Efficacy of P2B001 in patients with Early Parkinson's Disease: Analysis of an Integrated Phase 2b and 3 Database

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Objectives

Evaluate the efficacy of P2B001 versus placebo and marketed extended-release pramipexole (PramiER) in a pooled population of patients with early Parkinson's disease (PD) from phase 2b and 3 studies.

Background

- Conventional pharmacotherapy for people recently diagnosed with Parkinson's disease (PD) includes monotherapy with levodopa, a dopamine agonist, or an MAO-B inhibitor. The choice of initial therapy depends on the balance of providing symptomatic efficacy (lowest with MAO-B inhibitors and highest with levodopa) while minimizing common dopaminergic side-effects (lowest for MAO-B inhibitors and highest for dopamine agonists) and the risks for developing motor-complications (highest for levodopa).[1]
- P2B001 is an investigational, fixed-dose, once-daily, no titration, combination of low-dose, extended-release formulations of pramipexole and rasagiline (0.6/0.75mg), under investigation for patients with early PD.[2-4]
- The combination of pramipexole and rasagiline aims to improve striatal dopaminergic transmission via distinct and potentially synergistic mechanisms, while the lower doses allow for a favorable safety profile.[2]

Methods

- This was an integrated efficacy analysis of data from two randomized, controlled, 12-week studies of P2B001 in untreated PD patients:
  - Study 1 was a 12-week multicenter double-blind, placebo-controlled, phase 2b study (NCT01968460).[3]
  - Study 2 was a 12-week, double-blind, phase 3 study comparing P2B001 with its individual components or commercial doses of pramipexole-ER (PramiER) titrated to optimal dose (1.5–4.5 mg) (NCT03329508).[4]
- Eligible participants, in both studies, were adult (≥35 years old) male and females with early untreated PD, a disease duration <3 years from diagnosis, Hoehn & Yahr score <3, and mini-mental state examination (MMSE) score ≥26.
- Both studies included change from baseline to Week 12 in UPDRS Total scores as their primary endpoint (defined as the sum of Parts I-III in the phase 2b study and sum of Parts II+III in the phase 3 study) as well as assessment of Epworth Sleepiness Scale (ESS) scores (measured as a key secondary endpoint in the phase 3 study).
- For the purpose of this analysis UPDRS Total scores were defined as sum of Parts II+III [range 0–160].

Results

- The integrated modified-ITT analysis included 196 participants who received ≥1 dose of study drug and had ≥1 post-baseline UPDRS-Total score (Parts II+III) measurement (P2B001=196; placebo=50; PramiER=72).
- Baseline characteristics are provided in **Table 1**.

Table 1. Baseline characteristics

	Placebo (n=50)	P2B001 (n=196)	PramiER (n=72)
Age, years	64.6 ± 7.7	63.7 ± 9.1	63.9 ± 8.8
Male, n (%)	31 (62.0%)	136 (69.4%)	49 (68.1%)
White, n (%)	47 (94.0%)	186 (94.9%)	69 (95.8%)
Time since diagnosis, months	5.2 ± 7.7	5.9 ± 8.0	6.4 ± 8.4
UPDRS II+III	28.1 ± 9.2	29.7 ± 9.4	28.9 ± 10.1
Hoehn and Yahr, Stage 2 (%)	28 (56.0%)	130 (66.3%)	48 (66.7%)

- UPDRS results are shown in Figure 1. Results confirmed that 12-weeks treatment with P2B001 provided:
  - ✓ Significantly superior symptomatic efficacy on UPDRS Part II (ADL), Part III (Motor), and Total scores versus placebo.
  - ✓ Comparable efficacy to individually titrated PramiER.
- Patients treated with P2B001 had significantly less worsening in daytime-sleepiness than those treated with PramiER (**Figure 2a**) and significantly fewer patients shifted to excessive daytime sleepiness (ESS score >10) with P2B001 vs Prami-ER (**Figure 2b**).
- P2B001 was well-tolerated with an adverse event profile similar to placebo fewer sleep-related and dopaminergic adverse events than titrated doses of PramiER including somnolence, orthostatic hypotension, and neuropsychiatric side effects (**Table 2**).

Figure 1. P2B001 showed superior efficacy on UPDRS scores vs. placebo with comparable efficacy to PramiER*

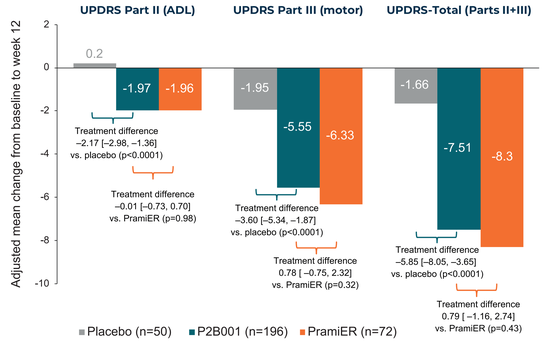
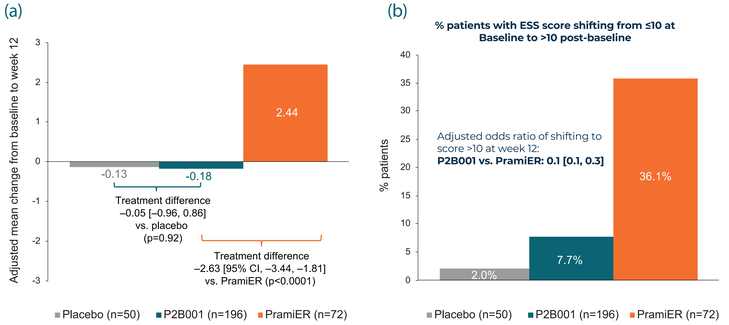


Figure 2: P2B001 had significantly less worsening in daytime-sleepiness than those treated with PramiER* (a) Change from baseline on ESS scores (b) % patients with ESS score shifting from ≤10 at baseline to >10 post-baseline**



*titrated optimized meand dose of PramiER 3.2 mg/day in Study 2
**the usual definition of excessive daytime sleepiness is an ESS score of 10 or more[5]

Conclusions

- These data support the potential of P2B001 as a first-line, once-daily treatment for people with early PD that requires no titration and has a favorable risk-benefit profile, including less daytime sleepiness, when compared to a conventional therapeutic option such as pramipexole ER

References

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