PD Patient Diaries Demonstrated ADS-5102 (Amantadine) Extended Release Capsules Improved ON Time Without Dyskinesia: Results From Pooled Phase 3 Clinical Trials

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Background

- ADS-5102 (amantadine) extended release capsules demonstrated improvement in both dyskinesia and OFF time in two phase 3 clinical trials and was approved as Gocovri® by the FDA for the treatment of levodopa induced dyskinesia (LID) in Parkinson's disease (PD) in 2017.[1,2,3]
- ADS-5102 is taken once daily at bedtime, and is specifically designed to provide high amantadine concentrations upon waking and throughout the day.[4]
- The pivotal trials demonstrated an improvement in "ON time without troublesome dyskinesia" (Good ON), a construct composed of two PD diary states: ON time without dyskinesia plus ON time with non-troublesome dyskinesia.

Good ON =	ON without dyskinesia	+	ON with non-troublesome dyskinesia

Objective

- To evaluate the extent to which ADS-5102–associated improvement in "ON without troublesome dyskinesia" resulted from an increase in ON without dyskinesia.

Methods

- Patients enrolled in phase 3 trials (EASE LID [NCT02136914] or EASE LID 3 [NCT02274766]) recorded time spent in the following PD diary states at baseline and endpoint (week 12): asleep, OFF, ON with troublesome dyskinesia, ON with non-troublesome dyskinesia, and ON without dyskinesia.
- We conducted mixed effect model repeat measurement (MMRM) analyses of the time spent in both ON with non-troublesome dyskinesia and ON without dyskinesia, following wake-up, for 162 of 198 (82%) enrolled patients (ADS-5102 n=85 and placebo n=77) with completed diaries at both timepoints, to evaluate changes in these states from baseline to week 12.
- Baseline demographics and PD characteristics for this patient population have been previously reported.[5]

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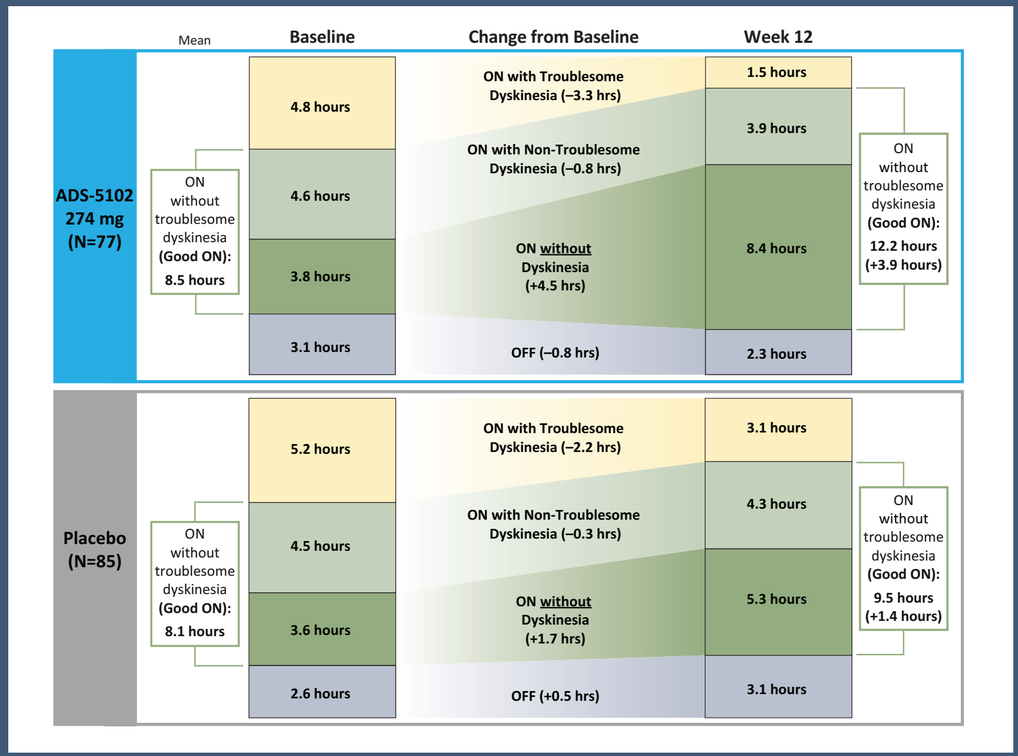
In Phase 3 trials ADS-5102 treatment more than doubled the time Parkinson's patients spent ON without dyskinesia



Results

- At baseline, patients experienced a mean 8.3 hours of Good ON (4.6 hours with non-troublesome dyskinesia + 3.7 hours ON without dyskinesia).
- At Week 12, Good ON increased by 3.9 hours to 12.2 hours for ADS-5102, vs a 1.4-hour increase to 9.5 hours for placebo [Central Figure].
- Moreover, the increase in Good ON with ADS-5102 was driven by time spent ON without dyskinesia (+4.5 hours) as opposed to ON with non-troublesome dyskinesia, which decreased (-0.8 hours).
  - Corresponding changes for placebo were +1.7 hours spent ON without dyskinesia and -0.3 hours ON with non-troublesome dyskinesia.
- As previously reported, ADS-5102 treatment also significantly reduced both OFF and troublesome dyskinesia.[5]
- Changes in diary states were significant for ADS-5102 vs placebo, as demonstrated by MMRM analyses [Table 1].
- The safety data for these phase 3 trials have been previously reported.[6]
  - The most common AEs for ADS-5102 (≥10% and more than placebo) were hallucination (21%), dizziness (16%), dry mouth (16%), peripheral edema (16%), constipation (13%), fall (13%), orthostatic hypotension (13%), urinary tract infection (10%).[3]

Table 1. MMRM Analysis of PD Diary Outcomes: Placebo-Adjusted Change from Baseline to Week 12 (N=162)

Diary State	LS mean (SE) treatment difference (hrs)	P-value
ON with troublesome dyskinesia	–1.5 (0.4)	<0.001
ON without troublesome dyskinesia	+2.5 (0.5)	<0.001
ON with non-troublesome dyskinesia	–0.5 (0.5)	0.298
ON without dyskinesia	+2.9 (0.6)	<0.001
OFF	–1.2 (0.3)	<0.001

Conclusion

- This post hoc analysis of PD diary data showed that ADS-5102 treatment more than doubled the daily time patients spent ON without dyskinesia.
- These results suggest that the ADS-5102 treatment effect to increase Good ON was driven by an increase in ON time without dyskinesia, as opposed to simply reducing the severity of dyskinesia from troublesome to non-troublesome.

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