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LETTER TO THE EDITOR

Screening for Fingolimod Associated Macular Oedema: Experience Versus Guidelines

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Abstract: We report adherence to United Kingdom national guidelines on surveillance for Fingolimod associated macular oedema (FAME) and the impact on clinical services at our unit. We conducted a 9-month study, measuring referral interval, visual function and performing OCT scans for all patients referred for FAME surveillance. 38 patients in total were seen, representing 9% of all new ophthalmic referrals during the study period. 26% were seen between 2 and 4 months after starting Fingolimod treatment, 74% between 3 and 4 months after starting Fingolimod treatment. The impact on clinical services is discussed.

Keywords: Fingolimod, guidelines, macular oedema, screening.

TO THE EDITOR,

Multiple Sclerosis (MS) is the most common demyelinating disease of the central nervous system. It affects 2.5 million people worldwide and is the primary cause of neurological disability of young adults.

Fingolimod (FTY720, Gilenya, Novartis) is a new oral therapy which sequesters lymphocytes involved in the immune-mediated process of MS in peripheral lymph nodes. Phase 3 clinical trials have shown that Fingolimod has a "superior efficacy with respect to relapse rates and MRI outcomes in patients with multiple sclerosis, as compared with intramuscular interferon beta-1a" [1] and "improved the relapse rate, the risk of disability progression, and end points on MRI" compared with placebo [2]. This drug is now "recommended as an option for the treatment of highly active relapsing-remitting MS in adults, if they have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon", according to UK national guidelines [3].

Both Phase 3 clinical trials identified macular oedema as a complication of Fingolimod [1, 2]. The summary of product characteristics states macular oedema with or without visual symptoms has been reported in 0.4% of patients treated with Fingolimod 0.5 mg, occurring predominantly within the first 3-4 months of therapy [4].

In the United Kingdom, the National Institute for Health Care Excellence (NICE) provides systematically developed recommendations and advice to improve health and social care, based on best available evidence. Among its many roles, NICE provides recommendations for good practice for those individuals and organisations involved in governing, commissioning, prescribing and decision-making about medicines [5]. In its final appraisal report, NICE recommends "an ophthalmological evaluation at 3-4 months after (Fingolimod) treatment initiation" [3].

Here we measure the adherence to NICE guidelines for surveillance of these patients at our unit, and measure the impact of delivery of NICE guidelines on clinical services.

Between 1st May 2013 and 15th January 2014, all new referrals to the eye clinic for Fingolimod surveillance were identified through a combination of MS nurse referral lists and ophthalmology clinic lists. Other than referrals made outside this time frame, no exclusion criteria were specified. For each patient, time interval between starting Fingolimod treatment and review in clinic was recorded. Visual symptoms, visual acuities for near and distance, slit-lamp biomicroscopy fundal assessment and Spectralis macular ocular coherence tomography (OCT) were also recorded.

During the study period, a total of 38 patients started on Fingolimod, were referred to the eye clinic for screening for associated maculopathy. These referrals made up 9% (38/403) of all new referrals seen in 2 ophthalmic consultant clinics (4 sessions per week) between 1st May 2013 and 15th January 2014. 26% of all referrals were seen between 3 and 4 months after starting Fingolimod treatment, 74% were seen between 2 and 4 months after starting Fingolimod treatment. (range 4-29 weeks).

All but one patient reported no new deterioration in visual function, and were found to have no macular oedema. One poorly controlled diabetic patient complained of increased blurring of vision in both eyes soon after Fingolimod commenced. He was seen 5 weeks after starting treatment; reduced visual acuities for near and distance were recorded for both eyes and bilateral macular oedema was

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noted both clinically and on OCT scans. Fingolimod was discontinued for this patient; at follow-up his vision had recovered and his macular oedema had diminished.

This study shows that adherence to the NICE guidelines produces a significant percentage of new referrals for Fingolimod surveillance at our unit. The numbers reported in this study may only represent the impact on services at a single unit, or may more broadly reflect the situation elsewhere. As a neuro-ophthalmology service within a large dedicated neurosciences centre, our unit may expect to receive a larger number of referrals in comparison with a general ophthalmology clinic, nevertheless, the resulting impact on services seems excessive, given the incidence of complications requiring further management, (although our study does not have the power to confirm the reported frequency of macular oedema).

The authors welcome information on any similar audits carried out in other units, such that data / impact on services can be compared.

In order to ease the pressure on already over-burdened outpatient clinics, the authors recommend patients' distance and near visual acuities and visual symptoms are monitored by the physicians prescribing Fingolimod, with referral to the ophthalmologist in the event of change.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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