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### Conflicts of Interest

The authors declare no conflicts of interest.

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## Melanoma in a Patient With Parkinson Disease

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### To the Editor:

There has been discussion of the link between melanoma and Parkinson disease (PD) in the literature, along with the possible causal relationship between levodopa and rasagiline therapy and the appearance of melanoma. We present the case of an 81-year-old woman, Caucasian, phototype III, home maker, with no history of sunburn

or family history of melanoma, who consulted for a pigmented lesion on the right cheek that had appeared a year earlier. Pathologic study led to a diagnosis of lentigo maligna and the lesion was excised. The patient had a personal medical history of idiopathic PD treated with Sinemet (levodopa/carbidopa) and Azilect (rasagiline) for the last 18 months. We reviewed the literature in order to

make an informed decision on whether or not to suspend these drugs in our patient.

The Sinemet prescribing information sheet warns of the possibility of levodopa activating melanoma, thereby contraindicating its use in patients with suspect skin lesions or a history of melanoma. The association between treatment with levodopa and melanoma was first described in 1972 by Skibba et al,<sup>1</sup> who published a case of the recurrence of melanoma following treatment with levodopa. The hypothesis stems from the fact that dopamine (the deficient neurotransmitter in PD) and melanin share common metabolic pathways and it is suggested that exogenous levodopa could have some effect on melanin synthesis, increasing melanogenesis and stimulating melanoma growth. Individual cases and series of cases along the same lines were published from the 1970s to the 1990s. In 2003, Fiala et al<sup>2</sup> published a review of all 43 cases published to date, adding a further 11 cases from their own institution in Texas, United States. They analyzed the average age at diagnosis of the 2 diseases; whether the diagnosis of melanoma occurred before or after initiating treatment with levodopa; the average time between starting treatment with levodopa and the appearance of the melanoma; and the average amount of levodopa consumed before the diagnosis of melanoma was made. The resulting data were heterogeneous and inconclusive on all fronts, whereby it was suggested that the relationship between treatment with levodopa and melanoma was more of a coincidence than a causal relationship.

In 2006, Olsen et al,<sup>3</sup> in Denmark, published a retrospective case-control study (cases: 8090 patients with PD; controls: 32 236 people from the central register) in which they measured the prevalence of cancer from 1943 until the date of diagnosis with PD (using the same date in the corresponding controls). They found a greater prevalence of melanoma in patients with PD (odds ratio [OR] 1.44; confidence interval [CI], 1.03-2.01); this prevalence increased in the year prior to diagnosis with PD (OR 3.2; CI, 1.26-8.1). These data led them to the conclusion that there must be a common environmental or genetic factor in both diseases and that the association between the 2 is not due to treatment with levodopa. In 2007, the same authors published a retrospective study of a cohort of 14 088 patients with PD in which they measured the incidence of cancer from diagnosis with PD to 2002.<sup>4</sup> They found an increased risk of melanoma compared with the general population (relative risk 1.85; CI, 1.37-2.46). There was a special link with melanoma in the idiopathic Parkinson group (OR 3.9; CI, 1.6-9.8), while this association was not statistically significant in the group of other forms of PD. Meanwhile, they confirmed that the risk of melanoma was not dependent on treatment with levodopa or on cumulative dose. They therefore concluded that the increased incidence of melanoma in patients with PD is

restricted to those with idiopathic PD and that this is not treatment dependent.

In the case of rasagiline, the prescribing information sheet of Azilect (authorized in 2005) warns of a possible link with the appearance of melanoma, meaning that any suspicious lesion should be assessed by a specialist. The warnings on the prescribing information sheet were based on the findings of a randomized and placebo controlled clinical trial<sup>5</sup> with 472 patients, in which 3 new cases of melanoma appeared (all in the treatment group). The results of a post-marketing study is currently pending.

In summary, there are no epidemiological studies that show a causal link between levodopa and melanoma, so this drug should not be withdrawn from patients with melanoma nor should its use be contraindicated in patients with a history of melanoma. We suggest modifying the prescribing information sheet to avoid anxiety in Parkinson patients who could also be affected by melanoma. At present there is a perceived link between PD and melanoma (see Zanetti et al<sup>6</sup>) although this has not yet been ascribed to a common genetic cause or the presence of an external factor associated with both entities. As for the use of rasagiline, further studies are needed before a position can be taken on the matter.

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#### Conflict of Interests

The authors declare no conflicts of interest.

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