Imiquimod cream – a novel patient-administered treatment for malignant and pre-malignant skin lesions

LAWRENCE SCERRI

It is a well established fact that the incidence of sun-related skin damage (photo-ageing) and neoplastic transformation (photo-carcinogenesis) has progressively increased in recent decades as a result of cultural and occupational trends leading to increased sun exposure and use of sunbeds, particularly in Caucasian populations.

Consequences of chronic sun-damage include actinic (solar) keratosis (AK), basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). AK presents as a scaly keratotic plaque which varies in thickness from thin to hypertrophic (including keratin horn). AKs are considered to be mildly pre-malignant, and the rate of transformation to invasive SCC is thought to be less than 1%. In fact most SCCs develop within a pre-existing AK. The in-situ pre-invasive form of SCC is known as intra-epithelial carcinoma or Bowen's disease. Clinically, this can sometimes look similar to superficial BCC. It typically presents as a flat scaly plaque on an erythematous background, rather like a psoriasiform plaque. It is most commonly found on the extremities, but sometimes also on the head, neck and trunk. The commonest clinical variants of BCC are nodular BCC and superficial BCC. Superficial BCC typically presents on the trunk or extremities as flat pink/red annular lesion often with some scale and a subtle raised translucent edge. It may also contain some pigment. Another name for superficial BCC is multi-centric BCC.

Apart from the common UV-related aetiology, AK, superficial BCC and Bowen's disease, have one other thing in common. They exhibit an excellent response rate to treatment with a topical immune response modulator known as Imiquimod (Aldara™). For AKs to respond to imquimod they must not be hypertrophic. Indeed, this product which comes as a 5% cream is licensed for treating these 3 types of lesions, apart from genital warts. Traditional treatments include: cryotherapy, curettage and cautery (C&C), topical 5-fluorouracil, and lately, photo-dynamic therapy (PDT) for AK; cryotherapy, C&C, excision, topical 5-fluorouracil, radiotherapy and PDT for superficial BCC; cryotherapy, C&C, excision, topical 5-fluorouracil and PDT for Bowen's disease.

Imiquimod acts through toll-like receptors, predominantly expressed on dendritic cells and monocytes, to induce production of cytokines and chemokines which promote both innate and adaptive cell-mediated immune response against the dysplastic/neolastic cells.

The recommended treatment regimes are: 5 times a week, Monday to Friday, for 6 weeks for superficial BCC; 5 times a week, Monday to Friday, for 6-12 weeks for Bowen's disease. For AK, it should be used three times per week on alternate days (Mon-Wed-Fri) for 4 weeks. After a 4 week treatment-free period lesions should be assessed and if any lesions persist treatment can be repeated for another 4 weeks. Maximum duration of treatment is 8 weeks.

A box of Imiquimod contains 12 packets, each containing 12.5mg of cream. The cream should be applied as a thin layer to the target area at bedtime and washed off with mild soap and water the following morning. Contact with the eyes, lips and nostrils should be avoided, and hands washed before and after application. No more than one packet should be used at each application. Partially used packets should not be saved or reused. Local skin inflammatory reactions are common. Flu-like symptoms such as malaise, fever, nausea, myalgias and rigors may also occasionally accompany local reactions. Patients should be forewarned about the possibility of these reactions. A rest period of several days may be taken if patients cannot tolerate the intensity of the reaction. The safety of imiquimod cream applied to areas of skin greater than 25cm^2 for treatment of AKs has not been established, and hence should be avoided. Exposure to sunlight should be avoided or minimized during use of imiquimod cream because of the possibility of increased susceptibility to sunburn. The safety of imiquimod in pregnancy and nursing mothers has not been established, and hence caution should be exercised in these situations.

Topical imiquimod represents a novel highly effective patient-administered treatment for non-hypertrophic AKs, superficial BCCs and Bowen's disease. In view of the high incidence of adverse reactions to this agent, prescribers must pay particular attention to appropriate patient selection and should take time to thoroughly explain the treatment regime and common side-effects during the initial consultation.