Safety and efficacy of P2B001 (low dose combination of extended-release pramipexole and rasagiline) in patients with early Parkinson's disease: Subgroup analyses from a Phase 3 randomized, controlled trial

For all baseline ages and disease severities, P2B001 provides consistent symptomatic control with comparable efficacy to marketed titrated PramiER, yet with reduced excessive daytime sleepiness

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Objectives

Evaluate the efficacy and safety of P2B001 for different subgroups of patients with early Parkinson's disease (PD).

Background

P2B001 is an investigational, fixed low-dose, once-daily combination of ER formulations of pramipexole and rasagiline (0.6/0.75mg). We have previously reported that P2B001 provided significantly superior symptomatic efficacy compared with each of its components, as well as comparable efficacy to optimally titrated marketed pramipexole-ER (PramiER), with reduced levels of excessive daytime sleepiness. Here, we evaluated the efficacy and safety of P2B001 in subgroups of patients categorized by age and baseline severity.

Methods

This was an international, multicenter, randomized, double-blind, parallel-group study in adult patients (35–80y) with early, untreated PD (<3y from diagnosis) comparing once-daily P2B001 with its individual components and to optimally titrated PramiER (mean dose of 3.2mg). Subgroups were categorized by age (≤median of 66 y vs. >median of 66 y) and baseline severity (≤median of 29 vs. >median of 29 on UPDRS Part II+III scores).

Results

The efficacy and safety profile of P2B001 was not significantly different in younger versus older patients, nor when patients were analyzed by baseline severity. Across all subgroups, P2B001 provided numerically greater symptomatic benefit versus its components, as assessed by Total-UPDRS and statistically significant greater benefit in Activities of Daily Living (UPDRS Part II) versus components. Comparable symptomatic efficacy versus marketed PramiER was confirmed in all subgroups, and P2B001 was consistently superior to PramiER on Epworth Sleepiness Scale scores. There were no apparent differences in the pattern or rates of treatment emergent adverse events or in discontinuation rates by subgroup.

Conclusions

For patients with different ages (younger vs older) and baseline symptom severities, these findings support consistent symptomatic control with P2B001, with comparable efficacy to marketed titrated PramiER, yet with reduced excessive daytime sleepiness.

Results

No meaningful differences in baseline characteristics between subgroups (all arms combined)

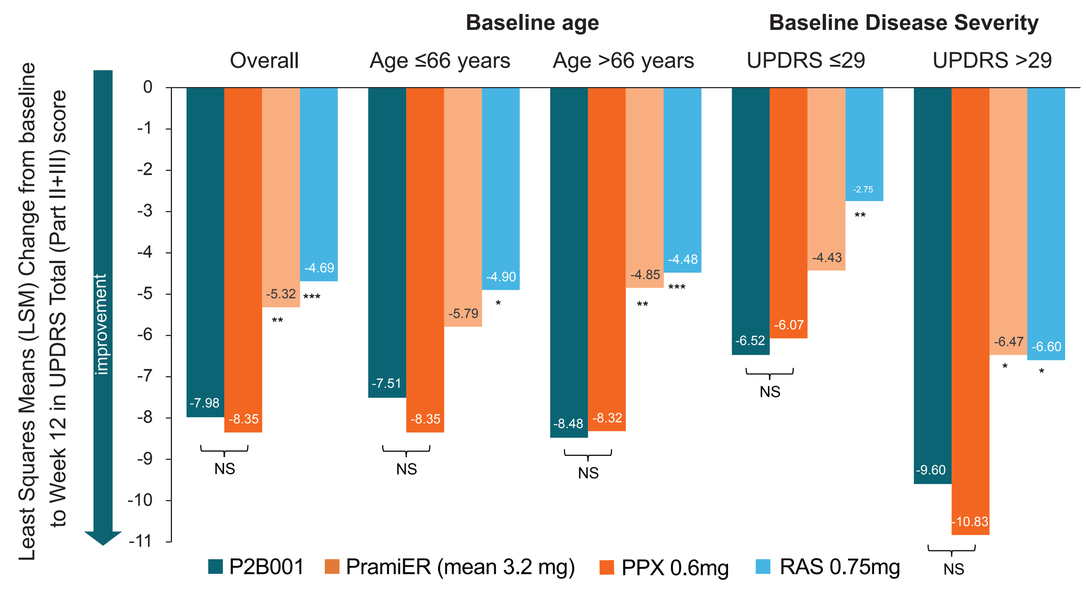
	Baseline age		Baseline Disease Severity		
	Age ≤66 years (n=261)	Age >66 years (n=246)	UPDRS-total ≤29 (n=256)	UPDRS-total >29 (n=251)	All (N=544)
Age, years ± SD	57.8 ± 6.5	72.1 ± 3.7	63.3 ± 9.1	66.3 ± 8.5	64.6± 9.1
Male, n (%)	172 (65.9%)	173 (70.3%)	170 (66.4%)	175 (69.7%)	369 (67.8%)
White, n (%)	247 (94.6%)	233 (94.7%)	239 (93.4%)	241 (96.0%)	516 (94.9%)
Time since diagnosis, months (SD)	5.6 ± 7.2	5.8 ± 7.6	5.4 ± 6.9	6.1 ± 7.9	5.2 ± 7.3
Modified Hoehn & Yahr stage (%)					
<2	29.5%	14.2%	34.8%	9.2%	22.3%
2	61.3%	70.7%	59.8%	72.1%	65.6%
2.5	9.2%	15.0%	5.4%	18.7%	11.6%
UPDRS Total score (SD)	29.0 ± 9.5	32.8 ± 10.7	23.1 ± 4.7	38.7 ± 8.4	30.8 ±10.3
UDPRS Part II ADL score (SD)	7.7 ± 3.6	8.5 ± 4.4	5.8 ± 2.5	10.4 ± 3.9	8.1± 4

Inclusion criteria: patients with PD; aged 35–80 years; Hoehn-Yahr <3; Disease duration <3 years from diagnosis; not on PD medication.

No apparent differences in the pattern or rates of treatment emergent adverse events (TEAEs) or in discontinuation rates by subgroup.

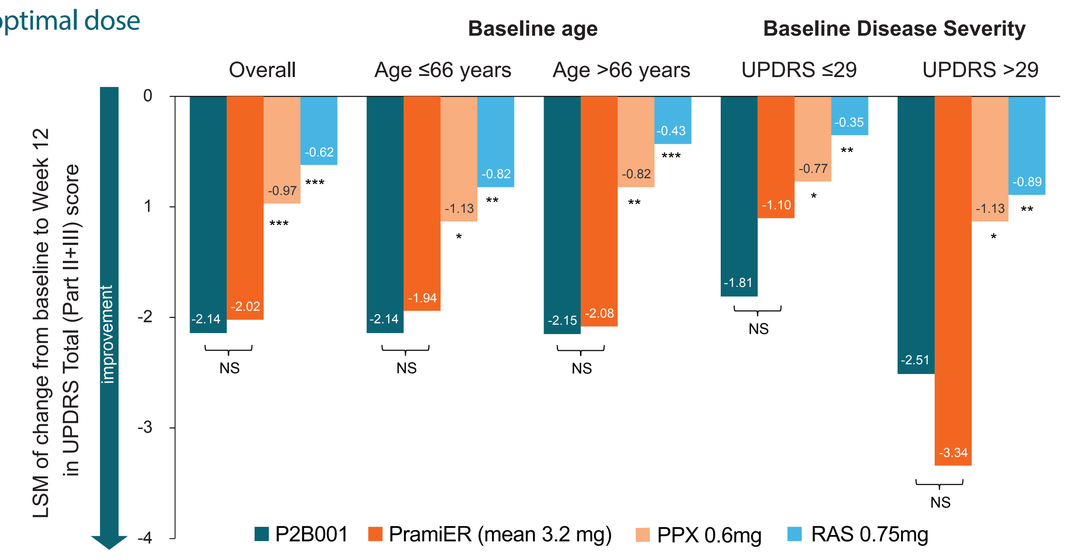
	Baseline age		Baseline Disease Severity		
	Age ≤66 years (n=268)	Age >66 years (n=251)	UPDRS-total ≤29 (n=262)	UPDRS-total >29 (n=256)	All (n=519)
All cause discontinuation					
P2B001	8 (10.4%)	5 (6.8%)	7 (9.0%)	6 (8.3%)	13 (8.7%)
PramiER	6 (14.6%)	1 (3.0%)	4 (8.9%)	3 (10.3%)	7 (9.5%)
PPX 0.6mg	6 (8.0%)	5 (6.8%)	4 (5.6%)	6 (8.0%)	11 (7.4%)
RAS 0.75mg	8 (10.7%)	5 (6.9%)	4 (6.0%)	9 (11.3%)	13 (8.8%)
Discontinued due TEAE					
P2B001	5 (6.5%)	3 (4.1%)	5 (6.4%)	3 (4.2%)	8 (5.3%)
PramiER	5 (12.2%)	0 (0%)	3 (6.7%)	2 (6.9%)	5 (6.8%)
PPX 0.6mg	3 (4.0%)	3 (4.1%)	3 (4.2%)	3 (4.0%)	6 (4.1%)
RAS 0.75mg	3 (4.0%)	1 (1.4%)	2 (3.0%)	2 (2.5%)	4 (2.7%)
≥1 TEAE					
P2B001	58 (75.3%)	54 (74.0%)	60 (76.9%)	52 (72.2%)	112 (74.7%)
PramiER	35 (85.4%)	29 (87.9%)	41 (91.1%)	23 (79.3%)	64 (86.5%)
PPX 0.6mg	55 (73.3%)	54 (74.0%)	52 (72.2%)	56 (74.7%)	109 (73.6%)
RAS 0.75mg	41 (54.7%)	46 (63.9%)	42 (62.7%)	45 (56.3%)	87 (59.2%)
≥1 Dopaminergic TEAE					
P2B001	38 (49.4%)	29 (39.7%)	32 (41.0%)	35 (48.6%)	67 (44.7%)
PramiER	28 (68.3%)	21 (63.6%)	32 (71.1%)	17 (58.6%)	49 (66.2%)
PPX 0.6mg	36 (48.0%)	36 (49.3%)	33 (45.8%)	39 (52.0%)	72 (48.6%)
RAS 0.75mg	25 (33.3%)	25 (34.7%)	26 (38.8%)	24 (30.0%)	50 (34.0%)

P2B001 provided consistently greater symptomatic benefit across all subgroups (UPDRS Total scores) versus its components and comparable efficacy versus marketed PramiER titrated to optimal dose



P values for differences of LSM between P2B001 and other treatments *p<0.05, **p<0.01, ***p≤0.001 vs P2B001. mITT population (patients who took ≥1 dose of study medication and had at least one measurement of UPDRS Total scores post baseline). Study was not powered for subgroup analyses.

P2B001 consistently provided significantly greater benefit across all subgroups in Activities of Daily Living (UPDRS Part II) versus components and comparable efficacy versus marketed PramiER titrated to optimal dose



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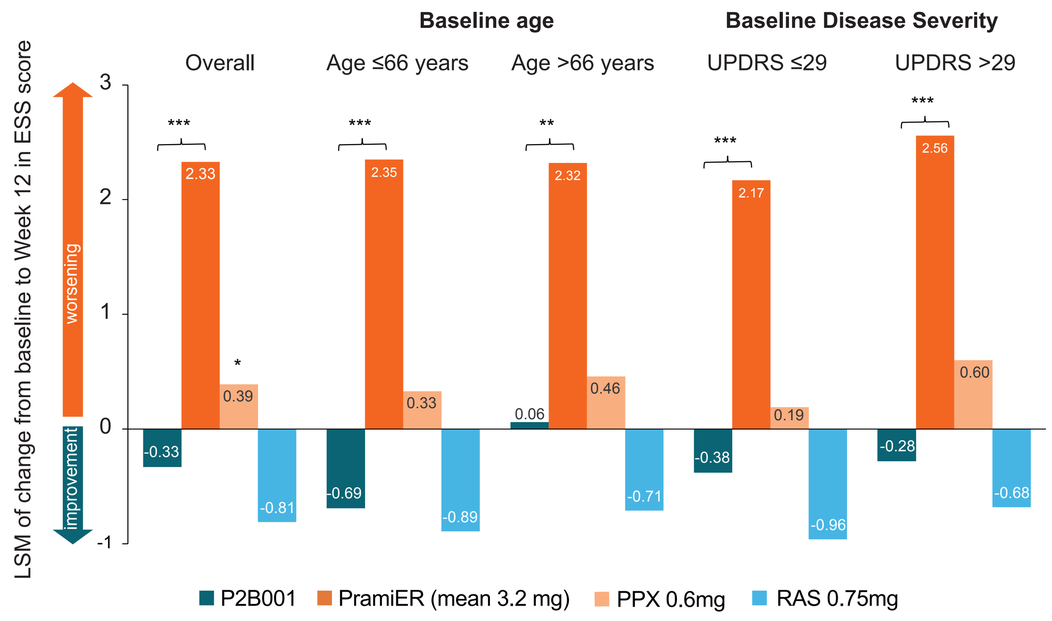
P2B001 was consistently superior to PramiER across all subgroups on Epworth Sleepiness Scale scores



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