

#AAD2019

*Highlights*  
**AEDV**

IN 77<sup>TH</sup> AAD CONGRESS

1-5 MARCH 2019

★ WASHINGTON ★

Scientific Initiative of:



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*Highlights*  
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**Cutaneous manifestations in  
systemic disease**

**Dra M<sup>a</sup> Elena de las Heras Alonso**

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# F0 –MULTIDISCIPLINARY MANAGEMENT OF CHRONIC GVHD .

09:00 – 11:00 AM; ROOM 103A

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- Chronic GCHD: A polymorphus disorder (diagnostic features)
  - Epidermal: lichen planus-like, poikiloderma
  - Dermal: lichen-sclerosus-like, morphea-like, scleroderma like
  - Subcutaneous: subcutaneous sclerosis, fasciitis
- What are the risk factors for flare of skin disease?
  - Recent decrease in immunosuppression
  - Donor lymphocyte infusion
  - Systemic infection (recent)
  - **Drug eruption (confusion in diagnosis)**
  - Stop/hold ECP: **Flares after stopping extracorporeal photopheresis!!**

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- How do I know if sclerotic skin is active?
  - Signs of evolving cGVHD
    - **New onset limb edema**
    - **Muscle cramping**
    - Decrease range of motion
    - Isomorphic involvement
  - **Flaring of other organ systems (app eGVHD)**
    - **Oral/ocular sicca SX (NIH: You tube – the concise oral exam)**
    - Generalized fatigue
    - Loss of appetite
    - Dyspnea
- Cutaneous GVHD: Evidence-based management: NIH 2014 Consensus
  - *Biol Blood Marrow Transplant 21 (2015): 1167-1187*
  - Very limited data
  - Clinical trials

# F0 –MULTIDISCIPLINARY MANAGEMENT OF CHRONIC GVHD .

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- Evidence for symptomatic treatment with emollients and antipruritic agents
- Skin directed vs systemic therapy (Topical corticosteroids, TCI, Phototherapy)
  - **Antihistamines may worsen sicca symptoms**
- Wound management (monitor for cutaneous infection)
- Systemic treatment:
  - First line: Steroids +/- calcineurin inhibitor
  - Second line: Sirolimus, MMF, ECP, imatinib, rituximab, HCQ, MTX
  - **JAK inhibitors:**
    - **Topical Ruxolitinib (currently recruiting, PI Dominique Pichard)**
    - **Oral Baricitinib (currently recruiting, PI Steve Pavletic)**
- Ibrutinib:
  - FDA approval for adults after failure of systemic therapy (August 2017). Side effects: infections, cytopenias, **hemorrhage: consider withholding for at least 3 to 7 days pre and post surgery because it inhibits platelet aggregation**
- Cell therapy:
  - Low dose IL-2
  - Mesenchymal stem cells
  - Combination approach

# F032 – GRANULOMATOUS DISORDERS OF THE ADULT SKIN 3:30 – 5:30 PM; ROOM 206

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- **Granuloma Annulare (GA)**
  - **Always take a biopsy to disclose sarcoidosis!!**
  - Systemic manifestations:
    - Generalized or atypical forms, refractory to treatment, > 60 or above.
    - **Associations: DM, autoimmune thyroiditis, HIV, Hep B+C, elevated lipids, lymphoproliferative and visceral malignancy.**
- Other clinical variants: **palmoplantar (paraneoplastic)**
- Differential Dx: sarcoidosis, elastolytic giant cell granuloma, reactive granulomatous dermatitis, necrobiosis lipoidica. *J Dermatol 2017; 44: 297-303.*
- Therapy ladder : **Phototherapy**
  - Steroids: top/il/oral.
  - Topical calcineurin inhibitors
  - Doxycycline
  - **Hydroxychloroquine**
  - Methotrexate
  - MFM
  - Acitretine
  - Biologics
  - Apremilast?/Statins?

*Improvement of 75% with HCQ or Phototherapy: wait 3 months to see results!*

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- **Necrobiosis lipoidica:**
  - Early/Middle/late stages (85% on the lower legs).
  - **Do not biopsy typical lesions located on shins! Biopsy atypical/ectopic lesions.**
  - Systemic manifestations: DM/retinopathy and nephropathy, ocular inflammation (retinal vasculitis in non-DM), joint immobility, autoimmune thyroiditis, IBD, RA.
  - Therapy: Phototherapy- **Avoid laser and PDT!**
    - **Glycemic control/No smoking/trauma avoidance!**
    - Steroid top/il
    - Topical calcineurin inh
    - Infliximab
    - ASA/ Dipyridamole/ Pentoxifiline/Niacinamide
    - **Hydroxychloroquine**
    - MMF/cyclosporine/MTX, hyperbaric O<sub>2</sub>
    - Biologics (infliximab)
    - Others (?): JAK inhibitors (ulcerative NL in a patient with polycitemia vera), apremilast, pioglitazone, thalidomide.

# F032 – GRANULOMATOUS DISORDERS OF THE ADULT SKIN 3:30 – 5:30 PM; ROOM 206

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- **Sarcoidosis:**
  - Specific (underlying granuloma) or non-specific (non-underlying granuloma)
  - Sarcoid lesions in tattoos (after 1-3 years)
  - Internal organ involvement: ocular, pulmonary, cardiac, neurologic
  - **Ask about palpitations!! (sign of cardiac involvement: sudden death).**
  - Associations: testicular cancer/lymphoma
  - Marker of multiple organ involvement: serum soluble interleukin-2 receptor more sensitive than angiotensin-converting enzyme. *J Dermatol* 2017; 44 (7): 789-797.
  - Therapy:
    - Steroids top/il. Oral or top calcineurin inhib.
    - **Doxycycline** better than minocycline 3 months.
    - **Hydroxychloroquine**
    - MTX
    - AZT/MMF/Leflunomide/Cyclophosphamide
    - Biologics: Infliximab/Adalimumab. Not effective Etanercept/Ustekinumab
    - Apremilast.

***Laser and PDT may induce sarcoidosis : use with caution!***



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- **Granulomatous drug reactions:**
  - Drug-induced accelerated rheumatoid nodulosis: tocilizumab.
  - Reactive granulomatous dermatitis to drugs and interstitial granulomatous drug reaction: bosutinib.
  - Drug-induced GA: not frequent.
  - Drug-induced sarcoidosis. *Chest* 2018; 154 (3): 664-677.
- **Immune check-point inhibitors** and the development of granulomatous reactions. *J Am Acad Dermatol* 2018; Aug 6.
- **Granulomatous/sarcoid like lesions associated with checkpoint inhibitors : a marker of melanoma response in a subset of melanoma patients.** *J Immunother Cancer* 2018; 6 (1): 14.
  - *Lesions may mimic melanoma recurrence*
  - *71% of reported patients with this reaction noted therapeutic response, stable disease or remission of primary.*

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- **GA/NL/Sarcoidosis Future therapies :**
  - **Gli-1 oncogene** is highly expressed in GA/NL and Sarcoidosis
    - Inhibitors of this pathway:
      - Vismodegib
      - Erismodegib
      - Glasdegib
      - Saridegib
      - Patidegib (topical)
  - **Adipophilin** is expressed in GA/NL and Sarcoidosis
    - PI3K inhibitors:
      - Duvelisib
      - Idelalisib