Title: Relevance of sun safety in patients commencing crizotinib for non-small cell lung cancer

Running Head: Crizotinib and photosensitivity

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Advanced non-small cell lung cancer (NSCLC) management has been increasingly characterized by therapies targeted at molecular alterations recognised to be oncogenic drivers. Aside from efficacy, such therapies have demonstrated favourable toxicity profiles compared to chemotherapy. Crizotinib, an inhibitor of ALK, MET and ROS1; was first reported as having benefit over chemotherapy for patients with metastatic NSCLC harbouring an anaplastic lymphoma kinase (ALK) translocation [1]. Subsequently, benefit has been demonstrated for patients with ROS1 proto-oncogene receptor tyrosine kinase rearrangements, noted amongst 1-2% of metastatic NSCLC cases [2].

Case Report

In 2019, a 57 year-old male of Chinese ethnicity, otherwise well and a never-smoker, presented in cardiac tamponade. Pericardiocentesis fluid analysis confirmed lung adenocarcinoma with bilateral pleural effusions and a 19mm right lung primary on imaging. ROS1 rearrangement was subsequently demonstrated via Fluorescence In-Situ Hybridisation, and crizotinib 250mg PO BD commenced. An FDG-PET scan performed less than 3 weeks later demonstrated almost complete resolution of the primary and no other disease.

Six months after commencing crizotinib, towards the end of summer, the patient developed a diffuse erythematous maculo-papular rash over sun-exposed areas (arms, neck and face to a lesser degree, Figure 1). The patient was taking no other medications. Medical history was significant for ulcerative proctitis only.

The patient briefly trialled topical corticosteroids however found them ineffective. Avoidance of further sun exposure was advised, and wearing of long-sleeved shirts, long pants and a broad brim hat if outdoors. The rash improved significantly over a month with near complete resolution by 4 months. The patient continued crizotinib and remained in complete metabolic response on FDG-PET imaging in August 2020. The patient consented to use of his images for publication.

Discussion

Crizotinib has been reported to have good tolerability with more common side-effects including visual disorders, diarrhoea, oedema and liver dysfunction [1, 2]. Unlike other tyrosine kinase inhibitors, such as those directed against EGFR alterations, marked dermatological toxicities are uncommon with 11-13% of patients experiencing grade 1-2 rash in early trials [1, 2]. To our knowledge only three cases of dermatological photosensitivity requiring intervention have been reported. Oser et al describe a patient with metastatic ALK-translocated NSCLC who developed a grade 4 desquamating rash on sun-exposed areas, requiring systemic corticosteroids and ultimately crizotinib cessation 2 months following commencement, with marked oncological response noted [3]. Dabas et al, describe a patient with metastatic ROS1-rearranged NSCLC who developed photo-allergic dermatitis 5 months following crizotinib initiation following an episode of significant sun exposure, which resolved with use of systemic and topical corticosteroids, anti-histamines and emollients [4]. Ho et Chen, describe a patient who developed a lichenoid drug eruption on the extremities 4 weeks following drug commencement which sun exposure was noted to aggravate, who was treated with topical corticosteroids and continued treatment [5].

We suggest the case reported represents another example of photosensitive rash associated with crizotinib. Whilst uncommon, increasing crizotinib use highlights the importance of awareness regarding such toxicities, particularly if simple measures such as advising patients to exercise caution regarding sun exposure might be sufficient.

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Figure 1 – bilateral forearms demonstrate erythematous maculopapular rash

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