Parkinson's disease, levodopa dose escalation and NOURIANZ: a real-world assessment

NOURIANZ® (istradefylline) tablets
20 mg | 40 mg

Nobutaka Hattori, Daijiro Kabata, Shinji Asada, et al. Real-world evidence on levodopa dose escalation in patients with Parkinson's disease treated with istradefylline

PLoS One. 2023

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Study objective and outcome assessment[1]

Hattori et al conducted a retrospective observational Japanese study in 4026 patients to measure changes in LDD (mg/day) and LEDD (mg/day) before and after initiation with NOURIANZ. These changes were assessed monthly and were based on anonymized hospital records including prescription data between April 1, 2008 and April 30, 2019 for patients prescribed NOURIANZ and continued for at least 29 days. Baseline therapy was NOURIANZ with or without MAO-B inhibitors, COMT inhibitors, and dopamine agonists.

Inclusion/exclusion criteria[1]

- Eligible patients were diagnosed with PD and had a prescription for any LD formulation at least once during the observation period
- Patients were not included if they were diagnosed with early-onset or familial PD, secondary parkinsonism or other degenerative diseases of the basal ganglia, or only parkinsonism during the record collection period or if their LD treatment initiation occurred before 40 years of age

Study limitations[1]

- Available data were observational, uncontrolled, and retrospective in nature and were confined to what was recorded in the database
- Since the database did not contain wearing-off data, a non-NOURIANZ group of patients experiencing wearing off could not be established
- **The database did not include efficacy or safety data;** therefore, this analysis cannot directly determine how the attenuation of LDD increases in patients treated with NOURIANZ equates to a change in motor symptoms/complications or tolerability

NOURIANZ is the only adenosine A_{2A} receptor antagonist that works with levodopa/carbidopa to help treat "off" episodes in adult patients with PD.[2,3]

COMT, catechol-o-methyltransferase; LD, levodopa; LDD, levodopa daily dose; LEDD, levodopa equivalent daily dose; MAO-B, monoamine oxidase; PD, Parkinson's disease.

Indication

NOURIANZ® (istradefylline) is an adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes.

Important Safety Information

Warnings and Precautions

Dyskinesia: NOURIANZ in combination with levodopa may cause dyskinesia or exacerbate pre-existing dyskinesia. In clinical trials, 1% of patients treated with either NOURIANZ 20 mg or 40 mg discontinued treatment because of dyskinesia, compared to 0% for placebo.

Hallucinations / Psychotic Behavior: Because of the potential risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with NOURIANZ. Consider dosage reduction or discontinuation if a patient develops hallucinations or psychotic behaviors while taking NOURIANZ.

Please see additional Important Safety Information throughout.

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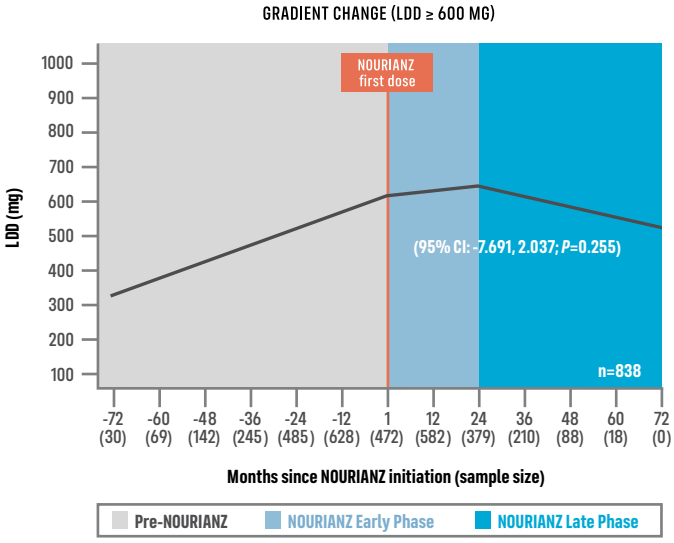
Assessment outcome[1]

- Patients receiving ≥600 mg/day of LD (n=838) prior to starting NOURIANZ demonstrated a **statistically significant reduction in the gradient of LDD escalation** during both the early (0-2 years) (95% CI: -6.493, -0371; *P*=0.028) and late (2-6 years) phases of treatment (95% CI: -9.223, -3.295; *P*<0.001)*
- Absence of definitive data on duration of NOURIANZ treatment limits the interpretation of the strength of any potential causal association between NOURIANZ treatment duration and change in pattern of LDD gradient change.



CI, confidence interval; ITSA, interrupted time series analysis.

**P* values among the 3 observation periods (pre-NOURIANZ, NOURIANZ early phase, and NOURIANZ late phase) were estimated using a self-controlled ITSA designed to explore patterns of LD dosage in patients with PD who were initiated on treatment with NOURIANZ.

Important Safety Information (continued)

Warnings and Precautions (continued)

Impulse Control / Compulsive Behaviors: Patients treated with NOURIANZ and one or more medication(s) for the treatment of Parkinson's disease (including levodopa) may experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge or compulsive eating, and/or other intense urges, and the inability to control these urges. In clinical trials, 1 patient treated with NOURIANZ 40 mg was reported to have impulse control disorder, compared to no patient on NOURIANZ 20 mg or placebo.

Drug Interactions: The maximum recommended dosage in patients taking strong CYP3A4 inhibitors is 20 mg once daily. Avoid use of NOURIANZ with strong CYP3A4 inducers.

Specific Populations

Pregnancy: Based on animal data, may cause fetal harm.

Hepatic impairment: The maximum recommended dosage of NOURIANZ in patients with moderate hepatic impairment is 20 mg once daily. Avoid use in patients with severe hepatic impairment.

Adverse Reactions

The most common adverse reactions with an incidence ≥5% and occurring more frequently than with placebo were dyskinesia (15%, 17%, and 8%), dizziness (3%, 6%, and 4%), constipation (5%, 6%, and 3%), nausea (4%, 6%, and 5%), hallucination (2%, 6%, and 3%), and insomnia (1%, 6%, and 4%) for NOURIANZ 20 mg, 40 mg, and placebo, respectively.

You are encouraged to report suspected adverse reactions to Kyowa Kirin, Inc. at 1-844-768-3544 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional Important Safety Information throughout.

Click here for full Prescribing Information.

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References: 1. Hattori N, Kabata D, Asada S, Kanda T, Nomura T, Shintani A, et al. Real-world evidence on levodopa dose escalation in patients with Parkinson's disease treated with istradefylline. *PLoS One*. 2023;18(12):1-13. **2.** NOURIANZ [package insert]. Kyowa Kirin, Inc., Princeton, NJ 08540. **3.** Isaacson SH, Betté S, Pahwa R. Istradefylline for OFF episodes in Parkinson's disease: a US perspective of common clinical scenarios. *Degener Neurol Neuromuscul Dis.* 2022;12:97-109.

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COMM-US-NOU-0392 February 2025

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