

TECNOLOGIA
e INNOVAZIONE
TERAPEUTICA
in DERMATOLOGIA
dalla ricerca alla pratica clinica

 9^a edizione
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ROMA

Novità diagnostiche e terapeutiche: malattie bollose

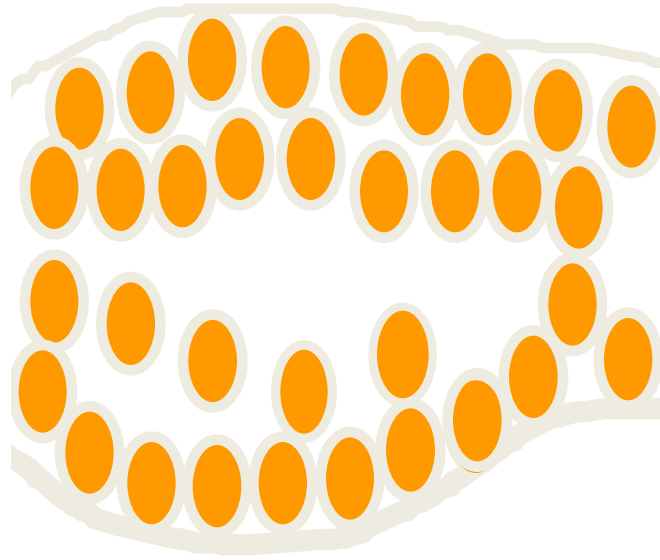
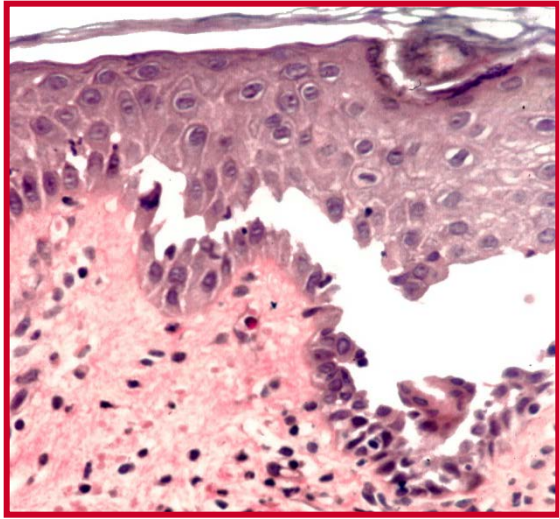
Giovanna Zambruno

Dermatology Unit &
Genetic and Rare Diseases Research Area



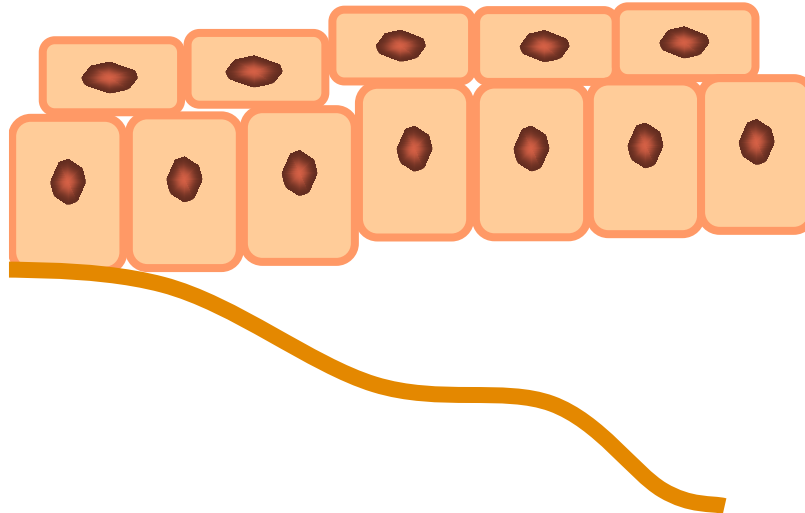
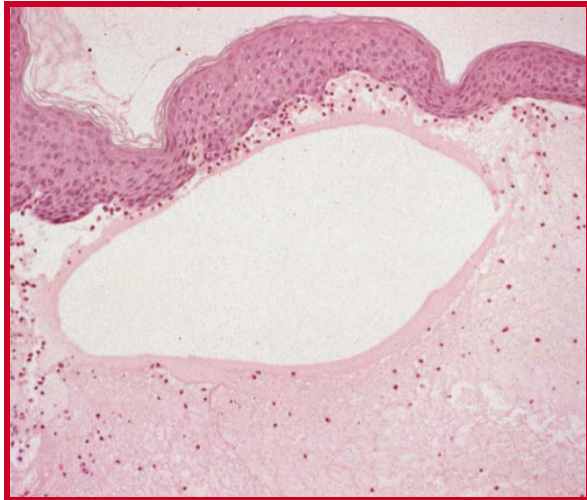
Bambino Gesù
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Autoimmune blistering diseases (AIBD)



**Intra-epithelial
blisters:**

Pemphigus



**Sub-epithelial
blisters:**

**Pemphigoid
diseases**

Outline

- Outcome measures for autoimmune blistering diseases (AIBD)
- AIBD treatment: European guidelines
- Pemphigus treatment: perspectives

AI BD are rare diseases: need for standardized outcome measures

- The rarity of AI BD has traditionally hampered the performance of sizeable randomized controlled trials
- The development and validation of standardized outcome instruments and disease definitions is pivotal to:
 - (i) performance of multicenter clinical trials, (ii) comparison of results from different trials, and (iii) informed therapeutic decision making

Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus

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J Am Acad Dermatol 2008;58:1043-6

Reliability and Convergent Validity of Two Outcome Instruments for Pemphigus

Misha Rosenbach¹, Dedee F. Murrell², Jean-Claude Bystry³, Sam Dulay¹, Sarah Dick¹, Steve Fakharzadeh¹, Russell Hall⁴, Neil J. Korman⁵, Julie Lin¹, Joyce Okawa¹, Amit G. Pandya⁶, Aimee S. Payne¹, Mathew Rose¹, David Rubenstein⁷, David Woodley⁸, Carmela Vittorio¹, Benjamin B. Werth¹, Erik A. Williams¹, Lynne Taylor⁹, Andrea B. Troxel⁹ and Victoria P. Werth^{1,10}

Journal of Investigative Dermatology (2009) **129**, 2404–2410

- Two outcome instruments for pemphigus, the **Pemphigus Disease Activity Index (PDAI)** and the **Autoimmune Skin Disorder Intensity Score (ABSIS)** were developed by the International Pemphigus Committee and the German blistering disease group, respectively
- The **PDAI assigns scores to defined anatomical regions based on the lesion number and size**, with about 45% of the score reflecting skin involvement and about 45% mucosal manifestations
- The **ABSIS is a general AIBD outcome instrument**, which includes an **objective component scored using body surface area and lesion type as weighting factors**, and a **subjective component related to patient discomfort during eating and drinking** (Pfutze M et al. *Eur J Dermatol* 2007;17:4-11)

PDAI scoring sheet

Skin	Activity		Damage
Anatomical location	Erosion/Blisters or new erythema		Post-inflammatory hyperpigmentation or erythema from resolving lesion
	0 absent 1 1–3 lesions, up to one >2 cm in any diameter, none > 6 cm 2 2–3 lesions, at least two > 2 cm diameter, none > 6cm 3 >3 lesions, none > 6 cm diameter 5 >3 lesions, and/or at least one >6 cm 10 >3 lesions, and/or at least one lesion >16 cm diameter or entire area	Number lesions if ≤ 3	0 absent 1 present
Ears			
Nose			
Rest of the face			
Neck			
Chest			
Abdomen			
Back, buttocks			
Arms			
Hands			
Legs			
Feet			
Genitals			
Total skin	/120		/12

Scalp

Scalp	Erosion/Blisters or new erythema	Number lesions if ≤ 3	Post-inflammatory hyperpigmentation or erythema from resolving lesion
	0 absent 1 in one quadrant 2 two quadrants 3 three quadrants 4 affects whole skull 10 at least one lesion > 6 cm		0 absent 1 present
Total Scalp (0–10)	/10		/1

PDAI scoring sheet

Mucous membrane

Anatomical Location	Erosion/Blisters		
	0 absent 1 1 lesion 2 2--3 lesions 5 >3 lesions or 2 lesions >2 cm 10 entire area	Number lesions if ≤ 3	
Eyes			
Nose			
Buccal mucosa			
Hard palate			
Soft palate			
Upper gingiva			
Lower gingiva			
Tongue			
Floor of mouth			
Labial bucosa			
Posterior pharynx			
Anogenital			
Total Mucosa	/120		

Total Activity Score:

Total Damage Score

ABSIS scoring sheet

Date:

Patient's weight (kg):

Legend for weighing factor (most dominant appearance of skin lesions):

1.5 *Erosive, exudative lesions*

1 *Erosive, dry lesions*

0.5 *Reepithelialized lesions (incl post inflamm erythema &/or hyperpigmentation)*

Skin Involvement (Max BSA)	Patient's BSA	Weighting factor
Head & neck (9%):		
L Arm including hand (9%):		
R Arm including hand (9%):		
Trunk (front & back) (36%):		
L Leg (18%):		
R Leg (18%):		
Genitals (1%):		

(Skin involvement total score: % BSA x weighing factor = 0–150 points) - will be calculated by the program

Oral Involvement:

I. Extent (enter 1 for presence of lesions, 0 absence of any lesion):

Upper gingival mucosa		Tongue	
Lower gingival mucosa		Floor of the mouth	
Upper lip mucosa		Hard palate	
Lower lip mucosa		Soft palate	
Left buccal mucosa		Pharynx	
Right buccal mucosa			

(Total score ranges from 0–11)

ABSIS scoring sheet

Severity (discomfort during eating/drinking)

Food	Level	Factor of Discomfort	Severity score
Water	1		
Soup	2		
Yogurt	3		
Custard	4		
Mashed potatoes/ scrambled egg	5		
Baked fish	6		
White bread	7		
Apple/ raw carrot	8		
Fried steak/ whole-grain bread	9		

(Severity score= Level multiplied by the factor of discomfort= 0–45 points)

<i>Legend for factor of discomfort</i>	
<i>1</i>	<i>Pain/bleeding occurred always</i>
<i>0.5</i>	<i>Pain/bleeding occurred sometimes</i>
<i>0</i>	<i>Never experienced problems</i>

PDAI and ABSIS: validation

- Internal and external studies evaluated inter-rater and intra-rater **reliability of PDAI** and **ABSIS** showing a **good to very good reliability of both** instruments (while Physician Global Assessment-PGA- proved much less reproducible), with **PDAI having the higher** inter-rater and intra-rater **intraclass correlation coefficients**
- Assessment of **convergent validity with PGA: higher correlation with PDAI than ABSIS**
- Need for (i) further longitudinal studies evaluating PDAI and ABSIS sensitivity to change, (ii) definition of clinically significant minimal change

Rosenbach M et al. J Invest Dermatol 2009;129:2404-10

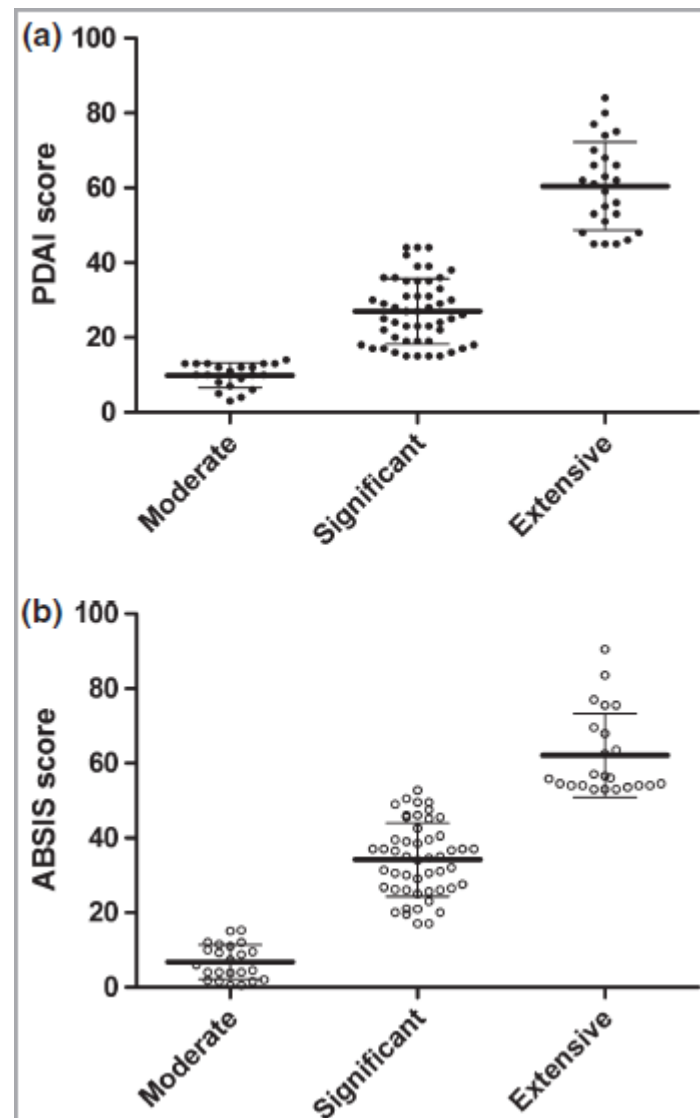
Kamiya K et al. J Dermatol Sci 2013;70:190-5

Patsatsi A et al. Acta Derm Venereol 2014;94:203-6

Rahbar Z et al. JAMA Dermatol 2014;150:266-72

PDAI and ABSIS: calculation of cut off values defining pemphigus activity subgroups

- A prospective multicenter (31 dermatology departments 6 countries), enrolled 96 consecutive patients with **newly diagnosed** pemphigus vulgaris (77) or foliaceus (19)
- Cut-off values defining **moderate**, **significant** and **extensive** subgroups were calculated based on the **25th and 75th percentiles of the ABSIS and PDAI scores**
- Cut-off values distinguishing moderate, significant and extensive pemphigus were **15 and 45 for PDAI**, and **17 and 53 for ABSIS**
- Usefulness in clinical trials and in the management of patients with pemphigus



PDAI and ABSIS: use in clinical trials

- Autoimmune Blistering Diseases Study (AIBD) (US, observational longitudinal study) (<http://clinicaltrials.gov/>, NCT02753777), **primary outcome: PDAI, BPDAI**, secondary outcomes: ABQoL, **ABSIS**
- Study of efficacy and safety of VAY736 (anti-BAFF antibody) pemphigus vulgaris (PV) (Novartis Pharmaceuticals, 4 countries, phase II) (NCT01930175), **primary outcome: change in PDAI at week 12, secondary outcome: change in ABSIS at week 12**
- A randomized, double-blind study to evaluate the efficacy and safety of rituximab versus mycophenolate mofetil in PV (Hoffmann-La Roche, 12 countries, 60 centers, 124 patients, phase III) (NCT02383589). Inclusion criteria: moderate-to-severely active disease based on PDAI, primary outcome: proportion of pts who achieve a complete remission on 0 mg prednisone and maintaining response >16 consecutive weeks
- Study of PRN1008 (a selective BTK inhibitor) in PV (Principia Biopharma, Inc., Australia, phase II) (NCT02704429). **Inclusion criteria: mild to moderate PV based on PDAI**

Instruments to evaluate disease activity: the bullous pemphigoid disease area index (BPDAI)

Definitions and outcome measures for bullous pemphigoid: Recommendations by an international panel of experts

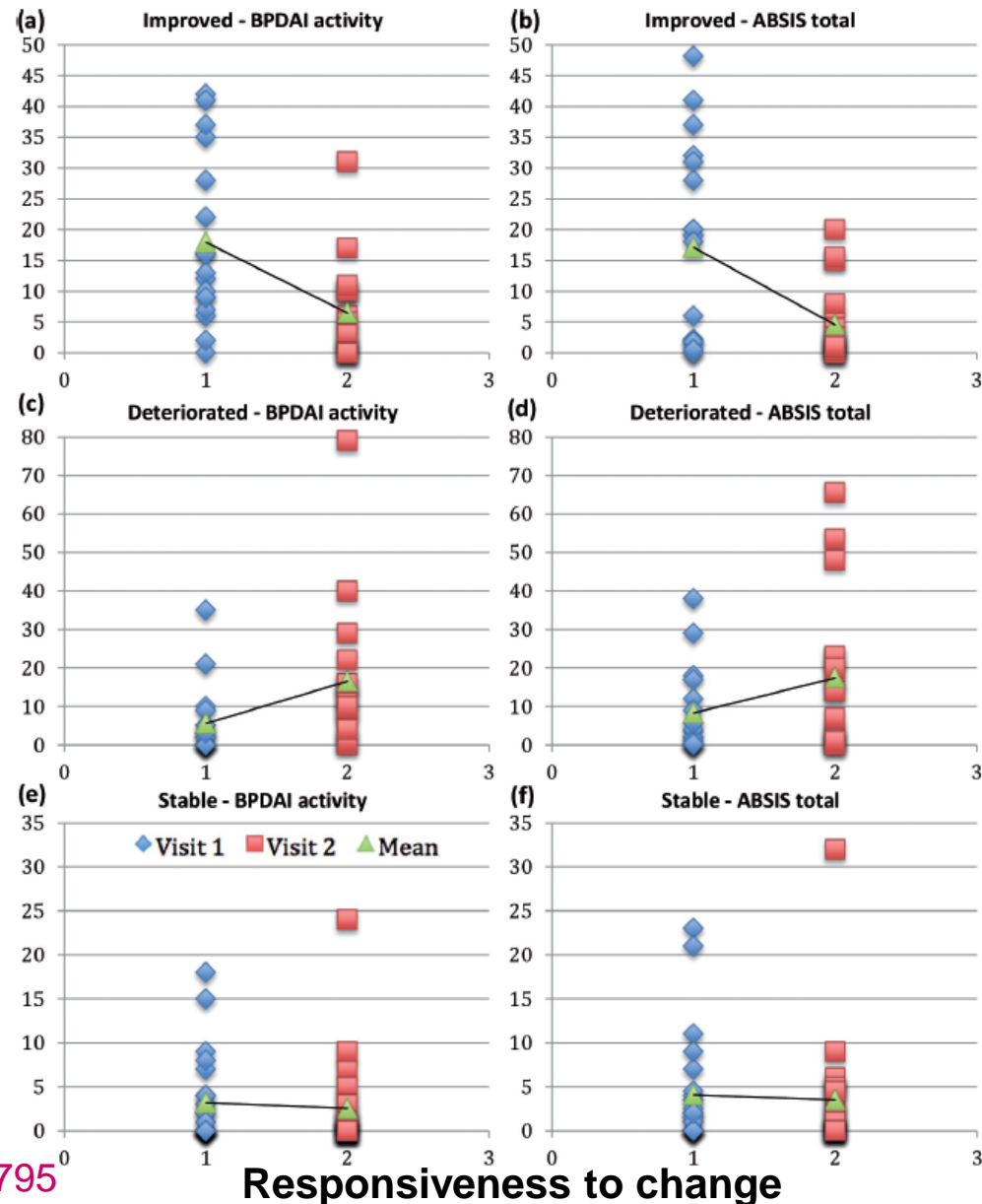
Dedee F. Murrell, MA, BMBCh, MD, FACD,^a Benjamin S. Daniel, MBBS,^a Pascal Joly, MD, PhD,^b Luca Borradori, MD,^c Masayuki Amagai, MD, PhD,^d Takashi Hashimoto, MD, PhD,^c Frédéric Caux, MD, PhD,^f Branka Marinovic, MD, PhD,^g Animesh A. Sinha, MD, PhD,^h Michael Hertl, MD,ⁱ Philippe Bernard, MD, PhD,^{ac} David Sirois, DMD, PhD,^j Giuseppe Cianchini, MD,^k Janet A. Fairley, MD,^m Marcel F. Jonkman, MD, PhD,ⁿ Amit G. Pandya, MD,^o David Rubenstein, MD, PhD,^p Detlef Zillikens, MD,^q Aimee S. Payne, MD, PhD,^s David Woodley, MD,^r Giovanna Zambruno, MD,^l Valeria Aoki, MD, PhD,^t Carlo Pincelli, MD,^u Luis Diaz, MD,^p Russell P. Hall, MD,^v Michael Meurer, MD, PhD,^x Jose M. Mascaro, Jr, MD,^y Enno Schmidt, MD,^q Hiroshi Shimizu, MD, PhD,^w John Zone, MD,^z Robert Swerlick, MD,^{ac} Daniel Mimouni, MD,^{ad} Donna Culton, MD,^p Jasna Lipozencic, MD, PhD,^g Benjamin Bince, MD,^{aa} Sergei A. Grando, MD, PhD, DSc,^{ag} Jean-Claude Bystryń, MD,^{ab} and Victoria P. Werth, MD^{s,af}

J Am Acad Dermatol 2012;66:479-85

BPDAI					
SKIN	ACTIVITY		ACTIVITY		DAMAGE
Anatomical location	Erosions/Blisters	Number of Lesions if <3	Urticaria/ Erythema / Other	Number of Lesions if <3	Pigmentation / Other
	0 absent		0 absent		Absent 0, present 1
	1 1-3 lesions, none > 1 cm diameter		1 1-3 lesions, none >6 cm diameter		
	2 1-3 lesions, at least one > 1 cm diameter		2 1-3 lesions, at least one lesion > 6 cm diameter		
	3 >3 lesions, none > 2 cm diameter		3 >3 lesions, or at least one lesion > 10 cm		
	5 >3 lesions, and at least one >2 cm		5 >3 lesions and at least one lesion > 25 cm		
	10 >3 lesions, and at least one lesion >5 cm diameter or entire area		10 >3 lesions and at least one lesion > 50 cm diameter or entire area		
Head					
Neck					
Chest					
Left arm					
Right arm					
Hands					
Abdomen					
Genitals					
Back/Buttocks					
Left leg					
Right leg					
Feet					
Total skin	/120		/120		

BPDAI and ABSIS: validation in BP

- Different studies evaluated the **reliability, validity and responsiveness** of **BPDAI** and **ABSIS** in **bullous pemphigoid**
- **BPDAI** demonstrated **excellent** reliability, validity and responsiveness, while **ABSIS** had moderate to good reliability, validity and responsiveness



Patsatsi A et al. Clin Dev Immunol 2012;2012:854795

Lévy-Sitbon C et al. Dermatology 2014;229:116-22

Wijayanti A et al. Acta Derm Venereol. doi: 10.2340/00015555-2473

BPDAI and ABSIS: clinical trials on BP

- Observational study assessing outcomes, treatment patterns and related costs in BP (France, multicenter) (<http://clinicaltrials.gov/>, NCT02837965), **BPDAI calculated at each visit**
- Evaluation of safety, efficacy and pharmacodynamic effect of bertilimumab (human Mab targeting eotaxin-1) in BP (Immune Pharmaceuticals, Israel, open label, phase II) (NCT02226146), **secondary efficacy outcome based on BPDAI reduction**
- Anti-IL-5 (mepolizumab) therapy in BP (Switzerland, randomized, placebo-controlled, phase II) (NCT01705795), **secondary outcome: changes in BP severity score over time (ABSIS)**
- Evaluation of fluid retention due to superpotent topical corticosteroid (France, open label, phase IV) (NCT02360202), **secondary outcome: change from baseline in BPDAI**

Instruments to evaluate disease activity: the mucous membrane pemphigoid disease area index (MMPDAI)

Definitions and outcome measures for mucous membrane pemphigoid: Recommendations of an international panel of experts

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J Am Acad Dermatol 2015;72:168-74

MMPDAI scoring sheet

Skin	Activity		Damage
Anatomic location	Erosion/blisters or new erythema		Postinflammatory hyperpigmentation or erythema from resolving lesion or scarring
	0 Absent 1 1-3 Lesions, up to 1 lesion >2 cm in any diameter, none >6 cm 2 2-3 Lesions, at least 2 lesions >2 cm diameter, none >6 cm 3 >3 Lesions, none >6 cm diameter 5 >3 Lesions, and/or at least 1 lesion >6 cm 10 >3 Lesions, and/or at least 1 lesion >16 cm diameter or entire area	No. of lesions if ≤ 3	0 Absent 1 Present
Ears			
Forehead			
Rest of the face			
Neck			
Chest			
Abdomen			
Shoulders, back			
Buttocks			
Arms and hands			
Legs and feet			
Anal			
Genitals			
Total skin	/120		/12
Scalp	Erosion/blisters or new erythema	No. of lesions if ≤ 3	Postinflammatory hyperpigmentation or erythema from resolving lesion /scarring
	0 Absent 1 1 Quadrant 2 2 Quadrants 3 3 Quadrants 4 Affects whole skull 10 At least 1 lesion >6 cm		0 Absent 1 Present
Total scalp (0-10)	/10		/1

MMPDAI scoring sheet

Mucous membrane	Activity		Damage
Anatomic location	Erosion/blisters		Postinflammatory hyperpigmentation or erythema from resolving lesion or scarring
Eyes (quadrants upper, lower, medial and lateral)*	0 No erythema 1 Light pink 2 Moderate pink 3 Dark pink 4 Bright red add up quadrants	Subtotal	0 absent 1 present
Left eye (0-16) x 0.625	/10	/16	
Right eye (0-16) x 0.625	/10	/16	
	0 absent 1 1 lesion 2 2-3 lesions 5 >3 lesions or 2 lesions >2 cm 10 entire area	Number lesions if ≤ 3	0 absent 1 present
Nasal			
Buccal mucosa			
Palate			
Upper gingiva			
Lower gingiva			
Tongue/floor of mouth			
Labial			
Posterior pharynx			
Anal			
Genital			
Total mucosa	/120		/12

Total activity score:

Total damage score:

Outline

- Outcome measures for autoimmune blistering diseases (AIBD)
- AIBD treatment: European guidelines
- Pemphigus treatment: perspectives

Management of bullous pemphigoid: the European Dermatology Forum consensus in collaboration with the European Academy of Dermatology and Venereology

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British Journal of Dermatology (2015) **172**, pp867–877

BP therapeutic ladder

Localized/limited disease with mild activity

First choice

Superpotent topical corticosteroids; in mild disease, on whole body except the face (1, validated)

In localized disease, on lesions only (3, nonvalidated)

Second choice

Oral corticosteroids (1, validated for prednisone)

Tetracycline + nicotinamide (2, nonvalidated)

Dapsone, sulfonamides (3, nonvalidated)

Topical immunomodulators (e.g. tacrolimus) (4, nonvalidated)

Generalized disease

First choice, primary treatment

Superpotent topical corticosteroids on whole body sparing the face (1, validated)

Oral corticosteroids (1, validated for prednisone)

Second choice, as adjunctive therapy

Combination with or introduction of:

Azathioprine (1, nonvalidated)

Mycophenolate (1, nonvalidated)

Tetracycline + nicotinamide (2, nonvalidated)

Methotrexate (3, nonvalidated)

Chlorambucil (3, nonvalidated)

Third choice

Combination with and/or introduction of:

Anti-CD20 or anti-IgE monoclonal antibody (4, nonvalidated)

Intravenous immunoglobulins (3, nonvalidated)

Immunoadsorption (4, nonvalidated)

Plasma exchange (1, nonvalidated)

Cyclophosphamide (3, nonvalidated)

GUIDELINES

Pemphigus. S2 Guideline for diagnosis and treatment – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV)

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JEADV 2015, 29, 405–414

Pemphigus: therapeutic algorithm

First-line treatment	Comments
(1) Predniso(lo)ne	(Ad 1) Initially 0.5 mg to 1.5 mg/kg/day. Optimal dose not validated. Taper by 25% reduction in biweekly steps, at <20 mg/d more slowly. Add proton pump inhibitors/ H2 blockers, vitamin D and calcium
Second-line treatment (in refractory disease or in case of contraindications to glucocorticoids)*	Comments
(1) Azathioprine or (2a) Mycophenolate mofetil or (2b) Mycophenolic acid	(Ad 1) 1–3 mg/kg/day. Check TPMT activity prior to treatment. Start with 50 mg/day. Steroid-sparing effect demonstrated (Ad 2a) 2 g/day. Steroid-sparing effect demonstrated. Raise daily dose by 1 capsule/ week to increase GI tolerance (Ad 2b) 1440 mg/day. Steroid-sparing effect demonstrated. Raise daily dose by 1 capsule/ week to increase GI tolerance
Third-line treatment (in refractory disease or in case of contraindications to immunosuppressants)	Comments
(1) Anti-CD20 monoclonal antibody (rituximab)	(Ad 1) 2×1 g i.v. (2 weeks apart) or 4×375 mg/m ² (each 1 week apart). Exclude hypersensitivity to mouse proteins. PML is a rare but potentially fatal complication
(2) Intravenous immunoglobulins	(Ad 2) (2 g/kg/month). Exclude IgA deficiency before treatment. Has been used in combination with rituximab and cyclophosphamide
(3) Immunoabsorption	(Ad 3) 2 cycles à 4 days (2.5-fold total plasma volume/d), 4 weeks apart. Has been used in combination with rituximab and cyclophosphamide
(4) Cyclophosphamide	(Ad 4) 500 mg as i.v. bolus or given orally at 2 mg/kg/day. Steroid-sparing effect demonstrated. Consider secondary sterility, haemorrhagic cystitis and secondary cancer
(5) Dapsone	(Ad 5) 100 mg/day or up to ≤ 1.5 mg/kg/day. Check serum G6PD activity before treatment. Steroid-sparing effect demonstrated
(6) Methotrexate	(Ad 6) 10–20 mg/week. Substitute folate 5–15 mg on the following day

*Immunosuppressants are commonly used in combination with glucocorticoids. Based on the current evidence, they have a glucocorticoid-sparing effect and may lead to glucocorticoid-free remission.

Outline

- Outcome measures for autoimmune blistering diseases (AIBD)
- AIBD treatment: European guidelines
- Pemphigus treatment: perspectives

Rituximab immunotherapy in pemphigus

- The **anti-CD20 monoclonal antibody rituximab**, first approved for use in B-cell malignancies, is increasingly used to treat **cases of severe, therapy-resistant pemphigus forms**
- A recent meta-analysis of **30 studies** (comparative trials, n=4, and case series) including **578 pemphigus** patients treated with rituximab, in most cases administered in an **adjuvant setting**, showed:
 - **complete remission in the large majority (77.5%)** of pemphigus patients after **one cycle of rituximab**
 - mean time to disease control was 1.1 month and to remission 5.8 months, with a remission duration of 14.5 months and a **40% overall relapse rate**
 - **Serious adverse events in 3.3%: infectious complications** (sepsis, pneumonia, osteomyelitis, etc.)

Rituximab as first-line adjuvant therapy in pemphigus vulgaris

- Phase III, randomized, double-blind, active-comparator, parallel-arm multicenter study to evaluate the efficacy and safety of **rituximab (1,000 mg X 2) compared with mycophenolate mofetil (1 g/day) (MMF)** in patients with **moderate-to-severely active** pemphigus vulgaris **requiring 60-120 mg/day oral prednisone** (or equivalent)
- Hoffmann-La Roche: 12 countries, 60 centers; estimated enrollment: 124 patients (<https://clinicaltrials.gov/NCT02383589>)
- **Primary outcome: proportion of pts** who achieve a **complete remission on 0 mg prednisone** and **maintaining response ≥ 16 consecutive weeks** [time frame: 52 weeks]

Table II. Anti-CD20 and anti-B cell monoclonal antibodies*

Antibody (generation)	Antibody features		Activity (compared to rituximab)			Additional features (compared to rituximab)
	Type	CDR	CDC	ADCC	Apoptosis	
Veltuzumab/IMMU-06/hA20 (second)	I	Humanized	=/+	=	=	Slower off-rate; largely identical to rituximab
Obinutuzumab/GA-101 (third)	II	Humanized	—	+++	+++	50-fold greater binding; strong induction of apoptosis
Ofatumumab/2F2/HuMax-CD20 (second)	I	Human	+++	+	=	Completely human; slower off-rate; binds the small extracellular part of CD20
Ocaratuzumab/AME-133v (third)	I	Humanized	=	+	=	Higher binding affinity for FcγRIIIa; 10-fold increase in ADCC
PRO131921/rhuMAb v114 (third)	I	Humanized	+	++	=	30-fold greater binding affinity to FcγRIII; 2- to 10-fold greater CDC and ADCC activity
Belimumab	Anti-BAFF	Human	=	=	++	Targets a B cell—activating factor, rather than CD20

- A randomized, partial-blind, placebo-controlled **phase II trial** evaluating the **efficacy, safety, pharmacokinetics and pharmacodynamics** of VAY736, a BAFF receptor **modulator**, in the treatment of patients with **mild to moderate pemphigus vulgaris**
- Novartis Pharmaceuticals, 4 countries, 6 center; Estimated Enrollment: 32 pts (<https://clinicaltrials.gov/NCT01930175>)
- **Primary outcome:** efficacy of a **single intravenous dose** of VAY736 in **reducing the clinical disease activity** in pemphigus vulgaris patients. The effect of VAY736 on clinical disease activity will be measured by the change in PDAI between baseline and week 12

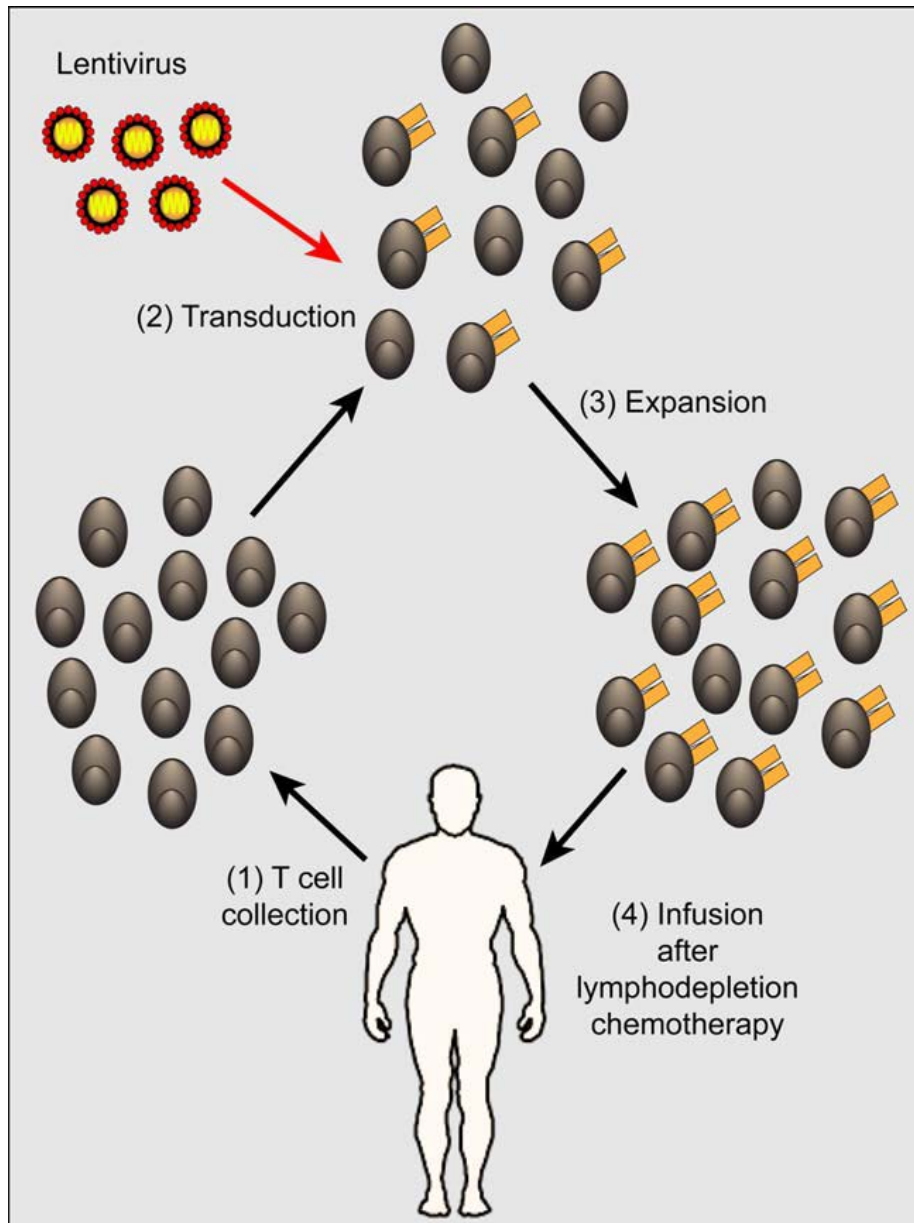
Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease

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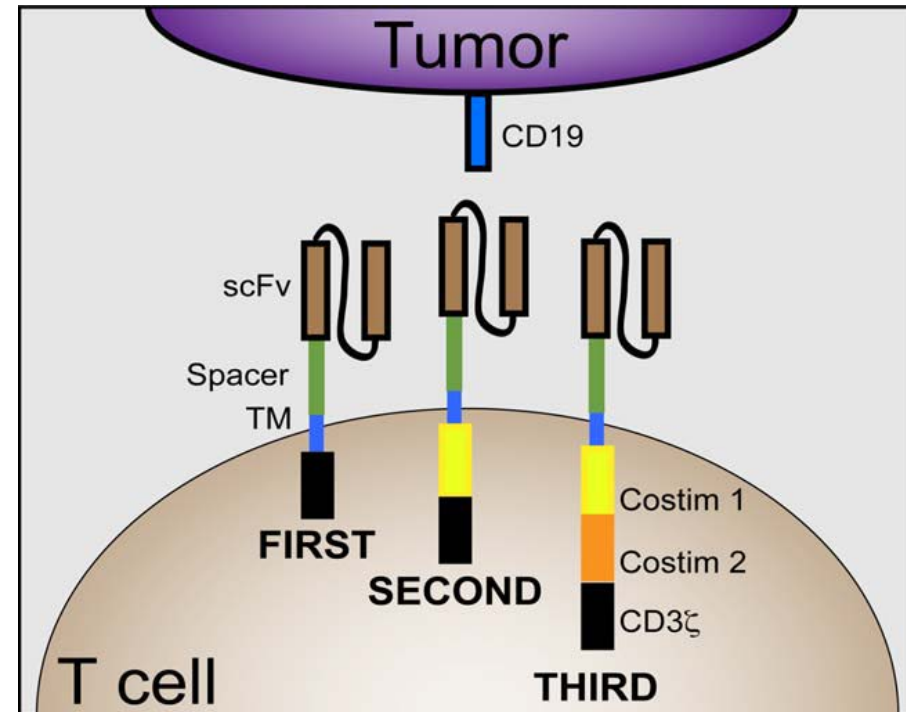
Science 2016; 353:179-84

- Chimeric antigen receptors (CAR) are chimeric proteins combining an extracellular antigen-recognition domain (a single chain variable fragment –scFv- derived from a monoclonal antibody specific for a tumor antigen) with intracellular signaling domains of the T-cell receptor. The engineered receptor allows autologous transduced cytotoxic T cells to recognize and kill cells expressing the targeted antigen
- CAR T-cell immunotherapy directed against CD19 has shown remarkable activity against several B-cell malignancies. It is being developed for an increasing number of solid tumors

CAR T-cell immunotherapy

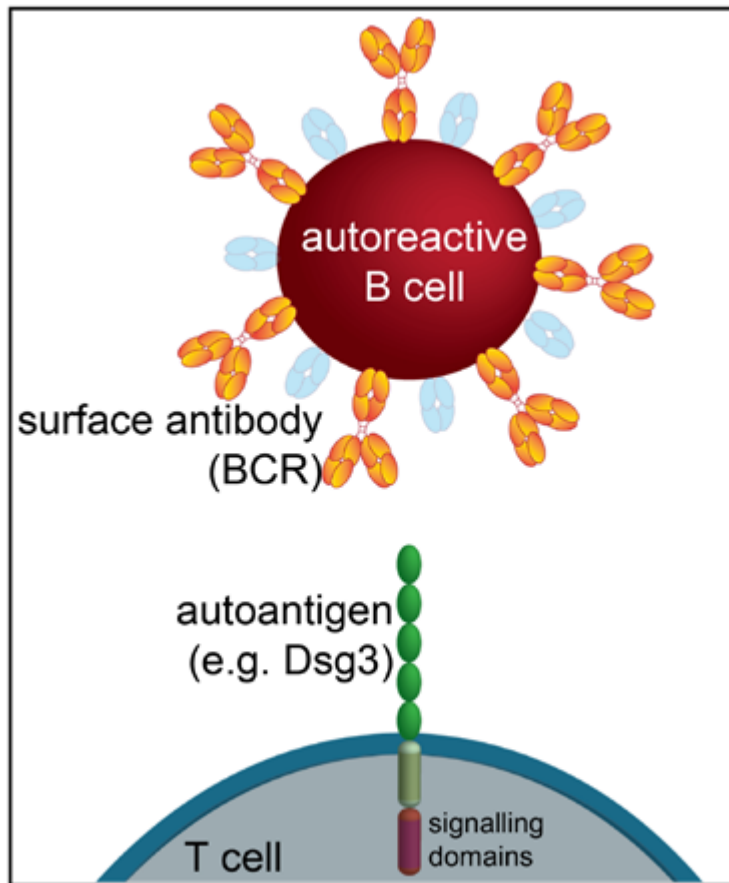


Schematics of CAR T-cell immunotherapy

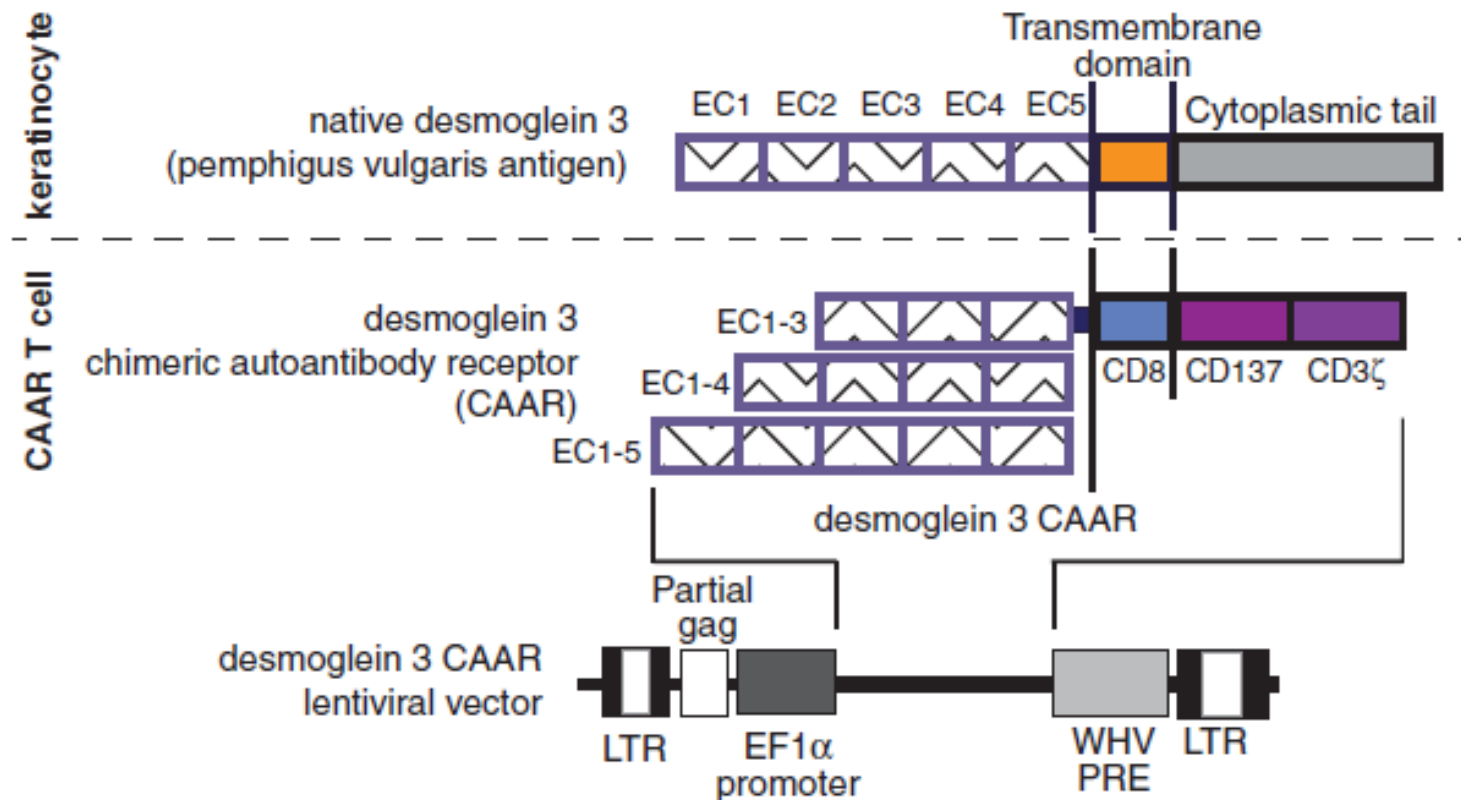


CAR T-cell immunotherapy designs for B cell malignancies

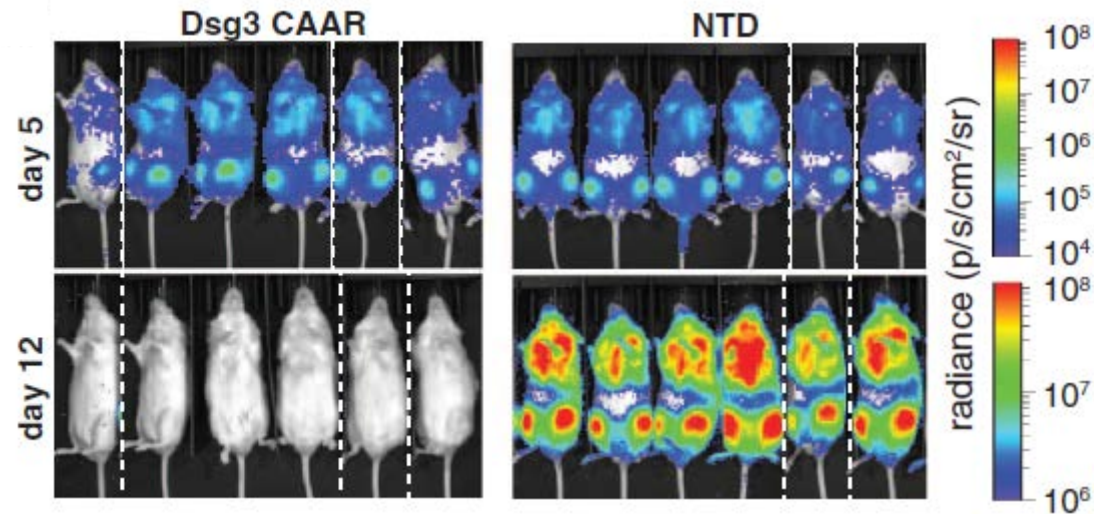
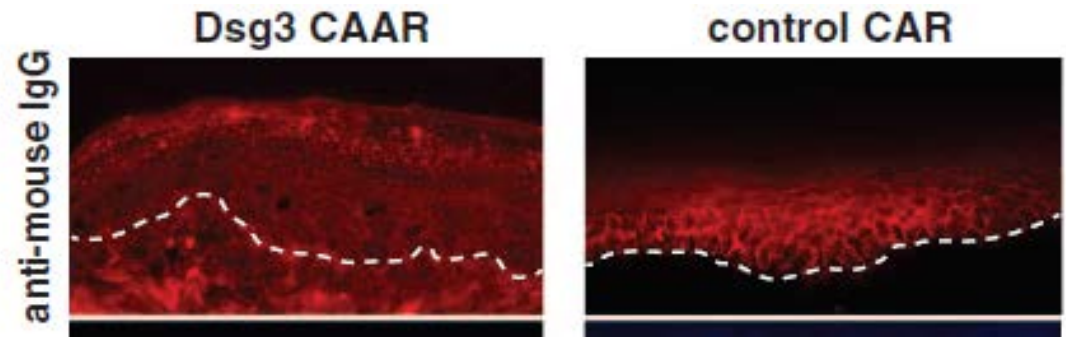
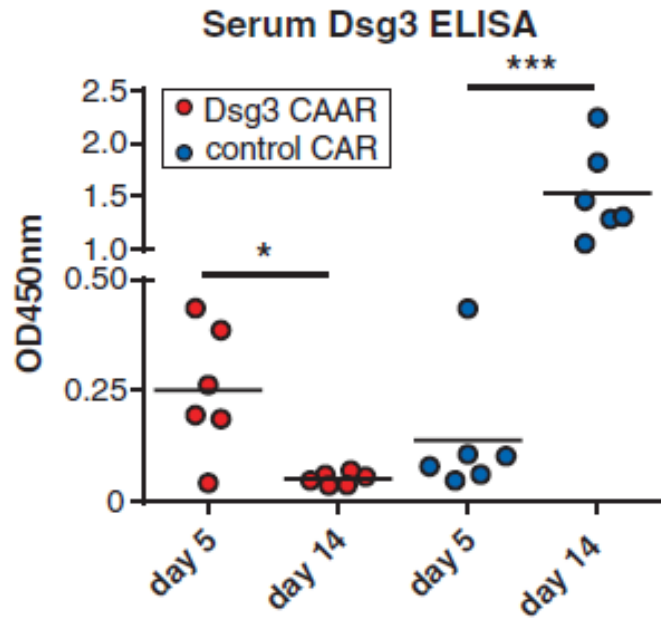
CAAR T-cell immunotherapy for pemphigus: the concept



A chimeric autoantibody receptor (CAAR) was created with the extracellular domains of desmoglein 3 (Dsg3) as the extracellular domain in order to engineer T cells to kill autoimmune B cells expressing anti-Dsg3 surface antibodies (BCR) in pemphigus vulgaris



- **Dsg3 CAAR-T cells were able to kill anti-Dsg3 B cells in vitro**, as assessed using antibody secreting hybridomas that target the Dsg3 EC1/EC2/EC3-4 domains and K562/Nalm6 cell lines expressing anti-EC1 or EC2 IgG cloned from patients
- The Dsg3 EC1-4 CAAR was selected as the best construct combining potency and breadth of target recognition



In a PV mouse model, Dsg3 CAAR T cells injection resulted in drop of anti-Dsg3 serum autoantibodies, negative DIF and lack of blistering, and significantly delayed or no hybridoma/Nalm6 cells overgrowth

CAAR T-cell immunotherapy for pemphigus

- In pemphigus models, CAAR T cells expressing Dsg3 specifically kill anti-Dsg3 B cells, even in the presence of circulating autoantibodies and, possibly, without off-target toxicity
- CAAR T-cell immunotherapy represents a targeted therapy approach for pemphigus and, in a more general way, autoantibody-mediated autoimmune diseases. It has the potential for generation of curative long-term memory CAAR T cells

Limits

- Short-term observations of CAART safety and efficacy in preclinical models
- Risk/benefit ratio of a therapy approach based on T cell transduction with lentiviral vectors in autoimmune diseases versus relapsing/therapy refractory lethal cancers

TECNOLOGIA
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Grazie dell'attenzione!