54 Reduced Dyskinesia and OFF Time in PD Patients with DBS Following Switch From Amantadine IR to ADS-5102 (Amantadine) Extended Release Capsules: Analysis of 2-Year Open-Label Trial (EASE LID 2)

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Background

- ADS-5102 (amantadine) extended release capsules demonstrated significant improvement in both dyskinesia and OFF time in two phase 3 clinical trials, and was approved as Gocovri® by the FDA in 2017 for the treatment of levodopa induced dyskinesia (LID) in Parkinson's disease (PD).[1,2]
- ADS-5102 is taken once daily at bedtime and is specifically formulated to provide high amantadine concentrations upon waking that are sustained throughout the day.[3]
- The EASE LID 2 trial (NCT02202551) showed long-term effect on dyskinesia and OFF and included 24 patients with DBS who were using amantadine IR at enrollment.[4,5]

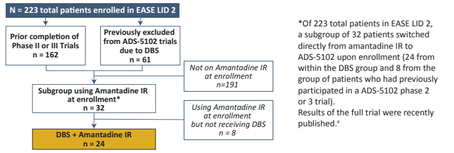
Objective

- To evaluate motor complications and safety outcomes among PD patients with DBS who switched directly from immediate-release (IR) amantadine to ADS-5102 (amantadine) extended release capsules upon enrollment in the 2-year open-label EASE LID 2 trial.

Methods

- Of 223 patients enrolled in EASE LID 2, 61 had DBS and 24 of these 61 were taking amantadine IR (DBS + Amantadine IR) at enrollment [Figure 1].

Figure 1.



*Of 223 total patients in EASE LID 2, a subgroup of 32 patients switched directly from amantadine IR to ADS-5102 upon enrollment (24 from within the DBS group and 8 from the group of patients who had previously participated in a ADS-5102 phase 2 or 3 trial). Results of the full trial were recently published.[4]

- Upon enrollment in this trial, patients taking amantadine IR were switched directly to ADS-5102 (dosed at 137 mg QHS in week 1 and 274 mg QHS thereafter).
- Adverse events (AEs) and persistence on treatment were evaluated, and efficacy (change in dyskinesia and OFF) was assessed at regular intervals through week 100 using the MDS-UPDRS Part IV Total and item scores.
- Analyses for the DBS+IR group were conducted post-hoc.

Results

Table 1. Baseline Demographics

	DBS+IR (N=24)	All Patients (N=223)
Age, mean (SD), years	59.2 (12.2)	63.7 (9.3)
Gender, male, n (%)	16 (66.7)	131 (58.7)
Time since PD diagnosis, mean (SD), years	15.3 (7.9)	11.8 (5.3)
Duration of dyskinesia, mean (SD), years	8.2 (4.4)	5.3 (3.7)
Duration of levodopa treatment, mean (SD), years	11.6 (5.8)	9.3 (4.7)
Levodopa dosage, mean (SD), mg/day	634 (380)	756 (457)

Table 2. Reasons for discontinuing study drug

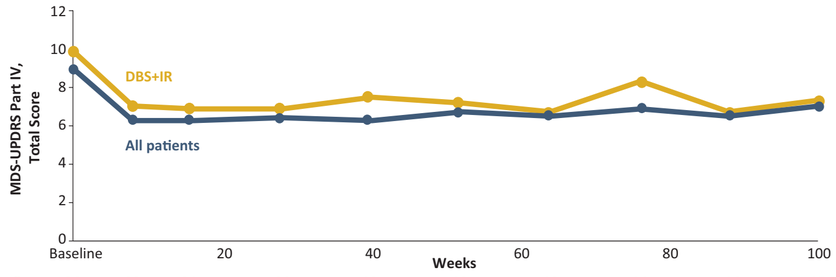
Reason, N (%)	DBS+IR (N=24)	All Patients (N=223)
Subjects who completed the study	15 (62.5)	129 (57.8)
Subjects who withdrew from the study	9 (37.5)	94 (42.2)
Adverse event	4 (16.7)	41 (18.4)
Death	0	7 (3.1)*
Consent withdrawn	2 (8.3)	20 (9.0)
eGFR <50 mL/min/1.73m^2		5 (2.2)
Need excluded medication	1 (4.2)	3 (1.3)
Lost to follow-up	1 (4.2)	2 (0.9)
Sponsor's decision	1 (4.2)	2 (0.9)
Protocol violation	0	1 (0.4)
Other**	0	13 (5.8)

*None of the deaths were considered by the investigator to be due to study drug.
**Discontinuations for "other" reasons were mostly administrative or resulted from other medical issues.

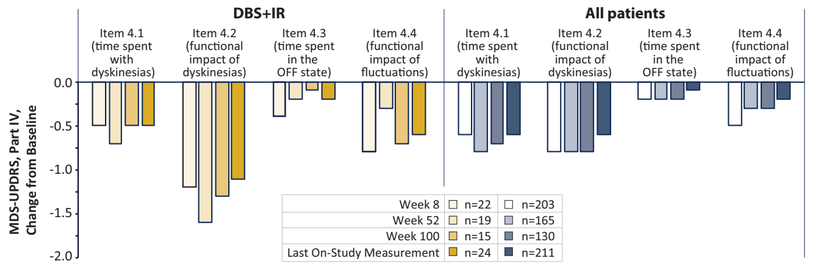
References: 1. Pahwa R, et al. *JAMA Neurol.* 2017;74:941-949. 2. Oertel W, et al. *Mov Disord.* 2017;32:1701-1709. 3. Hauser RA, et al. *Clin Pharmacokinetics.* 2019;58(1):77-88. 4. Tanner C, et al. *J Parkinsons Dis.* 2020 (in press). 5. Isaacson SH, et al. *Mov Disord Clin Pract.* 2018;5:183-190.

In this 2-year, open-label trial, ADS-5102 provided sustained improvement in dyskinesia and OFF for patients with DBS who switched from amantadine IR and overall

Mean Improvement in Motor Complication Scores Over 2 Years



Mean Improvement in Dyskinesia and OFF Item Scores Over 2 Years



Results

- Of 24 DBS + Amantadine IR patients enrolled, 19 (79.2%) completed 1 year and 15 (63%) completed the 2 year trial.
- A safety summary for the DBS+IR group relative to all enrolled patients is shown in Figure 3 and Table 3. The most commonly reported AEs for the DBS+IR group were similar to those seen in the overall population [Table 3].
- At baseline, the mean MDS-UPDRS Part IV total score for the DBS+IR group was 9.8.
- Following ADS-5102 initiation, the MDS-UPDRS Part IV total score decreased (indicating reduced motor complications) by a mean 2.7 points at week 8 (the first post-baseline study visit). This effect was similar to that seen for all patients and was maintained through week 100 (mean change, -2.8) [Central Figure].
- Evaluation of MDS-UPDRS Part IV item scores showed improvement in both daily duration and functional impact of dyskinesia. Item scores improved by week 8 and were maintained through week 100. Reductions in item scores for the DBS+IR group were consistent with those seen for all patients in the study [Central Figure].

Figure 3. Safety Overview

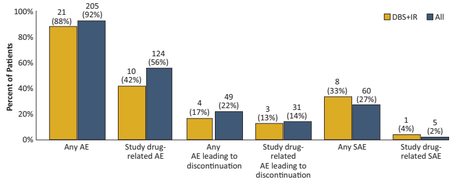


Table 3. Adverse Events (≥10% in either group)

Adverse Events	DBS+IR (N=24)	All Patients (N=223)
Fall	7 (29%)	73 (33%)
Peripheral edema	7 (29%)	36 (16%)
Hallucination (pooled)	6 (25%)	54 (24%)
Hallucination, visual	6 (25%)	52 (23%)
Hallucination, auditory	1 (4%)	5 (2%)
Local swelling	3 (13%)	3 (1%)
Osteoarthritis	3 (13%)	7 (3%)
Urinary tract infection	3 (13%)	23 (10%)
Dizziness	2 (8%)	22 (10%)
Nausea	1 (4%)	22 (10%)
Constipation	0 (0%)	30 (14%)

Conclusion

- This exploratory analysis suggests that ADS-5102 was well tolerated and provided sustained improvement in dyskinesia and OFF among PD patients with DBS who switched directly from amantadine IR.
- These results are consistent with previously reported improvements in dyskinesia and OFF among all patients enrolled in this 2-year open-label trial,[4] and suggest that ADS-5102 treatment may provide additional benefit for PD patients who experience motor fluctuations and/or dyskinesia, despite DBS, amantadine IR, or both.

Disclosures: C Tanner receives grants from the Michael J. Fox Foundation, the Parkinson's Foundation, the Department of Defense, BioElectron, Roche/Genentech, Biogen Idec and the National Institutes of Health, compensation for serving on Data Monitoring Committees from Biotie Therapeutics, Voyager Therapeutics and Intec Pharma and personal fees for consulting from Neurocrine Biosciences, Adamas Pharmaceuticals, Inc., Biogen Idec, 23andMe, Alexza, Grey Matter, Acorda and CNS Ratings. P Agarwal is a consultant and/or speaker for Adamas Pharmaceuticals, Inc., Acadia, Amneal, US WorldMeds, and Kyowa Kirin, and has research support from CHDI Foundation, US WorldMeds, Lilly USA, Biogen MA Inc., Acadia Pharmaceuticals, Genentech (Roche), Prilenia Therapeutics, Sun Pharma Advanced Research Company (SPARC), Centogene AG, Massachusetts General Hospital, and MJ Fox Foundation. D Chernick, A Formella, and J Hubble are employees of and own stock in Adamas Pharmaceuticals, Inc.

Presented at the 3rd Pan American Parkinson's Disease and Movement Disorders Congress, February 14–16, 2020, Miami, FL

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