#WCD2019

AEDV HIGHLIGHTS

24th World Congress of Dermatology (WCD)

10-15 JUNIO 2019

Milàn

Patrocina:

janssen Immunology
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organiza:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA
AEDV 1909

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24th World Congress of Dermatology (WCD)

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Milán

Systematic and autoimmune disease

Raquel Rivera

Dermatologia HU 12 de Octubre Madrid

Patrocina: Janssen Immunology, Pharmaceutical Companies of Johnson & Johnson

Organiza: Academia Española de Dermatología y Venereología AEDV 1909

AEDV HIGHLIGHTS

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SY: New oral Small molecules

Patrocina: Janssen Immunology, Pharmaceutical companies of Johnson & Johnson

Organiza: Academia Española de Dermatología y Venereología AEDV 1909

2019 update of the EULAR recommendations for the management of systemic lupus erythematosus

Ann Rheum

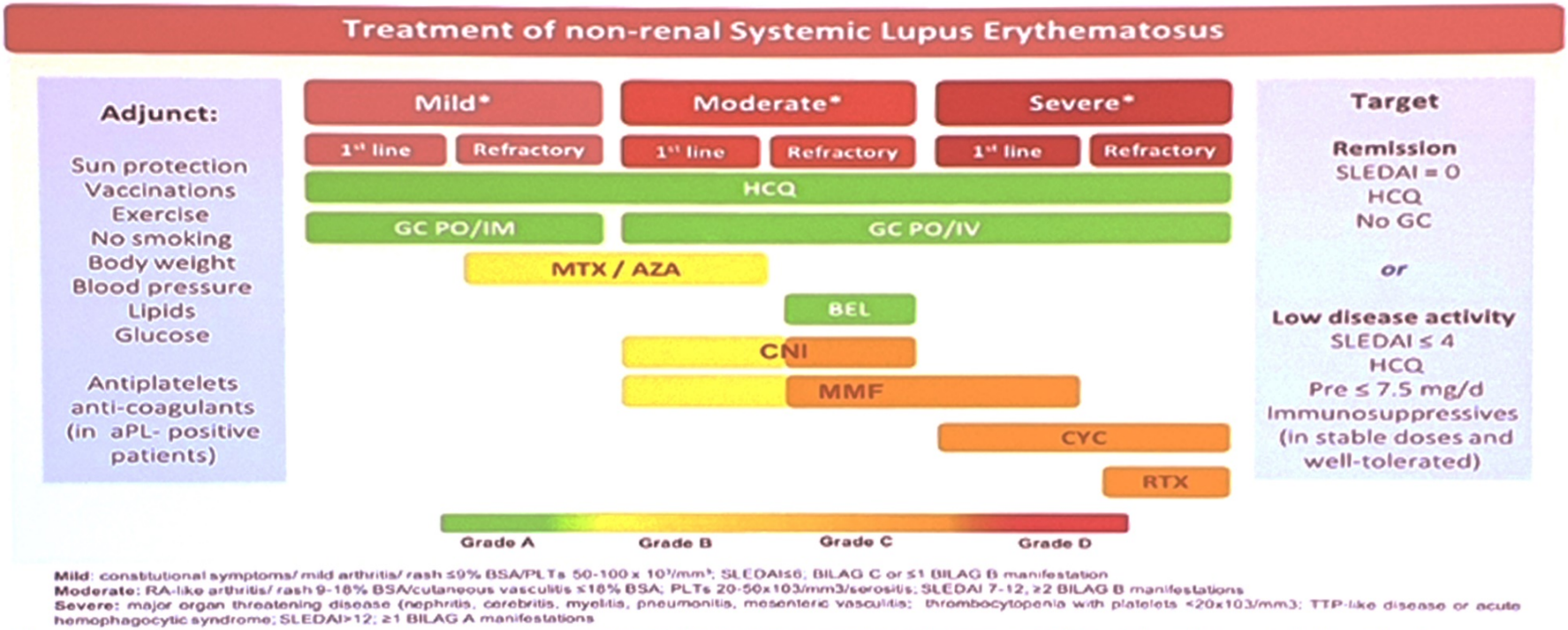

Figure 1 Treatment of non-renal SLE—recommended drugs with respective grading of recommendation. aPL, antiphospholipid antibodies; AZA, azathioprine; BEL, belimumab; BILAG: British Isles Lupus Assessment Group disease activity index; CNIs, calcineurin inhibitors; CYC, cyclophosphamide; GC, glucocorticoids; HCQ, hydroxychloroquine; IM, intramuscular; MMF, mycophenolate mofetil; MTX, methotrexate; Pre, prednisone; PO, per os; RTX, rituximab; PLTs: Platelets; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

- The first biologic agent approved for SLE, Belimumab, has been in clinical practice for more than 5 years with overall positive results.

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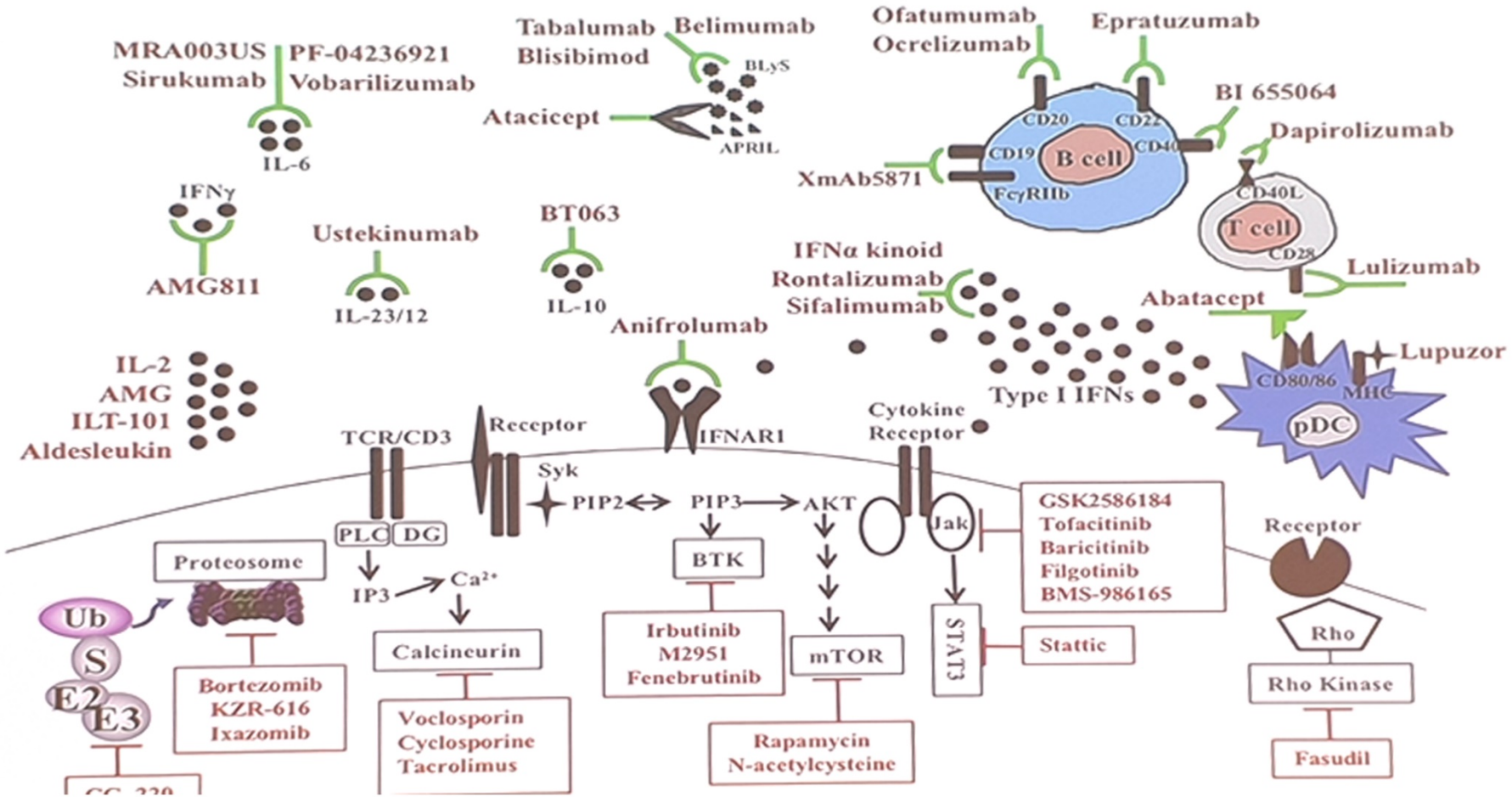
POTENTIAL NOVEL TREATMENT OPTIONS FOR SLE



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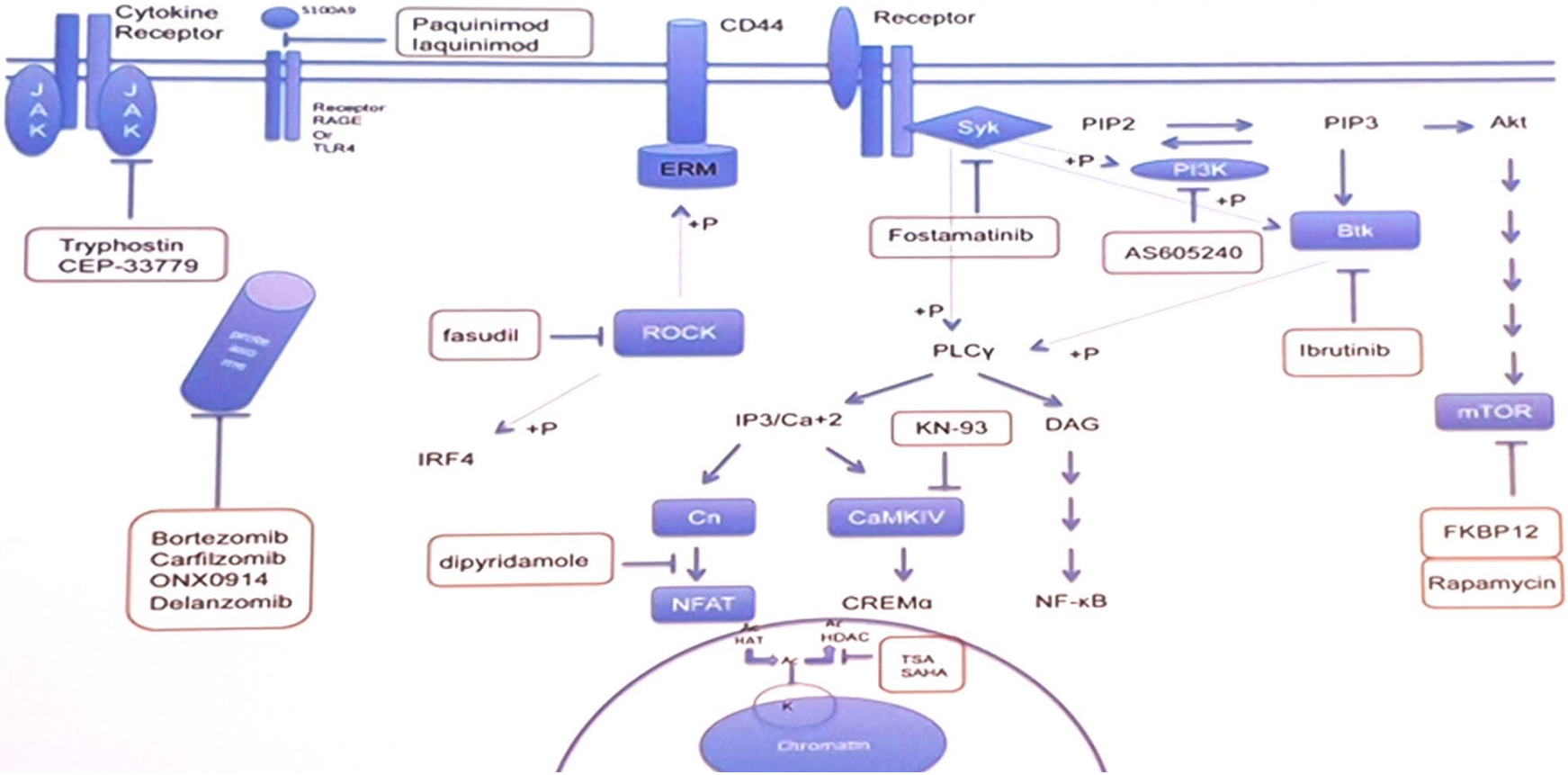
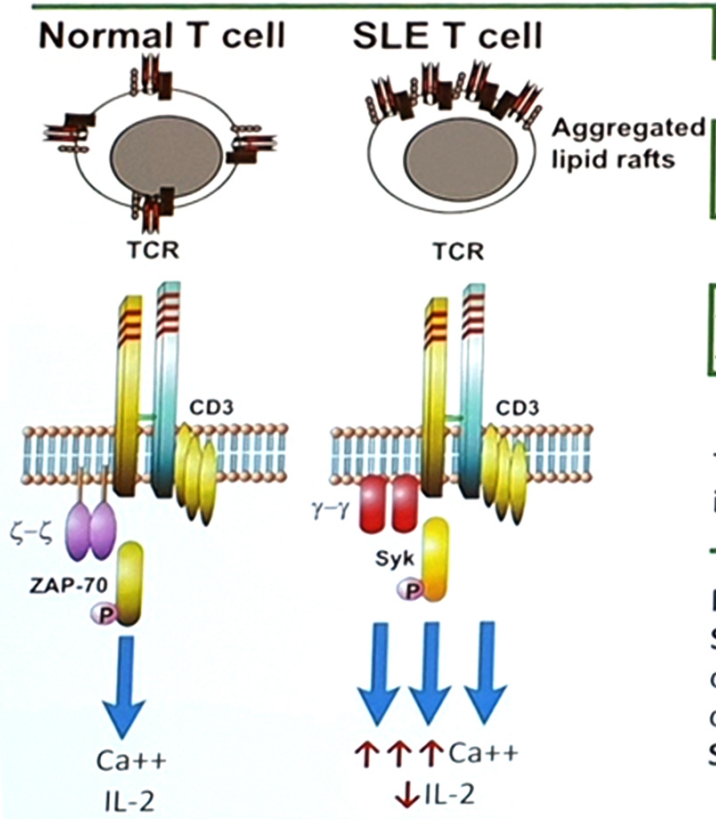
SMALL MOLECULE INHIBITORS INVOLVED IN THE POSSIBLE FUTURE TREATMENT OF SLE



SPLEEN TYROSINE KINASE (SYK) INHIBITION



Syk: expressed in hematopoietic, stromal, endothelial and epithelial cells.

↓

Recruited and activated at phosphorylated tyrosines on immunoreceptors, including BCR, TCR, Fc receptors (FcR), integrins and C-type lectins.

↓

Activation of Syk: mobilization of intracellular calcium and regulation o gene transcription programs.

↓

The key role of BCR and TCR in antigen recognition and of FcR in handli immune complexes, places Syk in the epicenter of SLE pathogenesis.

Normal T cell: CD3/TCR complex signaling through CD3ζ chain and ZAP-7
SLE T cell: CD3/TCR signals through the FcRγ chain and Syk. The F chain/Syk complex populates lipid rafts, which are pre-cluste contributing to the hyperexcitable T cell phenotype. **Therefore, targe Syk represents a promising therapeutic strategy in SLE**.

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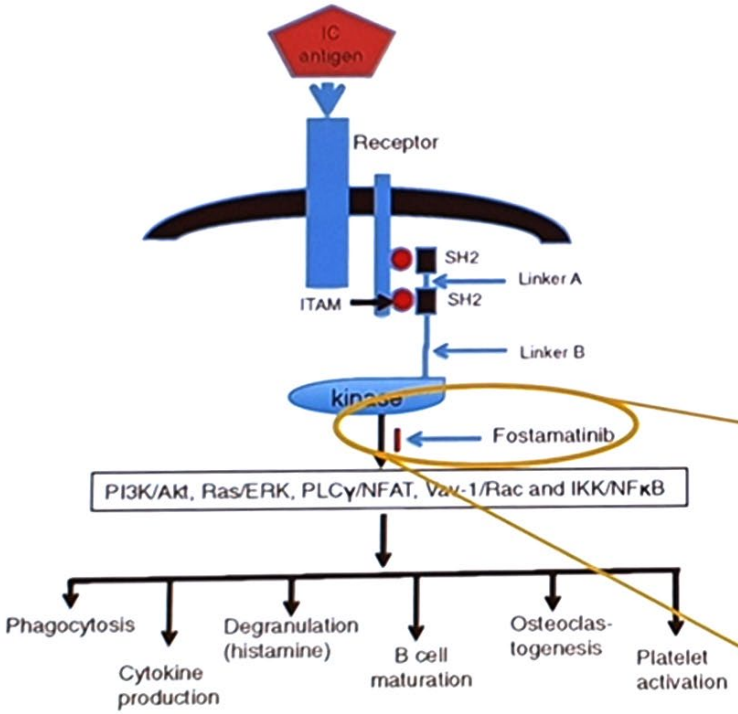
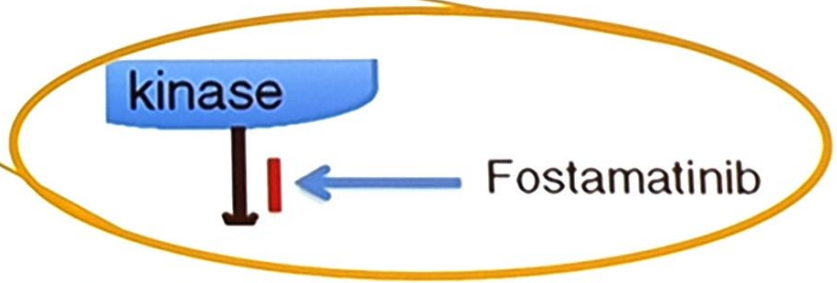
FOSTAMATINIB (R788)



Engagement of Syk and downstream effects. Following aggregation of FcR by immune complex (IC), the phosphorylation of ITAM tyrosine leads to the recruitment of Syk to the receptor in an interaction mediated by its tandem pair of SH2 domains. Active Syk initiates signaling pathways of PI3K/Akt, Ras/ERK, PLCγ/NFAT, Vav-1/Rac, and IKK/NFκB and then generating downstream effects, such as phagocytosis, cytokine production, degranulation, B-cell maturation, osteoclastogenesis, and platelet activation.



Targeting Syk in Autoimmune Rheumatic Diseases *Guo-Min Deng, Vasileios C. Kyttaris and G*

TOFACITINIB

Ann Rheum Dis. 2019 Apr 20. pii: annrheumdis-2019-215455. doi: 10.1136/annrheumdis-2019-215455. [Epub ahead of print]

Successful treatment of arthritis and rash with tofacitinib in systemic lupus erythematosus: the experience from a single centre.

You H[#1], Zhang G[#2], Wang Q[1], Zhang S[1], Zhao J[1], Tian X[1], Li H[2], Li M[3], Zeng X[3].

- 10 SLE patients treated with 10 mg/die of Tofacitinib
- Four patients quickly achieved resolution of arthritis and six patients of rash
- No significant serological improvement was observed in level of C3 and anti-dsDNA

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JAK/STAT PATHWAY

Baricitinib

- JAK1/JAK2 inhibitor efficacious for treatment of RA, approved in the EU for this indication.
- Currently a phase III study in SLE (ClinicalTrials.gov, numbers NCT03616912 and NCT03616964) is ongoing. A phase two study was completed.

Solcitinib (GSK2586184)Selective JAK1 inhibitor

- A study in SLE was terminated due to lack of efficacy and increased toxicity.

BMS-986165

- A phase II study of, a selective Tyk2 inhibitor, in 400 patients with SLE is currently ongoing (NCT03252587).

Lancet. 2018 Jul 21;392(10143):222-231. doi: 10.1016/S0140-6736(18)31363-1.

Baricitinib for systemic lupus erythematosus: a double-blind, randomised, placebo-controlled, phase 2 trial.

Wallace DJ[1], Furie RA[2], Tanaka Y[3], Kalunian KC[4], Mosca M[5], Petri MA[6], Dörner T[7], Cardiel MH[8], Bruce IN[9], Gomez E[10], Carmack T[10], DeLozier AM[10], Janes JM[10], Linnik MD[11], de Bono S[10], Silk ME[10], Hoffman RW[10]

INTERPRETATION: The **baricitinib** 4 mg dose, but not the 2 mg dose, significantly improved the signs and symptoms of active **systemic lupus erythematosus** in patients who were not adequately controlled despite standard of care therapy, with a safety profile consistent with previous studies of **baricitinib**. This study provides the foundation for future phase 3 trials of JAK1/2 inhibition with **baricitinib** as a new potential oral therapy for **systemic lupus erythematosus**.

Current Rheumatology Reports (2018) 20:34
https://doi.org/10.1007/s11926-018-0745-1

SYSTEMIC LUPUS ERYTHEMATOSUS (G TSOKOS, SECTION EDITOR)

New Trials in Lupus and where Are we Going

Aikaterini Thanou[1] · Joan T. Merrill[1]

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CALCINEURIN INHIBITION

- **Voclosporin** has an increased potency and faster elimination compared to cyclosporine
- In patients with lupus nephritis (AURA-LN), low-dose of voclosporin showed superiority compared to placebo in the rate of complete response at 24 weeks (OR 2.03, p =0.045).

RheumNow

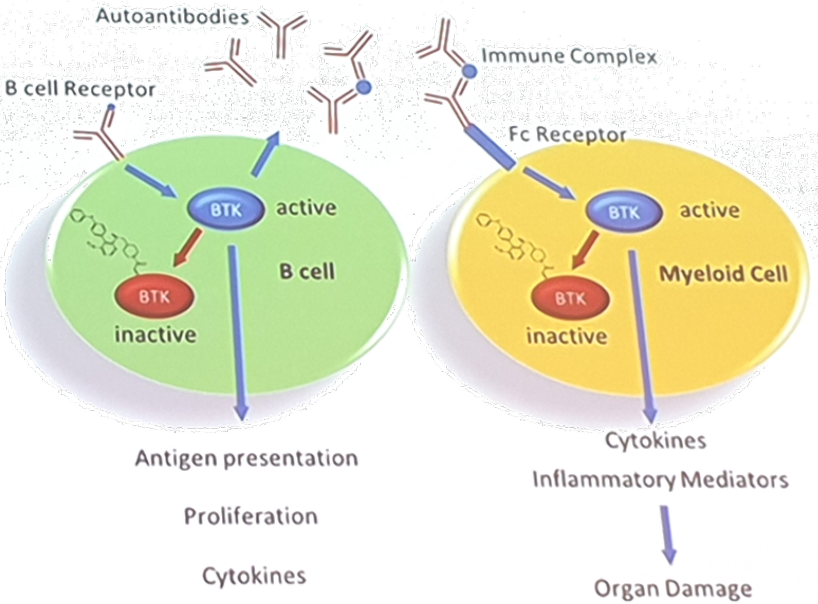
Friday, 07 Jun 2019

mTOR Inhibition with Sirolimus Effective in Lupus

BRUTON'S TYROSINE KINASE (BTK) INHIBITION

- Bruton's tyrosine kinase (Btk) is a **Tec-family kinase** that is expressed in most hematopoietic cells.
- Btk plays a crucial role in the development and activation of B-cells through its activation via the BCR.

- ***Ibrutinib***, an oral BTK inhibitor (PCI-32765) showed improvements in renal disease in SLE-model mice.



A. Honigberg, et al., The Bruton tyrosine kinase inhibitor PCI-32765 blocks B-cell activation and is efficacious in models of autoimmune disease and B-cell malignancy, Proc. Natl. Acad. Sci. U. S. A. 107 (2010) 13075–13080.

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Dermatomyositis

LENABASUM

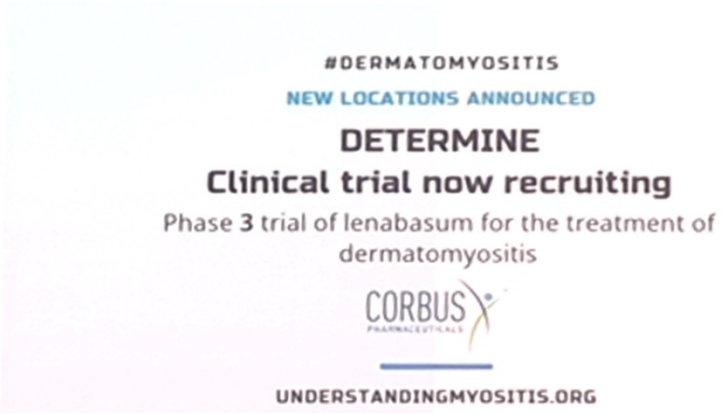
Phase 2 studies on diffuse cutaneous systemic sclerosis, dermatomyositis and cystic fibrosis have shown clinical benefit and positive impact on inflammatory and immunological markers

Phase 3 trial **DETERMINE** is designed to evaluate the efficacy and safety of lenabasum for the treatment of dermatomyositis (NCT03813160).

FRI0470

A PHASE 2 STUDY OF SAFETY AND EFFICACY OF LENABASUM (JBT-101), A CANNABINOID RECEPTOR TYPE 2 AGONIST, IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS

V.P. Werth[1,2], E. Hejazi[1,2], S.M. Pena[1,2], J.S. Haber[1,2], J. Okawa[1,2], R. Feng[1,2], K. Gabre[2], J.S. Concha[1,2], C. Cornwall[3], N. Dgetluck[3], S. Constantine[3], B. White[3].
[1]Philadelphia Veteran Affairs Medical Center, [2]University of Pennsylvania, Philadelphia, [3]Corbus Pharmaceuticals, Inc., Norwood, USA



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Dermatomyositis

JAK/STAT PATHWAY

Study of Tofacitinib in Refractory DM (STIR) (NCT03002649)

- Phase 1 study regarding the safety and efficacy of Janus kinase (JAK) inhibitor, tofacitinib, in adults with active, treatment-refractory dermatomyositis

Outcome Measures

Primary Outcome Measures :

1. Number of participants who achieve International Myositis Assessment and Clinical Studies (IMACS) Definition of Improvement (DOI) [Time Frame: Up to 12 weeks]

   IMACS DOI is 3 of any of the 6 core set measures (CSM) improved by ≥ 20%, with no more than 2 CSM worsening by ≥25% (worsening measure cannot include the manual musc

Secondary Outcome Measures :

1. Change from baseline in CDASI activity score [Time Frame: Up to 16 weeks]
2. Safety and tolerability of tofacitinib as assessed by frequency of adverse events reported and observed [Time Frame: Up to 16 weeks]
3. Safety and tolerability of tofacitinib as assessed by incidence of adverse events reported and observed [Time Frame: Up to 16 weeks]

JAK1/2 inhibitor **ruxolitinib** improved skin lesions in Dermatomyositis
Ruxolitinib inhibits the expression of cytokines characteristic for CLE in 20 vitro and has also been found to be effective in CLE-skin lesions105

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Dermatomyositis

APREMILAST

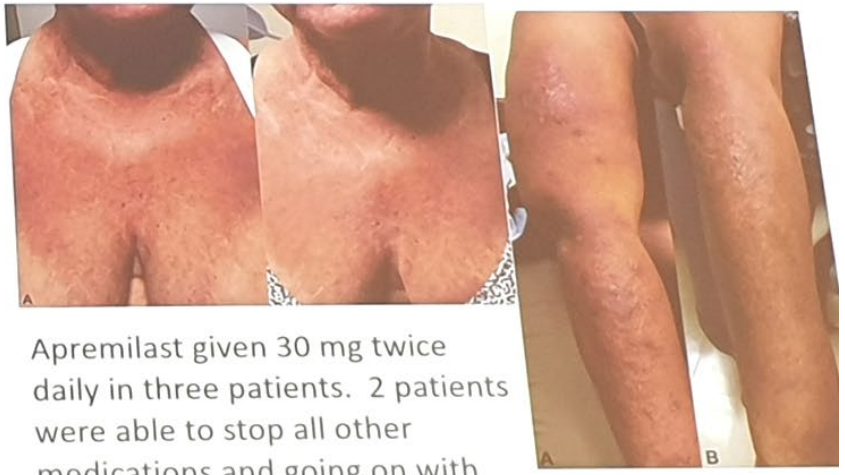
- Apremilast: phosphodiesterase-4 (PDE-4) inhibitor
- Potential role for the treatment of dermatomyositis through interfering with the Th1 and Th2 response.

A **phase 2** study on apremilast is evaluating the safety and efficacy of this drug in the treatment of cutaneous disease in patients with recalcitrant DM.

Evaluating Safety & Efficacy of Apremilast in the Treatment of Cutaneous Disease in Patients With Recalcitrant Dermatomyositis (NCT03529955)

Apremilast as a potential treatment for moderate to severe dermatomyositis: A retrospective study of 3 patients

Carole Bitar, MD,[a] Jalal Maghfour, MS,[b] Hoang Ho-Pham, MD,[c] Brittany Stumpf, MD,[a] and Erin Boh, MD, PhD[a]
New Orleans, Louisiana



Apremilast given 30 mg twice daily in three patients. 2 patients were able to stop all other medications and going on with apremilast as a monotherapy

JAK inhibitors

- JAK inhibitors as a new approach to block cytokine signalling
- Narrow therapeutic window , long term use?
- Smal mollecules can be used oral or topical
- In AD, rapid control of itch

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Milán

SY: Wound healing

Patrocina:

Janssen Immunology

PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organiza:

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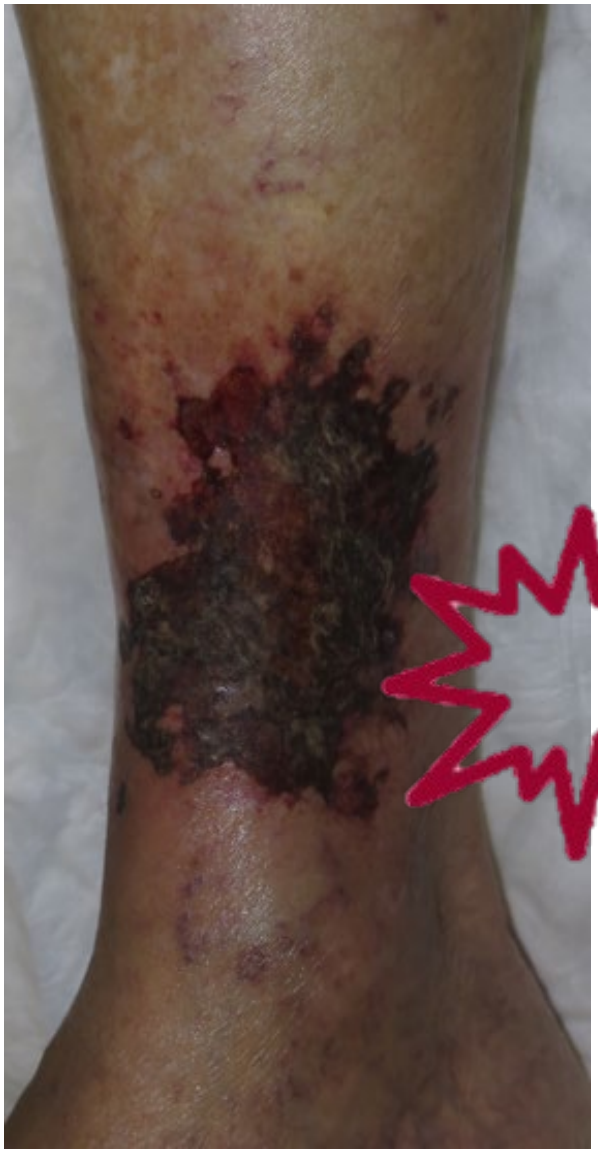
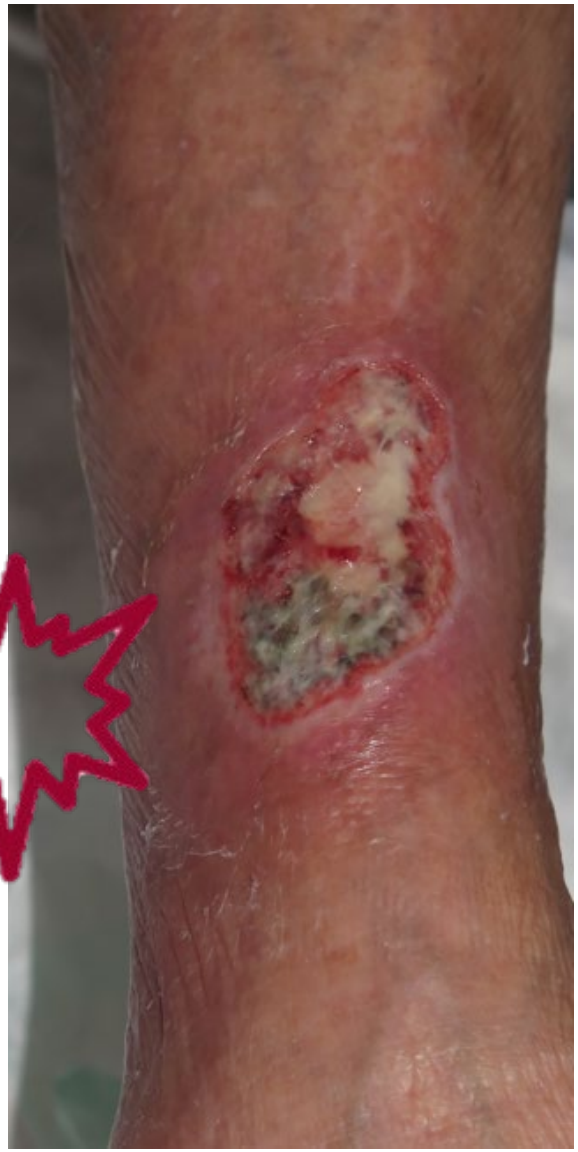


Rapidly progressive wounds after minor trauma



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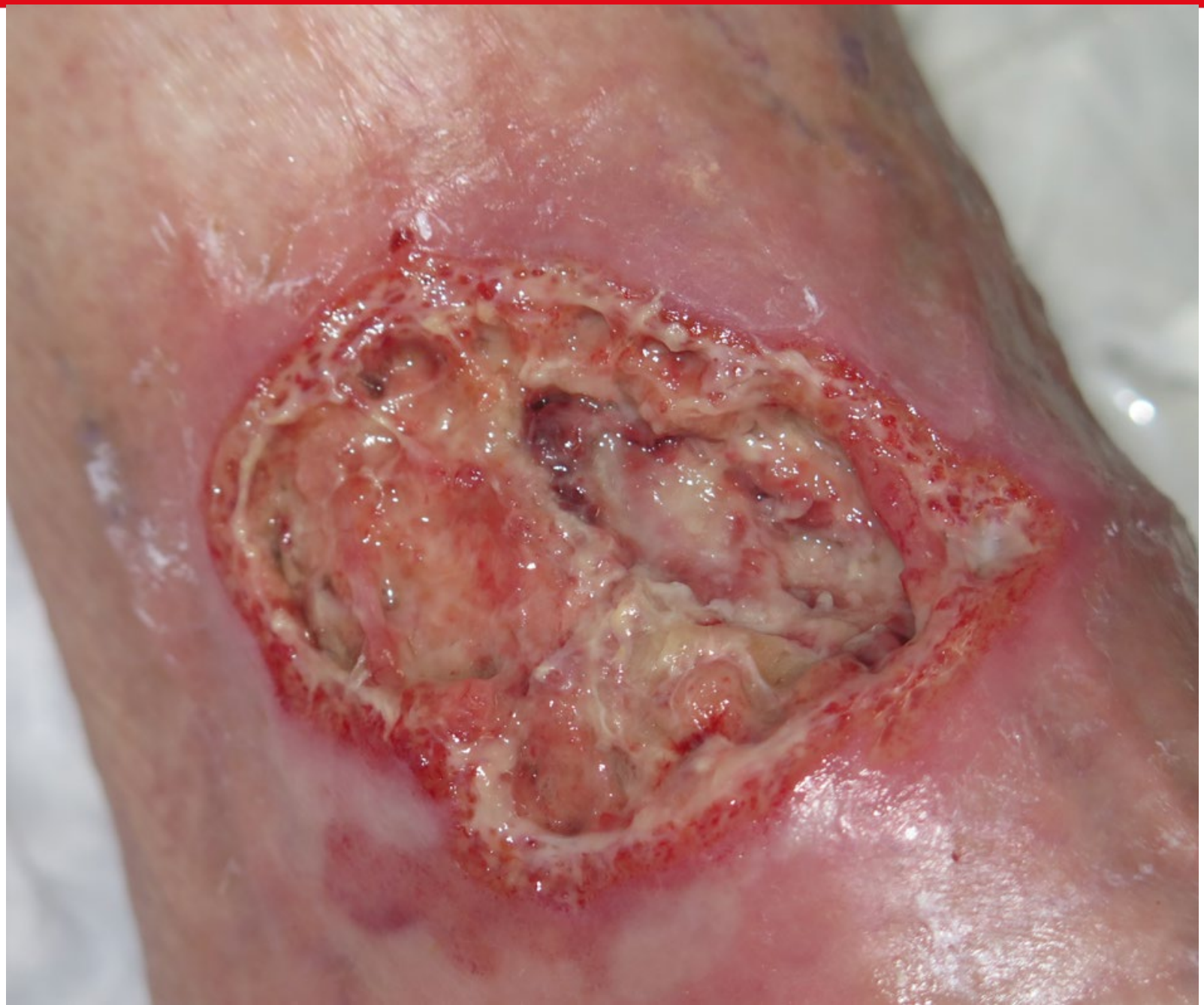

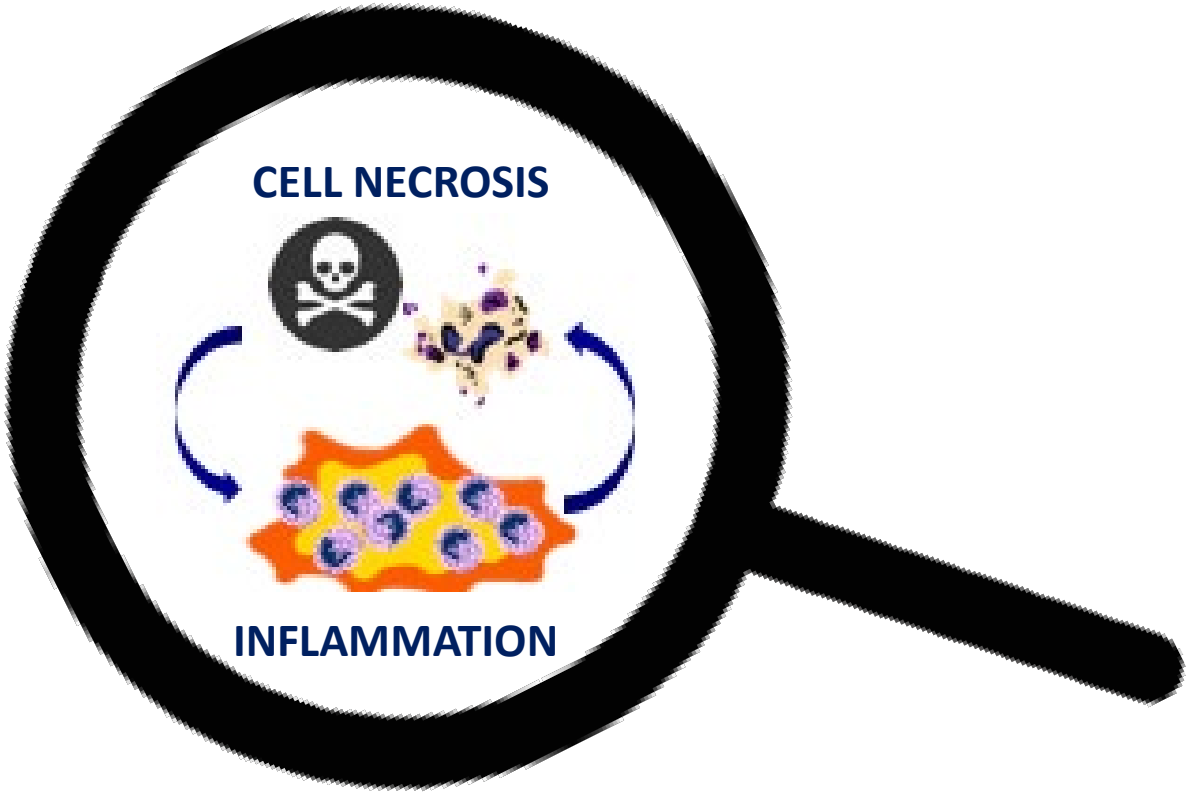

What is hidden behind a wound after trauma in erderly people?

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Research Article

Dermatology

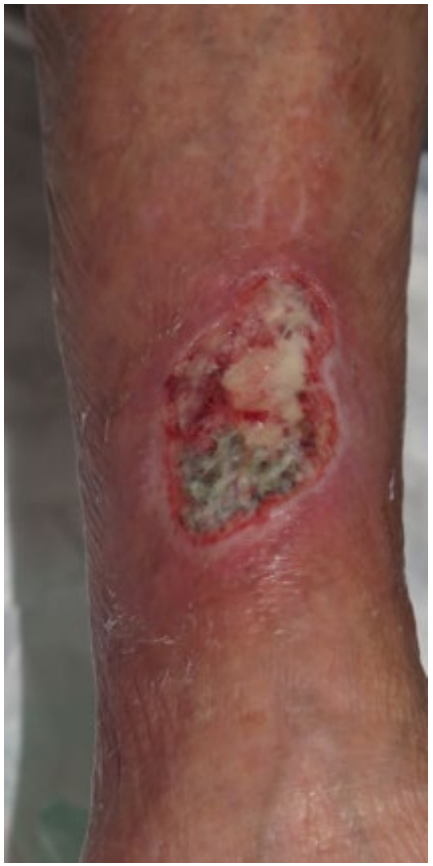
Dermatology 2018;234:194–197
DOI: 10.1159/000492669

Received: July 16, 2018
Accepted after revision: August 6, 2018
Published online: September 10, 2018

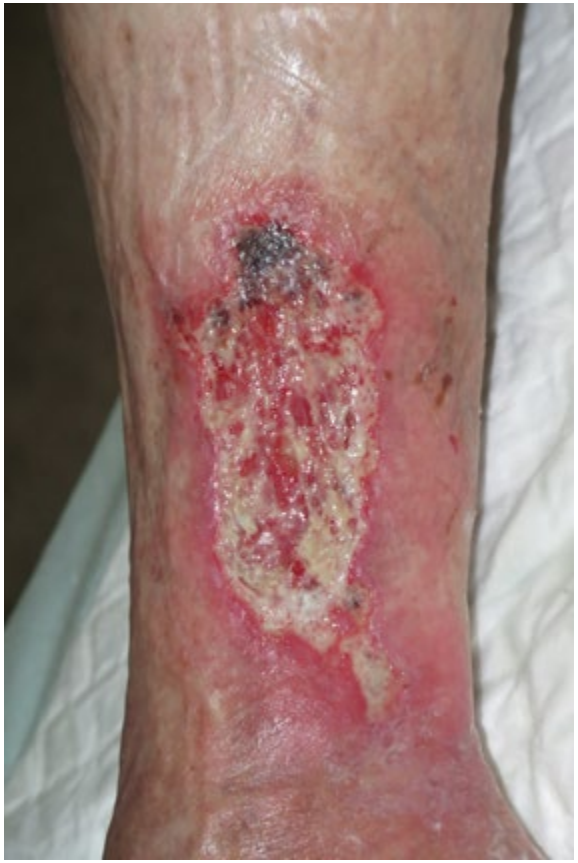
Cutaneous Arteriolosclerosis Is Not Specific to Ischemic Hypertensive Leg Ulcers

Jean-Benoît Monfort[a] Karine Cury[b] Philippe Moguelet[c] François Chasset[a]
Claude Bachmeyer[d] Camille Francès[a] Annick Barbaud[a] Patricia Senet[b]

Arteriolopatic ulcer secondary to trauma in the elderly



Martorell hypertensive ischemic leg ulcer




HOW TO
STOP THIS
VICIOUS
CYCLE?

Martorell Hypertensive Ischemic Ulcer Successfully Treated With Punch Skin Grafting

Elena Conde Montero, PhD[1]; Soledad Guisado Muñoz, RN[2]; Laura Pérez Jerónimo, RN[2]; Alicia Peral Vazquez, RN[2]; Juan Jesus Montoro López, RN[2]; Celia Hocajada Reales, MD[2]; Ofelia Baniandrés Rodriguez, PhD[1]; and Pablo de la Cueva Dobao, PhD[1]

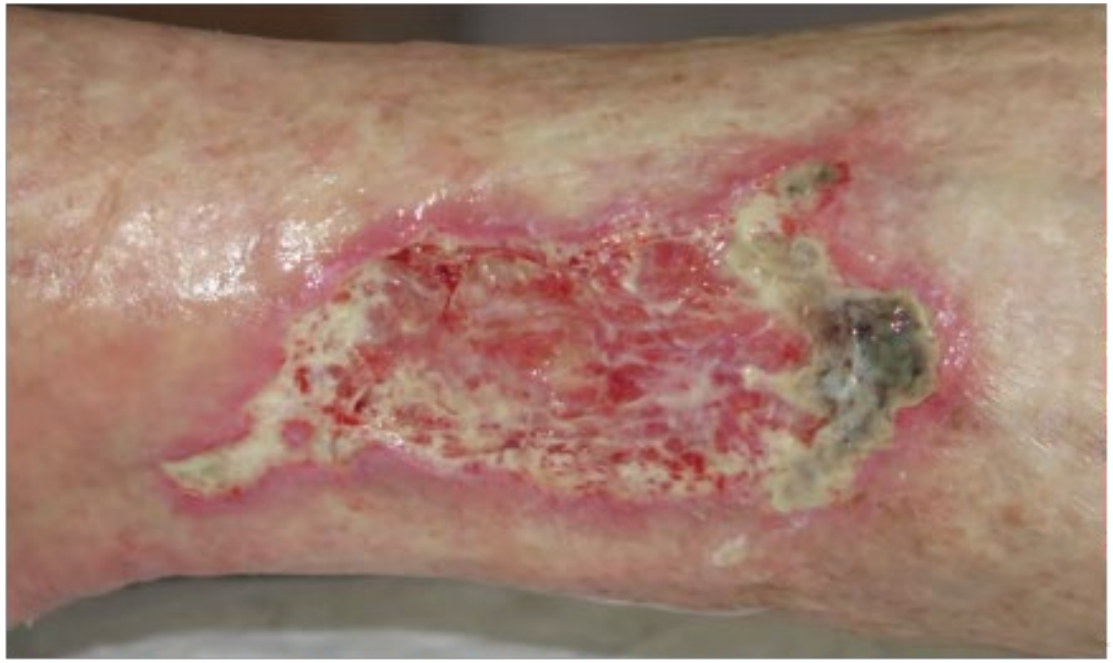


Figure 1. A 10-cm x 5-cm superficial ulcer on the distal medial aspect of the patient's left leg, with slough in the wound bed and erythrocyanotic margins.

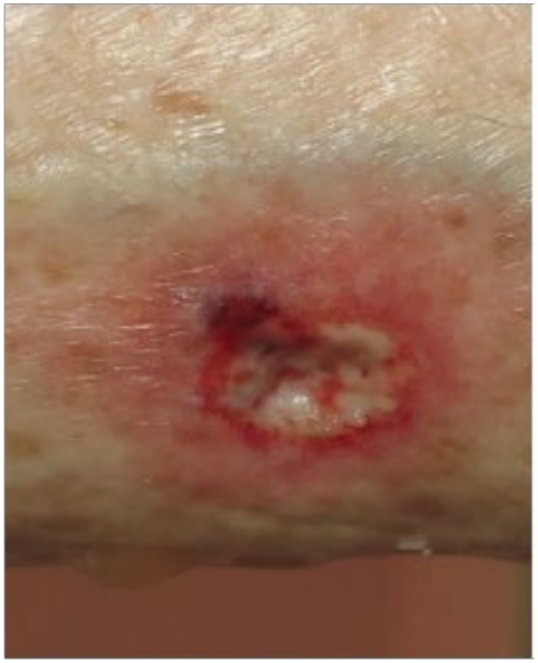


Figure 2. A 1-cm ulcer on the anterolateral supramalleolar region of the right leg with livid halo and slough in the wound bed.

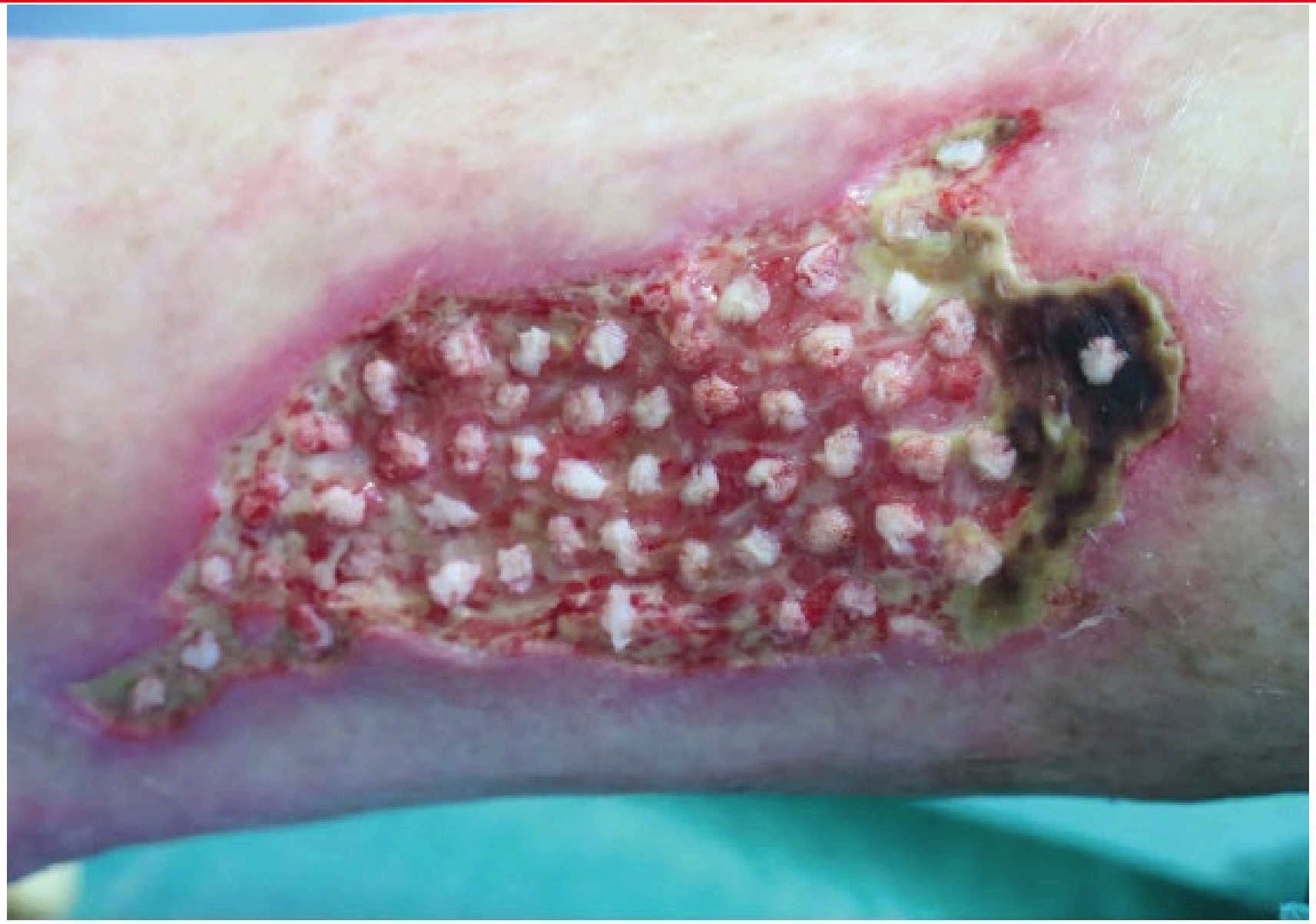
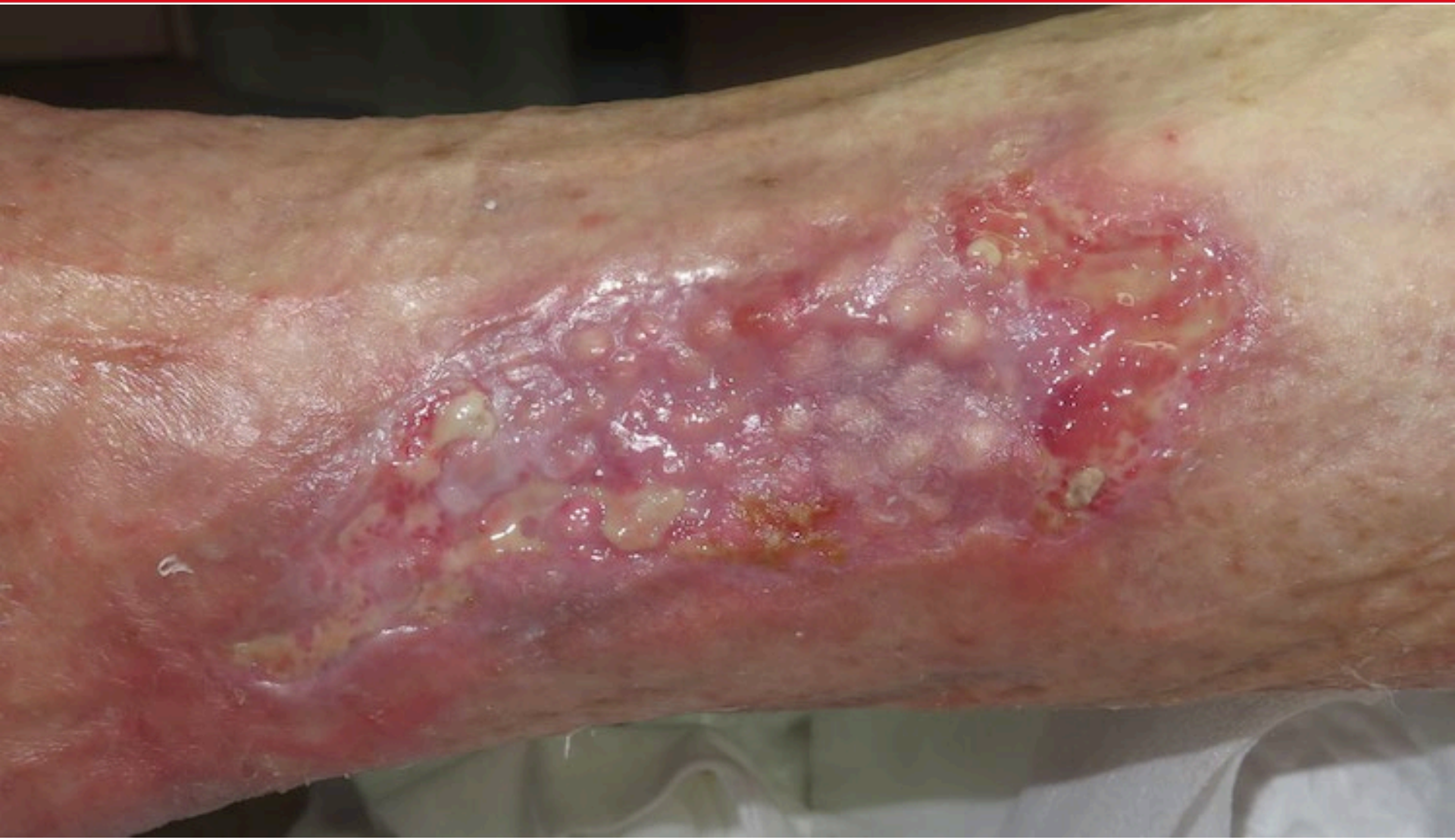


Figure 3. Punch skin grafts placed on the wound bed.



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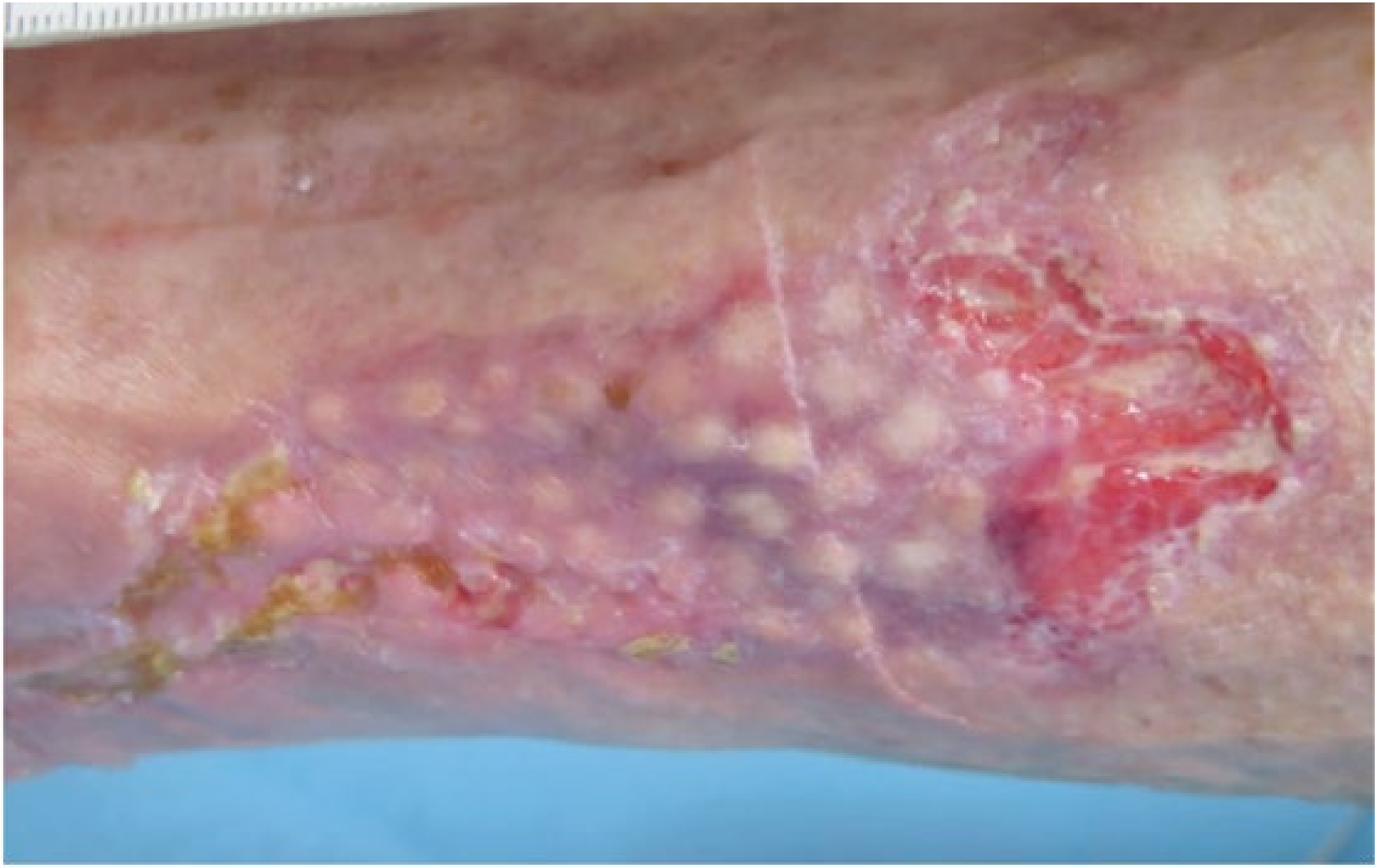


Figure 5. Clinical evolution at week 4 post punch skin grafting.

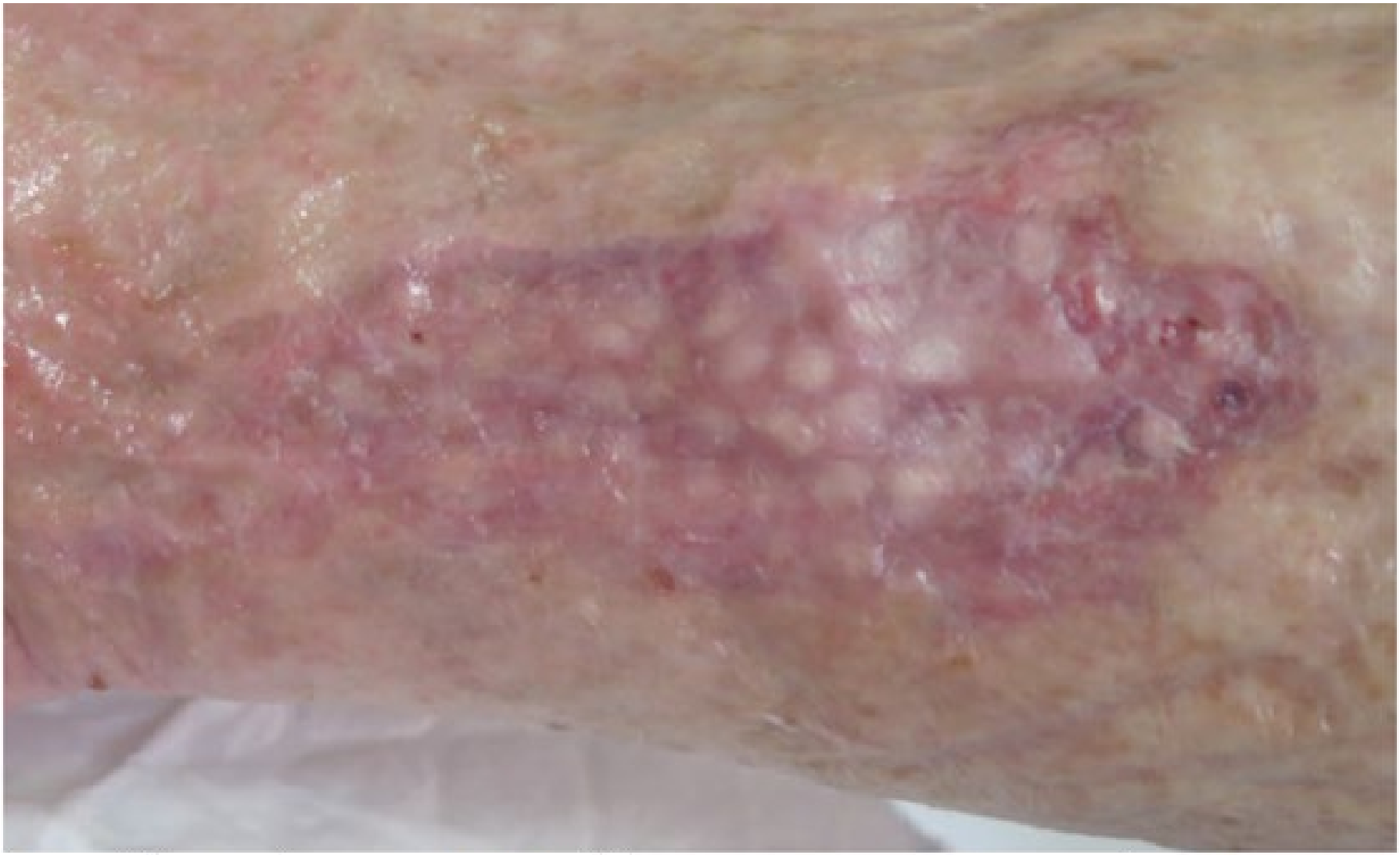
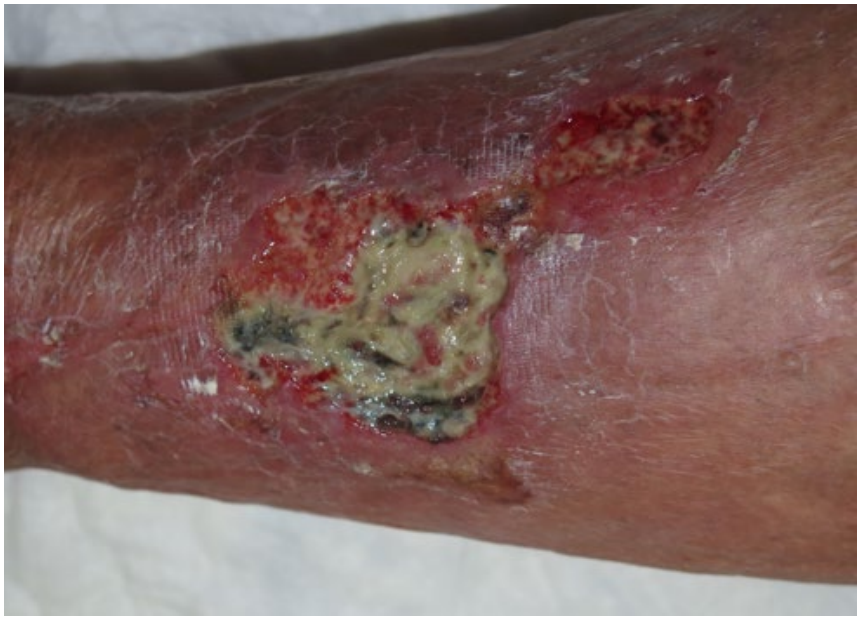
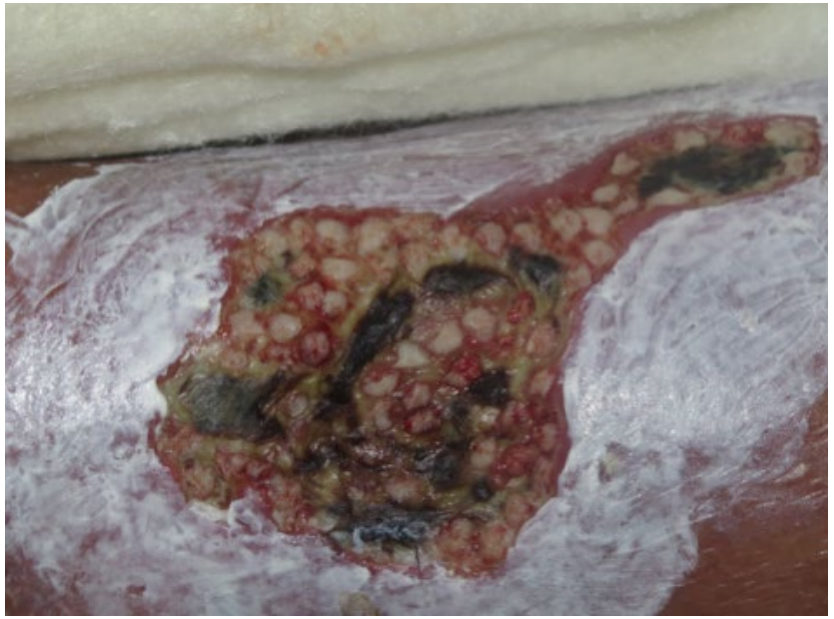
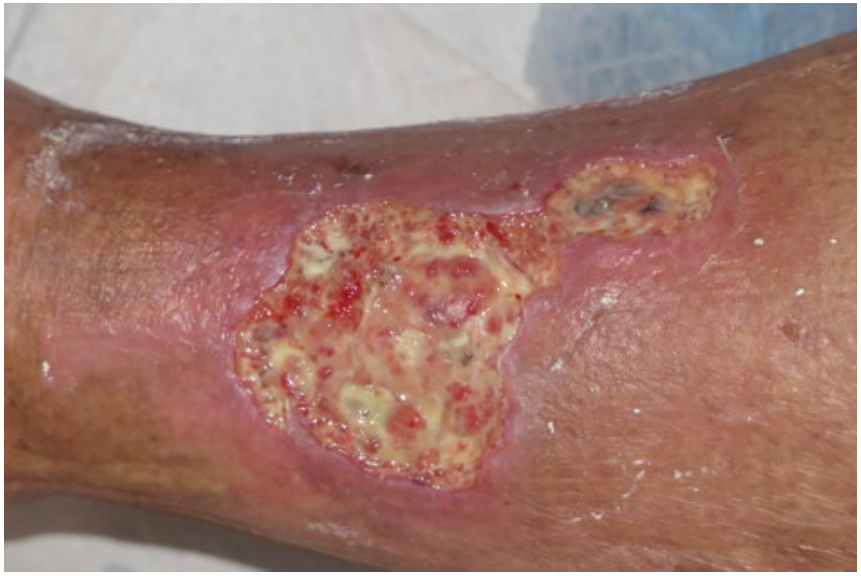
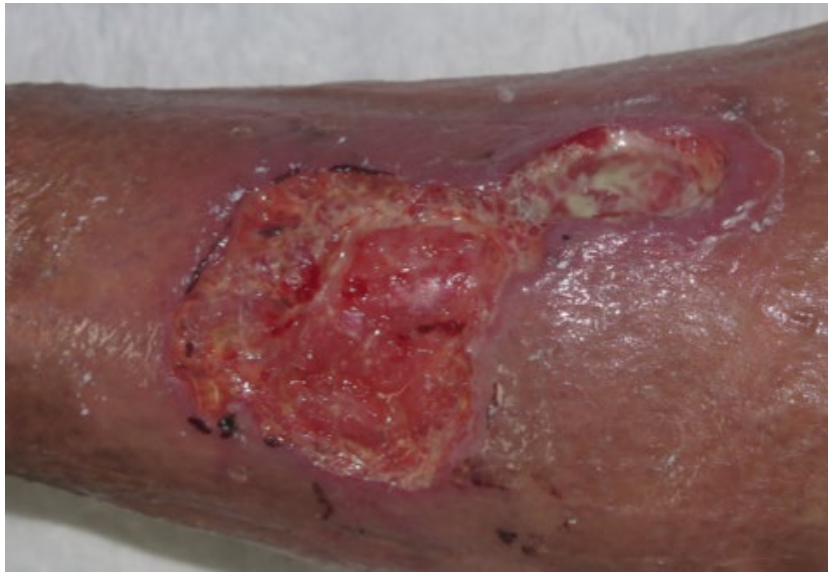
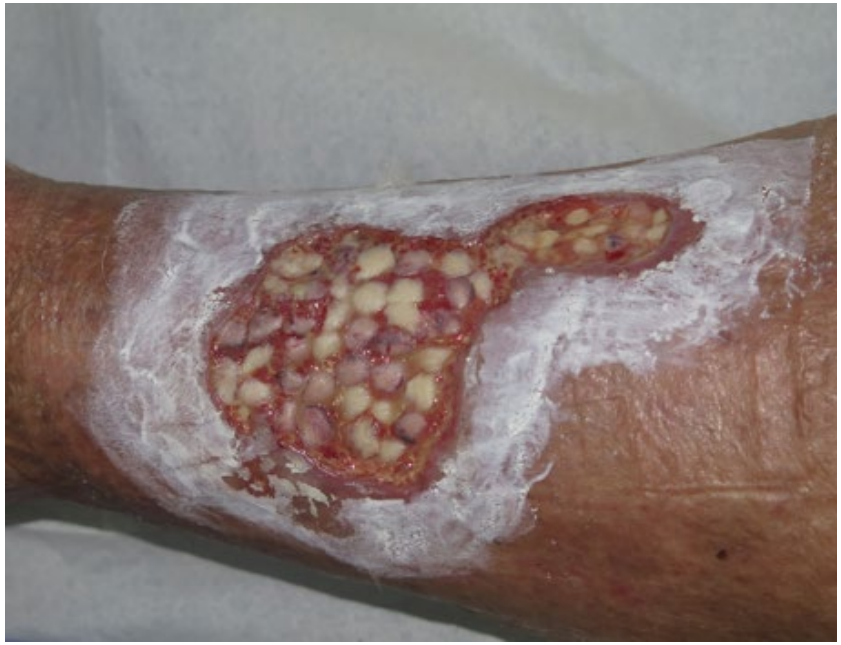
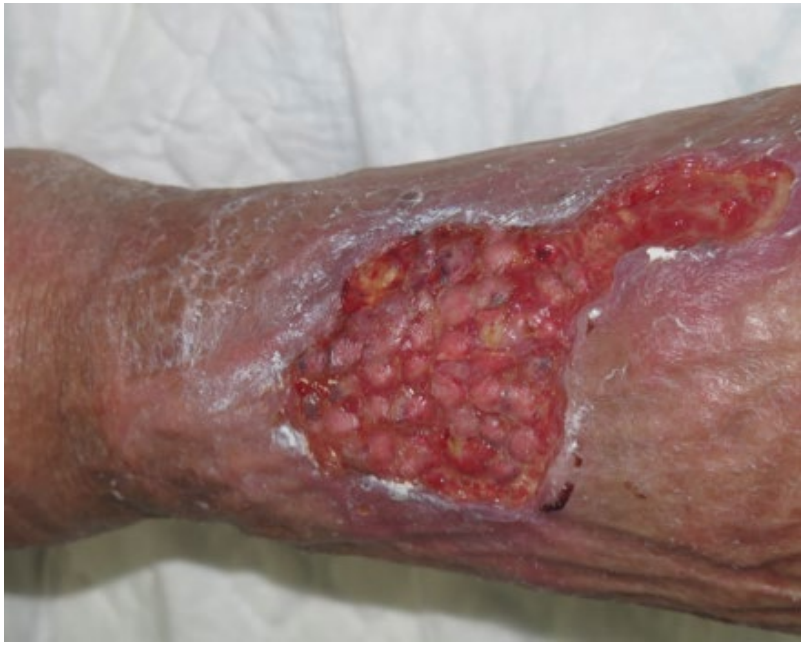


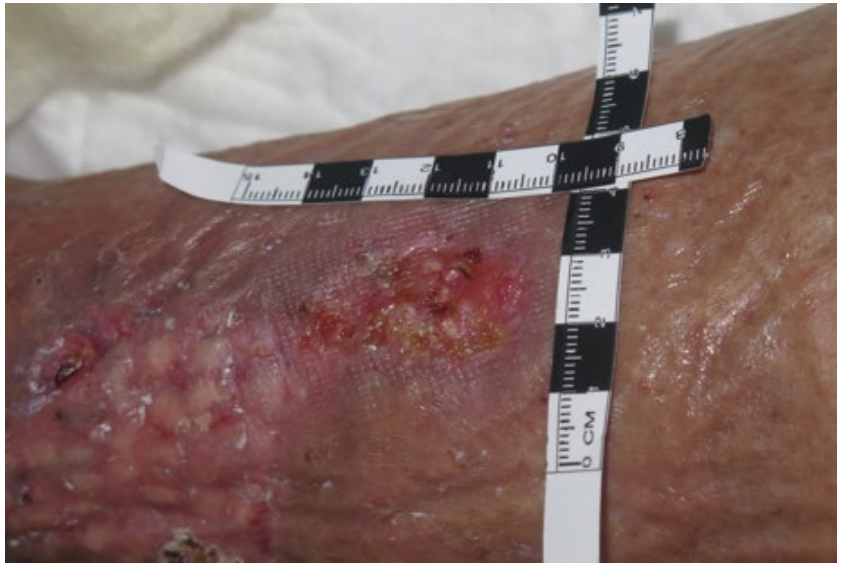
Figure 6. Complete epithelialization at week 7 post initial punch skin grafting.

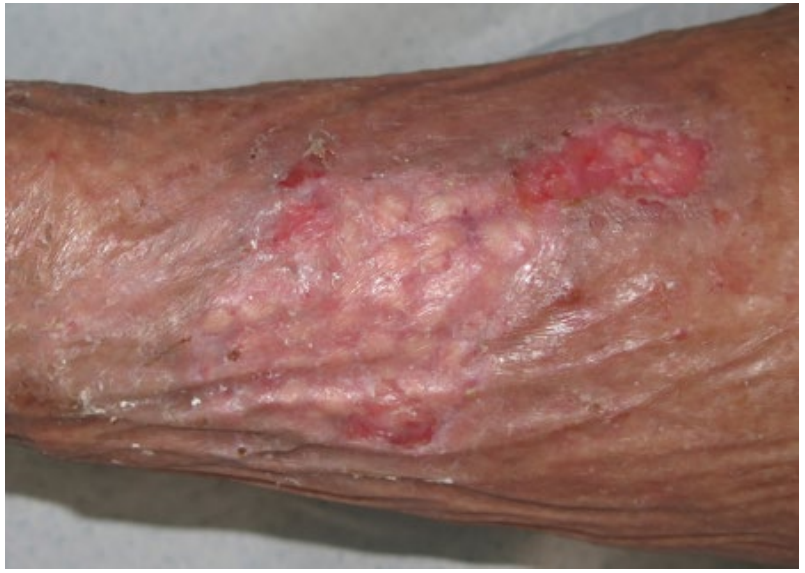
Sequential punch grafting









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