PATIENT INFORMATION LEAFLET:  
Actinic Keratosis

What are actinic keratosis?
Actinic keratosis (AK) (also known as ‘solar keratosis’ and ‘senile keratosis’) is generally classified a premalignant skin lesion although a few authors challenge this view and they believe that it represents an early variant of an in situ Squamous cell carcinoma (SCC).

Who is affected by actinic keratosis?
The main risk factors for AK are fair skin, advanced age, use of phototoxic drugs and high lifetime cumulative UV exposure. Immunosuppressed patients have higher risks of progression of AK into invasive SCC (iSCC) and development of metastasis.

What causes actinic keratosis?
AK is caused by chronic exposure to UV radiation. DNA mutations with UVB- signatures are found in all AKs. At a molecular level, the function of tumour suppressor proteins such as p53 is usually suppressed, leading to a clonal expansion of tumoral keratinocytes. UVA radiation can cause, at a lower extent, the same genetic damages and in addition they cause oxidative damages that can contribute to the malignant transformation of keratinocytes.

Can it be inherited?
A few hereditary phenotypic features, such as fair skin and red/blond hair, are relevant risk factors. Genetic syndromes associated with impaired DNA repair mechanisms or deficiency in melanin biosynthesis have a higher risk as well.

What does actinic keratosis look like?
Clinically, AKs typically present as erythematous and scaly patches or plaques. AKs are classified with the clinical Olsen (I-III) score according to their thickness or with the histological KIN (I-III) score according to the degree of dysplasia.

Sometimes, isolated AKs develop on apparently normal skin but, more often, multiple lesions develop on a skin with other clinical signs of chronic sun damage, including spider veins, pigmentary spots, yellowish hue and wrinkles.

Chronic sun exposed areas such as scalp, face, hands, and arms are the most involved. It has been demonstrated that photo aged skin surrounding multiple AKs (the so called “cancerization field”) harbours the same molecular damages of AK and iSCC and it represent a risk factor for the development of additional AKs.

How is actinic keratosis diagnosed?
Clinical examination and dermoscopy are sufficient in almost all cases. However if the diagnosis is not sure or the progression to iSCC is suspected, a biopsy is recommended.

Why and how is actinic keratosis treated?
The biological behaviour of a single AK cannot be predicted: it may disappear spontaneously, it may remain unchanged for decades or it may progress to an iSCC. The risk of progression of a single AK is low but the cumulative risk becomes high in patients with multiple AKs.

Therefore, due to the low but unpredictable risk of progressions into an iSCC, all AKs should be treated regardless of their number and thickness. Furthermore, if multiple lesions are present, the cancerization field of the surrounding photo damaged skin must be treated as well.
Several different treatments are available. The choice of the treatment modality depends on several factors: the clinical thickness, size, number and localization of lesions, patient's age and general health condition and patient's reliability to perform home treatments. Treatment options belong to 2 groups: lesion-directed physical treatments that only aim to the removal of lesions and field-directed chemical treatments that aim at the removal of lesions and the recovery of the surrounding photo-damaged skin as well.

Physical treatments are suggested in case of isolated lesions (≤5 AK on a limited body area).

The most common ones are:
- Cryotherapy: freezing lesions with liquid nitrogen is easy, effective and cheap. The procedure is usually well tolerated although it may cause pain, redness, swelling, crusting, blisters formation, with healing over several weeks.
- Curettage: lesions are scraped with a surgical instrument called curette. Curettage alone has a limited effectiveness but it is often used to remove scales of thick lesions in order to improve the efficacy of other treatments.
- Surgical excision: surgery is highly effective but it is rarely used because it is invasive and expensive and scars are a frequent complication.
- CO2-laser, Erbium(Er):YAG-laser: ablative lasers are expensive and less practical than cryotherapy with similar or lower efficacy and safety.

Drugs are approved for the treatment of multiple (≥6) AKs that are clustered in a limited body area with other clinical features of chronic actinic sun damage.
Topicals containing Ingenol mebutate 0.015/0.05%, 5-fluorouracil (FU) 0.5/5%, 0.5% 5-FU + 10% Salicylic Acid (SA), Imiquimod 2.5% /3.75%/5%, and diclofenac 3% in 2.5% Hyaluronic Acid are applied to the lesions and the surrounding skin and the consequent inflammatory and immunologic reactions lead to the clearance of lesions and improve the clinical, histologic and molecular damages of the cancerization field. All treatments are performed by the patient himself at home, and according to their approval status, drugs differ for efficacy, tolerability, toxicity, size of the area that can be treated in a single treatment cycle, overall duration of treatment and cost.
Creams containing 5-aminolaevulinic acid (ALA) or methylaminolevulinate (MAL) are also available. In this case, the application of the drug is followed by an irradiation with artificial or natural light that is delivered by the doctor or nurse.

Prevention
It is important to reduce sun exposure. Patients should always use protective clothing, sunscreen SPF 50+, and avoid tanning beds, especially for patients with fair skin type.

Good tips
1. Think to AKs if you have one or more red scaling patches on sun-exposed skin.
2. If you were already diagnosed with AKs you are at risk to develop further lesions in the future.
3. Be alert to the development of a nodule or ulcer with bleeding that might indicate an invasive skin cancer that requires urgent attention.
4. AK is a pre-cancerous lesion. Seek medical advice to choose the best therapeutic option.
5. A careful sun protection can decrease the risk of developing AKs.

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Single crusty erythematous lesion on the right ala of nose. The lesion developed a few months before and it did not modify with time. The patient often removed mechanically the scales causing mild bleeding.

Olsen III Actinic keratosis

Several small erythematous crusty lesions with variable thickness stand on the severely photoaged bald skin of a 52 year old gardener. Olsen I, II and III Actinic keratoses

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