behaviour of NMSC. There is a good deal of evidence that shows that azathioprine and cyclosporin, as well as other agents, adversely affect such cancers.[2,3] A direct carcinogenic effect has been described in transplant patients for both azathioprine and cyclosporin, beside their primary immunosuppressive role. The former acts as mutagen and photosensitizer by increasing the level of its metabolite 6-thioguanine, while the latter seems to upregulate the transforming growth factor β (TGF-β), a cytokine implicated in cells proliferation and transformation.

Immunological cancer surveillance systems in patients using these drugs in the long term are known to be impaired in the detection and eradication of precancerous lesions. Finally, evidences suggest that also immunosuppression related to HIV/AIDS, non-Hodgkin lymphoma and chronic lymphocytic leukaemia may increase the risk of developing more aggressive SCCs.[4,5]

Even assuming that no immunosuppressed individuals were present in Gerring *et al*'s[1] sample, we believe that considering immunosuppression among the potential prognostic factors is mandatory as far as NMSC are concerned. This is extensively outlined in many studies, including major reviews and meta-analysis.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Response to 'The importance of immunosuppression as risk and prognostic factor for periorbital non-melanoma skin cancers'

We would like to thank Dr Albanese for his interest in our recent publication, RC Gerring *et al.*[1] Although there is no data specifically looking at periorbital skin malignancies, there is significant evidence to support an increased risk for the development of nonmelanoma skin cancer after solid organ transplant at an approximate rate of 65–250-fold for squamous cell carcinoma and 10-fold for basal cell carcinoma as compared to the general population.[2,3]

The pathophysiology underlying these significantly increased skin cancer rates is thought to be through both the carcinogenic action of immune suppressive agents,[4,5] as well as impaired eradication of precancerous changes related to immune suppression.[6] Among transplant patients, known risk factors for the development of skin cancer after transplantation include fairer skin type, level of immune suppression, and degree of ultraviolet exposure.[3,7] Bone marrow transplantation has also been shown to increase the risk of nonmelanoma skin cancers in both children[8] and adults.[9] Given the increasing incidence of both solid organ and bone marrow transplantation, and increased survival after these therapies, immune suppression state in relation to skin cancer is an especially important topic of interest.

Unfortunately, we were not able to obtain this historical patient information consistently as part of our retrospective chart review (study time period of 2002–2012). We were able to obtain historical patient data with regards to skin cancer history, however, significant prior medical history data was often limited. For this reason, we were not able to include immune suppression as part of our analysis. We do, however, appreciate its importance as a potential prognostic indicator and will consider this upon any potential future research.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Hydroxychloroquine use: the potential impact of new ocular screening guidelines

Hydroxychloroquine (HCQ) has been widely prescribed by Rheumatologists since the 1950s. Retinal toxicity, particularly with treatment duration >5 years, is a recognised complication. The British Society for Rheumatology (BSR) recently updated its screening guidelines:[1]

> *'Patients should have baseline formal ophthalmic examination, ideally including objective retinal assessment for example using optical coherence tomography (OCT), within 1 year of commencing HCQ……*
>
> *(and) annual eye assessment (ideally including optical coherence tomography) if continued for >5 years'*

This reflected availability of data from OCT, and recognition that risk of HCQ-induced retinal toxicity is greater than previously thought. We set out to quantify HCQ use in England and Wales, to understand the impact of the new guidelines on ophthalmology services.

Estimate of new starters/year

Data from the Healthcare Quality Improvement Partnership (HQIP) Early Inflammatory Arthritis national audit and The Early Rheumatoid Arthritis Network (ERAN) were reviewed. ERAN (2001–2011) reported HCQ use of 22%. HQIP (2014–2016) reported 51.7% of patients newly diagnosed with rheumatoid arthritis (RA) were commenced on HCQ. The higher reported usage in HQIP may reflect a movement towards combination therapy in contemporary practice.

The Systemic Lupus International Collaborating Clinics Inception Cohort reported 67% of SLE patients commence HCQ in the first year.[2]

Extrapolating using UK disease incidence data for RA and Lupus,[3,4] and an adult population of 47 300 000, this equates to around 11 000 new HCQ initiations per year in England and Wales.

Individuals that are established on HCQ

Considerable effort is needed to bring established patients in line with the new guidelines. NHS Digital provides summary data from England on community expenditure and prescribing.[5] In 2016, 58 810 415 HCQ 200 mg tablets were dispensed, equating to 161 124 prevalent users (assuming 200 mg daily dose).

Horizon scanning and time trends

Within rheumatology, treatment guidelines have substantially evolved in the last decade, with recommendations for intensive therapy advocating targets of disease remission. Strategy trials have demonstrated cost benefits to combination therapy.

NHS Digital provides a useful data source for examining the time trends of HCQ use (Figure 1).

Implications

Retinal assessment based on the new BSR guidance will significantly increase pressure on NHS resources. This will include a transient catch up period for established HCQ users requiring additional screening, as well as an increased burden for new starters. This brings the cost-benefit of HCQ into question.

The Royal College of Ophthalmologists (RCOphth) is undertaking an independent review of the evidence, and new guidelines with collaborative recommendations are imminent.

Conflict of interest

Mark Yates is funded by the BSR. James Galloway is on the RCOphth hydroxychloroquine guidelines committee. The remaining authors declare no conflict of interest.

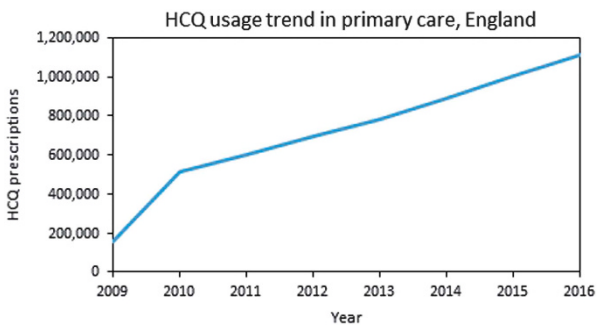

Figure 1 Source: *http://content.digital.nhs.uk/catalogue/PUB23631/pres-cost-anal-eng-2016-trend.zip* (accessed on 14 May 2017).