Amantadine for levodopa induced dyskinesias in PD: Prevalence, clinical correlates, and treatment outcomes in the PPMI study cohort

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Introduction

Levodopa induced dyskinesias (LIDs) represent a common, disabling complication of Parkinson's disease (PD), typically emerging after 5-10 years of levodopa-treatment.

Excessive fluctuations in dopamine levels are regarded as an important etiological mechanism. Medical management is mainly based on strategies to reduce such fluctuations, e.g. by levodopa dose-fractioning or invasive continuous infusion-systems or deep brain stimulation (DBS). An extended-release (ER) formulation of amantadine, an NMDA-receptor antagonist with anti-cholinergic/ and dopamine-releasing properties, was approved for LIDs treatment in 2017. Here, we examined use patterns of amantadine in a large observational PD-cohort.

Methods

PPMI is an international registry study on PD progression/biomarkers (https://www.ppmi-info.org). Clinimetric, demographic, genotype and DAT imaging data on 1340 subjects with PD were accessed November- 2025. Dyskinesia prevalence was assessed by MDS-UPDRS 4.1/ 4.2. MDS-UPDRS, MoCA, Scopa, Quip, MSEADL, Hoehn & Yahr (HY), Falls/Freezing, DAT scan data, along with demographics, genotype and co-medication data were analysed by PCA/O-PLS, exploring overall correlation structure, factors discriminating subjects with/without amantadine, and factors discriminating subjects who discontinued amantadine. For PCA and O-PLS, UV-scaling and auto log-transform were applied through-out. Significance was determined by cross-validation. Error bars represent standard errors estimated by cross-validation. Software: Umetrics SIMCA 18.

Descriptive statistics on amantadine use in the PPMI PD cohort

The mean duration of diagnosis (min - max) was 6.3 years (1 - 25 years). The time course of amantadine use is illustrated in Figure 1. Doses are displayed in Figure 2.

At their last visit, 315 (23.5%) subjects reported dyskinesias (UPDRS 4.1 ≥1). Among these, 93 (29.5%) were treated with amantadine at the last visit. Of all subjects treated with amantadine, 86 (31.5%) eventually discontinued.

Kaplan-Meier discontinuation analysis

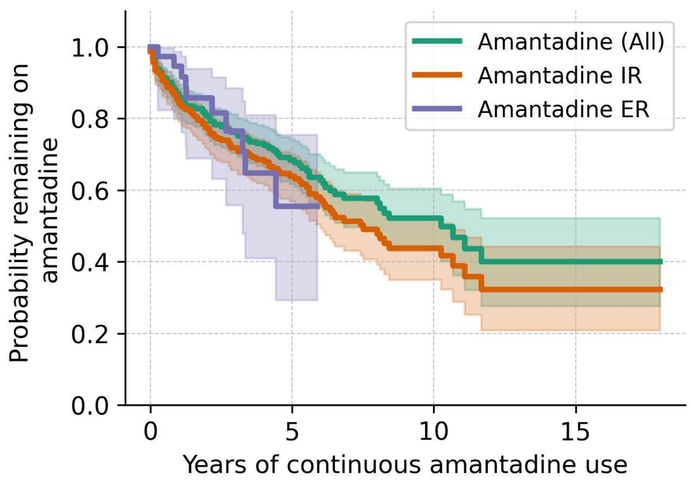

Fig 1. Kaplan-Meier estimate of discontinuation probability. Event = discontinuation; patients censored at withdrawal or at data cutoff

Distribution of amantadine doses

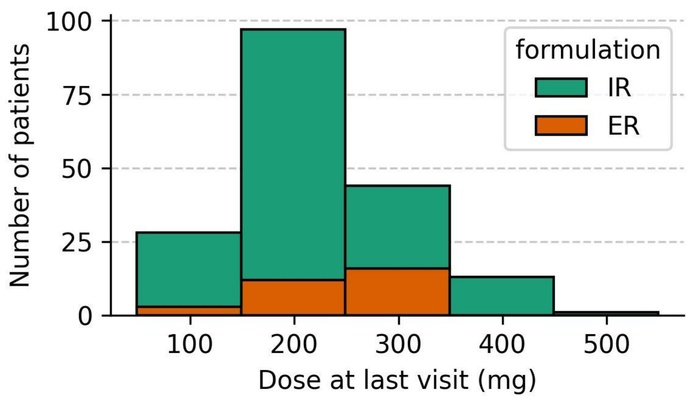

Fig 2. Histogram of amantadine doses (amantadine HCl equivalent) for all subjects

Data used in the preparation of this poster was obtained on 2025-12-17 from the Parkinson's Progression Markers Initiative (PPMI) Database (www.ppmi-info.org/access-data-specimens/download-data) RRID:SCR_006431. For up-to-date info on the study visit www.ppmi-info.org. PPMI – a public-private partnership – is funded by the Michael J. Fox Foundation for Parkinson's Research, and funding partners including a consortium of industry players, non-profit organizations and private individuals.

Overall correlation structure (All subjects)

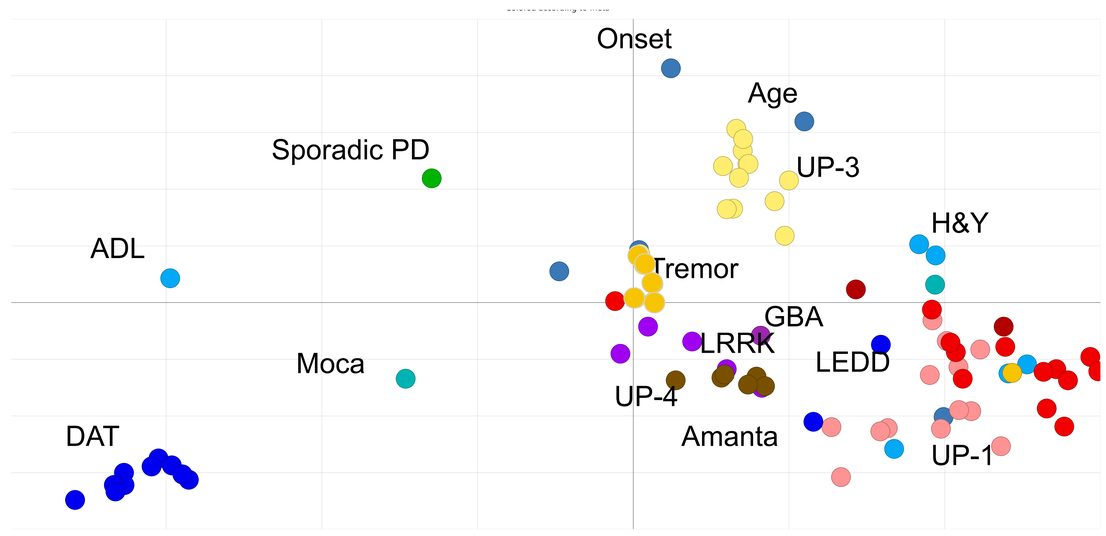

Fig 3. PCA loadings component 1 vs. component 2 showing overall correlation structure. Severity related items cluster to the right, opposed to MoCA, ADL, and DAT signal. Tremor items (gold) are independent. UP= MDS-UPDRS, LEDD: L-Dopa equivalents, ADL: MSE-ADL. Purple: PD genotype. R2X pc 1: 22%, pc 2 7%.

Troublesome dyskinesia – with *vs.* w/o amantadine

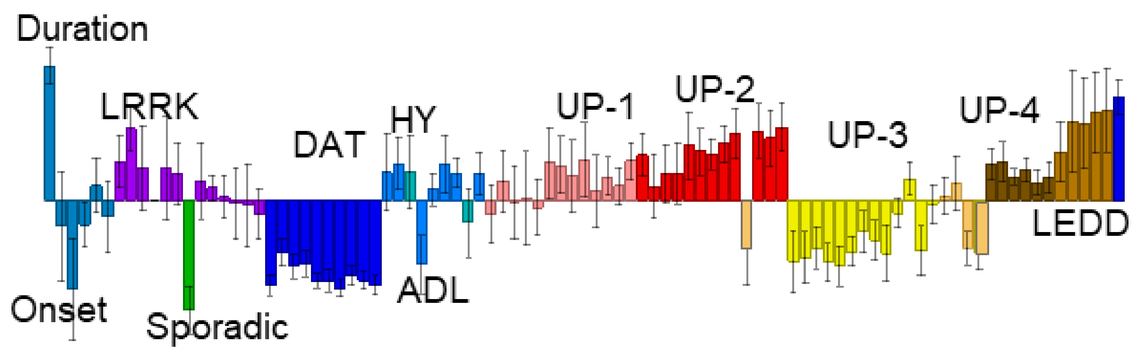

Fig 4. Predictive coefficients (SE) from significant O-PLS component model discriminating subjects with troublesome dyskinesia (MDS-UPDRS 4.2 ≥ 2) with vs. without amantadine. Positive = higher in amantadine treated subjects). Gold bars: tremor items from MDS-UPDRS 2/3. Note reverse direction of MDS-UPDRS part 3 compared to other severity related measures.

Amantadine – discontinued *vs.* continued

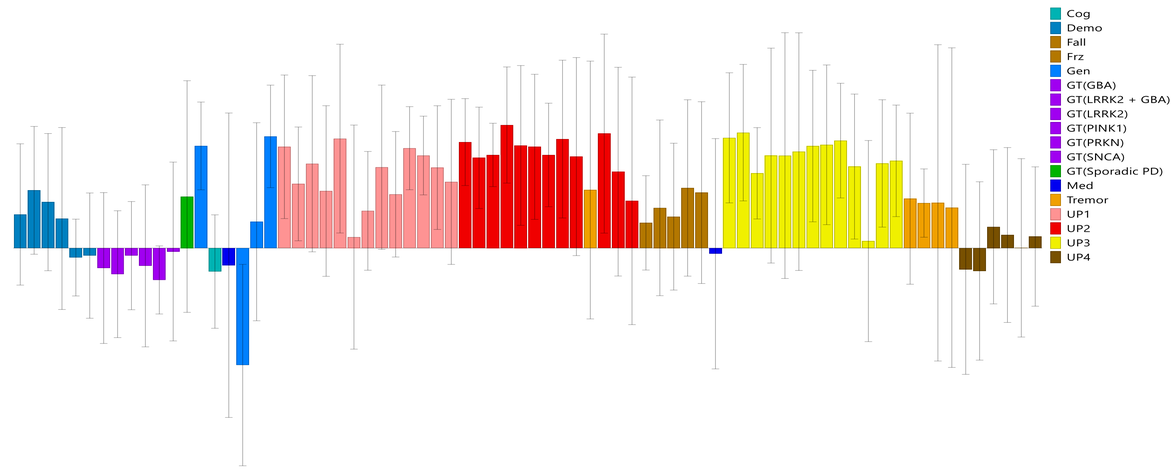

Fig 5. Predictive coefficients (SE) from significant O-PLS component model discriminating subjects discontinuing *vs.* continuing amantadine. Positive = higher in subjects discontinuing amantadine. Gold bars: tremor items from MDS-UPDRS 2/3. Overall pattern is that more severe subjects, eg regarding H&Y, MDS-UPDRS parts 1-3 (except tremor), MSE-ADL, are more likely to discontinue amantadine.

Conclusions

Amantadine use was reported for ~30% of subjects with dyskinesia. Approximately one third discontinued amantadine. A majority received daily doses <300 mg.

Sporadic PD was associated with higher DAT signals, less clinical severity and less dyskinesias & amantadine use. MDS-UPDRS-4 (Complications of therapy) was independent of general PD-severity measures. Also, tremor items formed a separate cluster, not correlated to general severity.

Dyskinetic subjects receiving amantadine were generally more severe, except on tremor items, and tended to be of the "genetic" subtype, esp LRRK, while sporadic PD was associated with less amantadine use.
Also, MDS-UPDRS part 3 was generally lower in those receiving amantadine.

Subjects discontinuing amantadine tended to be more severe overall, but no strong signals were observed.

In summary, around 30% of dyskinetic subjects used amantadine, most at relatively low doses. Around one third discontinued as the disease progressed.