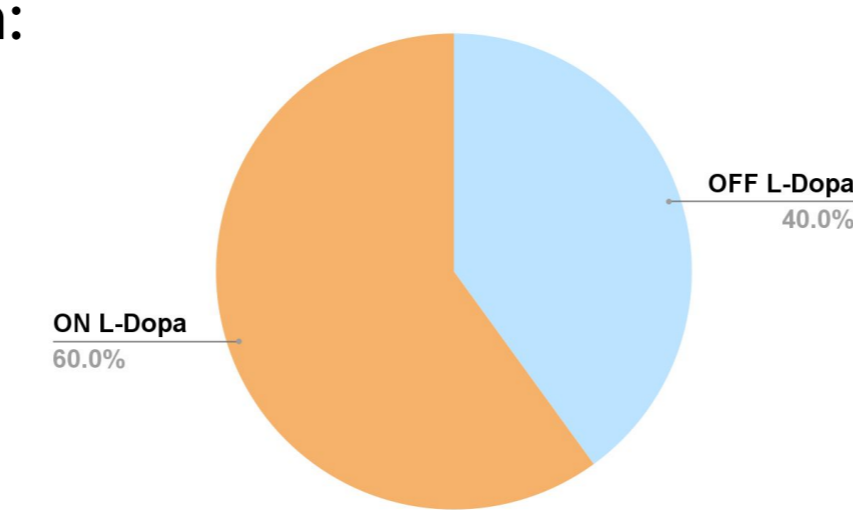
- The results of a pre-specified analysis of proportion of data collected in the practically-defined ON and OFF states are shown in **Figure 3**.

**Figure 3. Proportion of digital data collected in practically-defined OFF and ON L-DOPA states.**

A: FAS population:



B: L-DOPA population:



**Table 2. Prasinezumab vs. placebo progression in FAS, L-DOPA OFF+ON, and in L-DOPA OFF and ON state data separately.**

Nominal p-values from GAMMs comparing group differences in progression of digital scores. All group differences p < .2 favored the prasinezumab group.

Score	FAS population		L-DOPA group					
	76	104	Time point (week)					
			OFF+ON		OFF		ON	
76	104	72	104	72	104	72	104	
Simple sum (as in PASADENA <sup>2</sup> )	.06	.07	.14	.18	.02	.03	.78	.88
Bradykinesia score	.82	.65	.82	.65	.10	.13	.52	.45
HT - Median turn speed	.58	.83	.74	.45	.55	.94	.50	.14
HT - Median turn amplitude	.97	.98	.60	.89	.51	1.00	.99	.78
ST - CoV intertap interval	.70	.80	.71	.47	.37	.06	.92	.90
UT - Median turn speed	.07	.09	.38	.36	.66	.52	.58	.81
UT - CoV step time	.32	.46	.76	.87	.43	.48	.56	.86
RT - Total power	0.21 <sup>a</sup>	.064 <sup>a</sup>	.14 <sup>a</sup>	.02 <sup>a</sup>	.015	.007	.59	.96
PT - Total power	.03	.03	.051	.058	.059	.11	.61	.56

<sup>a</sup>MMRM results. CoV, coefficient of variation; HT, Hand Turning; PT, Postural Tremor; RT, Rest Tremor; ST, Speeded Tapping (Dexterity); UT, U-Turn.

## Conclusions

- DHT data collected at home during the PADOVA study comprised a mixture of data collected in the practically-defined ON and OFF states.
- When analyzed separately, nominal and early group differences in progression favoring prasinezumab were observed in the OFF but not ON L-DOPA states for global motor and tremor progression.
- These post-hoc findings, which require confirmation in a prospective study with larger sample sizes, are supportive of the PADOVA in-clinic MDS-UPDRS Part III OFF results.

## Results: post-hoc analyses of L-DOPA subgroup only

**Table 3. Baseline characteristics of digital L-DOPA subgroups.**

Means (SDs) are shown.

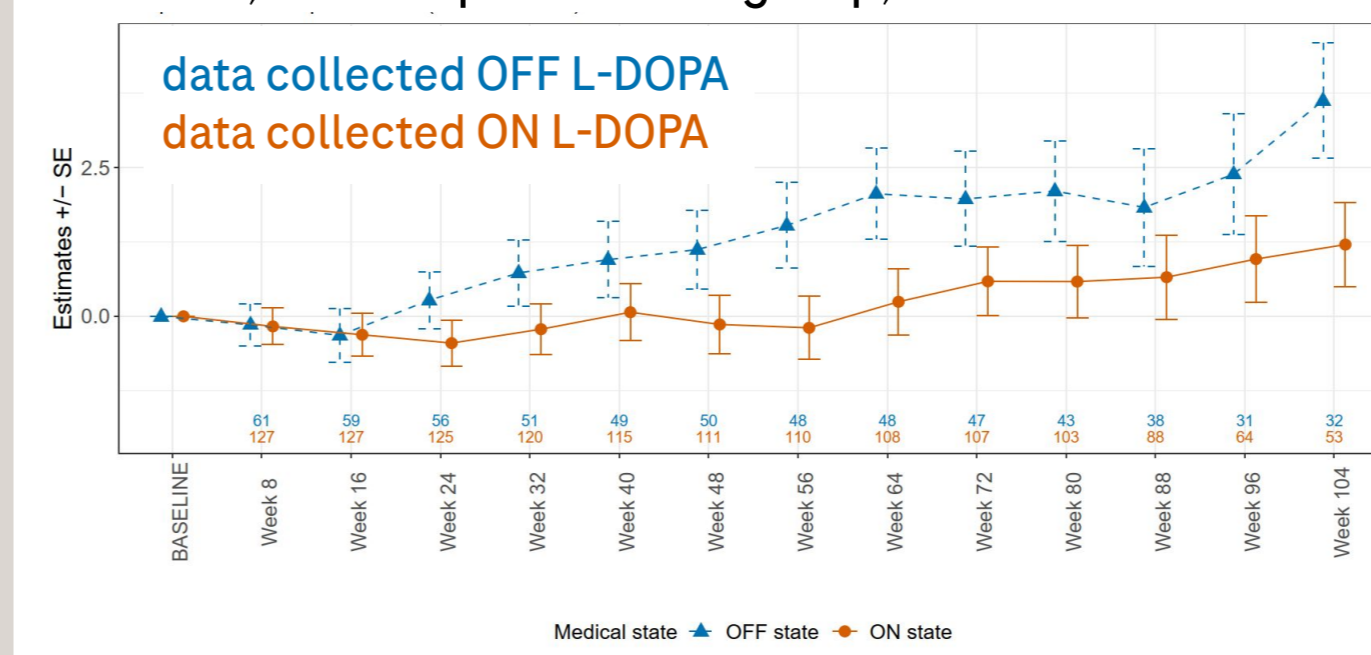
Variable	L-DOPA subgroup		
	placebo	prasi	all
n	71	67	138
Age (y)	66.5 (7.7)	65.7 (6.9)	66.1 (7.3)
Gender (% M)	62.0%	67.2%	64.5%
H&Y stage = 1	15.5%	8.9%	12.3%
H&Y stage >=2	84.5%	91.1%	87.7%
MDS-UPDRS part III (OFF)	25.7 (12.9)	26.57 (10.4)	26.2 (11.7)
MDS-UPDRS part III (ON)	20.5 (11.6)	20.2 (10.0)	20.3 (10.8)
Tremor dominant (%)	57.7%	52.2%	55.1%

<sup>a</sup>Individuals can be represented in both ON and OFF datasets.

- L-DOPA placebo subgroup progression was greater in digital data collected in the OFF compared to ON L-DOPA states [Figure 4], similar to OFF/ON progression rates in MDS-UPDRS Part III scores<sup>3</sup>

**Figure 4. Progression of global motor signs (Simple Sum score) measured in the practically-defined OFF vs. ON state)**

MMRM; L-DOPA placebo subgroup; standard error bars.



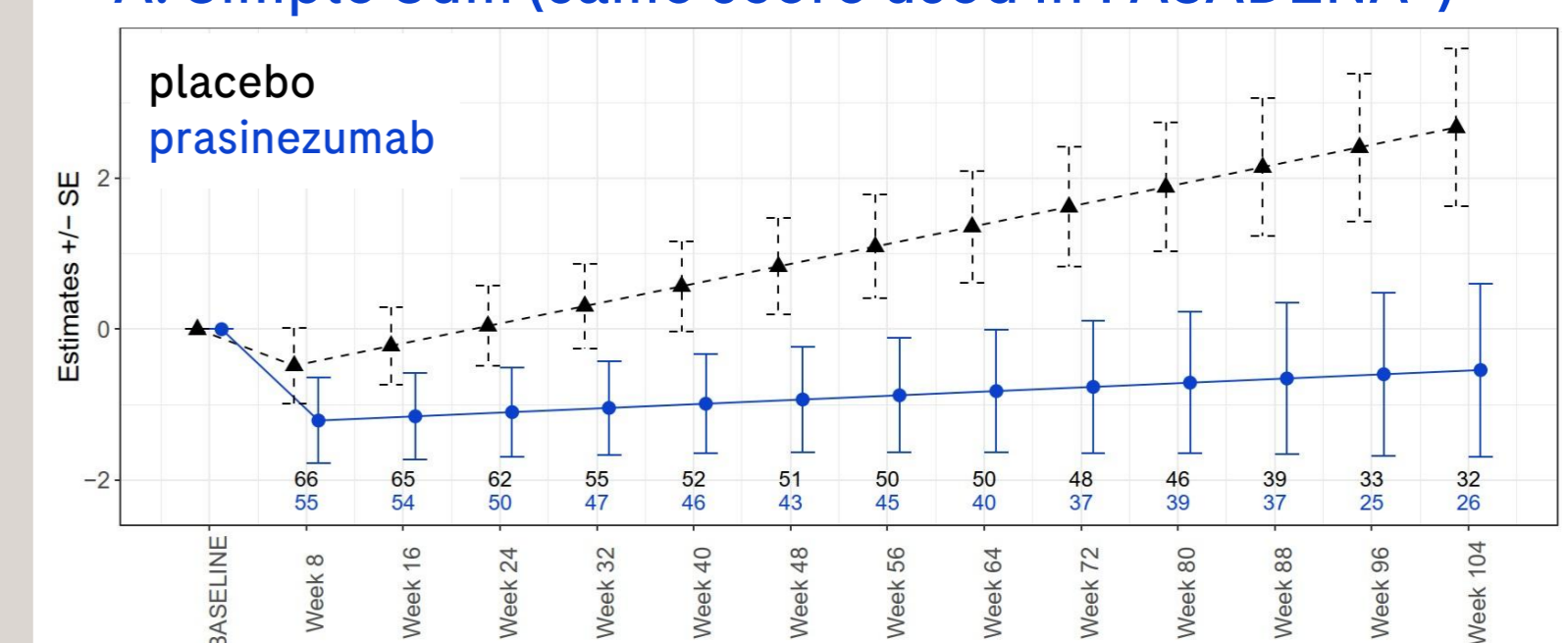
- Post-hoc analyses in the L-DOPA population showed nominal group differences favoring prasinezumab in data collected in OFF but not in the ON state [Table 2] [Figure 5].

## Post-hoc results (cont.)

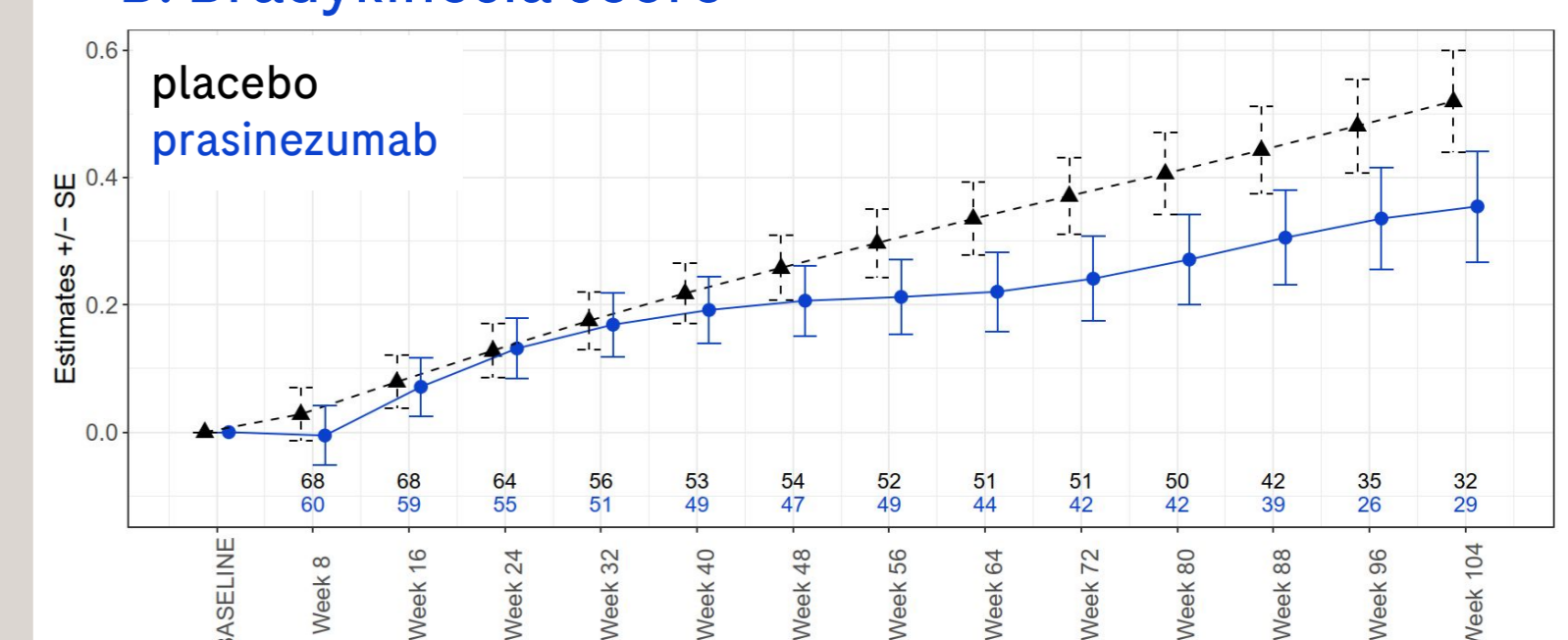
**Figure 5. GAMM models of progression of L-DOPA subgroup digital data collected in OFF state.**

Estimated mean change from baseline to week 104 (standard error bars) for select digital scores and features (A-D). Bottom: sample sizes, per group and time point.

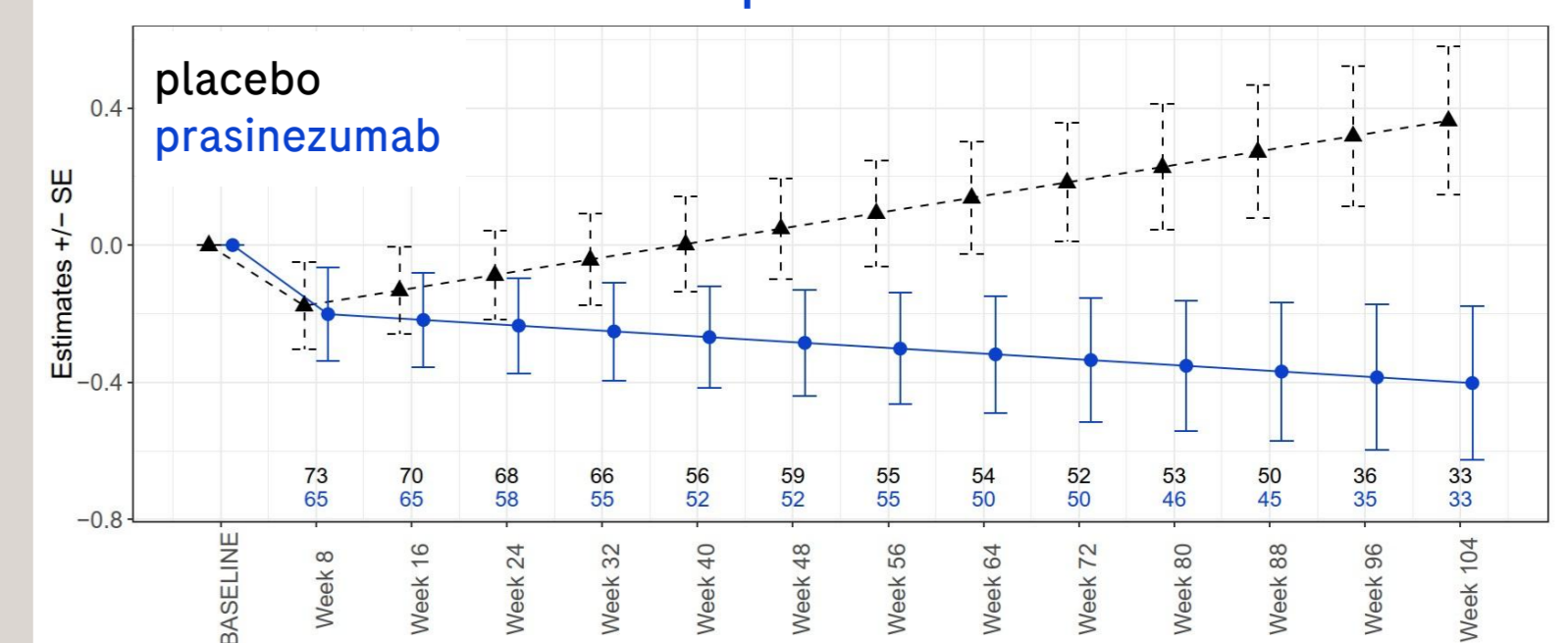
**A: Simple Sum (same score used in PASADENA<sup>2</sup>)**



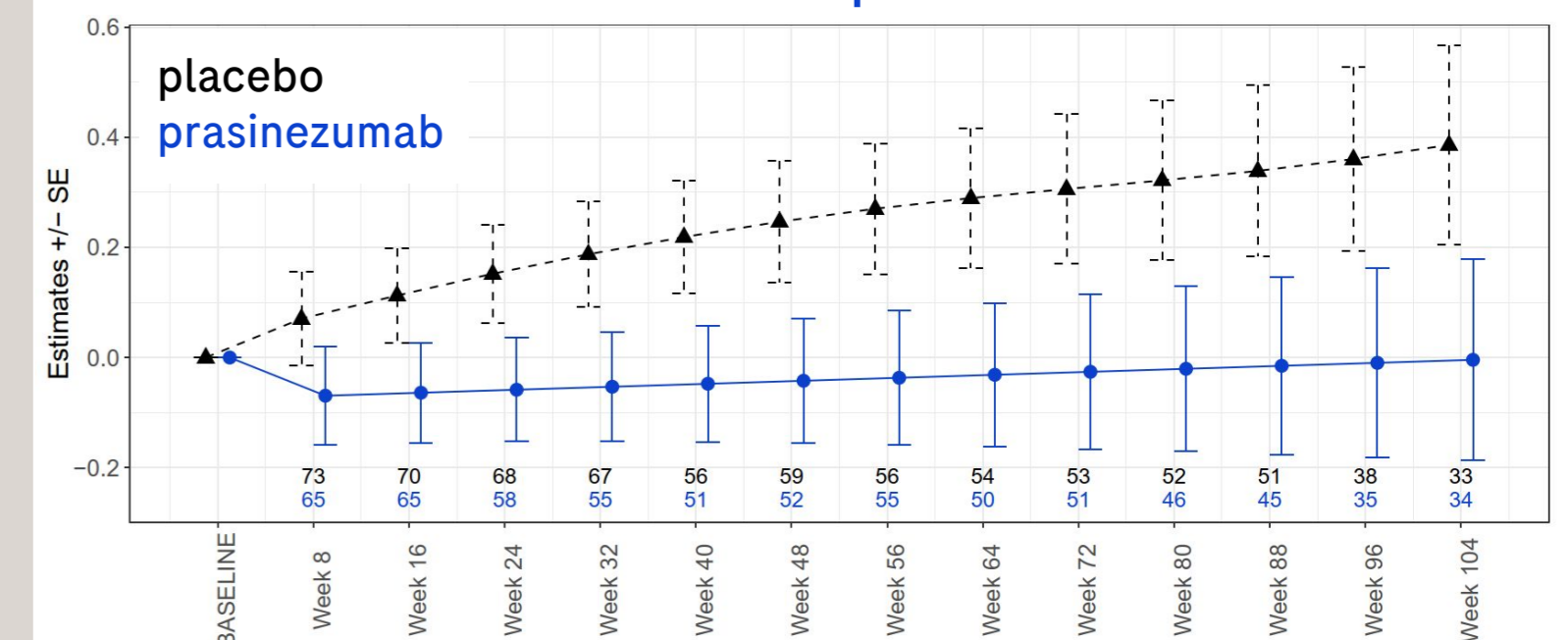
**B: Bradykinesia score**



**C: Rest Tremor - total power**



**D: Postural Tremor - total power**



## Discussion

- The prespecified analyses of remotely collected digital data in the PADOVA study showed no differences between placebo and prasinezumab progression.
- The digital data collected at home contained an unexpected mixture of data collected in the practically-defined OFF and ON states (L-DOPA group). Consistent with known clinical findings<sup>3</sup>, progression was greater in OFF than in ON scores.
- Post-hoc analyses of L-DOPA group OFF, but not ON, DHT data showed nominal group differences in motor sign progression favoring prasinezumab. These differences were apparent early and most pronounced in the global motor Simple Sum and tremor scores.
- These results support the PADOVA in-clinic OFF MDS-UPDRS Part III findings.
- The post-hoc findings require confirmation in a prospective study with larger cohorts.

## References

- Nikolcheva, T., et al. *Mov Disord.* 2025; 40 (suppl 1).
- Taylor, K. I., et al. *NPJ Digit. Med.* 2025, 8(1), 365.
- Simuni, T. et al. *Mov Disord.* 2018; 33, 771-782.

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## Disclosures

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