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Welcome to this review of the 26th European Academy of Dermatology and Venereology 2017 Congress held in Geneva, Switzerland on 13-17 September 2017.

This review has been created to allow those unable to attend, but with a keen professional interest, to access a summary of some of the presentations. Selection and review of the research has been carried out independently by Associate Professor Pablo Fernández Peñas of the University of Sydney and Westmead hospital, Sydney who attended the meeting.

Highlights of this review include a number of presentations on the currently hot topic of atopic eczema, with one speaker reporting that there are more than 630 studies ongoing. For example we report an interesting discussion of the role of barrier, allergy and pruritus in the pathogenesis of atopic eczema and a review of the use of antibody-based therapies in this indication. Other highlights include a report discussing the role of pigment in the development of melanoma and an update which detailed new molecules under development for cutaneous lymphomas.

We hope you enjoy these selections, and as always, look forward to hearing your comments and feedback.

Kind Regards,

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Melanoma therapy 2017

Speaker: Prof. Martin Röcken

Summary/Comment: The lecture was centered in the recent papers about lymph-node dissection outcomes. Although there is enough evidence that lymph-node dissection does not provide any melanoma specific survival at three years, Prof. Röcken showed some data suggesting that there could be differences at five years and 12 years. He insisted that the procedure has minimal side effects and that there is less secondary metastasis in the lymph node area (quite evident as lymph nodes have been removed). Regarding new treatments, he would use anti-PD1 agents in patients with good general status and limited tumour load, regardless of mutation status. BRAF and MEK inhibitors would be used for patients with extensive tumour load if they harbor the BRAF mutation. If the tumour load is extensive, but patients are BRAF wildtype, anti CTLA-4 would be the drug of choice. Although it is undeniable the quick effect of MAPK inhibitors in high tumour load patients, the use of these molecules in worse cases seems to be one of the factors to suggest that they are less effective than anti-PD1 agents. This is still a controversial topic. One recent paper has shown that patients that stopped immunotherapy due to side effects had responses as good as patients that continued treatment. This should give hope to patients if their treatment is stopped due to adverse events, and encourage the treatment of these events with immunosuppressants, knowing that outcomes won't be worse. Finally, he questioned the observed benefit of immunotherapy in the adjuvant stage due to the high cost of the drugs and safety profile. A dilemma that patients, clinicians and payers are facing regularly.

Reference: Spotlights 1, September 14th 2017; D1T01.1F

Do we need pigment to develop melanoma?

Speaker: Prof. David E Fisher

Summary/Comment: This was a very interesting presentation about melanoma research. Black mice with BRAF mutations that activate the RAS/RAF/MEK/ERK pathway develop multiple nevii. On the other hand, 50% of red mice with the same changes develop melanoma without UV light. If the red mice are albino… no melanoma appears. These data suggest that pheomelanin is a procarcinogenic that does not need UV light, and that its effects can be enhanced by UV light. Extending these results to humans, he hypothesised that amelanotic melanomas may contain pheomelanin. He reported that his team has already found 3 of 3 human amelanotic melanomas tested to have pheomelanin using special imaging systems. This will be quite revolutionary if confirmed, and new tools to detect pheomelanin in the skin will be needed soon. At the same time, he reported experiments to rescue dark pigment in pheomelanin mice, activating MITF. There are molecules (SIK inhibitors) that can be applied topically and which can activate brown colour in mice skin. If this could be applied to humans, we will have a new revolution in skin colour. The last part of the lecture was about the role of mutations in immunologic response. Mice injected with highly mutated melanomas can reject them, but cannot reject melanomas with only two mutations. Interestingly, after these mice rejected the highly mutated melanomas, if they were challenged with the 2 mutations melanomas, some of them rejected this also (epitope spreading?). Prof. Fisher hypothesised the possible role of creating inflammation in melanomas with imiquimod or lasers to create inflammation that could lead to an anti-melanoma response. In our group, we are using DPCP (diphenylcyclopropenone) in patients with cutaneous metastasis to stimulate immune reactions. This research gives more support to our treatment approach.

Reference: Plenary Lectures A, September 14th 2017; PLA-03

Drug eruptions

Speaker: Prof. Knut Brockow

Summary/Comment: Clinically, acute cutaneous drug reactions are classified into four main groups: maculopapular reactions, drug-rash with eosinophilia and systemic symptoms (DRESS), Steven-Johnson and toxic epidermal necrosis (SJS-TEN) syndrome, and pustular reactions. These reactions do not fit in the classical Cooms and Gell classification. Type IV reactions have been divided into four groups to accommodate for these reactions. Regarding mechanism, mast cell mediators and receptors such as MrgprB2 could explain pseudo-allergic drug reactions. For classical drug reactions, specific HLA types have been involved in reactions to specific molecules. This has been explained by molecules being able to interact with the specific HLA. Due to the need for a defined conformational structure, molecules belonging to the same group (e.g. penicillins and cephalosporines) do not always cross react.

Reference: Spotlights 2, September 15th 2017; D2T01.1C

Pathogenesis of atopic dermatitis in the perspective of barrier, allergy, and pruritus

Speaker: Prof. Kenji Kabashima

Summary/Comment: Filaggrin mutations are related to atopic dermatitis and other diseases such as ichthyosis, allergic contact eczema, asthma and rhinitis. This disrupted barrier together with environmental challenges to the skin lead to activation of keratinocytes and production of TSLP (thymic stromal lymphopoietin, similar to IL-7 and important in T cell maturation). This induces a Th2 reaction, critical in atopic eczema. Large molecules are captured by Langerhan cells and trigger TSLP production by keratinocytes. It has been shown that the absence of Langerhan cells diminishes atopic dermatitis. On the other hand, small molecules reach the dermal dendritic cells and this triggers allergic contact eczema. TSLP is also involved in itch, but there are many other mediators. The itch/scratch system was probably developed to fight parasites. Interestingly, Th2 responses are also involved in parasite infestations. Atopic dermatitis has links with these evolutionary mechanisms, and TSLP has a central role. The speaker did not elaborate, but molecules interfering with TSLP function may be another target in the treatment of atopic dermatitis.

Reference: Atopic Dermatitis, September 15th 2017; D2T10.2A

Genetics and regulation of the barrier

Speaker: Prof. Michael J Cork

Summary/Comment: Low natural moisturising factor, increased pH and increased protease activity (PAR2) lead to epidermal barrier dysfunction. To prevent atopic eczema, the skin barrier should be repaired by optimal emollients and wash products. The speaker argued that a single occlusive emollient, although it helps to reduce transepidermal water loss, does not restore the barrier. He suggested that more sophisticated emollients may restore the barrier better by adding lipids, correcting pH, modifying proteases, etc. He stressed, as the previous speaker, that there is a randomised controlled trial showing that regular application of emollients reduces the prevalence of atopic dermatitis.

Reference: Atopic Dermatitis, September 15th 2017; D2T10.2B

Systemic treatments of atopic dermatitis: A critical evaluation

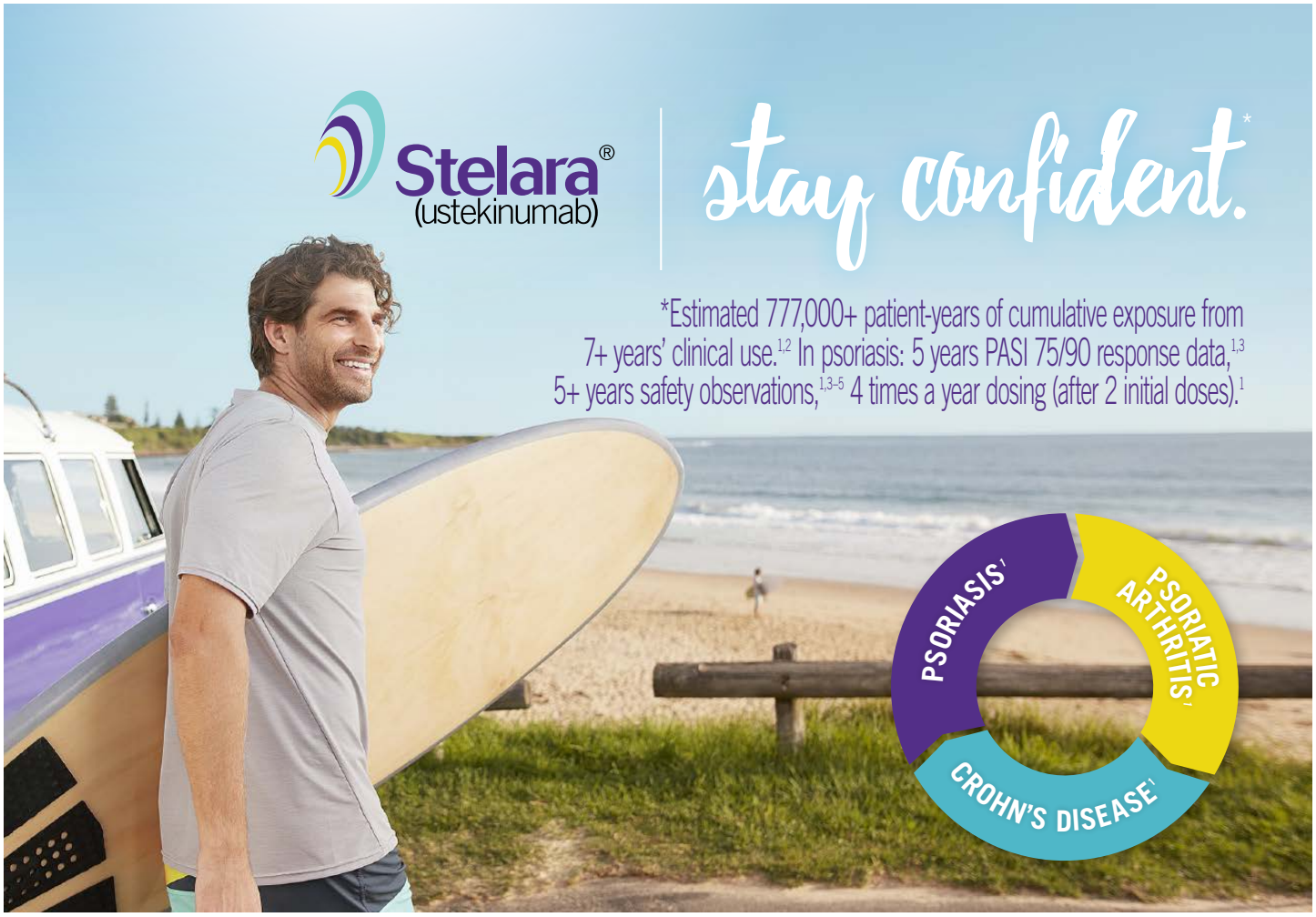
Speaker: Prof. Julien Seneschal

Summary/Comment: This was a good review of the evidence for treatment of atopic dermatitis with systemic therapies. Prof. Seneschal discussed a few papers:

- Methotrexate vs azathioprine (2012): similar efficacy and good safety profile
- Methotrexate vs cyclosporine (2017 in press): at 8 weeks cyclosporine was better but at 24 weeks there were small differences
- Mycophenolate vs cyclosporine (2017): both effective

There is a retrospective study comparing methotrexate, azathioprine, cyclosporine and the combination of methotrexate and azathioprine. He reported that cyclosporine is effective even at low doses (< 3 mg/kg) in 2 weeks, and that systemic steroids are rapidly effective but have an unfavourable safety profile in long-term treatment. In his opinion, the treatment plan should be: cyclosporine (RCT, higher evidence) then methotrexate, followed by azathioprine (due to long-term side effects) and lastly mycophenolate (due to lack of enough studies). Personally, I treat atopic eczema patients long-term with methotrexate as my first option, using cyclosporine and prednisone as rescue medications. As the speaker, I use azathioprine as second and mycophenolate as third line.

Reference: Atopic Dermatitis, September 15th 2017; D2T10.2D



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PASI: Psoriasis Area and Severity Index. **STELARA® ustekinumab (rmc) vials MINIMUM PRODUCT INFORMATION (Plaque psoriasis, psoriatic arthritis, **Crohn's disease*) INDICATIONS:** Moderate to severe plaque psoriasis in adults who are candidates for photo- or systemic therapy; signs and symptoms of active psoriatic arthritis in adults where response to previous non-biological DMARD therapy has been inadequate; **moderately to severely active Crohn's disease in adults who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a TNFα antagonist or have medical contraindications to such therapies.* **DOSE: Psoriasis:** Subcutaneous injection. 45 mg at Weeks 0 and 4, then every 12 weeks. Alternatively, in patients weighing >100 kg, 90 mg at Weeks 0 and 4, then every 12 weeks. If inadequate response, consider treatment every 8 weeks. Discontinue if no response after 28 weeks. **Psoriatic Arthritis:** Subcutaneous injection. 45mg at Weeks 0 and 4, then every 12 weeks. Some patients weighing >100kg received a 90mg dose in clinical trials and observed a clinical benefit. Discontinue if no response after 28 weeks. ****Crohn's Disease:*** *Single initial intravenous tiered dose based on body weight using STELARA 130 mg vial (weight ≤ 55kg = 260 mg [2 vials]; weight > 55kg to ≤ 85 kg = 390 mg [3 vials]; weight > 85 kg = 520 mg [4 vials]). Then subcutaneous injection. 90 mg 8 weeks after the intravenous dose, then every 8 weeks. In some patients a subcutaneous dose of 90 mg 8 weeks after the intravenous dose, then every 12 weeks may be acceptable according to clinical judgment. Consider discontinuing if no evidence of benefit by Week 16.* **CONTRAINDICATIONS:** Severe hypersensitivity to ustekinumab or to any of the excipients. Do not administer to patients with a clinically important active infection. **PRECAUTIONS: Serious infections:** STELARA may increase risk of infections and reactivate latent infections. Serious bacterial, fungal and viral infections have been observed. Use with caution in patients with chronic or recurrent infections. **Tuberculosis (TB):** Evaluate for TB prior to initiating treatment. Do not administer to patients with active TB. Treat latent TB before administration. Consider anti-TB therapy in patients with suspected TB. Monitor patients for TB. **Malignancies:** STELARA may increase risk of malignancies. Malignancies have been observed. Use with caution in patients with known malignancy or history of malignancies. Patients should be monitored for the appearance of non-melanoma skin cancer. **Hypersensitivity reactions:** Discontinue immediately if serious hypersensitivity reactions including anaphylaxis and angioedema occurs. **Immunisations:** Do not give live bacterial or viral vaccines. Consider secondary transmission of live vaccines from contacts. **Immunosuppression:** STELARA should not be used in combination with photo- or systemic therapy. **Immunotherapy:** Use with caution in patients receiving allergy immunotherapy. **Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** If RPLS is suspected, STELARA should be discontinued and appropriate therapy instituted. **Serious Skin Conditions:** Physicians should be alert for symptoms of erythrodermic psoriasis or exfoliative dermatitis. STELARA should be discontinued if a drug reaction is suspected. **Use in Pregnancy:** Category B1. **ADVERSE EFFECTS:** Serious: serious infections and malignancies. Common: URTIs, nasopharyngitis, dizziness, headache, **oropharyngeal pain,* diarrhoea, nausea, **vomiting,* pruritus, back pain, myalgia, arthralgia, fatigue, injection site erythema, injection site pain. See full PI for other adverse effects. Adverse events: serious cardiovascular events, suicidality, hypersensitivity (including rash, urticaria), serious hypersensitivity reactions including anaphylaxis and angioedema. **PRESENTATION:** Pack of 1 single use 45 mg vial for subcutaneous use, and **pack of 1 single use vial for intravenous use (Crohn's disease only).* Store at 2°C – 8°C. Refrigerate. Do not freeze or shake. Protect from light by storing in original carton. **Date of preparation:** 8 March 2017

*Please note changes to Product Information as **italicised text*

REFERENCES: 1. STELARA (ustekinumab) Approved Product Information 28 February 2017. 2. Janssen data on file. 3. Kimball AB et al. J Eur Acad Dermatol Venereol 2013;27:1535-1545. 4. Langley RG et al. Br J Dermatol 2015;172:1371-1383. 5. Papp KA et al. Br J Dermatol 2013;168:844-854.

Antibody-based therapies of atopic dermatitis

Speaker: Prof. Tilo Biedermann

Summary/Comment: This was a quick review of an amazing landscape. Prof. Biedermann classified the molecules into three groups: not effective, no data, some data.

1. Not effective:
   - Mepolizumab (anti-IL5): patients with high eosinophils may respond
   - Omalizumab (anti-IgE)
   - Rituximab (anti-CD20)
   - Infliximab (anti-TNF)
   - Etanercept (anti-TNF)
   - Ustekinumab (anti-IL12-23): recent paper showing no differences
   - Alefacept
   - Efalizumab
   - Tocilizumab (anti-IL6): effective but increased bacterial infections
2. No data
   - Anti-IL17
   - Anti-IL22
3. Some data
   - Nemolizumab (anti-IL31): good response in itch, but inflammation may not be reduced
   - Tralokinumab (antil-IL13): phase 2b showed some response
   - Tezepelumab (anti-TSLP): some effects in asthma
   - Dupilumab (anti-IL4R): EASI 50-80% sustained to 52 weeks. The main side effect is conjunctivitis

Reference: Atopic Dermatitis, September 15th 2017; D2T10.2C

The epidermal barrier to the environment - new concepts

Speaker: Dr Leopold Eckhart

Summary/Comment: The concept of a tight junction barrier in the epidermis has been discussed since the beginning of the century. This layer separates the stratum corneum and part of the stratum granulosum from the rest of the living epidermis, and it is critical for fluid retention. The process of cell death is always pro-inflammatory, regardless of the mechanism. Cornification (preferred term to apoptosis to describe stratum corneum formation) is also pro-inflammatory. The tight junction barrier has an anti-inflammatory role. When this layer is damaged, signaling from the cornification process reaches the dermis and triggers inflammatory responses. These danger signals trigger the release of IL1b, IL36, IL37 and IL38.

Reference: ESDR session: Translational dermatology, September 15th 2017; D2T09.3D

Modern therapies for cutaneous lymphomas

Speaker: Dr Emmanuella Guenova

Summary/Comment: After a quick review of the range of new molecules in development, the speaker focused on three molecules. IPH4102 is a CD158K/KIR3DL2 inhibitor. This is a diagnostic and prognostic factor in cutaneous T cell lymphoma, and the phase I has been completed showing some responses. Mogamulizumab is a CCR4 inhibitor. Phase II has been finished. In published results from phase I and II an overall response rate of 37% was found, higher in Sezary syndrome than mycosis fungoides. The molecule is already approved in Japan for adult T cell leukaemia/lymphoma. Brentuximab is an anti-CD30 antibody. A phase III trial has been published with a 56.3% response rate compared to 12.5% with physician's choice (methotrexate or bexarotene). Peripheral neuropathy was seen in 67% of patients and it was not always reversible.

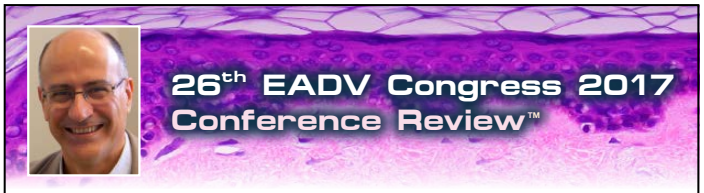
Reference: New drugs, new indications, new side effects, 16th September 2017; D3T06.4A

New drugs for atopic dermatitis

Speaker: Prof. Kilian Eyerich

Summary/Comment: This was another talk about atopic eczema that reviewed mainly small molecules. After an introduction about dupilumab (one of the main stars in all lectures as the first biologic effective in atopic eczema), and a quick review of tralokinumab, nemolizumab and ustekinumab, JAK inhibitors took central stage. These included tofacitinib (JAK1/3), ruxolitinib (JAK1/2), baricitinib (JAK1/2) and upadacitinib (JAK1 inhibitor). There were mentions of the incidence of haematological adverse events due to the inhibition of some of the JAK pathways. AHR agonists, PDE4 inhibitors and bacterial lysates are other molecules in development. To highlight how hot the topic of atopic eczema is now, the speaker reported that there are more than 630 studies ongoing, and 139 still recruiting patients in clinical trial databases.

Reference: New drugs, new indications, new side effects, 16th September 2017; D3T06.4B



Selection of papers and comments are provided by A/Prof Pablo Fernández-Peñas, MD, PhD, FACD

Pablo Fernández-Peñas is Associate Professor in Dermatology at the University of Sydney, Head of the Department of Dermatology at Westmead Hospital and Head of Research at the Skin and Cancer Foundation Australia in Sydney, Australia. Previously, he was Staff Specialist (Dermatology) at Hospital Universitario de la Princesa and Clinical Professor at the Universidad Autonoma, both in Madrid, Spain. Since moving to Sydney in 2007, A/Prof Fernández-Peñas has expanded dermatological services, and research and education opportunities in Western Sydney. He opened the Dermatology Comprehensive Clinical Centre at Westmead Hospital, and has built strong links with the Westmead Cancer Care Centre and the Skin and Cancer Foundation Australia, participating in melanoma, non-melanoma skin cancer, cutaneous lymphoma, hidradenitis and psoriasis clinical trials, and leading research projects in onco-dermatology and quality of life. He has opened clinics for severe psoriasis, cutaneous lymphoma, graft versus host disease, and melanoma at Westmead Hospital, and severe eczema at the Skin and Cancer Foundation Australia. His main fields of interest are immunology, onco-dermatology, quality of life in dermatology, and information technologies and codification. He has 100+ publications in peer review journals, has participated in 30+ clinical trials, and has been invited to lecture in national and international meetings.

