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Everyday decision making on biologic use for psoriasis patients

Speaker: P Foley
Department of Medicine, the University of Melbourne, Australia

Since the introduction of biologics, there has been significant progress in the management of psoriasis in recent years. Achieving sustainable clear or almost clear skin such as PASI 90 and 100 has become the target for treatment according to many international guidelines. Long term efficacy and safety profiles should be taken into the consideration in the choice of biologics. Among the various biologics available, IL-17 and IL-23 inhibitors are associated with the lowest number needed to treat to achieve PASI90/100 in the short term from week 10 to 16. Head to head date show high efficacy and similar speed of response for IL-17 and IL-23 inhibitors. IL-23 inhibition is associated with consistent response regardless of prior therapy. It provides a durable high response even after treatment withdrawal. It also shows improvement of nail and joint disease. Risankizumab, an IL-23 inhibitor, was well tolerated up to 256 weeks of continuous exposure with no new safety signals noted and similar long term incidence of adverse events as that of week 16.

Learning points:

Risankizumab, an IL-23 inhibitor, has demonstrated durable and complete clearance with a favourable safety profile, simpilicity of dosing regimen (12-weekly dosing regimen after initiation), and sustainability (maintenance of response after withdrawal).

Atopic dermatitis: Hope is on the horizon

Speaker: P Foley
Department of Medicine, the University of Melbourne, Australia

Atopic dermatitis (AD) induced itch and scratching which contributes to skin related complications such as excoriation and infection. These can magnify into significant well-being, life-style and economic consequences. Moderate to severe AD is associated with multiple comorbidities, such as food allergy, anxiety, diabetes and obesity, hypertension and heart disease. The impact of AD is multifactorial. The treatment targets should include more than one domain. Only a minority of patients with moderate to severe AD receive systemic treatment. This suggests that inadequate control of AD remains high. There are several new and emerging systemic therapies. These include IL-13 inhibitors (Tralokinumab and Librikizumab) and IL-31 inhibitor (Nemolizumab) and JAK inhibitors (Baricitunib, Abrocitunib and Upadacitunib). Most of them showed efficacy in phase III

trials. Ongoing long term extension trials of targeted therapies should further characterise their safety profiles.

Learning points:

Emerging target therapies, such as IL-13 inhibitors (Tralokinumab and Librikizumab) and IL-31 inhibitor (Nemolizumab) and JAK inhibitors (Baricitunib, Abrocitunib and Upadacitunib) offer more systemic treatment options for moderate to severe atopic dermatitis.

Multidisciplinary approach in psoriatic disease's management

Speaker: CSM Wong
Hong Kong College of Dermatology & The Hong Kong Society for Paediatric Dermatology, Hong Kong

With multiple epidemiological studies, psoriasis is more accurately classified as a systemic disease associated with comorbidities such as metabolic syndrome, cardiovascular disease, hepatic disease, chronic kidney disease, cancer, osteoporosis and depression. The most reported comorbidities included hypertension (35%), depression (33%) and arthritis (30%) in one recent large survey. In QMH psoriasis clinic, the most common comorbidities included hypertension (68%), overweight (BMI >25, 59%) chronic liver disease (57%) and fatty liver disease (NAFLD, 50%). Screening for comorbidities should be part of the managing strategy in psoriasis patients. British Association of Dermatologists (BAD) recommends biologic therapy earlier in the treatment pathway in people with psoriasis who fulfil the severity criteria and who have active psoriatic arthritis or psoriasis that is persistent that relapses rapidly. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) also strongly recommended IL-17 inhibition biologic therapy for all domains of psoriasis comorbidities. IL-17 inhibition has demonstrated not only improvement of skin condition, but also significant improvement in symptoms associated with pre-PSA and stabilisation of structural joint changes. In addition, IL-17 inhibition might have a beneficial effect on CV risks by improving endothelial function and reduction in non-calcified plaque burden and total atheroma volume.

Learning points:

a. Psoriasis represents a systemic disease with a great physiological burden and impact of patient's quality of life.
b. Multidisciplinary approach in psoriasis disease management is suggested.
c. Advanced treatment in biologics therapy is promising.

Update dermatitis management targeting oxidative stress

Speaker: G Pellacani
Professor, Department of Department of Dermatology, University of Modena and Reggio Emilia, Italy

Atopic dermatitis is a multifactorial chronic inflammatory disease. Pathophysiology of atopic dermatitis is related to many factors such as immune regulatory abnormalities, skin barrier dysfunction, microbiome, race, and environment. There is a profound link between oxidative stress and atopic eczema. Inflammatory cells like neutrophils, eosinophils and macrophages can produce reactive oxygen species that perpetuate the inflammation and lead to epithelial damage. Environment pollution also contribute to the source of oxidative stress. Reactive oxygen species cause lipid peroxidation, DNA, mitochondrial, protein damage and hence impairment of skin barrier function.

Exploring the association between inflammation and oxidative stress in atopic dermatitis may help us in formulating new

treatment strategies. Antioxidants, skin barrier enhancer, anti-inflammatory drug and immune regulatory agents may be combined in the treatment of atopic dermatitis. Topical antioxidants such as Furfuryl palmitate (Relizema), have been recently integrated into moisturisers in the treatment of mild to moderate atopic dermatitis.

Learning points:

The exploring the association between inflammation and oxidative stress in atopic dermatitis may help us in formulating new treatment strategies.

Atopic dermatitis - topical treatment focus on methylprednisolone aceponate

Speaker: D Thaci
Institute and Comprehensive Centre for Inflammation Medicine, University Lubeck, Germany

Atopic dermatitis (AD) displays a high level of phenotypic variability. Topical corticosteroid is the commonest treatment.

Methylprednisolone Aceponate (MPA) is a topical corticosteroid indicated across different types of eczema, including AD and contact dermatitis. It is applied once daily with a maximum treatment duration of 12 weeks in adults and 4 weeks in children.

MPA is rapidly absorbed because of its lipophilicity. It is metabolised by skin esterases to produce the active metabolite methylprednisolone propionate (MPP). Once MPP dissociates from the glucocorticoid receptor, it enters the bloodstream and is deactivated in the liver before being excreted mainly in urine. Rapid deactivation renders MPP largely unavailable for absorption into systemic circulation. MPA has a therapeutic index of 2.0 indicating a favorable efficacy to adverse events rate, which means it has a similar side effect profile to topical 1% hydrocortisone but with much higher efficacy.

The efficacy of MPA for the treatment of childhood AD has been demonstrated in clinical trials. In children with AD, MPA provided relief from the symptoms of AD including itch in the majority of children (65%) within 3 days while 97% of the patients achieved significant improvement or cleared signs and symptoms by the end of treatment. Children (2-14 years) with AD treated with MPA cream or elomet once daily for 1-4weeks showed comparable results as well. Proportion of patients with complete healing or a marked improvement in symptoms was similar between MPA cream and elomet

MPA can also be used for facial eczema (commonly 1-2 weeks and a maximum of 4 weeks) with good efficacy.

MPA has a very favourable side effect profile. One of the most common adverse events associated with topical corticosteroid is skin atrophy, particularly following long-term use. It has been shown that MPA cream did not lead to any significant reduction in skin thickness compared with vehicle, while betamethasone valerate significantly decreased skin thickness compared with vehicle. Also, MPA ointment induced less frequent and less severe atrophy and telangiectasia compared Elomet - a TCS with similar potency ($p<0.001$).

For the systemic absorption and possible hypothalamic-pituitary-adrenal axis suppression by the use of topical corticosteroid, MPA has been demonstrated not to cause serum cortisol to fall below normal levels of cortisol, while topical clobetasol propionate suppressed cortisol levels.

In summary, MPA is a potent topical anti-inflammatory corticosteroid and has a favourable efficacy to adverse event rate. It has comparative

efficacy with less frequency of application to other similar potent topical corticosteroids in the treatment of AD. It provides early relief from itch in AD and demonstrates symptomatic relief in a range of eczema. Most importantly, it is generally well tolerated treatment of eczema with limited topical and systemic side effects.

Learning points:

1. MPA is lipophilic and hence rapidly absorbed when applied to skin.
2. It is a potent anti-inflammatory corticosteroid with efficacy comparable with elomet.
3. It has a favourable side effect profile which does not cause any skin atrophy or any systemic steroid absorption.

Latest treatment advanced with IL-23 as target for psoriasis

Speaker: D Thaci
Institute and Comprehensive Centre for Inflammation Medicine, University Lubeck, Germany

Long term suboptimal management of psoriasis can lead to irreversible physical and psychological burden e.g. disease progression, lost opportunities, deteriorated quality of life. The growing availability of effective and safe treatment for psoriasis and psoriatic arthritis has made high skin clearance increasingly possible. Achieving high levels of skin clearance (PASI 90/100) with IL-23 inhibitors e.g. Guselkumab, has been reported in studies.

IL-23 plays an important role in the pathophysiology of psoriasis. A number of IL-23 inhibitors have been approved for the treatment of moderate-to-severe psoriasis e.g. Guselkumab, Thildrakinzuma and Risankizuma, while the newest one Mirikizumab is undergoing Phase 3 trial.

Study has shown that Guselkumab has significantly faster and higher PASI 90 responder rate than Adalimumab (80% vs 50%). Secondary analysis of 2 randomised clinical trials also reveals that Guselkumab has better efficacy than Adalimumab in treatment of scalp psoriasis and palmoplantar psoriasis, while it is similar for nail psoriasis. Guselkumab has demonstrated superiority over Secukinumab in long term efficacy (esp in obese patient) to maintain PSAI 90 response and long term efficacy of Guselkumab has been reported that 80% patient can maintain PASI 90 with 5-year use of Guselkumab. Furthermore, Guselkumab is also effective in the treatment of psoriatic arthritis.

Studies have proved that Guselkumab has an excellent safety profile. There is no significant difference in overall infection or malignancy rate, while the superficial candida infection or tinea infection appears to be less when compared with Secukinumab.

Learning points:

1. Guselkumab is one of the IL-23 inhibitors that has been approved for the treatment of moderate-to-severe psoriasis.
2. It has better efficacy than adalimumab and Secukinumab.
3. It has excellent safety profile with no increase in overall infection or malignancy rate.