Immunobullous Disease

Tips for Management and Future Therapies

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Relevant Disclosures

- Investigator: Argenx

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Objectives

- At the conclusion of this presentation, participants will be able to:
  - Develop treatment plans for immunobullous patients which will lead to the best outcomes
  - Understand the appropriate diagnostic tools for different clinical scenarios
  - List potential future therapies for the treatment of immunobullous diseases

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Pemphigus and Bullous Pemphigoid Tip 1

- Use steroids

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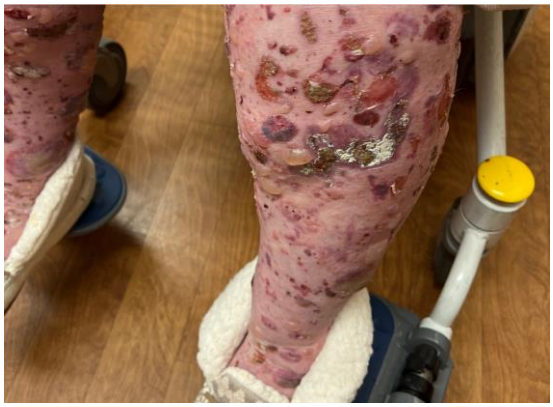
Case 1

- 70 year old female
- Diagnosed with BP 9/2022
  - PMH significant for T2DM
- No new medications
- Initial therapy
  - Doxycycline 100mg BID
  - Prednisone 20mg x 5 days, 10mg x 10 days
- 10/5 – Minocycline/clobetasol
- 10/26 – 14 day prednisone taper
- 11/22 – Mycophenolate and triamcinolone



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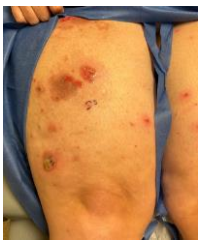
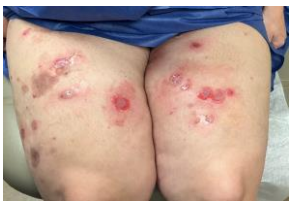
Case 2

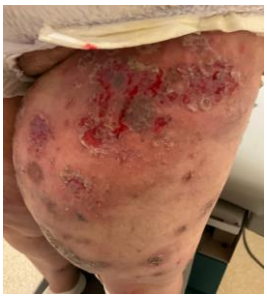
- 46 year old female
- Nonspecific H&E findings, DIF negative x 2
- No new medications, no significant PMH
- Prednisone tapers
  - August - 19 day taper
  - September - 15 day taper
  - October - 28 day taper
  - Doxycycline and mycophenolate started in November (no prednisone)
  - December – ELISA for desmogleins 1 and 3
    - Dsg 1 - 54
    - Dsg 3 - 173



September



October



November

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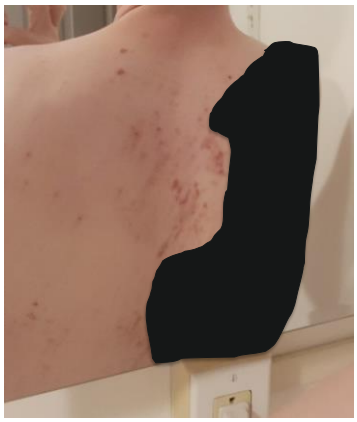
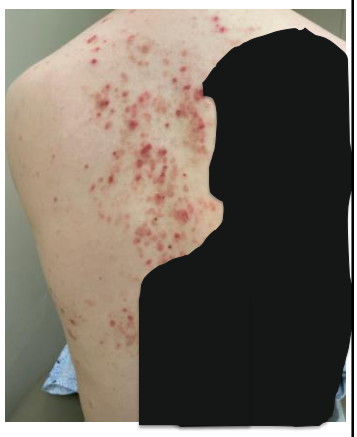
Case 3

- 38 year old male
- Diagnosed with pemphigus foliaceous
- No new medications, no significant PMH
- Prednisone taper
  - 40 – 20 – 10, 5 days at each dose





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Use of prednisone in AIBD

- Avoid rapid tapers!
  - Decreases in prednisone should be on the order of 5 – 10mg every 2-4 weeks (for both bullous pemphigoid and pemphigus)
- Even with the addition of steroid sparing therapy (excluding rituximab), be cautious about stopping prednisone in the setting of active disease
- Work closely with patient's primary care provider to manage potential corticosteroid induced side effects

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Murrell DF et al. (2023) UpToDate
Murrell DF et al. J Am Acad Dermatol. 2020 Mar;82(3):575-585

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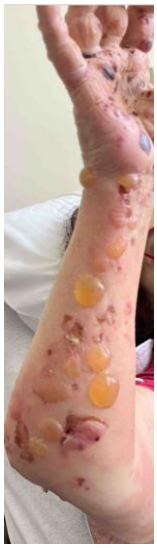
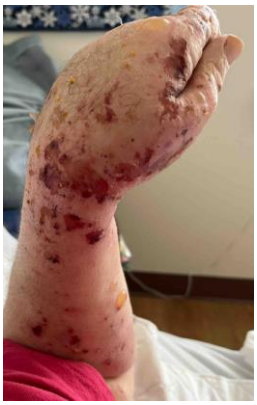
Prednisone in BP

- 70 year old female
- Diagnosed with BP
- PMH notable for T2DM
- No new medications around the time that BP was diagnosed
- Being treated with topical steroids, doxycycline 100mg BID

- Started on 40mg x 2 weeks, 30mg x 2 weeks, 20mg for 4 weeks, 10mg for 2 months
- Doxycycline was discontinued
- Sliding scale insulin was added when patient was on higher doses of prednisone





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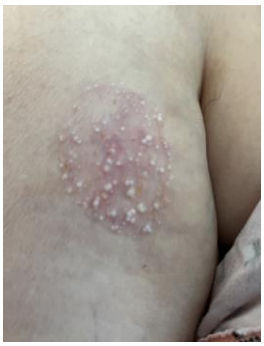

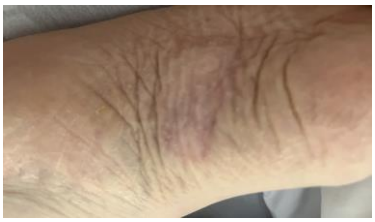

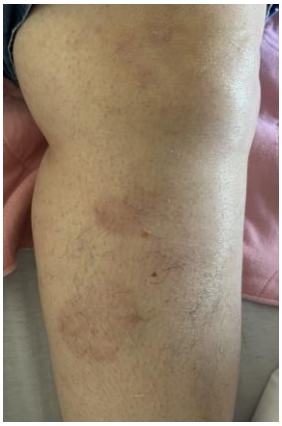

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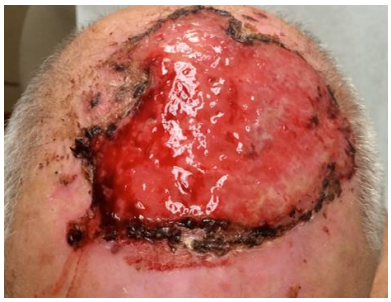
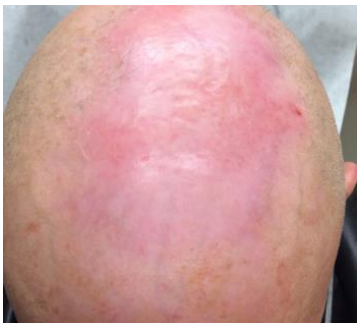
Prednisone in (non-BP) pemphigoid



- Started on prednisone 60mg daily for 2 wks, then 50mg daily for 2 wks, then decrease by 10mg every month



- Consistent response to moderate to high dose oral prednisone
- Inconsistent response to adjuvant therapy:
  - Pulse dexamethasone (30mg daily for 3 days)
  - Mycophenolate mofetil
  - Azathioprine
  - Dapsone
  - Intralesional corticosteroid injection
  - Topical corticosteroids
  - Rituximab was denied by insurance

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Pemphigus and Bullous Pemphigoid Tip 2

- Get patients off steroids
- Rituximab

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Limitations of steroid sparing therapies (That aren't rituximab)

- Bullous pemphigoid
  - Cochrane Database of Systemic Reviews (updated August 2023)
    - "The effectiveness of the addition of plasma exchange, azathioprine, mycophenolate mofetil, dapsone, or mepolizumab to prednisolone or prednisone has not been established"

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Singh S et al. Cochrane Database of Systematic Reviews 2023, Issue 8

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Doxycycline in bullous pemphigoid patients

Doxycycline versus prednisolone as an initial treatment strategy for bullous pemphigoid: a pragmatic, non-inferiority, randomised controlled trial

*Hywel C Williams, Fenella Wojnarowska, Gudula Kirtschig, James Mason, Thomas R Godec, Enno Schmidt, Joanne R Chalmers, Margaret Childs, Shernaz Walton, Karen Harman, Anna Chapman, Diane Whitham, Andrew J Nunn, on behalf of the UK Dermatology Clinical Trials Network BLISTER Study Group**

- Control of blister development at week 6
  - 74% of doxycycline patients versus 91% of prednisolone patients
- Severe, life-threatening, and fatal events
  - 18% of doxycycline patients versus 36% of prednisolone patients
- Doxycycline is a reasonable addition to prednisone in all BP patients and could be considered as monotherapy in the mildest cases of BP

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Williams HC et al. Lancet (London, England), 389(10079), 1630–1638

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Limitations of steroid sparing therapies (That aren't rituximab)

Treating Pemphigus Vulgaris with Prednisone and Mycophenolate Mofetil: A Multicenter, Randomized, Placebo-Controlled Trial

Stefan Beissert[1], Daniel Mimouni[2,3], Amrinder J. Kanwar[4], Neil Solomons[5], Veena Kalia[5] and Grant J. Anhalt[6]

- Percentage of patients reaching the primary endpoint (disease control on ≤10mg prednisone) was the same between patients taking prednisone + MMF versus prednisone + placebo (69% vs. 63.9%)

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Beissert S et al. Journal of Investigative Dermatology. Volume 130, Issue 8, 2010

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Rituximab

First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomised trial

Pascal Joly, Maud Maho-Vaillant, Catherine Prost-Squarcioni, Vivien Hebert, Estelle Houivet, Sébastien Calbo, Frédérique Caillot, Marie Laure Golinski, Bruno Labeille, Catherine Picard-Dahan, Carle Paul, Marie-Aleth Richard, Jean David Bouaziz, Saphie Duvert-Lehembre, Philippe Bernard, Frederic Caux, Marina Alexandre, Saskia Ingen-Housz-Oro, Pierre Vabres, Emmanuel Delaporte, Gaelle Quereux, Alain Dupuy, Sebastien Debarbieux, Martine Avenel-Audran, Michel D'Incan, Christophe Bedane, Nathalie Bénéton, Denis Jullien, Nicolas Dupin, Laurent Misery, Laurent Machet, Marie Beylot-Barry, Olivier Dereure, Bruno Sassolas, Thomas Vermeulin, Jacques Benichou, Philippe Musette, and the French study group on autoimmune bullous skin diseases

- Anti-CD20 monoclonal antibody
- 1000mg on days 1 and 14, 500mg at months 12 and 18
- Patients in the rituximab group underwent a more rapid taper of their prednisone
  - 3 and 6 months versus 12 and 18 months in the prednisone alone group
- Patients in complete remission off therapy at month 24
  - 89% of rituximab patients versus 34% of prednisone alone

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Joly P et al. Lancet (2017), 2031–2040

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Rituximab

Rituximab versus Mycophenolate Mofetil in Patients with Pemphigus Vulgaris

V.P. Werth, P. Joly, D. Mimouni, E. Maverakis, F. Caux, P. Lehane, L. Gearhart, A. Kapre, P. Pordeli, and D.M. Chen, for the PEMPHIX Study Group*

- 1000mg on days 1, 15 with 2 additional doses at 6 months (2 weeks apart)
- Sustained complete remission at week 52
  - 40% rituximab patients versus 10% mycophenolate patients

Werth VP et al. (2021). The New England journal of medicine, 384(24), 2295–2305

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Rituximab

- 2 doses of 1000mg, 2 weeks apart
- Follow up doses as needed
- Should be offered to almost all patients with pemphigus vulgaris and most patients with pemphigus foliaceous
- Should be considered in BP patients not responding to moderate to high-dose prednisone
  - Literature review of 122 BP patients treated with rituximab
    - Complete remission in 70.5%
    - Partial remission in 23.8%

Cao P et al. Front Immunol. 2022 Jun 13;13:928621

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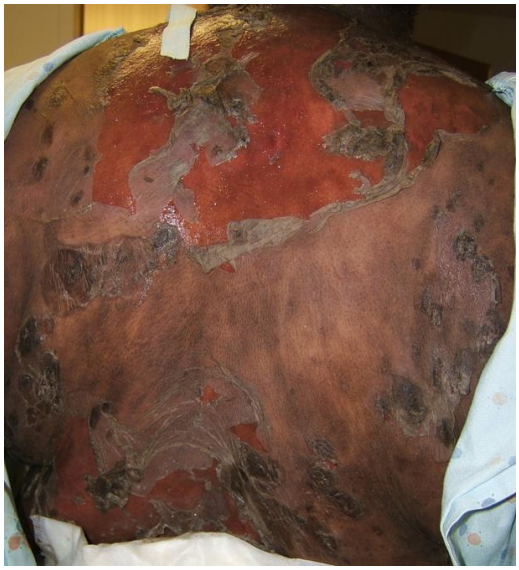
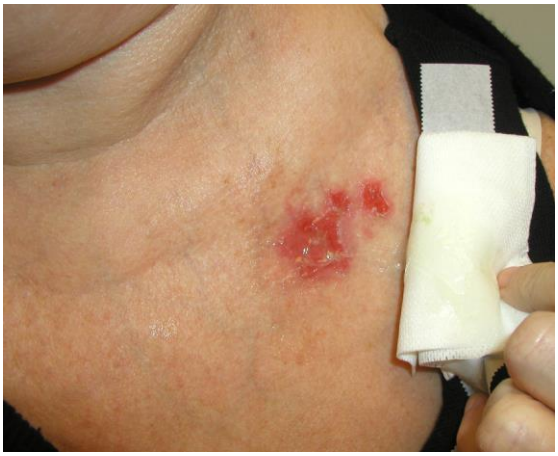
Severe pemphigus vulgaris



Mild pemphigus vulgaris



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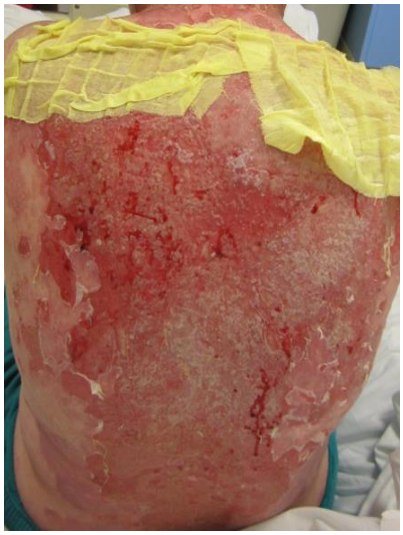
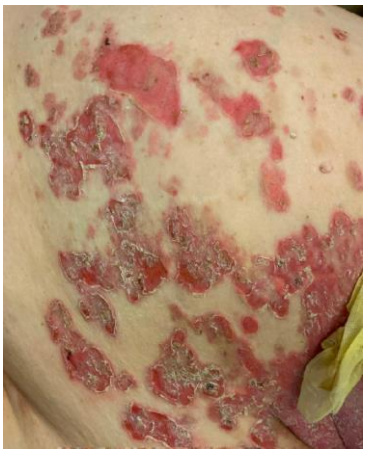
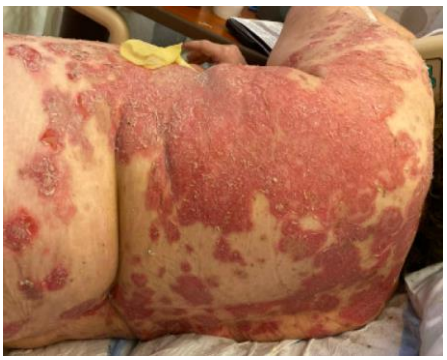
Pemphigus foliaceous







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Rituximab

- Just initial 2 doses? Yes
- Routine follow up doses? No – not routinely
- Use of antibody titers to determine redosing? Sometimes

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Rituximab

- Lymphoma versus RA protocol for pemphigus
  - Literature review demonstrated CR in 66.66% of the lymphoma protocol patients compared to 75% of the RA protocol patients
  - Single institution retrospective study demonstrated that patients receiving the lymphoma protocol had a higher odds ratio of achieving complete remission off therapy
- Standard follow up doses versus "as needed" follow up dosing
  - Retrospective study comparing just initial two doses of 1000mg versus the initial dose plus 500mg at months 6 and 12
  - 71% relapse rate versus 40% relapse rate

Zakka LR et al. Dermatol Ther (Heidelb). 2012 Dec;2(1):17
Kushner CJ et al. JAMA Dermatol. 2019;155(12):1404–1409
Rashid H et al. (2020). Journal of the American Academy of Dermatology, 83(5), 1503–1505.

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Rituximab

- Vaccination recommendations
  - Prior to immunosuppression
    - ≥2 weeks for non-live vaccines
    - ≥4 weeks for live vaccines
  - Following rituximab therapy
    - For non-live vaccines, wait at least 3 months, ideally 6 months
    - Avoid live vaccines

Seree-Aphinan C et al. Front Immunol. 2023 Mar 15;14:1138765
Winthrop KL In: UpToDate, Kaufmann CA (Ed). 2023

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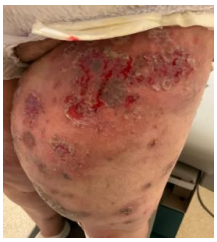
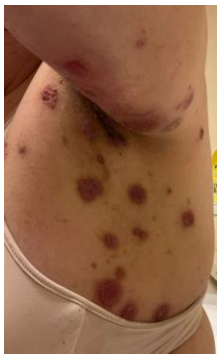
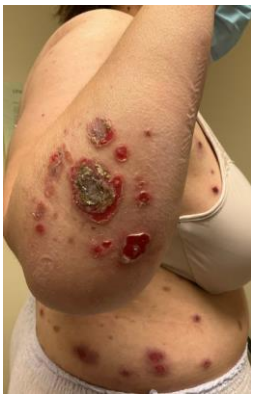
Using titers in disease management

- 46 year old female
- Baseline titers
  - Dsg 1 - 54
  - Dsg 3 – 173
- Initial treatment
  - Prednisone, 60 – 50 – 40 – 30, 2 weeks at each dose,then one month each of 20mg, 10mg
  - Rituximab 1000mg x 2 doses while taking the 20mg







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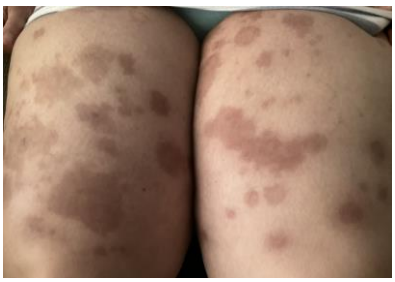
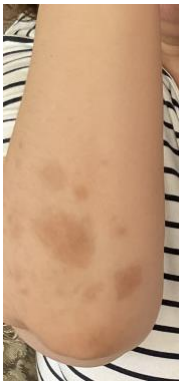
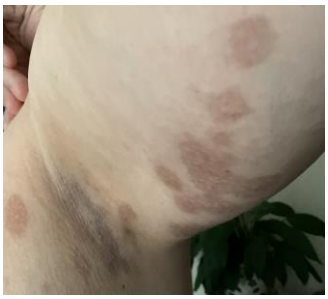




3 months post rituximab
Prednisone tapered to 0mg



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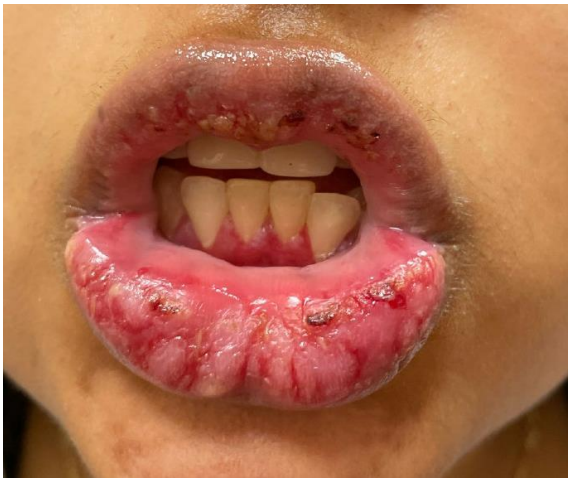
Using titers in disease management

- 25 year old female
- Approximately 8 months of oral erosions/blisters
- Prednisone improved lesions – had never been prescribed a longer course of medication
- Biopsy – “intraepithelial separation”, DIF unable to be performed because of denuded epithelium
- Antibody titers
  - Dsg 3 – 158
  - Dsg 1 – 16
- Initial treatment
  - Prednisone taper – 40mg x 2 weeks, 30mg x 2 weeks, then 20mg for a month
  - Rituximab 1000mg x 2 doses, 2 weeks apart



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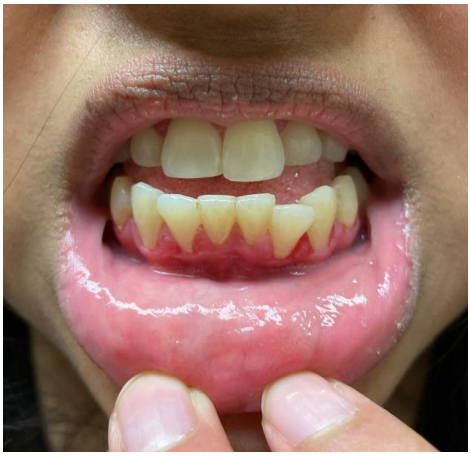

One month following rituximab
Prednisone 10mg

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  - Dsg 1 – 16
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  - Rituximab 1000mg x 2 doses, 2 weeks apart

- One month after rituximab
- Patient still complaining of gingival sloughing
- Still developing oral blisters while on 10mg prednisone
- Repeat titers
  - Dsg 3- 140
  - Dsg 1 - <19
- Repeat rituximab, 500mg x 1 dose

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Bullous Pemphigoid Tip

- Take a good medication history

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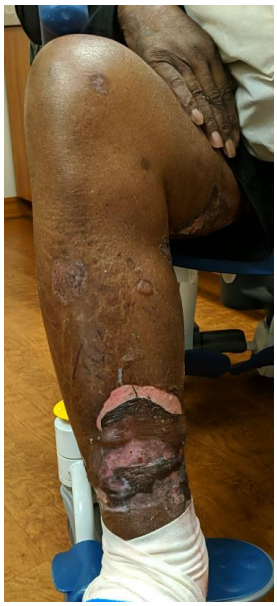
BP Case 2

- 80 year old male
- Referred for management of BP
- Multiple prednisone tapers over the previous several months
- Started linagliptin around the time of the start of his BP
- Linagliptin discontinued, slow prednisone taper
- Currently on low dose prednisone



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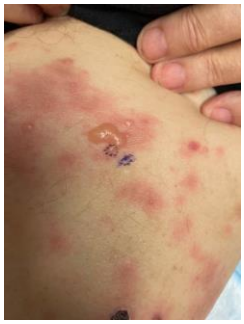
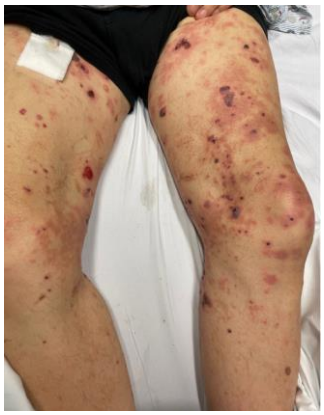
BP Case 2

- 78 year old male
- Diagnosed with metastatic urothelial carcinoma
- On month 10 of a planned 1 year course of nivolumab
- Subepidermal bullae with eosinophils, IgG and C3 at the BMZ
- BPAg 180 – 53
- BPAg 230 - <9





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Drug Associated BP

A Systematic Review of Drug-associated Bullous Pemphigoid

Matthew J. VERHEYDEN[1], Asli BILGIC[2,3] and Dédée F. MURRELL[2,4]
[1]School of Medicine, University of Notre Dame, [2]St George Hospital, Department of Dermatology, Sydney, Australia, [3]Antalya Research and Training Hospital, Antalya, Turkey and [4]Faculty of Medicine, University of New South Wales, Sydney, Australia

- 250 case reports
- DPP4-inhibitors and PD-1/PD-L1 inhibitors made up ~25% of reported cases
- Treatment
  - Withdraw medication
  - Prednisone, rituximab

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Verheyden MJ et al. Acta Derm Venereol. 2020 Aug 17;100(15)

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Paraneoplastic Pemphigus Tip 1

- Have a high degree of suspicion for PNP in the setting of certain clinical and histologic findings

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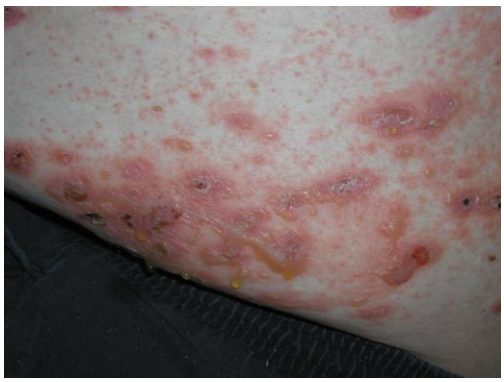
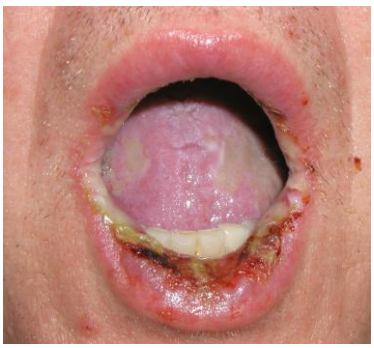
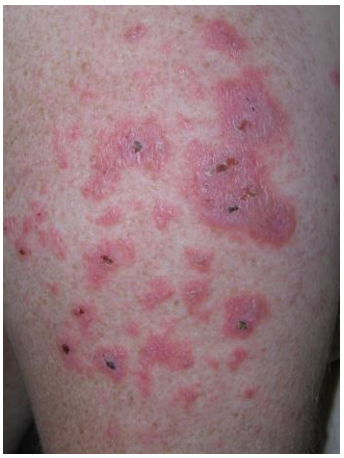
PNP Case 1

- 56 year old male with rash, blisters, oral erosions
- No new medications
- No significant PMH







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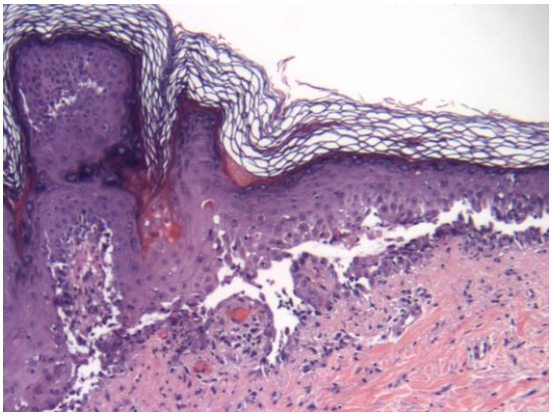
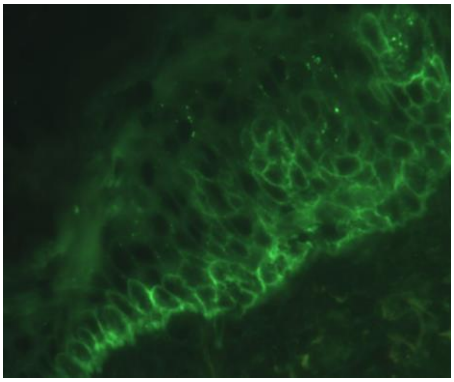
PNP Case 1

Suprabasal clefting with acantholysis



Intracellular IgG and C3



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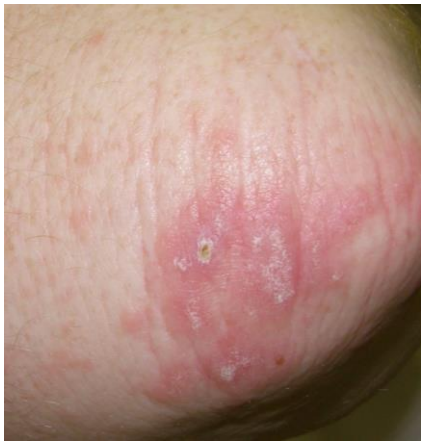
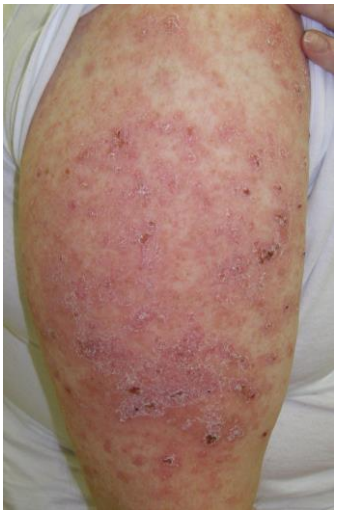
PNP Case 1

- Initial improvement with corticosteroids
- Worsening rash with tapering doses of corticosteroids





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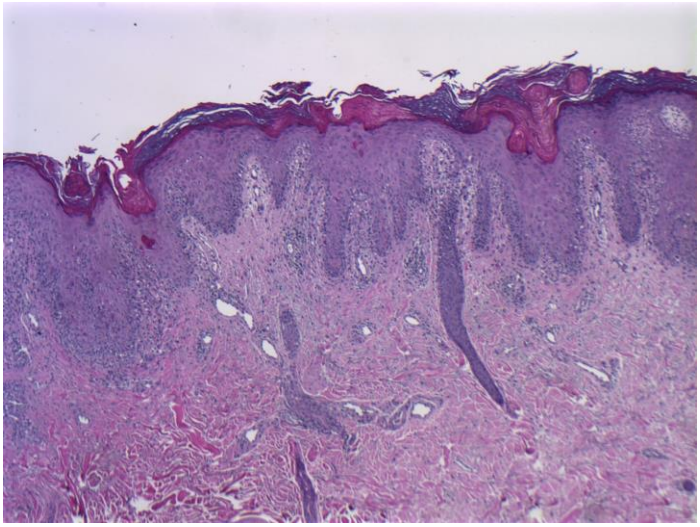
PNP Case 1

Lichenoid reaction pattern



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Paraneoplastic Pemphigus

- Autoimmune bullous disease in which antibodies are directed against multiple epithelial antigens in addition to desmogleins
- Also known as Paraneoplastic Autoimmune Multiorgan Syndrome (PAMS)
- Occurs in association with multiple malignancies
  - NHL
  - CLL
  - Castleman's
  - Waldenstrom's
  - Thymoma
- Involves both humoral and cell mediated autoimmunity

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Paraneoplastic Pemphigus
Diagnosis

- In addition to suprabasal clefting classically found in PV, PNP patients may also show lichen planus-like or EM-like changes
  - This may be the first indication of PNP and workup for malignancy should be considered
    - CT scan of chest, abdomen, pelvis
    - CBC, SPEP
- Specific DIF findings (immunoreactants at both epithelial cell surface and basement membrane zone) may only be present in less than half of PNP patients
- IIF on murine bladder and ELISAs to envoplakin and periplakin are sensitive tests, but may not be immediately available

Joly P. et al. (2000) JAAD, 43(4), 619–626

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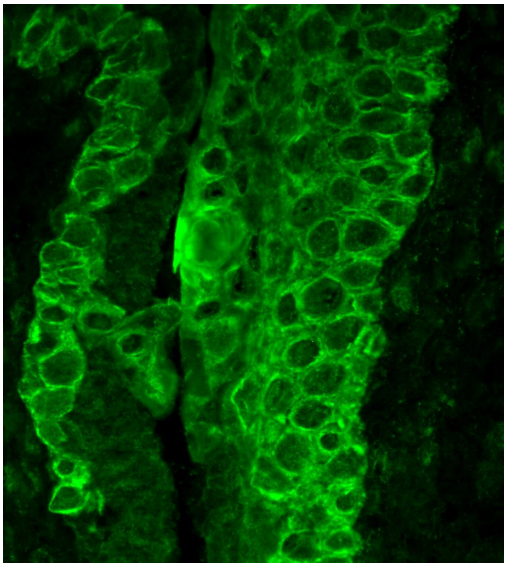
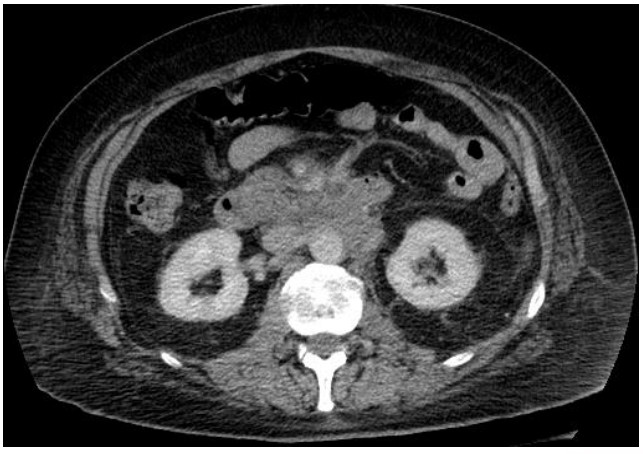
PNP Case 1



IIF on murine bladder



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Paraneoplastic Pemphigus Tip 2

- Be aware of lichenoid PNP in patients that have received rituximab
- Initial immunofluorescence testing may be negative

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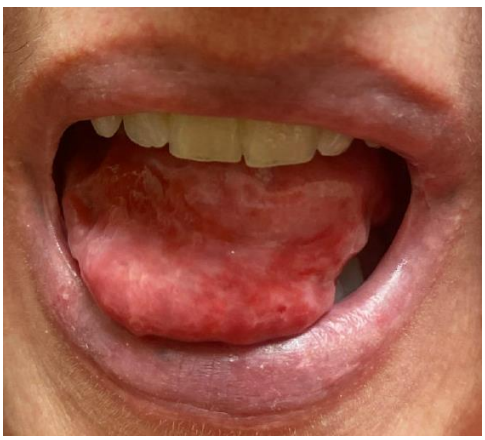
PNP Case 2

- 63 year old female with SJS from rituximab
- Patient with CLL, was initiated on a regimen of fludarabine, cyclophosphamide, rituximab and developed a severe mucositis
- Diagnosed with SJS secondary to rituximab, treated with dexamethasone for close to 2 years
- Multiple skin biopsies demonstrated lichen planus-like reaction



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PNP Case 2

- 2 years following diagnosis SJS secondary to rituximab, biopsy performed for DIF on buccal mucosa
  - Negative
- IIF on human skin
  - Negative
- Desmoglein ELISA
  - Dsg3 titers: 44 U/ml (Normal <20)
- IIF on rat bladder
  - Positive

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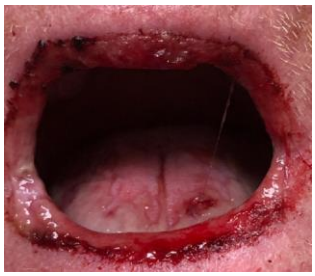
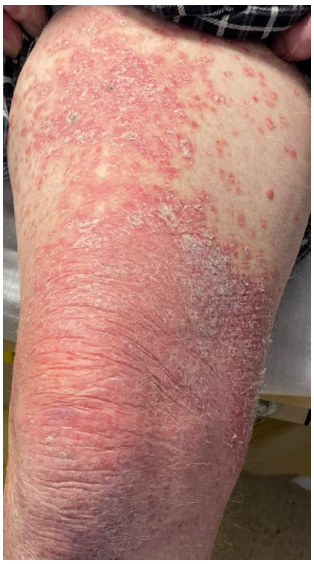
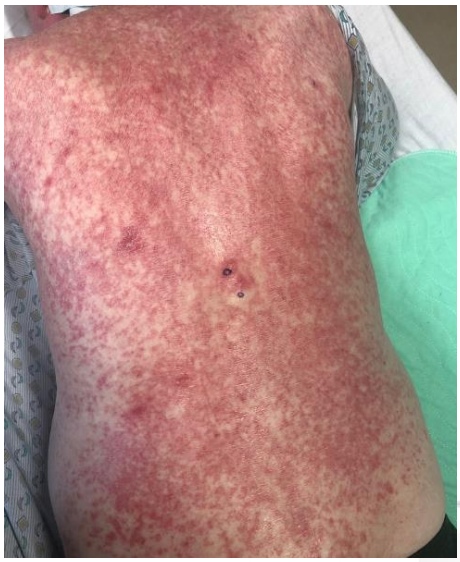
PNP Case 3







- 71 year old male
- CLL – diagnosed with SJS secondary to rituximab
- Initial antibody testing negative
- IIF on rat bladder – positive
- Envoplakin ELISA - positive

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PNP without antibodies

Lichenoid paraneoplastic pemphigus in the absence of detectable antibodies

Deborah L. Cummins, MD,[a] Daniel Mimouni, MD,[b] Julia Tzu, BS, Nicole Owens, MD,[c]
Grant J. Anhalt, MD,[a] and Jon H. Meyerle, MD[a]
Baltimore, Maryland; Petah Tikva and Tel Aviv, Israel; and Fort Sam Houston, Texas

- 4 patients that had received rituximab for the treatment of CLL
- Severe mucosal erosions/ulcerations
- Lichenoid pattern of inflammation
- DIF, IIF, immunoprecipitation all failed to demonstrate antibodies

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Cummins DL et al. J Am Acad Dermatol. 2007 Jan;56(1):153-9

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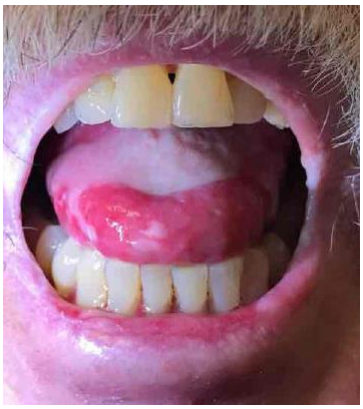
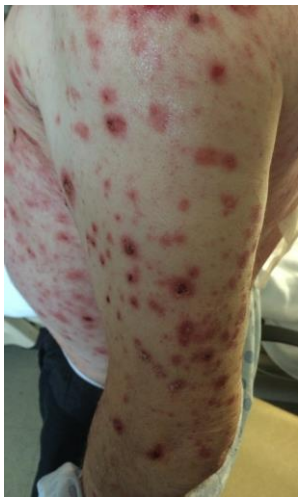
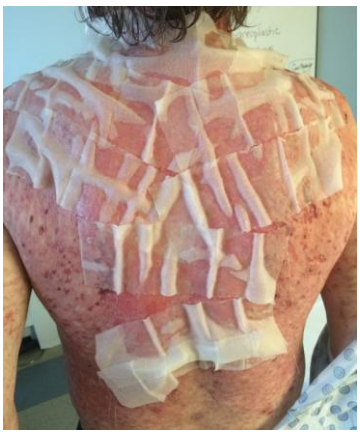
PNP without antibodies







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Lichenoid PNP

- PNP is both a B-cell and T-cell mediated disease
- When patients receive rituximab, the B-cell component of the disease is rendered inactive
  - Negative antibody testing
- All three patients were diagnosed with SJS secondary to their chemotherapy
  - Importance of correct diagnosis – chemotherapy can be continued in these patients

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Mucous Membrane Pemphigoid Tip 1

- Utilize subspecialists

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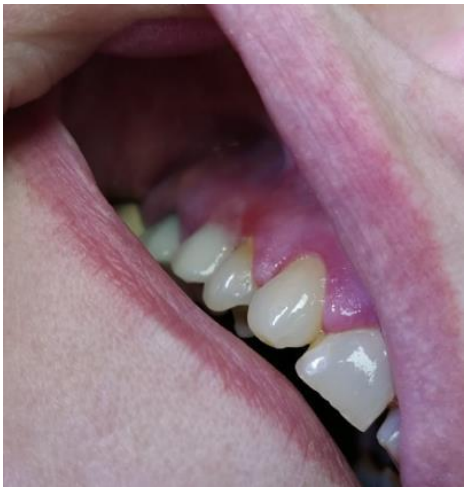
Case

- 63 year old female
- 5 month history of oral ulcers
- Biopsy results demonstrating "inflammation"
- Repeat biopsy with nonspecific H&E findings, negative DIF
- IIF testing was negative
- Trial of hydroxychloroquine without improvement
- Patient referred to dental surgeon for repeat gingival biopsy



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Pemphigoid Algorithm

H&E – submucosal split
Immunoglobulins at the mucosal/submucosal junction
Prominent lichenoid infiltrate not present

IgA only → Linear IgA Disease

IgG, +/- IgA, +/-C3 → Mucous Membrane Pemphigoid
Epidermolysis Bullosa Acquisita

If DIF is negative and suspicion for an immunobullous disease is still high, the best option is to probably repeat the DIF
Indirect IF is often negative in MMP patients

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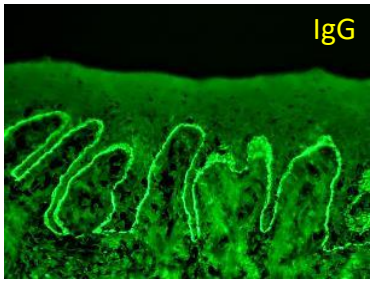

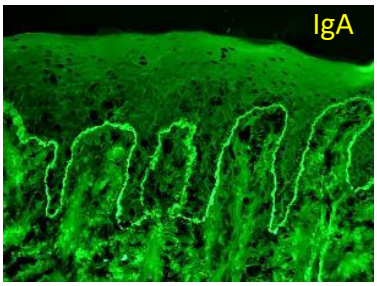

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Mucous Membrane Pemphigoid
Tip 2

- Determine if patient has scarring or non-scarring disease

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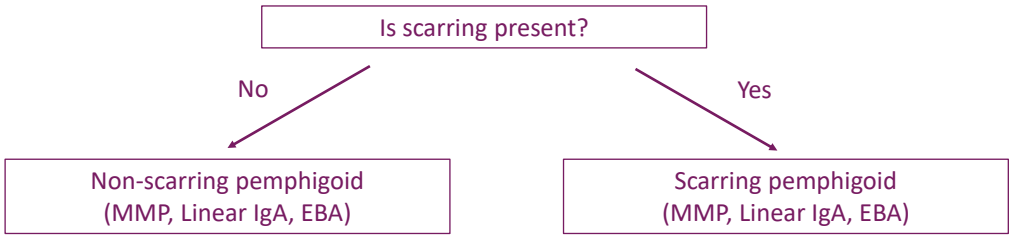
Pemphigoid Group
Diagnosis

- With predominant oral mucous membrane involvement, more important than the precise diagnosis (MMP versus EBA versus Linear IgA) is assessing whether or not scarring is present
- Eyes, esophagus, larynx, genital
- Take a good history – history of regurgitation, stridor, foreign body sensation
- Eye exam should be done in all patients with oral pemphigoid lesions



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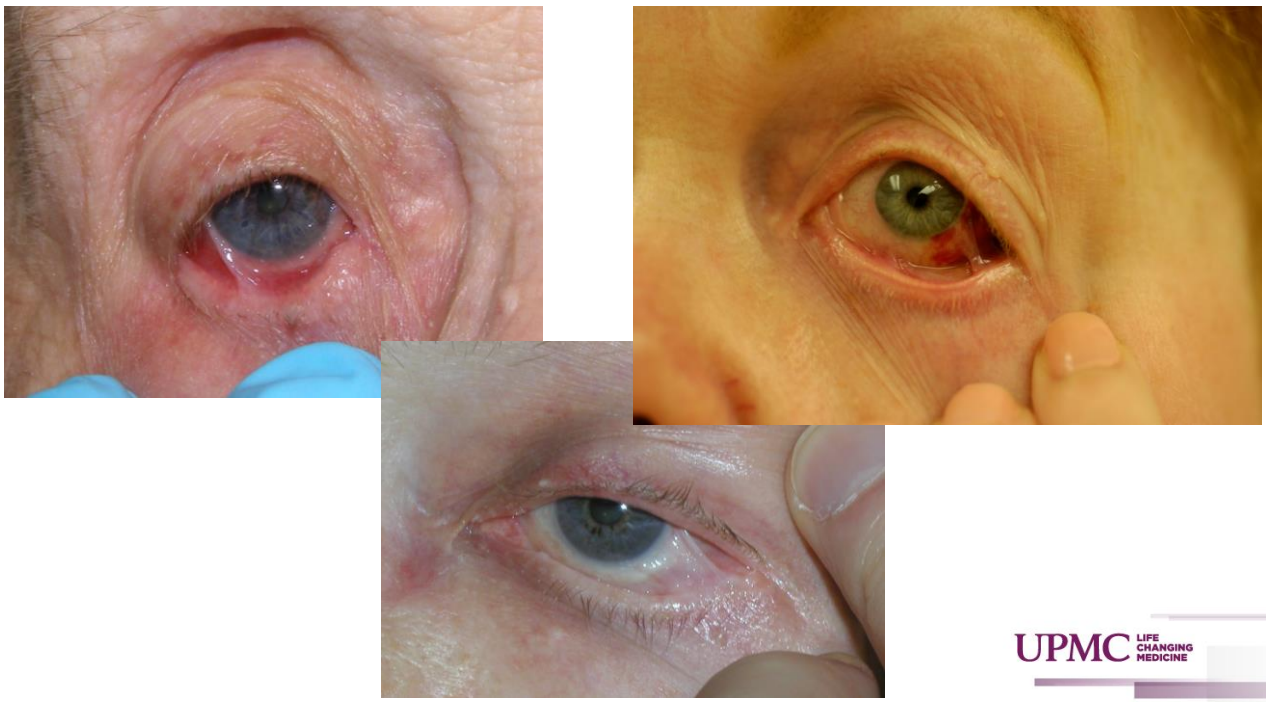

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Pemphigoid Group

Therapy

Is scarring present?

No → Non-scarring pemphigoid (MMP, Linear IgA, EBA)

Yes → Scarring pemphigoid (MMP, Linear IgA, EBA)

Usually only affects the oral mucosa
Can be symptomatic
Initial treatments should be non-aggressive
Topical corticosteroids, doxycycline, dapsone, colchicine

Serious sequelae can develop if not treated aggressively (blindness, esophageal stenosis, laryngeal stenosis)
Systemic corticosteroids + cyclophosphamide + rituximab

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Archives of Dermatology Vol 138, Mar 2002

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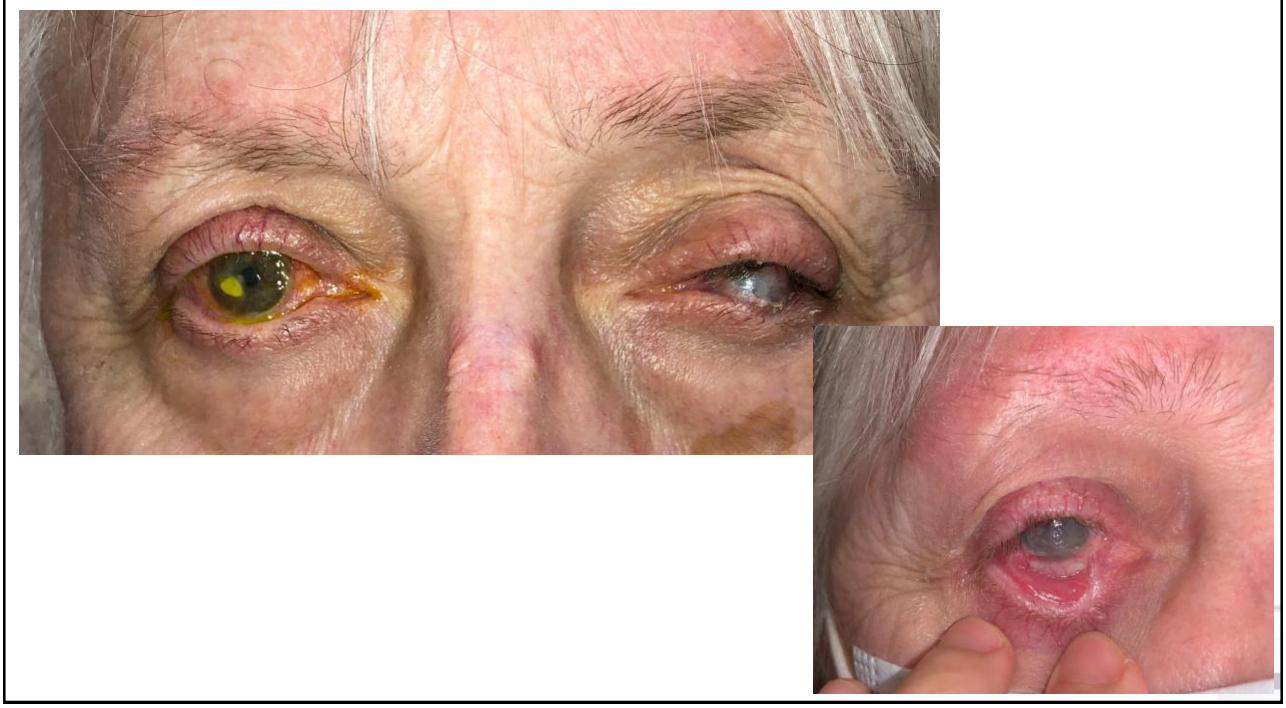

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Potential Future Therapies

- Therapies targeting B-cells
  - Anti-CD20 – ofatumumab, veltuzumab, ocrelizumab, tositumomab, obinutuzumab
  - Anti-CD19 – blinatumomab, inebilizumab
  - CD22 modulators – epratuzumab
  - Anti-APRIL – atacicept
  - Anti-BAFF – belimumab
  - Bruton tyrosine kinase inhibitors – irbutinib, rilzabrutinib, tirabutinib
  - CAAR T-cell therapy
- Therapies targeting pathogenic antibodies
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  - CD40-CD40L inhibition
  - Polyclonal regulatory T-cells

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Bishnoi A et al. (2021). Indian journal of dermatology, venereology and leprology, 87(5), 611–620
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  - Anti-IgE antibodies – omalizumab, legulizumab
- Therapies targeting cytokines, chemokines, complement
  - Anti-complement C1s – sutimlimab
  - IL4 receptor antagonist – dupilumab
  - Anti-IL5 – mepolizumab
  - IL5 receptor antagonist - benralizumab
  - Anti-eotaxin-1 – bertilimumab
  - Anti-IL17 – ixekizumab
  - Anti-C5aR1 – avdoralimab
  - Anti-C5 and anti-LTB4 – nomacopan
  - Anti-IL23 – tildrakizumab
  - Anti-IL12/23 – ustekinumab
- Miscellaneous
  - Syk inhibitors – fostamatinib
  - CD40-CD40L inhibition
  - Polyclonal regulatory T-cells

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Bishnoi A et al. (2021). Indian journal of dermatology, venereology and leprology, 87(5), 611–620
Maglie R et al. Front Med (Lausanne). 2023 Feb 6;10:1128154

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Potential Future Therapies

- Therapies targeting B-cells
  - Anti-CD20 – ofatumumab, veltuzumab, ocrelizumab, tositumomab, obinutuzumab
  - Anti-CD19 – blinatumomab, inebilizumab
  - CD22 modulators – epratuzumab
  - Anti-APRIL – atacicept
  - Anti-BAFF – belimumab
  - Bruton tyrosine kinase inhibitors – irbutinib, rilzabrutinib, tirabutinib
  - CAAR T-cell therapy
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Bruton Tyrosine Kinase Inhibitors

- BTK is a signaling protein linking B-cell receptor to B-cell proliferation, activation, and survival
- Taken as a daily oral dose
- CR at week 24
  - 22% of rilzabrutinib, 18.8% of tirabrutinib patients
- Rilzabrutinib extended to one year of therapy
  - 50% CR rate

Original Article

A multicenter, open-label, uncontrolled, single-arm phase 2 study of tirabrutinib, an oral Bruton's tyrosine kinase inhibitor, in pemphigus

Jun Yamagami[a], Hideyuki Ujiie[b], Yumi Aoyama[c], Norito Ishii[d], Chiharu Tateishi[e], Akira Ishiko[f], Tomoki Ichijima[g], Shunsuke Hagihara[h], Koji Hashimoto[i], Masayuki Amagai[a,*]

Proof of concept for the clinical effects of oral rilzabrutinib, the first Bruton tyrosine kinase inhibitor for pemphigus vulgaris: the phase II BELIEVE study*

D.F. Murrell,[1] A. Patsatsi,[2] P. Stavropoulos,[3] S. Baum,[4] T. Zeeli,[5] J.S. Kern,[6] A.-V. Roussaki-Schulze,[7] R. Sinclair,[8] I.D. Bassukas,[9] D. Thomas,[10] A. Neale,[10] P. Arora,[10] F. Caux,[11] V.P. Werth,[12] S.G. Gourlay[10] and P. Joly[13] on behalf of the BELIEVE trial investigators

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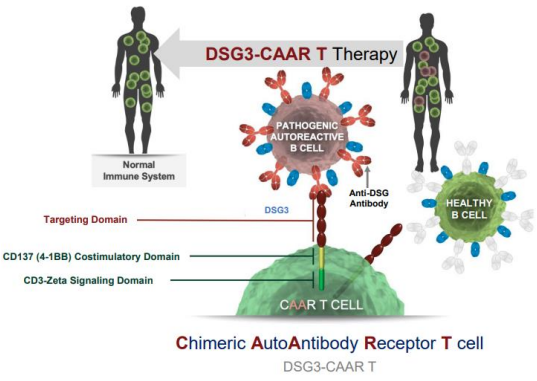
CAAR T-cell therapy

- Chimeric autoantibody T cells (CAAR T)
  - T cells from the patient engineered to express Dsg3 protein
    - Specifically bind to autoreactive anti-Dsg3 B cells
  - No dose limiting toxicities
  - Persistence of the DSG3-CAAR T cells
  - No clear pattern of change in anti-DSG3 antibody levels



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Chang DJ et al. EADV Congress (2022). Milan, Italy
Volkov JR. ASGCT Annual Meeting (2023). Los Angeles, CA

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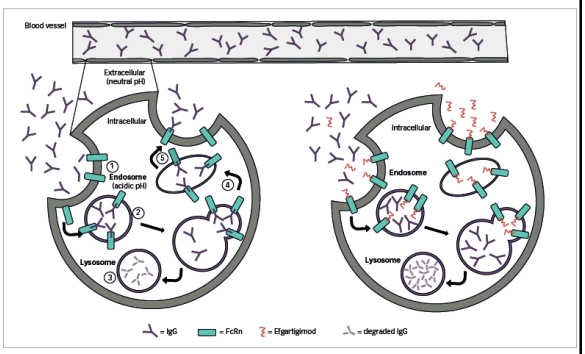
Efgartigimod

- Human derived Fc1 fragment that binds to the neonatal Fc receptor (FcRn)
- Promotes degradation of IgG
- Open-label phase II trial
  - 34 patients with PV or PF
  - Different IV doses and durations of induction, maintenance therapy
  - Mostly mild AEs reported at varying doses
  - Early disease control in 90% of patients
  - Decreases in overall IgG (40-50%) and anti-Dsg1 (61% reduction) and anti-Dsg3 (49% reduction) titers
- Current trial underway for BP patients

Figure 1: Efgartigimod mechanism of action



Vanoli F et al. touchREVIEWS in Neurology. 2022;18(2): 127-32

Goebeler M et al. British Journal of Dermatology, Volume 186, Issue 3, 1 March 2022, Pages 429–439

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Omalizumab, Legulizumab

- Anti-IgE antibodies (Legulizumab higher affinity for IgE)
- Phase 2 trial for legulizumab in BP was terminated
- 2 systematic reviews of BP patients treated with omalizumab
  - 55 and 56 patients
  - ~90% of patients in both studies received concurrent therapies
  - ~88% - 90% with response (CR and PR)

Cao P et al. Front Immunol. 2022 Jun 13;13:928621
D'Aguanno K et al. Journal of Cutaneous Medicine and Surgery. 2022;26(4):404-413

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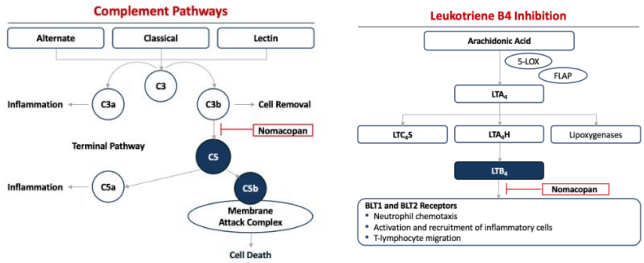
Nomacopan

JAMA Dermatology | Original Investigation

Evaluation of Nomacopan for Treatment of Bullous Pemphigoid
A Phase 2a Nonrandomized Controlled Trial

Christian D. Sadik, MD, PhD; Hanan Rashid, MD; Christoph M. Hammers, MD, PhD; Gilles F.H. Diercks, MD, PhD; Anke Weidinger, MD; Stefan Beissert, MD; Franziska Schauer, MD; James Fettiplace, MD, PhD; Diamant Thaçi, MD; Yenting Ngai, PhD; Miles A. Nunn, PhD; Detlef Zillikens, MD; Barbara Horváth, MD, PhD

- Inhibitor of both the complement cascade and LTB4 formation
- Decrease in BPDAI scores
- Phase III study in BP was withdrawn



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Akari Website. 2023

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Dupilumab

JAMA Dermatology | Original Investigation

Evaluation of Dupilumab in Patients With Bullous Pemphigoid

Liuqi Zhao, MD; Qijun Wang, MD; Guirong Liang, MD; Yuxi Zhou, MD; Nam Yiu, MD; Baoqi Yang, MD; Guiying Zhang, MD, PhD; Wei Li, MD; Suying Feng, MD; Panpan Shang, MD; Xixue Chen, MD; Xuejun Zhu, MD; Jie Zheng, MD, PhD; Meng Pan, MD, PhD; Mingyue Wang, MD, PhD

- Monoclonal antibody that binds to the IL4Ra receptor, inhibiting both IL4 and IL13 activity
- Retrospective study from 5 centers
- 87% of patients achieved disease control at 4 weeks
  - 60.6% of these patients were also on systemic corticosteroids (mean dose 0.3mg/kg/day)
  - Only 5.5% of patients were on dupilumab monotherapy
- Overall CR rate of 35.6% during study

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Zhao L et al. JAMA Dermatol. 2023 Aug

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The End

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