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Sir,

MEK inhibitors: a new class of chemotherapeutic agents with ocular toxicity

We read with interest Duncan *et al*'s[1] article published in the August edition of the *Eye*.

We have made similar observations in patient's taking R05126766 (a combined RAF and MEK inhibitor) for advanced stage cancers and found retinal changes to be common.

MEK inhibitors act upon the mitogen-activated protein kinase (MAPK) pathway, which is upregulated in a number of cancers. R05126766, the first-in-human combined RAF/MEK inhibitor, offers dual inhibition on the MAPK pathway and superior cascade blockage.[2,3] Ocular toxicities were reported in up to 50% of patients.[2]

Despite increased use of MEK inhibitors,[3,4] there has been limited ophthalmic literature. We would like to share our experiences regarding them.

We retrospectively analysed clinical notes for a 15-patient cohort, commenced on R05126766 monotherapy, as part of an ongoing prospective phase 1/2 trial. Each patient had baseline ophthalmic assessment and at least one follow-up while taking R05126766. The examinations were performed by the same consultant ophthalmic specialist (PU).

Retinal changes, including central serous retinopathy and pigment epithelial detachments were seen in eight patients. Six patients were symptomatic, describing blurred vision, scotomas, and two patients described a blue discolouration. We also noted that 75% of the patients who developed ocular toxicity complained of a rash, compared with only one patient (14%) without ocular toxicity. Please see Table 1 for results summary.

Table 1 Summary table showing results for the eight patients

Case no	*Age*	*Sex*	*Type of cancer*	*Signs*	*Confirmed on OCT*	*Onset*	*Rash*
1	57	M	Colorectal	Bilateral CSR	Yes	1 Month	Yes
2	50	M	Adrenal	Bilateral CSR	Yes	Day 1	Yes
3	62	M	Metastatic melanoma	unilateral CSR	Yes	1 Week	Yes
4	54	M	Metastatic melanoma	Bilateral PED	No	2 Months	Yes
5	64	M	Metastatic colorectal	Unilateral PED	No	4 Months	No
6	40	F	Metastatic melanoma	Unilateral RPE changes	Yes	1 Week	Yes
7	58	M	Colorectal	Unilateral PED	No	1 Week	Yes
8	64	F	Metastatic melanoma	Unilateral PED	Yes	1 month	No

The onset of symptoms varied from 1 day to 4 months. Conclusive follow-up was not achieved because of poor patient health, with quite a number dying before resolution of their symptoms.

We have observed a high incidence of retinal pathologies in this small group of patients taking combined RAF/MEK inhibitors. We agree with the conclusions made by our colleagues Duncan *et al* and would recommend that baseline ophthalmic assessment with optical coherence tomography should be obtained in all patients before commencing MEK inhibitor chemotherapy.

As MEK inhibitors continue to be developed,[3,4] we predict an increased incidence of associated ocular toxicities, which may be more common than first realised. It is important, therefore, that general ophthalmologists are aware of these drugs. Further understanding of the aetiology and management of complications is needed.

Conflict of interest

The authors declare no conflict of interest.

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