AEDV HIGHLIGHTS
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Systemic diseases

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Skin diseases associated with inhibitors of cytokines and T-cell function Prof. Dr. Knut Schäkel

• Reactions in the area of injection with nearly every biologic. Most are moderate to mild
• Reactions to infusion with EV treatments
  • IFX 17% of patients- 1.5% infusions
  • Systemic treatment: Anti-H1, paracetamol
  • It can be prevented with pre-medication. In severe cases: systemics cortis
• Increase in risk of severe infections:
  • Especially IFX (RR 2.49) and Adalimumab (1.97)
  • It hasn’t been seen with Ustekinumab/ETN
• ↑ Risk Herpes Zoster in psoriasis: Not significant
• Candidiasis: ↑ with anti-IL17: 4.3% ixekizumab and 3.5% Secukinumab
• Psoriasis forms paradoxical reactions: Anti-TNF
• Lupus-like eruptions: described with anti-TNF 0.1-1%
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- Tumors:
  - Doesn’t seem to have global increase
  - There could be a ↑ risk of NMSC with anti-TNF

- Dupilumab in Atopic Dermatitis
  - Reactions in areas of injection
  - Unspecified conjunctivitis of uncertain mechanism which is normally mild-moderate

- Risk of Anaphylaxis with Omalizumab: Risk of 0.1%-0.2%
  - 80% are asthmatic
  - Previous anaphylaxis background
  - Appears within 30-60 mins

- Melanoma: anti-PD1/ anti-PD1L
  - 59% maculo-papular eruptions, 30% itching, 11% vitiligo
  - Immune reaction against melanocytes of healthy skin?
Raynaud:
- Calcium channel blockers, anti-PDE5, Fluoxetine (could be useful), Iloprost EV in severe cases

Digital ulcers:
- anti-PDE5, endothelin antagonists, Iloprost EV
- Complications: Infection, osteomyelitis, gangrene, amputation, ALT functional

Cutaneous Sclerosis:
- Exercise/Rehabilitation
- MTX, TPHT
- MFM, Cyclof
- RTX
- Telangiectasias: Make-up, Vascular Laser, IPL
- Calcinosis cutis: Multiple therapies but none has proven their efficacy
- Systemic Complications: depending on organ
  - Pneumonitis interstitial- Cyclof, MFM, TPHT
  - Pulmonary HT: endothelin antagonists, anti-PDE5
  - Renal Crisis: IECAs, Hemodialysis
- New treatments against developing target therapies, for now, none have shown efficacy
- Follow up of new EULAR 2017 guidelines
They have used a scarring model to investigate scleroderma and other fibrotic processes.

They objectify that implicated cells are macrophages that activate through myeloid cells and type 2 cell immunity via IL4R receptor by the action of IL4 and IL13.

These macrophages interfere in:
- Vascular stability
- Collagen formation
- Collagen fiber cross-linking

The type 2 cell immunity would be implicated in:
- Systemic Scleroderma
- Morphea
- Lipodermatosclerosis
- Scars y Keloids
- Disease graft against Escleroderiform hostage

Drugs which block IL4Rα in theses processes are being studied.
Improving our understanding of lupus pathogenesis - and prospects for its treatment D. Isenberg

- LES prognosis has changed drastically over the last years:
  - 1950s: 4 year survival: 50%
  - 2018: 15 year survival: 85%
- Until now, the treatment was based on drugs who’s utility was found in serendipia, without knowing how they acted (antipaludics, cCS, immunosuppressors)
- Over the last years, target therapies have been introduced to treat Lupus against:
  - CD20: Rituximab
  - BAFF: Belimumab, Tabaluma, Blisibimod, Atacicept
  - Interferon
  - Humanised Anti-CD20, CD40L, RFc gammaIIIB, BTK, P140, IL3R, JAK-STAT, Bcl2
- Until now, only Belimumab has proven efficacy (reaching end-points) LES randomised clinical trials
- The future Will consist on finding effective and safe treatments against target therapies
Belimumab for the Treatment of Cutaneous Lupus Erythematosus

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INTRODUCTION
Systemic treatment of Cutaneous Lupus Erythematosus (CLE) that does not respond to topical corticosteroids and general measures is mainly based on antimalarials, systemic corticosteroids and immunosuppressants. There is a small group of patients with CLE that do not respond or cannot tolerate these treatments, representing a therapeutic challenge since there are no clear-cut guidelines in these cases. Belimumab, an inhibitor of the B-cell survival stimulator (BLyS or BAFF) recently approved for the treatment of systemic lupus erythematosus (SLE), can be a promising option in these cases of CLE.

MATERIAL AND METHODS
Here we present the cases of two patients with CLE without SLE criteria who had a good response to belimumab.

RESULTS
The first case is a man in his 40s with an 8-year history of chronic discoid CLE who has received multiple systemic treatments (prednisone, hydroxychloroquine, azathioprine, mycophenolic acid and isotretinoin). Despite this, he has had no good control of his cutaneous disease, presenting multiple outbreaks and often the lesions have eroded.

The second case is a woman in his 30s with an 11-year history of subacute CLE and chilblain lupus in her hands and feet. Multiple systemic treatments (chloroquine, hydroxychloroquine, prednisone, isotretinoin, methotrexate, mycophenolic acid and azathioprine) have been used but her cutaneous lesions have persisted. In addition, she has presented osteopenia (diagnosed by bone densitometry) and herpes zoster as complications of systemic therapy. Due to the difficult handling of both cases of CLE, off label treatment with belimumab was requested with the usual regimen of 10 mg/kg IV on days 0, 14 and 28, and then every 4 weeks.

In the first patient all the active lesions disappeared with belimumab. Prednisone and mycophenolic acid could be discontinued 8 and 23 months respectively after initiating belimumab and hydroxychloroquine could be reduced. In the second patient subacute CLE lesions disappeared but mild chilblain lupus persisted. Furthermore, azathioprine could be stopped 10 month after initiating belimumab and prednisone has been tapered to minimum doses.

DISCUSSION
With the results observed in these 2 patients we conclude that belimumab could be an effective and well tolerated treatment in patients with refractory CLE, and can also have an important long-term steroid and immunosuppressant sparing capacity.