Keywords
Levodopa · Motor fluctuations · Opicapone · Parkinson’s disease · Real-world study

Abstract
Introduction: The OPTIPARK study confirmed the effectiveness and safety of opicapone as adjunct therapy to levodopa in patients with Parkinson’s disease (PD) and motor fluctuations under real-world conditions. The aim of this sub-analysis was to evaluate opicapone in the German patient cohort of OPTIPARK in order to provide country-specific data. Methods: OPTIPARK was an open-label, single-arm study conducted in routine clinical practice across Germany and the UK. Patients with PD and motor fluctuations received once-daily opicapone 50 mg for 3 months in addition to levodopa. The primary endpoint was Clinicians’ Global Impression of Change (CGI-C). Secondary assessments included Patients’ Global Impressions of Change (PGI-C), Unified Parkinson’s Disease Rating Scale (UPDRS) I–IV, Parkinson’s Disease Questionnaire (PDQ-8), and Non-Motor Symptoms Scale (NMSS). This sub-analysis reports outcomes from the German patients only. Results: Overall, 363 (97.6%) of the 372 patients included in the German cohort received ≥1 dose of opicapone and 291 (80.2%) completed the study. Improvements on CGI-C and PGI-C were reported by 70.8% and 76.3% of patients, respectively. UPDRS scores improved for activities of daily living during OFF time by −3.3 ± 4.5 points and motor scores during ON time by −5.3 ± 7.9 points. PDQ-8 and NMSS scores also demonstrated improvements. Treatment emergent adverse events considered at least possibly related to opicapone occurred in 37.7% of patients, with most being of mild or moderate intensity. Conclusion: Opicapone added to levodopa in patients with PD and motor fluctuations was effective and generally well tolerated in routine clinical practice across Germany.

Introduction
Levodopa, also known as L-DOPA, is an effective and generally well-tolerated dopamine replacement agent that is widely used to treat Parkinson’s disease (PD) [1–3].
However, long-term use of levodopa can cause wearing-off symptoms, other motor and non-motor fluctuations and dyskinesias, which can affect mobility, activities of daily living, and communication [4, 5]. Wearing-off symptoms are experienced by 40–50% of patients treated for 5 years and affect approximately two-thirds of patients after 10 or more years of levodopa therapy [6]. To manage these symptoms, catechol-O-methyltransferase (COMT) inhibitors are commonly used as an adjunct to levodopa [7, 8]. The inhibition of dopa decarboxylase (DDC) and COMT, two enzymes involved in metabolizing levodopa, increases levodopa bioavailability and its delivery to the brain, thereby ameliorating wearing-off symptoms [9–12].

Opicapone is a once-daily COMT inhibitor developed for increased potency and longer-acting COMT inhibition [7, 9, 13–15]. Two large randomized trials (BIPARK-I and -II) demonstrated that opicapone is generally well tolerated and efficacious in reducing OFF-time in patients with PD and end-of-dose motor fluctuations [15, 16], which led to the drug’s approval in Europe as adjunctive therapy to preparations of levodopa/DDC inhibitors [17].

While randomized-controlled trials are essential for assessing the efficacy and safety of new treatments, they are usually conducted in highly selective patient populations under restricted conditions that do not mimic real-life situations [18–20]. Evidence from everyday clinical practice is encouraged to complement data from randomized controlled trials, and is now being used more frequently to support regulatory decision-making and pharmacovigilance studies [19, 21, 22]. OPTIPARK was a prospective, open-label, single-arm study on the use of opicapone in patients with PD and motor fluctuations across Germany and the UK under clinical practice conditions, with the primary aim of evaluating the change in the clinician’s view of their patients’ global PD condition after 3 months of treatment. OPTIPARK was the first study to confirm the effectiveness, safety and tolerability of once-daily opicapone 50 mg in routine clinical practice [23]. This report focuses on a sub-analysis of the German cohort only and will provide clinicians with data on the effectiveness and tolerability of opicapone 50 mg in routine clinical practice specifically in Germany.

**Methods**

**Study Design**

The study design has been described previously [23]. In brief, a prospective open-label, single-arm, multicenter trial investigating the effectiveness of opicapone 50 mg in levodopa-treated patients with PD who experience motor fluctuations was carried out...

---

**Fig. 1.** Patient disposition.
between November 2016 and July 2018 at 68 specialist neurology centers across Germany and the UK (EudraCT number: 2016-002391-27). This sub-analysis will report the outcomes from the German patients only who were treated at 49 centers across Germany.

Patients received opicapone 50 mg capsules once-daily at bedtime, at least 1 h after the last daily dose of levodopa/DDC inhibitor. The total duration of treatment within the German cohort was 3 months.

**Study Population**

Patients with idiopathic PD aged ≥30 years were eligible if they reported symptoms of motor fluctuations as identified by at least one symptom on the 9-Symptom Wearing-off Questionnaire (WOQ-9) [24]. They also had to be Hoehn and Yahr stages I–IV (during ON) and treated with 3–7 daily doses of levodopa/DDC inhibitor. Details of the inclusion and exclusion criteria have previously been reported [23].

**Study Assessments**

Endpoints were assessed at baseline, 1 month and 3 months or at any early discontinuation visit. The primary endpoint was the Clinicians’ Global Impression of Change (CGI-C; 7-point scale, from very much improved to very much worse), which assessed the clinician’s view of the patient’s global PD condition after 3 months of treatment with opicapone 50 mg. Secondary assessments included the Patient’s Global Impression of Change (PGI-C), WOQ-9 assessments, the Unified Parkinson’s Disease Rating Scale (UPDRS) sections I–IV during ON and/or OFF time [25], the Parkinson’s Disease Questionnaire (PDQ-8) [26], the Non-Motor Symptoms Scale (NMSS) [27] and change from baseline in total daily levodopa dose and dosing frequency. Safety was assessed through reporting of treatment emergent adverse events (TEAEs) as well as vital signs and routine physical and neurological examinations.

**Statistical Analysis**

No sample size estimation was performed. The safety population included all patients who received ≥1 dose of opicapone. Effectiveness was assessed in the full analysis set which included all patients in the safety population who had ≥1 CGI-C recorded post-baseline. Analyses were primarily descriptive; missing values for the primary outcome measure (CGI-C) at 3 months was imputed using the last observation carried forward method.

**Results**

**Patient Disposition and Baseline Characteristics**

Three-hundred and seventy-two patients were enrolled at 49 centers across Germany. Of these, 363 (97.6%) patients received at least one dose of opicapone (safety set) and 349 (93.8%) had at least one post-baseline CGI-C assessment and were included in the full analysis set (Fig. 1). A total of 72 (19.8%) patients prematurely terminated the trial and discontinued treatment with opicapone. While 54 patients (14.9%) withdrew due to a TEAE (including 11.0% [n = 40] due to an at least possibly related TEAE), two (0.6%) withdrew because of lack of efficacy. A high proportion of patients (92.6%) complied with ≥80% of doses. The mean ± standard deviation (SD) treatment compliance was 99.7 ± 8.19%. Of the 291 patients who completed the trial, 248 patients (71.1%) continued to receive opicapone by prescription.

Baseline characteristics of the safety set are provided in Table 1. The study population was comprised of white Caucasian patients with a mean ± SD age of 67.8 ± 9.2 years, a mean ± SD time since diagnosis of 100.3 ± 58.7 months and a mean ± SD duration of motor fluctuations

| Table 1. Baseline characteristics (safety set) |
|-----------------------------------------------|
| Category                                      | N = 363 |
| Age, years; mean ± SD (range)                 | 67.8 ± 9.21 (45–87) |
| Age categories, n (%)                         |        |
| ≥30 to <65                                    | 125 (34.4) |
| ≥65 to <85                                    | 233 (64.2) |
| ≥85                                           | 5 (1.4) |
| Sex (M/F), n (%)                              |        |
| White                                         | 363 (100.0) |
| Duration of Parkinson’s disease, months       |        |
| Mean ± SD                                     | 100.3 ± 58.74 |
| Median (range)                                | 89 (5–420) |
| Duration of motor fluctuations, months        |        |
| Mean ± SD                                     | 29.7 ± 39.47 |
| Median (range)                                | 14.5 (0–324) |
| Symptoms (WOQ-9 assessment), n (%)            |        |
| Tremor                                        | 215 (61.6) |
| Any slowness of movement                      | 333 (95.4) |
| Mood changes                                  | 189 (54.2) |
| Any stiffness                                 | 287 (82.2) |
| Pain/aching                                   | 206 (59.0) |
| Reduced dexterity                             | 317 (90.8) |
| Cloudy mind/slowness of thinking              | 154 (44.1) |
| Anxiety/panic attacks                         | 71 (20.3) |
| Muscle cramping                               | 204 (58.5) |
| Total levodopa daily dose, mg; mean ± SD      | 552.9 ± 244.61 |
| Median (range)                                | 500.0 (100–1,500) |
| Adjunct therapies, n (%)                      |        |
| Rasagiline                                    | 96 (26.4) |
| Pramipexole                                   | 92 (25.3) |
| Amantadine                                    | 89 (24.5) |
| Ropinirole                                    | 80 (22.0) |
| Safinamide                                    | 64 (17.6) |
| Rotigotine                                    | 54 (14.9) |
| Piribedil                                     | 44 (12.1) |

SD, standard deviation; WOQ-9, Wearing-off Questionnaire (9 items). * Assessed in the full analysis set. # Patients could take ≥1 adjunct therapy.
of 29.7 ± 39.5 months. Total mean ± SD levodopa daily dose in the safety set was 552.9 ± 244.61. The majority of patients (80.7%) received another levodopa adjunct medication: the most common reported adjunct medications were rasagiline (26.4%), pramipexole (25.3%), and amantadine (24.5%).

**Clinician and Patient Global Impressions of Change**

The majority of patients (70.8%) demonstrated clinical improvements after 3 months of treatment with opicapone 50 mg, as judged by the investigators (CGI-C), with 41% reporting as much or very much improved (Fig. 2a). Patients’ self-rated levels of improvement (PGI-C) were consistent with the PGI-C results of the primary OPTIPARK study, with the majority of patients (76.3%) reporting an improvement after 3 months of treatment with opicapone 50 mg (Fig. 2b). Similar results were already reported at the 1-month assessment, with 72.8% and 71.2% of patients reporting improvements on CGI-C and PGI-C, respectively.
Presence of Symptoms as Assessed by the WOQ-9
The proportions of patients reporting the overall presence of individual symptoms on the WOQ-9 decreased from baseline to 3 months (Fig. 3). Similar improvements in all nine symptoms were also observed after 1 month of treatment.

Rating Scale Outcomes
Assessments of UPDRS scores after 3 months of opicapone treatment demonstrated no alterations in mentation, behavior and mood (Part I scores) and clinically relevant improvements in activities of daily living (ADL, Part II) during ON and OFF time, motor scores (Part III) during ON time and total scores (Parts II + III) during ON time (Table 2). After 3 months of treatment, UPDRS IV scores were reduced by 0.9 ± 1.8 points.

Patients’ quality of life (as assessed by the PDQ-8) and non-motor symptoms (as assessed by the NMSS) were also improved after 3 months of opicapone treatment. A mean ± SD improvement of −3.1 ± 12.5 points and −7.7 ± 18.6 points was observed for PDQ-8 and NMSS, respectively. Improvements to cognition and sleep quality among patients were reported, with a mean ± SD of −1.4 ± 6.09 and −1.2 ± 6.14, respectively.

Levodopa Dosing
After 3 months of opicapone treatment, most patients remained on the same total daily levodopa dose (no change: 88.7%; increase: 6.5%; decrease: 4.8%) and levodopa dosing frequency (no change: 79.7%; increase: 10.0%; decrease: 10.3%), resulting in an overall mean change of approximately −4 mg/day. For patients who reported dopaminergic adverse events (full analysis set), most patients (67.2%) remained on the same total daily levodopa dose, 13.4% received a higher dose and 19.4% a lower dose, resulting in an overall mean change of −23.9 mg/day.

Safety and Tolerability
Overall, 252 (69.4%) patients reported TEAEs, which were mostly mild or moderate (Table 3). Few patients (8.0%) experienced serious TEAEs, including one death due to endocarditis that was considered unrelated to
treatment. A total of 137 (37.7%) patients reported TEAEs that were at least possibly related to treatment. Similar to the pivotal studies, the most frequent TEAEs (>5%) considered possibly treatment-related were dyskinesia (5.8%), dizziness (5.2%) and dry mouth (4.4%); diarrhea was reported in 3 (0.8%) patients. Serious TEAEs considered at least possibly treatment-related were reported in 5 (1.4%) of patients and TEAEs leading to premature termination occurred in 40 (11.0%) patients. The most common TEAEs leading to withdrawal were nausea (2.2%) and constipation (1.4%). Of note, no dyskinesia led to treatment interruption or discontinuation. There were no relevant changes in vital signs, and physical and neurological examinations throughout the study.

### Discussion

PD is the second most common neurodegenerative disorder globally, and its prevalence is expected to rise with the aging population [28]. In Germany, nearly 300,000 people aged 50 years or over have been diagnosed with PD, and the number of hospitalizations for the treatment of PD in the country continues to rise [28, 29].

Currently, levodopa is the standard treatment offered to patients with PD; however, continued use of levodopa monotherapy has been associated with wearing-off symptoms, such as motor fluctuations or dyskinesia [12, 30]. The limited half-life and bioavailability of levodopa has resulted in the investigation of various strategies to optimize levodopa treatment, including the introduction of COMT inhibitors such as opicapone [7, 31].

This sub-analysis of the OPTIPARK study is the first study to confirm the effectiveness, safety and tolerability of once-daily opicapone 50 mg in patients with PD and motor fluctuations in routine clinical practice across

### Table 2. Scale assessments

| Scale | UPDRS Part I (mentation, behavior and mood); mean ± SD | UPDRS Part II (ADL during OFF); mean ± SD | UPDRS Part II (ADL during ON); mean ± SD | UPDRS Total scores (Part II + III); mean ± SD | UPDRS Part IV (complications of therapy); mean ± SD | PDQ-8 Total score; mean ± SD |
|-------|-------------------------------------------------------|------------------------------------------|------------------------------------------|--------------------------------------------|-------------------------------------------------|-----------------------------|
|       | Baseline (n = 349) 2.4±2.1 | Baseline (n = 348) 16.8±6.8 | Baseline (n = 348) 11.3±6.2 | Baseline (n = 349) 38.4±17.4 | Baseline (n = 349) 5.0±2.6 | Baseline (n = 349) 29.4±16.6 |
|       | 3 months (n = 349) 1.9±1.9 | 3 months (n = 348) 13.1±6.4 | 3 months (n = 290) 9.0±5.2 | 3 months (n = 291) 30.2±15.2 | 3 months (n = 291) 3.9±2.4 | 3 months (n = 291) 25.5±16.0 |
|       | Change from baseline (n = 291) −0.4±1.5 | Change from baseline (n = 288) −3.3±4.5 | Change from baseline (n = 291) −5.3±7.9 | Change from baseline (n = 291) −7.3±10.1 | Change from baseline (n = 291) −0.9±1.8 | Change from baseline (n = 291) −3.1±12.5 |
|       |                                    |                                    |                                    |                                    |                                    |                                    |
|       | ADL, activities of daily living; NMSS, Non-Motor Symptoms Scale; UPDRS, Unified Parkinson’s Disease Rating Scale; PDQ-8, Parkinson’s Disease Questionnaire; SD, standard deviation. |

### Table 3. Incidence of treatment emergent adverse events

| TEAE category | N = 363 |
|---------------|---------|
| Any TEAE      | 252 (69.4) |
| Any treatment-related* TEAE | 137 (37.7) |
| Any serious TEAE | 29 (8.0) |
| Any treatment-related* serious TEAE | 5 (1.4) |
| Any TEAE leading to discontinuation | 54 (14.9) |
| Any treatment-related* TEAE leading to discontinuation | 40 (11.0) |
| Any serious TEAE leading to discontinuation | 5 (1.4) |
| Any TEAE leading to death | 1 (0.3) |

TEAE, treatment emergent adverse event. * Treatment-related TEAEs were any TEAEs that were considered at least possibly related by the investigator and include the events with missing relationship assessment.
Opicapone Use in Clinical Practice across Germany. The majority of patients demonstrated clinical improvements 3 months after starting treatment, in line with the findings previously reported in the primary OP-TIPARK study, with 70.8% of patients in the German cohort showing clinical improvement on the CGI-C compared with 71.3% of patients in the overall OP-TIPARK population [23]. Treatment with opicapone 50 mg was also generally well tolerated in this patient group, with frequency and type of adverse events as expected for a dopaminergic therapy in patients with PD.

Treatment with opicapone was also associated with an improvement in overall quality of life, as assessed using the PDQ-8. Despite optimized anti-PD therapy (according to clinicians’ judgment) and the fact that most (80.7%) patients received levodopa plus another PD medication, UPDRS motor and ADL scores improved (by 5.3 and 3.3 points, respectively). These data are comparable to findings in the original OPTIPARK cohort, which reported UPDRS motor and ADL score increases of 4.6 and 3.0, respectively [23]. Effects of this magnitude have been reported to be clinically relevant [32–34] and may therefore indicate that treatment with opicapone not only increases ON time, but also improves the quality of ON time. Consistent with previous studies in patients with PD [15, 16], this sub-analysis also suggested an overall improvement in non-motor symptoms, such as cognition and sleep quality, which are an important source of disability and a contributor to worse quality of life [35, 36].

The majority of adverse events experienced in this patient cohort were mild to moderate in severity. As reported for the overall patient population of the OP-TIPARK study, adverse events were the most common reason for withdrawal from the study and the rate of serious TEAEs considered at least possibly related to treatment was low.

Strengths of this study lie in its size, broad inclusion criteria and routine practice setting. Although this study permitted inclusion of a broad range of disease severities (Hoehn and Yahr stages 1–4), we did not capture sufficient data in this pragmatic study to analyze by subgroups. Other weaknesses include those inherent to open-label studies without placebo control, where both the clinician and patient have expectations from treatment. However, despite these limitations, these real-world data complement evidence from clinical trials and confirm that opicapone added to levodopa in patients with PD and motor fluctuations is effective and generally well tolerated in routine clinical practice across Germany.

Conclusions

This study demonstrates the effectiveness, safety, and tolerability of once-daily opicapone 50 mg in patients with PD and motor fluctuations in real-world settings in Germany. Patients’ and clinicians’ perceptions about the global PD condition of patients included in this German cohort were improved with the addition of opicapone 50 mg as adjunct therapy to levodopa. In line with findings from the original OPTIPARK study cohort, opicapone was generally well tolerated, ameliorated motor and non-motor symptoms, and improved quality of life. These findings confirm the clinical utility of opicapone 50 mg as an effective adjunct therapy option for the management of motor fluctuations in levodopa-treated patients with PD in routine clinical practice across Germany.

Acknowledgments

Editorial assistance was provided by Katrin Male from mXm Medical Communications funded by BIAL. We thank the study staff and patients involved in the trial. OPTIPARK study German investigators: Csaba Antal Zolnai, Claudius Bartels, Andreas Barth, Kriemhild Barth, Stephan Behrens, Arnfin Bergmann, Rolf Bodenschutz, Rommy Born, Moritz Brandt, Sebastian Brock, Bernd Brockmeier, Christof Brücke, Norbert Brüggemann, Bernhard Bühler, Uwe Bungard, Lukas Cepek, Ilona Csoyi, Max Deist, Carl Detlev Reimers, Ulrich Dölle, Sylke Domke, Imanuel Dzialowski, Georg Ebersbach, Heike Eggert, Karla Eggert, Reinhard Ehret, Jana Engel, Urban Fietzek, Anke Friedrich, Michael Fritzingner, Florin Gandor, Klaus Gehring, Stephan Gierer, Stephanie Gierer, Vasil Gjaurov, Doreen Gruber, Özkan Günes, Thomas Haas, Kirsten Hahn, Anna Eszter Haraszi, Rolf Hartmann, Bernhard Haslinger, Eva Heiss, Heinz P. Herbst, Frank Hoffmann, Werner E. Hofmann, Günter Höglinger, Wolfgang Jost, Anna-Maria Kavicic, Christoph Kellinghaus, Bertold Klemperer, Fabian Klostermann, Thomas Knoll, Natalia Koleva-Alazeh, Jiri Koschel, Diana Waltraud Kraft-Safavi, Almut Kronenberger, Andrea Kühn, Andreas Kupsch, Thomas Lehnhoff, Peter Laumen, Paul Lingor, Karla Lippmann, Michael Lorrain, Fabian Maass, Siegfried Muhlack, Thomas Müller, Michael Nagel, Stephan Neudecker, Katja Odin, Christian Oehlwein, Hakan Orbasli, Wolfram von Pannwitz, Heidi Pape, Robert Pfister, Tino Prell, Reinhard Puzich, Daniela Rau, Rene Reese, Gerd Reifschneider, Gernot Reimann, Stefani Ries, Christoph Rieth, Charlotte Rewitzer, Ali Safavi, Alexander B. Schmied, Johannes Schwarz, Wolfgang Schwarz, Joachim Springub, Inga Suttrup Claus, Vera Tadic, Klaus Tiel-Wilck, Lars Tönges, Jens Tröger, Christoph Schrey, Alexander Schulze, Sven Thonke, Tobias Wächter, Achim S. Wannenmacher, Tobias Warneck, Bettina Wieder, Martin Wimmer, Christian Winkler, Otto Witte, Dirk Woitalla, Samis Zella, and Uwe Ziebold.
Statement of Ethics

This study protocol was reviewed and approved by Ethics Committees at all the multiple participating sites. The lead Ethics Committee was at the Technical University Dresden, Dresden, Germany, reference number EK 353082016. The trial was conducted in accordance with the Declaration of Helsinki and International Conference on Harmonization Good Clinical Practice Guidelines. All patients provided written informed consent.

Conflict of Interest Statement

H.R. reports acting on advisory boards, gave lectures, and received research grants from Abbvie, BIAL, Desitin, Eisai, Kyowa Kirin, Novartis, TEVA, UCB Pharma, and Zambon. K.E. reports acting on advisory boards, gave lectures, and received research grants from Abbvie, Accorda, Adamas, Adexx, Alkahest, Apopharma, Benevolent, Bial, Biogen, Biohaven, Biotie, Desitin, Impax, Kyowa Kirin, Novartis, Pfizer, Retrotepo, Roche, Stada, UCB, and Zambon. C.O. held lectures and created posters for BIAL. T.W. reports acting on advisory boards, gave lectures, and received research grants from AbbVie, Archimedex, Bayer, Bial, Biogen, Desitin, Kyowa, Licher, Pfizer, Phagenesis, Stada, Teva, UCB, and Zambon. A.L. is funded by the Reta Lila Weston Institute of Neurological Studies, Institute of Neurology, University College London, and reports consultancies from Britannia Pharmaceuticals and BIAL. He also reports grants and/or research support from the Frances and Renee Hock Fund and honoraria from Britannia Pharmaceuticals, Profile Pharma, UCB, Roche, BIAL, STADA, NordicInFu Care, and NeuroDerm. M.K. and P.S.S. are employed by BIAL – Portela & Cª, S.A.

References

1 Fackrell R, Carroll CB, Grosset DG, Mohamed B, Reddy P, Parry M, et al. Noninvasive options for “wearing-off” in Parkinson’s disease: a clinical consensus from a panel of UK Parkinson’s disease specialists. Neurodegener Dis Manag. 2018;8(5):349–60.
2 Girasole AE, Lum MY, Nathaniel D, Bair-Marshall CJ, Guenther CJ, Luo L, et al. A subpopulation of striatal neurons mediates levodopa-induced dyskinesias. Neuron. 2018;97(4):787–95.e6.
3 Lane EL. L-DOPA for Parkinson’s disease—a bittersweet pill. Eur J Neurosci. 2019;49(3):384–98.
4 Athulya RT, Jayakrishnan S, Lye R, Alapat PJ. Predictors of levodopa-induced dyskinesias in Parkinson’s disease. Ann Indian Acad Neurol. 2020;23(1):44–7.
5 Chapuis S, Ouchchane L, Metz O, Gerbaud L, Durif F. Impact of the motor complications of Parkinson’s disease on the quality of life. Mov Disord. 2005;20(2):224–30.
6 Mizuno Y, Shimoda S, Origasa H. Long-term treatment of Parkinson’s disease with levodopa and other adjunctive drugs. J Neural Transm. 2018;125(1):35–43.
7 Fabbri M, Ferreira JJ, Lees A, Stocchi F, Poewe W, Tolosa E, et al. Opicapone for the treatment of Parkinson’s disease: a review of a new licensed medicine. Mov Disord. 2018;33(10):1528–39.
8 Poewe W. The role of COMT inhibition in the treatment of Parkinson’s disease. Neurology. 2004;62(1 Suppl 1):S31–8.
9 Almeida L, Rocha JF, Falcao A, Palma PN, Loureiro AI, Pinto R, et al. Pharmacokinetics, pharmacodynamics and tolerability of opicapone, a novel catechol-O-methyltransferase inhibitor, in healthy subjects: prediction of slow enzyme-inhibitor complex dissociation of a short-living and very long-acting inhibitor. Clin Pharmacokinet. 2013;52(2):139–51.
10 Montioli R, Voltattorni CB, Bertoldi M. Parkinson’s disease: recent updates in the identification of human dopa decarboxylase inhibitors. Curr Drug Metab. 2016;17(5):513–8.
11 Montioli R, Cellini B, Dindo M, Oppici E, Voltattorni CB. Interaction of human Dopa decarboxylase with L-Dopa: spectroscopic and kinetic studies as a function of pH. Biomed Res Int. 2013;2013:161456.

Funding Sources

The study was funded by BIAL. Two authors (P.S.S. and M.K.) were employed by the funder and participated in the study design, data collection, data management, and data analysis of the primary study and/or the sub-analysis. The funder of the study had no other role in data interpretation or in the decision to submit the manuscript for publication. BIAL also supported reporting of study results by procuring medical writing support for the manuscript.

Author Contributions

H.R., K.E., C.O., T.W., and A.L. were study investigators of the primary study and were involved in the study design, data collection, and data interpretation. P.S.S. and M.K. participated in the study design, data collection, data management, and data analysis. All authors provided critical review of the manuscript and approved the final draft.

Data Availability Statement

The dataset supporting the conclusions of this article is included within the article. The study sponsor (BIAL) undertakes to share, upon request, anonymized patient-level, study-level clinical trial data (analyzable data sets), and other information (such as protocols) from this clinical trial to qualified researchers as necessary for conducting legitimate research. Information is provided at www.bial.com.

DOI: 10.1159/000523771

Eur Neurol 2022;85:389–397

Reichmann/Eggert/Oehlwein/ Warnecke/Lees/Kemmer/Soares-da-Silva

396

End
Opicapone Use in Clinical Practice across Germany

17 European Medicines Agency. Ongentys, INN-opicapone. Summary of product characteristics. 2021 [cited 2021 Oct 11]. Available from: https://www.ema.europa.eu/en/documents/product-information/ongentys-epar-product-information_en.pdf.

18 Mahajan R. Real world data: additional source for making clinical decisions. Int J Appl Basic Med Res. 2015;5(2):82.

19 Kim HS, Lee S, Kim JH. Real-world evidence versus randomized controlled trial: clinical research based on electronic medical records. J Korean Med Sci. 2018;33(34):e213.

20 Bhida A, Shah PS, Acharya G. A simplified guide to randomized controlled trials. Acta Obstet Gynecol Scand. 2018;97(4):380–7.

21 Food and Drug Administration. Submitting documents using real-world data and real-world evidence to FDA for drugs and biologics guidance for industry. 2021 [cited 2021 Oct 11]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submitting-documents-using-real-world-data-and-real-world-evidence-fda-drugs-and-biologics-guidance.

22 Cave A, Kurz X, Arlett P. Real-world data for regulatory decision making: challenges and possible solutions for Europe. Clin Pharmacol Ther. 2019;106(1):36–9.

23 Reichmann H, Lees A, Rocha JF, Magalhães D, Soares-da-Silva P, OPTIPARK Investigators. Effectiveness and safety of opicapone in Parkinson’s disease patients with motor fluctuations: the OPTIPARK open-label study. Transl Neurodegener. 2020;9(1):9.

24 Stacy M, Hauser R, Oertel W, Schapira A, Sethi K, Stocchi F, et al. End-of-dose wearing off in Parkinson disease: a 9-question survey assessment. Clin Neuropharmacol. 2006;29(6):312–21.

25 Fahn S, Elton R. UPDRS Program Members. Unified Parkinson’s disease rating scale. In: Recent developments in Parkinson’s disease: MacMillan Healthcare Information; 1987. Vol. 2; p. 153–64.

26 Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N. The PDQ-8: development and validation of a short-form Parkinson’s disease questionnaire. Psychol Health. 1997;12(6):805–14.

27 Chaudhuri KR, Martinez-Martín P, Brown RG, Sethi K, Stocchi F, Odin P, et al. The metric properties of a novel non-motor symptoms scale for Parkinson’s disease: results from an international pilot study. Mov Disord. 2007;22(13):1901–11.

28 Prell T, Siebecker F, Lorrain M, Eggers C, Lorenz S, Klucken J, et al. Recommendations for standards of network care for patients with Parkinson’s disease in Germany. J Clin Med. 2020;9(5):1455.

29 Nerius M, Fink A, Dobhlhammer G. Parkinson’s disease in Germany: prevalence and incidence based on health claims data. Acta Neurol Scand. 2017;136(5):386–92.

30 Cilia R, Cereda E, Akpelu A, Sarfo FS, Cham M, Laryea R, et al. Natural history of motor symptoms in Parkinson’s disease and the long-duration response to levodopa. Brain. 2020;143(8):2490–501.

31 Poewe W, Antonini A. Novel formulations and modes of delivery of levodopa. Mov Disord. 2015;30(1):114–20.

32 Shulman LM, Gruber-Baldini AL, Anderson KE, Fishman PS, Reich SG, Weiner WJ. The clinically important difference on the unified Parkinson’s disease rating scale. Arch Neurol. 2010;67(1):64–70.

33 Hauser RA, Auinger P. Determination of minimal clinically important change in early and advanced Parkinson’s disease. Mov Disord. 2011;26(5):813–8.

34 Hauser RA, Gordon MF, Mizuno Y, Poepe W, Barone P, Schapira AH, et al. Minimal clinically important difference in Parkinson’s disease as assessed in pivotal trials of pramipexole extended release. Parkinsons Dis. 2014;2014:467131.

35 Chaudhuri KR, Yates L, Martinez-Martín P. The non-motor symptom complex of Parkinson’s disease: a comprehensive assessment is essential. Curr Neurol Neurosci Rep. 2005;5(4):275–83.

36 Chaudhuri KR, Schapira AH. Non-motor symptoms of Parkinson’s disease: dopaminergic pathophysiology and treatment. Lancet Neurol. 2009;8(5):464–74.