CASE REPORT

# Detection of a new melanoma in a patient treated with fingolimod

Yves Michiels,[1] Olivier Bugnon,[1,2] Jean-François Michiels,[3] Sophie Mazellier[3]

[1]Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland
[2]Community Pharmacy Unit, Pharmaceutical Sciences section, Universities of Geneva and Lausanne, Geneva, Switzerland
[3]Laboratoire Central d'Anatomie et Cytologie Pathologique, Centre Hospitalier Universitaire de Nice, Hôpital Pasteur, CHU Nice, Nice, France

**Correspondence to**
Dr Yves Michiels,
yves.michiels@hospvd.ch

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## SUMMARY

In addition to the TRANSFORMS, FREEDOMS, INFORMS studies, very few publications have identified new cases of skin cancer in patients treated with fingolimod. Here, we present the case of a 52-year-old Caucasian patient with relapsing remitting multiple sclerosis for 19 years, with a phototype II with blue eyes, light brown hair, no personal or family history of melanoma and a low number of naevi (<10). She did not experience intense sun exposure in childhood as well as severe sunburn and did not practise sessions in ultraviolet cabins.
This case is distinguished from other published cases, usually superficial spreading malignant melanoma by its unclassifiable histological character. The occurrence of skin cancers in patients with multiple sclerosis remains exceptional, but new cases have recently emerged requiring the strengthening of dermatological follow-up of such patients.

## BACKGROUND

In addition to the TRANSFORMS, FREEDOMS, INFORMS studies, very few publications have identified new cases of skin cancer in patients treated with fingolimod.

## CASE PRESENTATION

Here, we present the case of a 52-year-old Causasian patient with relapsing remitting multiple sclerosis for 19 years, with a phototype II with blue eyes, light brown hair, no personal or family history of melanoma and a low number of naevi (<10). She did not experience intense sun exposure in childhood as well as severe sunburn and did not practise sessions in ultraviolet cabins.

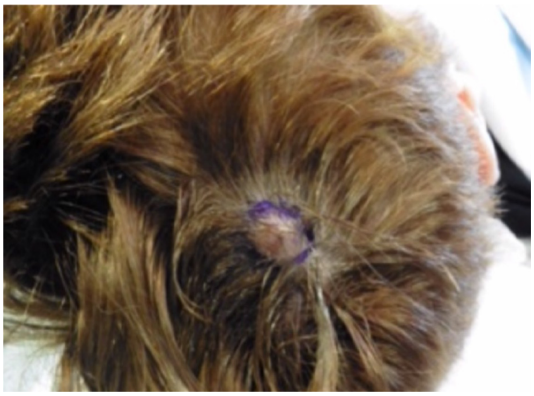

**Figure 1** Left parietal nodular cranial lesion.

## INVESTIGATIONS

This patient with multiple sclerosis has been treated with fingolimod 0.5 mg/day for 3 years following a therapeutic switch of natalizumab for positive seroconversion to John Cunningham virus. Two years later, she presented with a subcutaneous, mobile, nodular lesion of the scalp in the left parietal region. It had a bluish appearance and was non-pulsatile (figure 1). This lesion developed an inflammatory and painful character and a surgical excision was performed. The histological study showed a largely necrotic dermal tumour consisting of a cellular proliferation, positive after Fontana Masson staining. Immunohistochemistry showed positivity with PS100, HMB45 and Melan A, and total cytokeratin negativity. The diagnosis was a Clark Level IV unclassifiable malignant melanoma with a Breslow index of 13 mm (figure 2). Lymph node ultrasonography excluded lymph node involvement in the cervical and supraclavicular areas. Sentinel lymph node technique was done, the final clinical examination did not show a primary site or a sign of clinically regressing melanoma.

## TREATMENT

Treatment with fingolimod was stopped following this diagnosis, the patient did not present a relapse.

## OUTCOME AND FOLLOW-UP

Ensure better dermatological screening of melanoma in patients treated with fingolimod with regular follow-up

## DISCUSSION

This case is distinguished from other published cases, usually superficial spreading malignant melanoma by its unclassifiable histological character.[1] Although clinical trials or follow-up studies have not revealed any significant differences in the increase of cancers, especially melanomas, a large number of pharmacovigilance cases have been reported in recent years concerning almost all new oral or injectable molecules.[2 3] The occurrence of skin cancers in patients with multiple sclerosis remains exceptional, but new cases have recently emerged requiring the strengthening of dermatological follow-up of such patients.

Cases of melanoma have been reported for galitramer, natalizumab (more than 100 cases), dimethyl fumarate, alemtuzumab or cladribine.[2–6]

The relationship between cancer and multiple sclerosis is very complex to establish, and there is no obvious relationship despite a chronic inflammatory character promoting the cancer risk in



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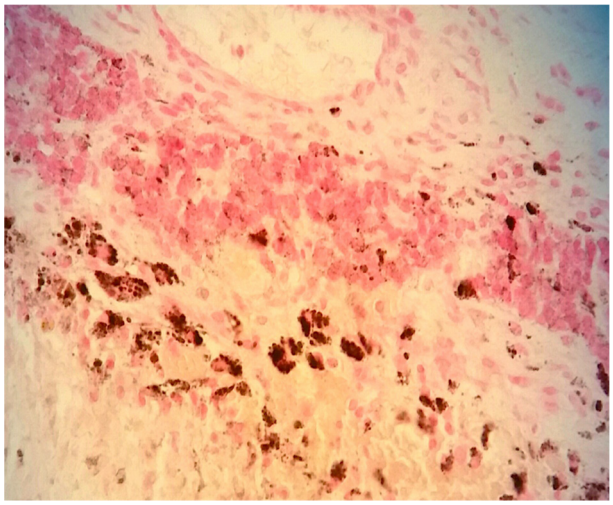

**Figure 2** Fontana-Masson colouring which stains the melanic pigment in black in the necrosis and in the few perennial pink cells (×40).

such patients. Tumour mechanisms are still poorly understood today and range between a decrease in general immune surveillance or a direct action on a specific receptor present on keratinocytes (fingolimod (SP1) or integrin α4β1 integrin for natalizumab).[2 3]

We can legitimately ask ourselves the question of the use of immunomodulatory molecules such as fingolimod continuously in such patients, because several studies have already revealed an increased incidence of melanomas or Merkel cell carcinoma in patients treated with immune suppressants.[7] Patients with fingolimod should have enhanced dermatological monitoring to detect early this type of skin cancer and must be able to practise regular self-monitoring.

A pharmacovigilance statement was made by a community pharmacist for this case indicating their potential role in the monitoring of such treatments.[2 3]

## Learning points

- Dermatological monitoring should be considered for patients treated with fingolimod.
- Patients should be warned of the need for dermatological follow-up.
- Patients can be educated to monitor possible melanoma.

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