Clinical utility of Ongentys®(opicapone) 50 mg confirmed by real-world data in Parkinson's disease patients with motor fluctuations

Clinical insights from principle investigator and lead author Prof. Dr. med. Heinz Reichmann, Department of Neurology, Technische Universitaet Dresden, Fetscherstrasse 74, 01307 Dresden, Germany

Heinz Reichmann is a member of the German Neurological Society, The European Neurological Society and is a fellow of the American Academy of Neurology. His major research interests cover etiopathogenesis and treatment in Parkinson's disease, premotor symptoms in Parkinson's disease, and neuroprotection.

OPTIPARK, a Phase IV, open-label study conducted in the UK and Germany under clinical practice conditions, supports the efficacy of Ongentys® 50 mg observed in the pivotal Phase III studies.[1]

Ongentys® 50 mg, as an adjunct to levodopa in patients with motor fluctuations, significantly improved perception of patients' global Parkinson's disease (PD) condition (≥70% as judged by clinicians and the patients themselves) 3 months after they started treatment with Ongentys® 50 mg.[1] Ongentys® is a once-daily catechol-O-methyltransferase (COMT) inhibitor. COMT inhibitor treatment is appropriate for PD patients taking levodopa/dopa decarboxylase inhibitor (DDCI) therapy where there is evidence of motor fluctuations.[1]

OPTIPARK: real-world clinical data in adult PD patients with motor fluctuations

Rationale for OPTIPARK

Findings from two pivotal Phase III studies, BIPARK I and II,[2,3] highlighted that global assessments using Clinician's Global Impression of Change (CGI-C) and Patient's Global Impression of Change (PGI-C) showed clinical improvements for Ongentys® 50 mg versus placebo[2,3] and entacapone[2] (CGI-C: p=0.0005 versus placebo, and p=0.007 versus entacapone; PCI-C: p=0.0091 versus entacapone).[2] The OPTIPARK open-label, prospective study set out to confirm these results in a real-life setting,[1] with CGI-C selected as the primary endpoint, and PGI-C as one of the secondary endpoints.

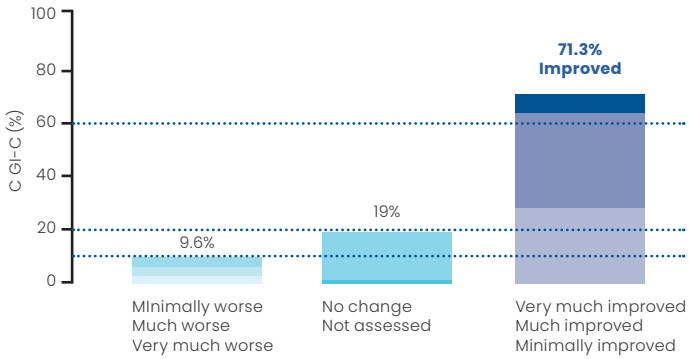
Study protocol and methodology for OPTIPARK (n=506 patients)[1]

- Key inclusion criteria: Men or women (≥30 years) with idiopathic PD reporting ≥1 symptom on the 9-symptom Wearing-off Questionnaire (WOQ-9), Hoehn and Yahr Stages I–IV (during ON), and treated with 3–7 daily doses of levodopa/DOPA decarboxylase inhibitor (DDCI)
- Treatment protocol: Ongentys® 50 mg once daily for 3 months (German sites) or 6 months (UK sites) in addition to current treatment with levodopa/DDCI. Total daily levodopa/DDCI dose could be adjusted according to the individual's condition throughout the study (except on Day 1)
- Primary endpoint: CGI-C after 3 months
- Secondary endpoints: PGI-C, the Unified PD Rating Scale (UPDRS), PD Questionnaire 8 items (PDQ-8), Non-Motor Symptoms Assessment Scale (NMSS)

Primary endpoint: OPTIPARK confirms the clinical utility of Ongentys® 50 mg

After 3 months treatment with Ongentys® 50 mg in a clinical setting of fluctuating PD patients, there were improvements in global PD condition: 71.3% of patients showed clinical improvement as rated by the CGI-C, with 43% reported as much or very much improved.[1]

Clinical Global Impression of Change (CGI-C) n=477

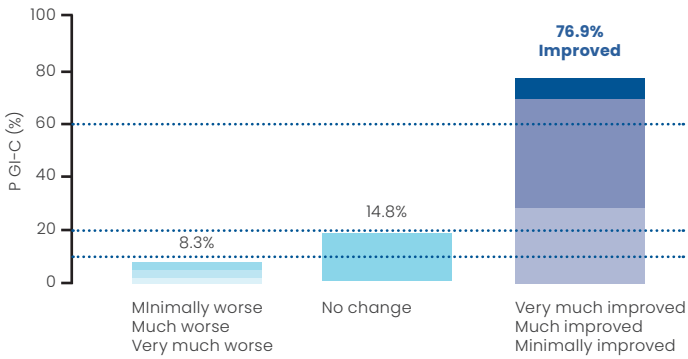


Source: Adapted from Reichmann H *et al. Transl Neurodegner* 2020[1]

Secondary endpoints: Ongentys® significantly improved motor scores, quality of life and non-motor symptoms

After 3 months treatment with Ongentys® 50 mg in UK and German PD patients, 76.9% self-reported a clinical improvement (PGI-C), with 48.1% of patients reporting they were much or very much improved.[1,4]

Patient's Global Impression of Change (PGI-C) (n=393)



Adapted from Reichmann H *et al. Transl Neurodegner* 2020[1,4]

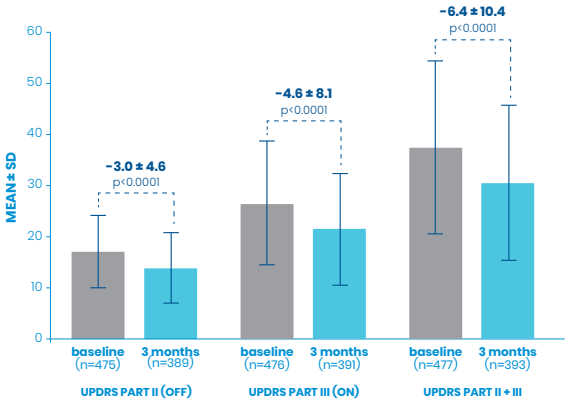
"In routine clinical practice, once-daily Ongentys® 50 mg as an adjunct to levodopa-treated PD patients with motor fluctuations significantly improved patients' perceptions about their global PD condition", ***Heinz Reichmann***

Both clinical and statistical improvements were evident for activities of daily living (ADL) and motor scores after 3 months. UPDRS scores showed a statistically significant improvement from baseline for ADL (UPDRS Part II) during OFF periods: mean±SD, −3.0±4.6 (p<0.0001), and motor scores (UPDRS Part III) during ON periods (−4.6±8.1, p<0.0001), as well as total scores (UPDRS Parts II + III), −6.4±10.4, p<0.0001.[1,4]

Prescribing information can be found on the following page

Motor scores in OPTIPARK[1,4]

Significant improvements in activites of daily living and motor scores (UPDRS II and III)

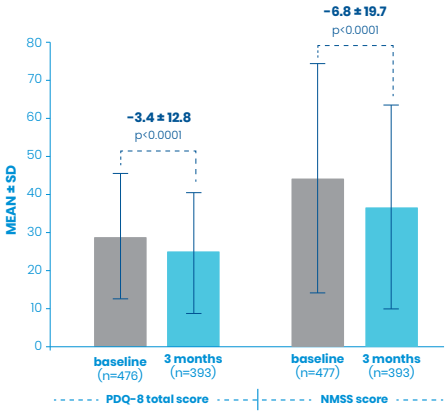


SD, standard deviation; UPDRS, Unified Parkinson's Disease Rating Scale.

There was also a statistically significant improvement in quality of life (PDQ-8) and non-motor symptoms (NMSS) versus baseline: PDQ-8 (mean±SD) −3.4±12.8 (p<0.0001); NMSS, −6.8±19.7(p<0.0001).[1]

Quality of life and non-motor symptoms[1]

Significant improvememts in quality of life (PDQ-39) and non-motor symptoms (NMSS)



NMSS, Non-Motor Symptom Scale; PDQ-8, Parkinson's Disease Questionnaire, 8 items; SD, standard deviation

Safety profile: The majority of drug-related treatment-emergent adverse events (TEAEs) were reported during the first week[5]

The safety profile in this large-open label study was comparable to adverse event data from the two pivotal studies.[2,3] In the 74.9% of patients who experienced TEAEs, the majority were mild or moderate in severity. Dyskinesia was the most common treatment-related TEAE (11.5%), leading to discontinuation in 1% of patients. The most common TEAE leading to withdrawal was nausea (2%).[1]

Clinical practice points:[1]

- This large real-life study in 495 patients treated with Ongentys® 50 mg mirrored a clinical setting through the inclusion of a broad population of fluctuating PD patients (Hoehn and Yahr I-III) compared to the two Phase III studies
- Despite optimised PD therapy (according to clinician's judgement), and most patients in OPTIPARK (78.8%) receiving levodopa/DDCI plus another PD medication, clinically significant improvements were reported for UPDRS motor and ADL scores
- More patients were judged by the clinician to have shown an improvement in OPTIPARK than reported in the pivotal Phase III studies (71.3% vs 59.6%)[6]

OPTIPARK confirms the clinical utility of Ongentys® 50 mg as an effective and generally well-tolerated adjunct option in patients with Parkinson's disease with motor fluctuations[1]

References

1. Reichmann H, *et al.* Effectiveness and safety of opicapone in Parkinson's disease patients with motor fluctuations: the OPTIPARK open-label study. *Transl Neurodegener* 2020;9:1–9.
2. Ferreira JJ, *et al.* Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: a randomised, double-blind, controlled trial. *Lancet Neurol* 2016;15:154–65.
3. Lees AJ, *et al.* Opicapone as adjunct to levodopa therapy in patients with Parkinson disease and motor fluctuations: a randomised clinical trial. *JAMA Neurol* 2017;74:197–206.
4. Reichmann H, *et al.* Correction to: Effectiveness and safety of opicapone in Parkinson's disease patients with motor fluctuations: the OPTIPARK open-label study. *Transl Neurodegener* 2020;9:14.
5. Lees A. Onset of drug-related adverse events in Parkinson's disease patients with motor fluctuations treated with opicapone in clinical practice: OPTIPARK post-hoc Analysis. *Mov Disord.* 2020;35(suppl 1),S462,abst 1029
6. Ferreira JJ, *et al.* Long-term efficacy of opicapone in fluctuating Parkinson's disease patients: a pooled analysis of data from two phase 3 clinical trials and their open-label extensions. *Eur J Neurol* 2019;26:953–60.

PRESCRIBING INFORMATION

Ongentys® (opicapone)

Please refer to the SPC before prescribing. **Presentation**: Capsules containing 50 mg of opicapone. **Indication**: Adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCI) in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations. **Dosage and administration**: The recommended dose is 50 mg of opicapone. It should be taken once daily at bedtime at least one hour before or after levodopa combinations. Ongentys is to be administered as an adjunct to levodopa treatment and enhances the effects of levodopa. Hence, it is often necessary to adjust levodopa dosage by extending the dosing intervals and/or reducing the amount of levodopa per dose within the first days to first weeks after initiating the treatment with opicapone according to the clinical condition of the patient. If one dose is missed, the next dose should be taken as scheduled. The patient should not take an extra dose to make up for the missed dose. **Elderly patients**: No dose adjustment is needed for elderly patients. Caution must be exercised in patients ≥ 85 years of age as there is limited experience in this age group. **Patients with renal impairment**: No dose adjustment is necessary in patients with renal impairment, as opicapone is not excreted by the kidney. **Patients with hepatic impairment**: No dose adjustment is necessary in patients with mild hepatic impairment (Child- Pugh Class A). There is limited clinical experience in patients with moderate hepatic impairment (Child- Pugh Class B). Caution must be exercised in these patients and dose adjustment may be necessary. There is no clinical experience in patients with severe hepatic impairment (Child-Pugh Class C), therefore, Ongentys is not recommended in these patients. **Contraindications**: Hypersensitivity to the active substance or to any of the excipients. Phaeochromocytoma, paraganglioma, or other catecholamine secreting neoplasms. History of neuroleptic malignant syndrome and/or non-traumatic rhabdomyolysis. Concomitant use with monoamine oxidase (MAO-A and MAO-B) inhibitors (e.g. phenelzine, tranylcypromine and moclobemide) other than those for the treatment of Parkinson's disease. **Pregnancy**: Ongentys is not recommended during pregnancy and in women of childbearing potential not using contraception. **Lactation**: Breast-feeding should be discontinued during treatment with Ongentys. **Warnings and precautions**: Opicapone enhances the effects of levodopa. To reduce levodopa-related dopaminergic adverse reactions (e.g. dyskinesia, hallucinations, nausea, vomiting and orthostatic hypotension), it is often necessary to adjust the daily dose of levodopa by extending the dosing intervals and/or reducing the amount of levodopa per dose within the first days to first weeks after initiating treatment with Ongentys, according to the clinical condition of the patient. Patients and care-givers should be made aware that impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments. Patients should be monitored regularly for the development of impulse control disorders and review of treatment is recommended if such symptoms develop. Increases in liver enzymes were reported in studies nitrocatechol inhibitors of catechol-O-methyltransferase (COMT). For patients who experience progressive anorexia, asthenia and weight decrease within a relatively short period of time, a general medical evaluation including liver function should be considered. **Excipients**: Ongentys contains lactose. Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. **Drug interactions**: Concomitant use of opicapone with MAO inhibitors (e.g. phenelzine, tranylcypromine and moclobemide) other than those for the treatment of Parkinson's disease is contraindicated. Concomitant use of opicapone and MAO inhibitors for the treatment of Parkinson's disease, e.g. rasagiline (up to 1 mg/day) and selegiline (up to 10 mg/day in oral formulation or 1.25 mg/day in buccal absorption formulation), is permissible. There is no experience with opicapone when used concomitantly with the MAO-B inhibitor safinamide. Therefore, their concomitant use should be considered with appropriate caution. Opicapone may interfere with the metabolism of medicinal products containing a catechol group that are metabolised by COMT, e.g. rimiterole, isoprenaline, adrenaline, noradrenaline, dopamine, dopexamine or dobutamine, leading to potentiated effects of these medicinal products. Careful monitoring of patients being treated with these medicinal products is advised when opicapone is used. Concomitant use with tricyclic antidepressants and noradrenaline re-uptake inhibitors (e.g. venlafaxine, maprotiline and desipramine) should be considered with appropriate caution. Particular consideration should be given to medicinal products metabolised by CYP2C8 and their co-administration must be avoided. Particular consideration should be given to medicinal products transported by OATP1B1 and their concomitant use should be considered with appropriate caution. **Adverse events**: Refer to the SPC for all side effects. Very common side effects (≥ 1/10): Dyskinesia. Common side effects (≥ 1/100 to < 1/10): Abnormal dreams, Hallucination, Hallucination visual, Insomnia, Dizziness, Headache, Somnolence, Orthostatic hypotension, Constipation, Dry mouth, Vomiting, Muscle spasms, Blood creatine phosphokinase increased. Uncommon side effects (≥ 1/1,000 to < 1/100): Decreased appetite, Hypertriglyceridaemia, Anxiety, Depression, Hallucination auditory, Nightmares, Sleep disorder, Dysgeusia, Hyperkinesia, Syncope, Dry eye, Ear congestion, Palpitations, Hypertension, Hypotension, Dyspnoea, Abdominal distention, Abdominal pain, Abdominal pain upper, Dyspepsia, Muscle twitching, Musculoskeletal stiffness, Myalgia, Pain in extremity, Chromaturia, Nocturia, Weight decreased. **Legal Category**: POM. **Basic UK NHS cost**: Ongentys pack of 30: £93.90. **Marketing authorisation numbers**: PLGB 21566/0004 EU/1/15/1066/003. **Marketing authorisation holder**: Bial-Portela & Ca., S.A., A Avenida da Siderurgia nacional 4745-457 Coronado (S. Romao e S. Mamede) – Portugal. **Further Information from**: Bial Pharma UK Ltd., Admiral House, St. Leonard's Road, Windsor, SL4 3BL, UK. **Job code**: UK/ON/2021/016. **Date of preparation**: March 2021.

Adverse events should be reported.
For UK healthcare professionals: reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bial on +44 (0)1628 531171 or bial@pharmalex.com

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