NOURIANZ® (istradefylline) with levodopa: Real World Data

NOURIANZ® (istradefylline) tablets 20 mg | 40 mg

Hatano T, Sengoku R, Nagayama H, et al. Impact of Istradefylline on Levodopa Dose Escalation in Parkinson's Disease: ISTRA ADJUST PD Study, a Multicenter, Open-Label, Randomized, Parallel-Group Controlled Study.

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Study objective and endpoints[1]

Hatano et al explored whether the addition of NOURIANZ, an adenosine A_{2A} receptor antagonist, can help reduce levodopa dose escalation in adult PD patients experiencing "wearing off". The primary endpoint was cumulative additional levodopa dose; the secondary endpoints were additional levodopa doses, changes in symptom rating scales, motor activity determined by a wearable device, and safety outcomes.[1,2]

Primary efficacy endpoint[1]:

- Over 37 weeks, the mean (± standard deviation [SD]) cumulative additional levodopa dose was lower in the NOURIANZ group (3229.8 ± 5692.7 mg) than in the control group (15,056.6 ± 5187.1 mg) (P<0.0001)

Secondary efficacy endpoint[1]:

- Over 37 weeks, the levodopa dose increase was significantly reduced in the NOURIANZ group compared to the control group (P<0.0001)
- The mean (± SD) add-on levodopa dose was significantly lower in the NOURIANZ group (25.0 ± 40.2 mg/day) than in the control group (73.6 ± 43.9 mg/day) at Week 36 (P<0.0001)

Secondary safety endpoints[1]:

- Fifteen patients (28.8%) in the NOURIANZ group and 7 patients (13.2%) in the control group experienced adverse drug reactions (ADRs). One patient in the NOURIANZ group dropped out of the study due to dyskinesia. The most common ADRs were dyskinesia, somnolence, and nausea (5.8% each) in the NOURIANZ group, and nausea (3.8%) in the control group. There were no serious ADRs in either group.

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.

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.

Please see additional Important Safety Information throughout.
Click here for full Prescribing Information.

Study limitations[1]

- Open-label study with performance bias, and the increase in levodopa dose may have been affected by the participants' judgment
- Diagnosis of PD was based on clinical features versus pathology, and some patients with atypical PD might have been included
- Association between accelerometry parameters and motor symptoms in PD patients was not validated
- CGI was used as a criterion for levodopa dose escalation based on methods such as those used by Watts et al
- Observation period of 37 weeks might not provide adequate time to identify alterations in the necessary levodopa dose; further long-term studies needed to confirm these results

The triaxial accelerometer monitoring system unique to this PD study helped to minimize subjective performance bias in assessing motor activity. Correlations were confirmed between accelerometry parameters and CGI-S, as well as MDS-UPDRS Part III.

CGI, clinical global impressions; CGI-S, Clinical Global Impressions–Severity scale; MDS-UPDRS, International Parkinson and Movement Disorder Society Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease.

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]

Important Safety Information (continued)

Warnings and Precautions (continued)

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.

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Click here for full Prescribing Information.

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References: 1. Hatano T, Sengoku R, Nagayama H, et al. Impact of istradefylline on levodopa dose escalation in Parkinson's disease: ISTRA ADJUST PD study, a multicenter, open-label, randomized, parallel-group controlled study. *Neurol Ther.* 2024;13(2):323-338. **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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