Farmaci innovativi in Dermatologia

Sergio Chimenti

Clinica Dermatologica – Università degli Studi di Roma "Tor Vergata"

La principale innovazione farmacologica in Dermatologia è rappresenta dall'Introduzione nella pratica clinica dei farmaci biologici

I farmaci biologici

- I farmaci biologici sono molecole ottenute mediante tecnologia del DNA ricombinante e dotate di una notevole specificità di azione
- Includono anticorpi, proteine di fusione e citochine
- Interagiscono nella patogenesi della malattia con meccanismi di blocco o stimolo, o con un effetto antagonista o di tipo citotossico

I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

Agenti anti-CD20

Rituximab

- Anticorpo monoclonale chimerico diretto contro il CD20, espresso dai linfociti B, dalle cellule pre-B e da molte cellule neoplastiche ad origine dai linfociti B
- Determina una lisi complemento-mediata delle cellule esprimenti il CD20

Agenti anti-CD20

Rituximab

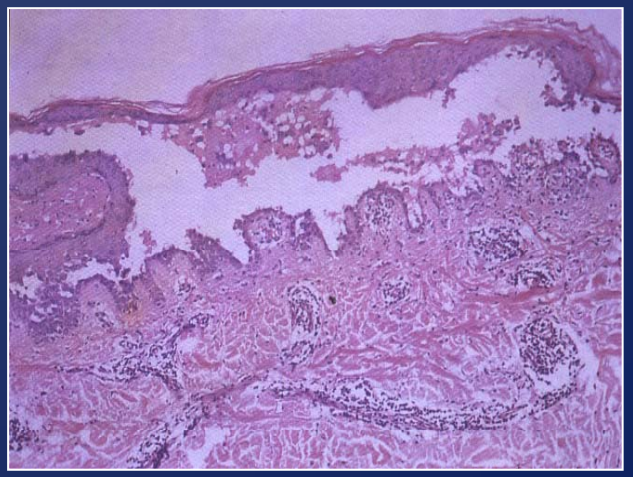
- Indicazioni terapeutiche dermatologiche:
  - Pemfigo
  - Linfomi cutanei a cellule B

- Posologia: 375 mg/m^2 e.v. 1 volta/settimana per 4 settimane

Pemfigo

Il termine pemfigo identifica un gruppo di patologie caratterizzate da una perdita di coesione intercheratinocitaria da cui risultano clinicamente la bolla ed istologicamente l'acantolisi con formazione di fenditure intraepidermiche









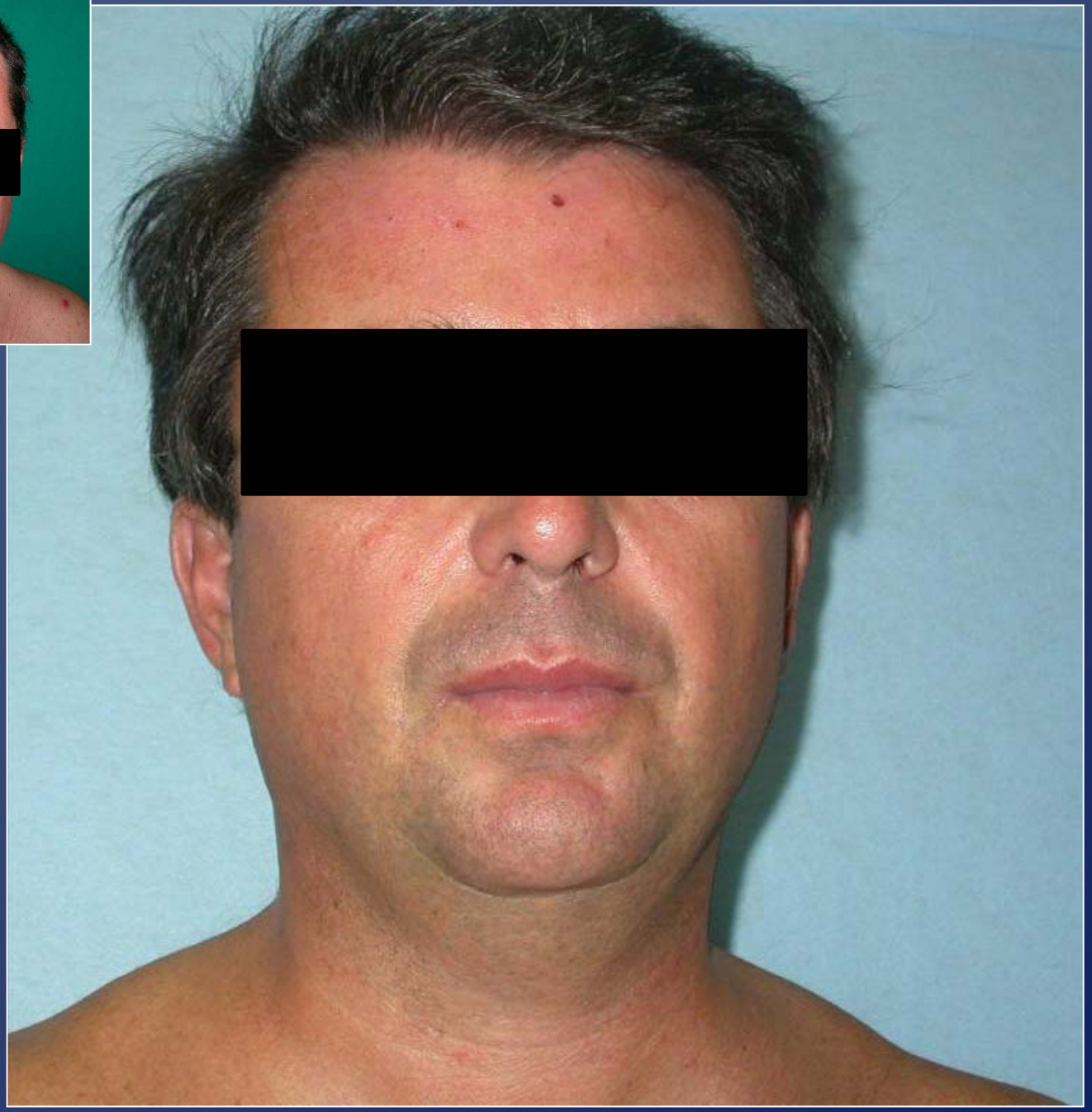
















Agenti anti-CD20

Rituximab

2006 Acta Dermato-Venereologica. ISSN 0001-5555

Long-lasting Remission of Pemphigus Vulgaris Treated with Rituximab

Maria Esposito, Elisabetta Capriotti, Alessandro Giunta, Luca Bianchi and Sergio Chimenti*

*Department of Dermatology, University of Roma "Tor Vergata", Viale Oxford 81, IT - 00133, Rome, Italy. *E-mail: chimenti@dermatologica.it*

Accepted June 20, 2005.

Linfomi cutanei a cellule B

WHO-EORTC classification for cutaneous lymphomas

Rein Willemze, Elaine S. Jaffe, Günter Burg, Lorenzo Cerroni, Emilio Berti, Steven H. Swerdlow, Elisabeth Ralfkiaer, Sergio Chimenti, José L. Diaz-Perez, Lyn M. Duncan, Florent Grange, Nancy Lee Harris, Werner Kempf, Helmut Kerl, Michael Kurrer, Robert Knobler, Nicola Pimpinelli, Christian Sander, Marco Santucci, Wolfram Sterry, Maarten H. Vermeer, Janine Wechsler, Sean Whittaker, and Chris J. L. M. Meijer

BLOOD, 15 MAY 2005 • VOLUME 105, NUMBER 10

Linfomi primitivi cutanei a cellule B

- *A basso grado di malignità ("indolent")*
  - Linfoma del centro follicolare
  - Linfoma della zona marginale
- *Aggressività intermedia ("Intermediate")*
  - Linfoma B diffuso a grandi cellule della gamba
  - Linfoma B diffuso a grandi cellule *(other)*
    - Linfoma B a grandi cellule intravascolare





Agenti anti-CD20

Rituximab

Acta Dermatol Venereol 2001

Systemic Therapy of Primary Cutaneous B-cell Lymphoma, Marginal Zone Type, with Rituximab, a Chimeric Anti-CD20 Monoclonal Antibody

R. Soda[1], A. Costanzo[1], M. Cantonetti[2], A. Orlandi[3], L. Bianchi[1] and S. Chimenti[1]*

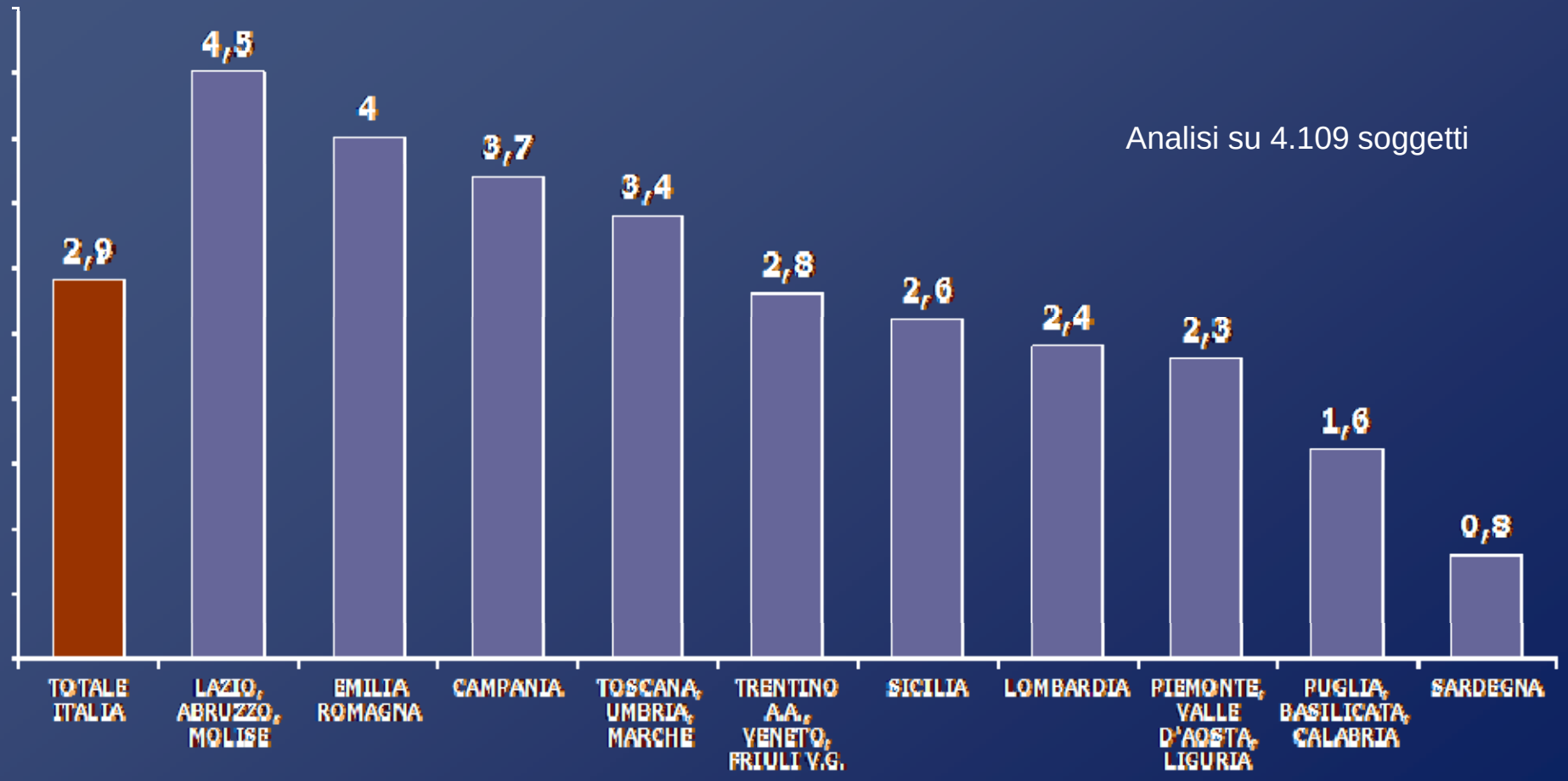
I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

Psoriasi

- La psoriasi (dal greco psora, squama) è una patologia infiammatoria a carattere cronico-recidivante con una prevalenza nella popolazione generale del 2.5-3%, che interessa, nella sua forma più comune, la cute con lesioni eritemato-squamose
- In una percentuale di pazienti compresa tra il 5 ed il 30% coesiste una artropatia sieronegativa che configura il quadro clinico della psoriasi artropatica

Prevalenza della psoriasi in Italia

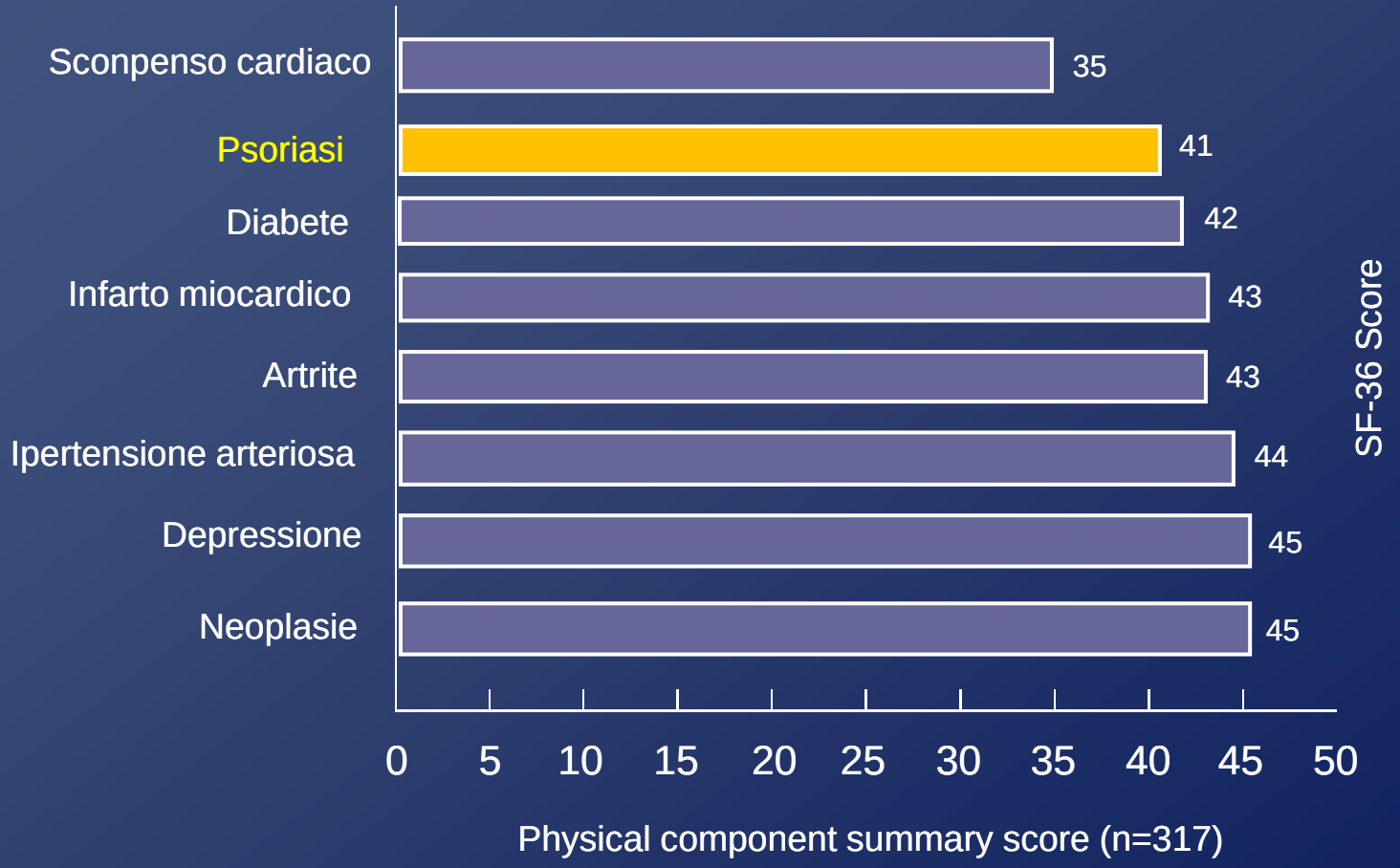


Analisi su 4.109 soggetti

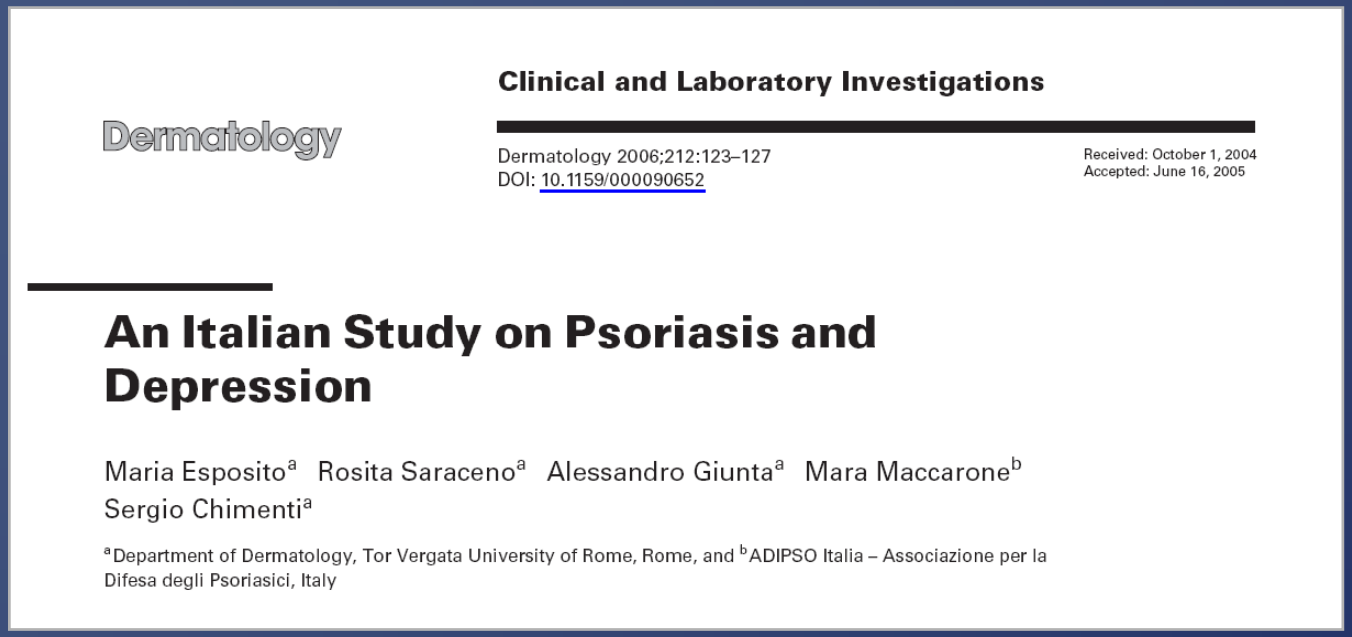
Fonte: Genstinpresa per ADIPSO

Psoriasis causes as much disability as other major medical diseases

Stephen R. Rapp, PhD,[a,b] Steven R. Feldman, MD, PhD,[c] M. Lyn Exum, MA,[a]
Alan B. Fleischer, Jr, MD,[c] and David M. Reboussin, PhD[b] *Winston-Salem, North Carolina*



Rapp SR, et al. *J Am Acad Dermatol.* 1999;41:401-407.



Clinical and Laboratory Investigations

Dermatology

Dermatology 2006;212:123–127
DOI: 10.1159/000090652

Received: October 1, 2004
Accepted: June 16, 2005

An Italian Study on Psoriasis and Depression

Maria Esposito[a] Rosita Saraceno[a] Alessandro Giunta[a] Mara Maccarone[b] Sergio Chimenti[a]

[a]Department of Dermatology, Tor Vergata University of Rome, Rome, and [b]ADIPSO Italia – Associazione per la Difesa degli Psoriasici, Italy

- "… questionnaires from 2391 patients, including 1528 men (63.9%) and 863 women (36.1%). Depressive symptoms were observed in 1482 patients (62% overall; females, 63%; males, 61%) ..."
- "…Emotional suffering due to psoriasis can lead to depression and suicidal ideation; indeed, recent studies have shown that psoriasis is associated with a high risk of suicide…"

I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

Agenti anti-TNF-alfa

Adalimumab

- Anticorpo monoclonale umanizzato diretto contro il TNF-alfa

Esperienza personale:

- 204 pazienti (145 M e 59 F)
  - 113 pazienti affetti da psoriasi artropatica
  - 84 pazienti affetti da psoriasi volgare
  - 3 pazienti affetti da psoriasi eritrodermica
  - 4 pazienti affetti da psoriasi pustolosa



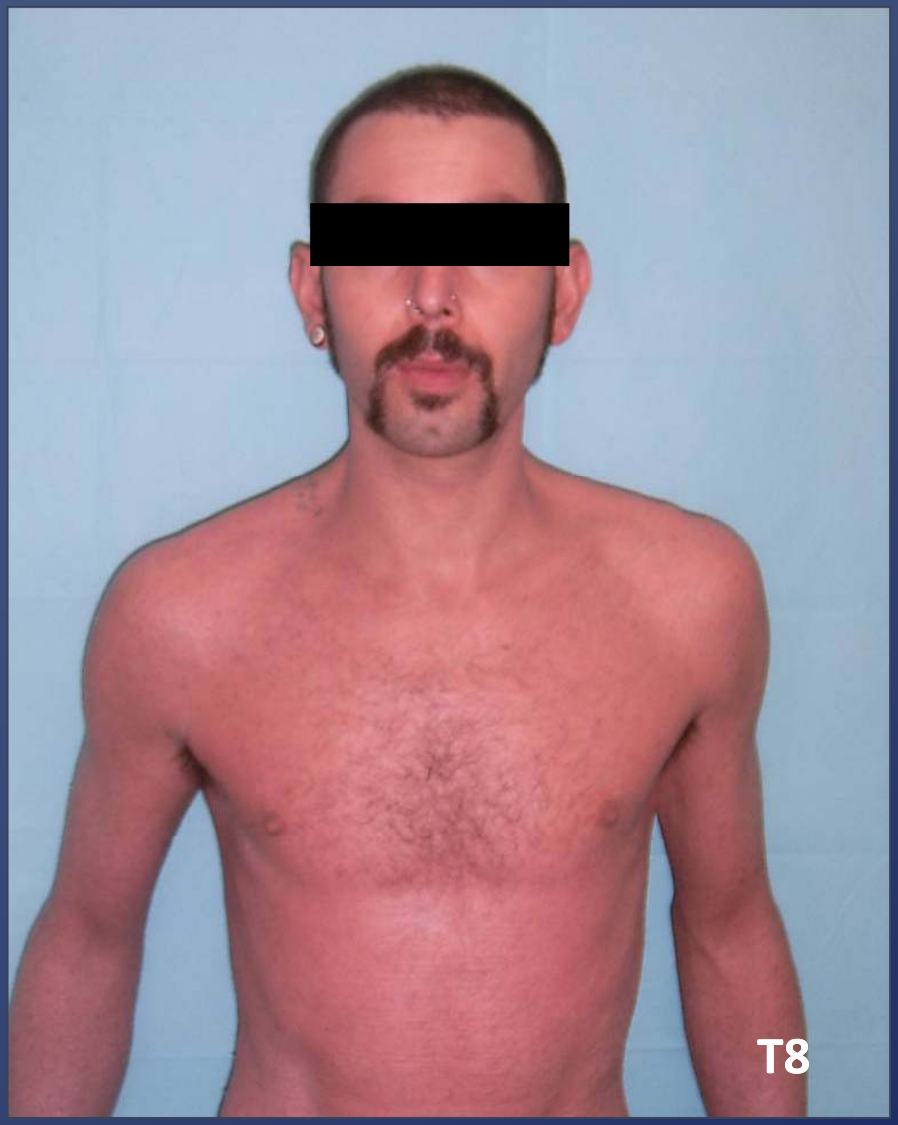


PASI: 24





PASI: 24





PASI: 13,2





PASI: 13,2



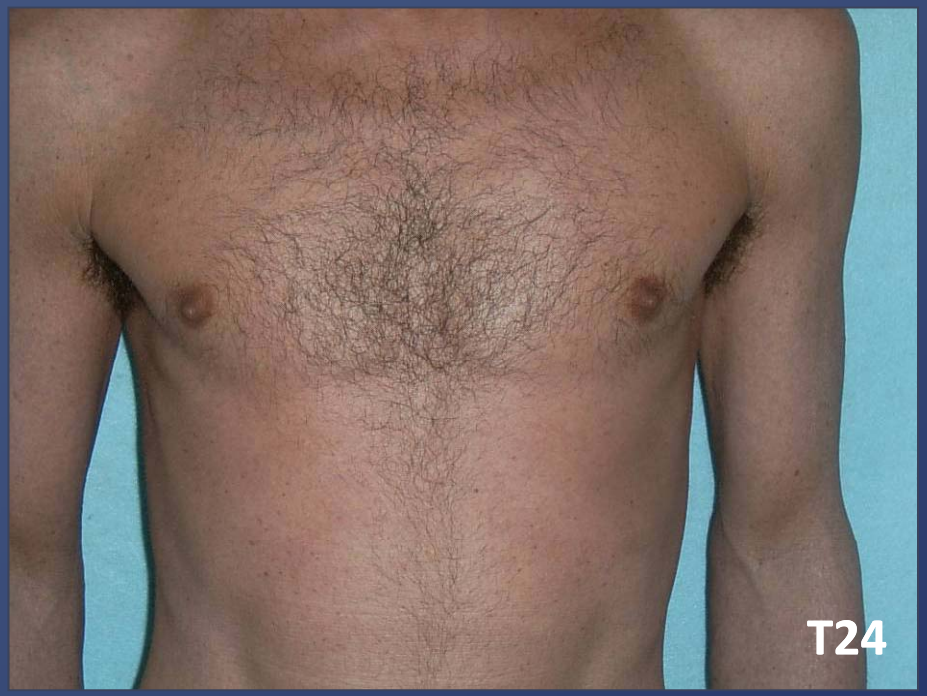


PASI: 4,8





PASI: 4,8



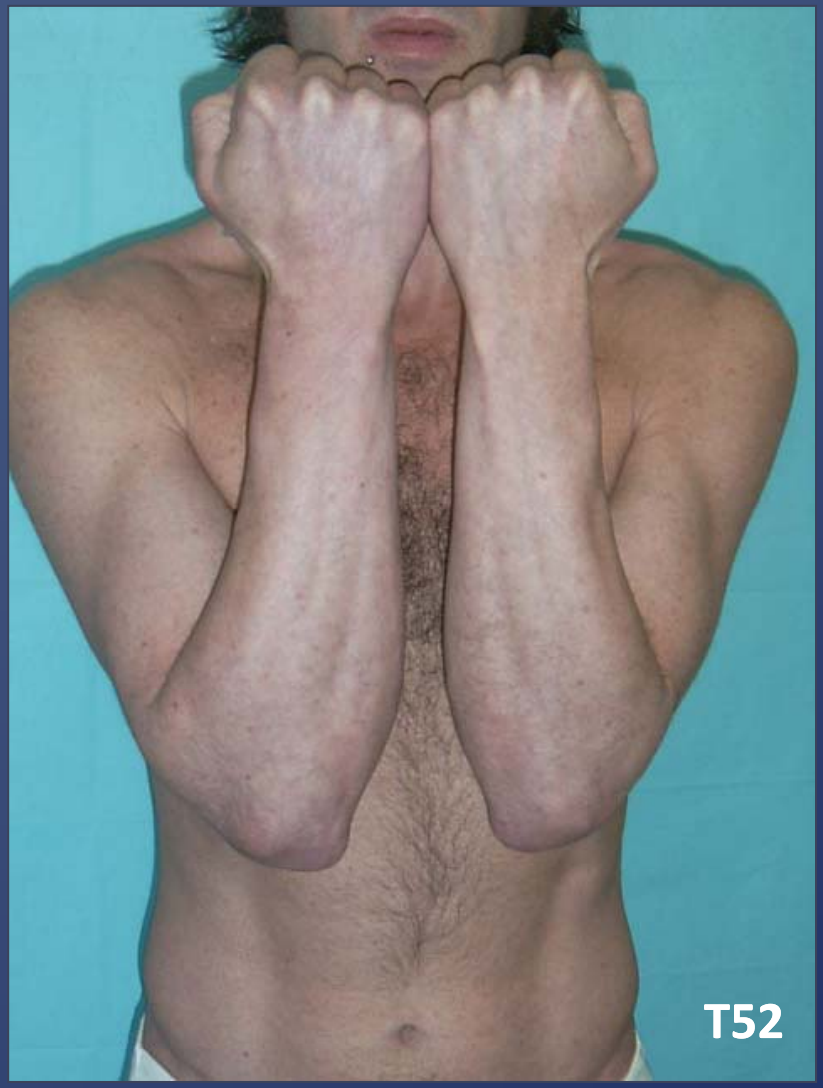


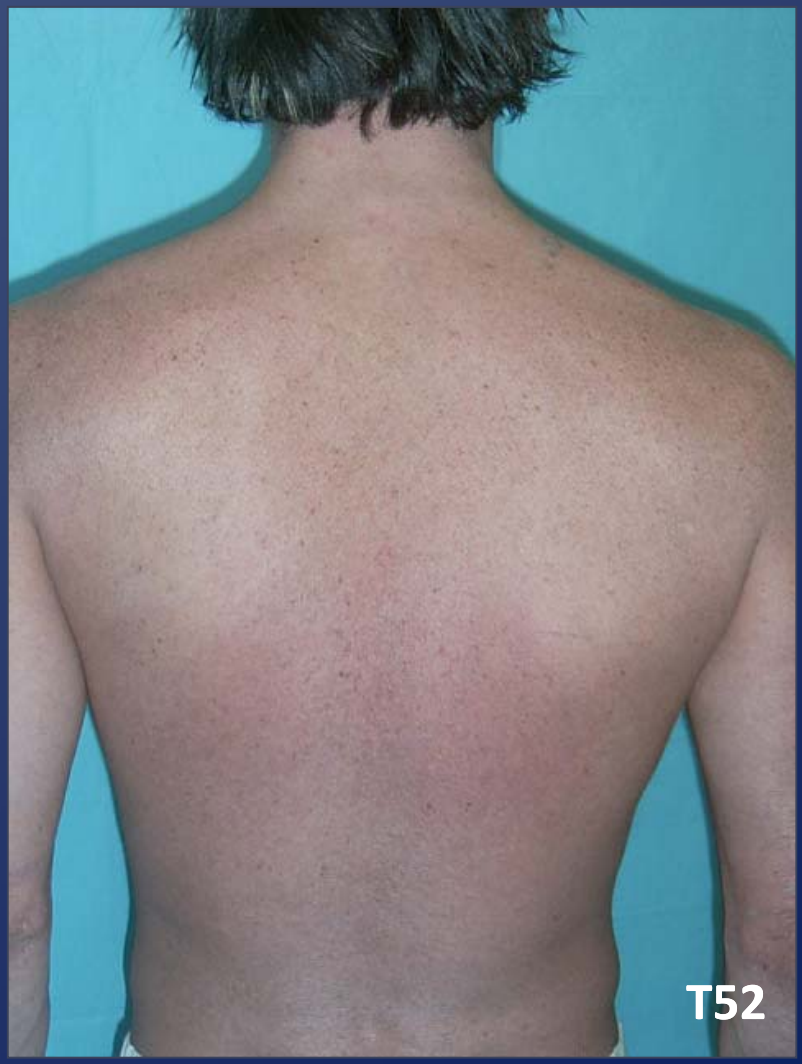
PASI: 0





PASI: 0





PASI: 0





PASI: 0

Università degli Studi di Roma "Tor Vergata"
Clinica Dermatologica

THERAPY

Adalimumab for severe psoriasis and psoriatic arthritis: An open-label study in 30 patients previously treated with other biologics

M. Papoutsaki, MD,[a] M. S. Chimenti, MD,[b] A. Costanzo, MD, M. Talamonti, MD,[a] A. Zangrilli, MD,[a] A. Giunta, MD,[a] Luca Bianchi, MD,[a] and S. Chimenti, MD[a]
Rome, Italy



Fig 2. A, Patient affected by plaque-type psoriasis at baseline. Same patient after 4 (**B**), 12 (**C**), and 24 (**D**) weeks of treatment with adalimumab.

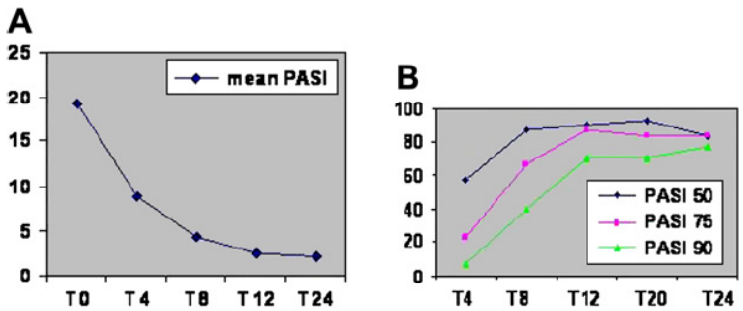
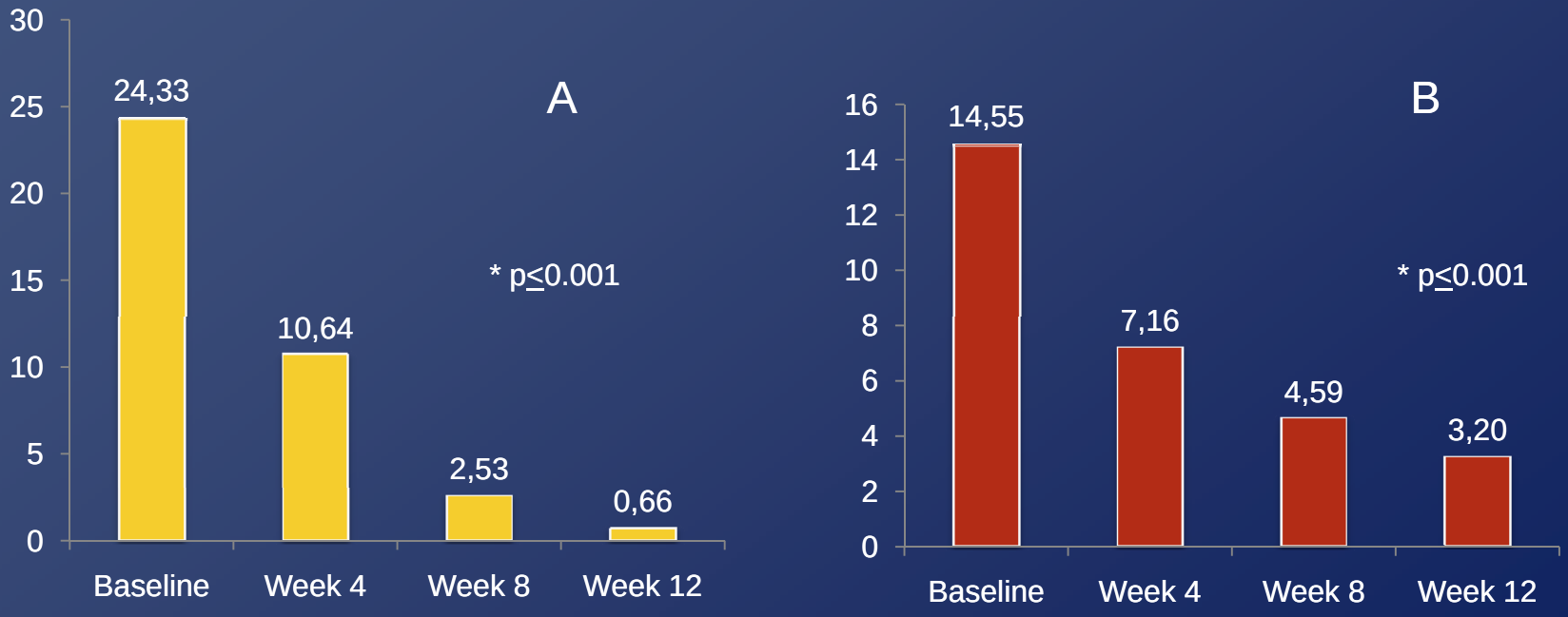


Fig 3. A, Mean PASI score at 24 weeks of treatment. **B**, PASI score (PASI 50, 75, 90) at 24 weeks of treatment.

A. Giunta, A. Zangrilli, M.S. Chimenti, M. Teoli, M. Talamonti, M.Bavetta, S. Chimenti

Long-term safety and efficacy of Adalimumab in the treatment of psoriasis: a 4 years open label study.

J Am Acad Dermatol, submitted



Miglioramento del PASI medio nella psoriasi volgare (A) e artropatica (B)

I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

Agenti anti-TNF-alfa

Etanercept

- Recettore solubile del TNF-alfa

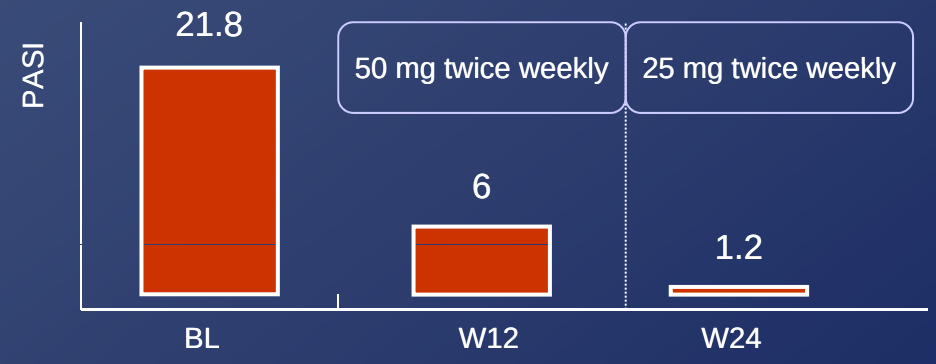
Esperienza personale:

- 601 pazienti (314 affetti da psoriasi volgare e 287 da psoriasi artropatica)
  - 251 in regime di trattamento intermittente
  - 63 in trattamento continuativo


T0


T0


T24


PASI
21.8
6
1.2
50 mg twice weekly
25 mg twice weekly
BL
W12
W24


T24

Safety and efficacy study on etanercept in patients with plaque psoriasis

DOI: 10.1111/j.1365-2133.2005.06306.x

Department of Dermatology,
University of Rome 'Tor Vergata',
Viale Oxford 81, 00133 Rome, Italy
E-mail: antonio.costanzo@uniroma2.it

A. COSTANZO
A. MAZZOTTA
M. PAPOUTSAKI
S. NISTICÒ
S. CHIMENTI

Costanzo A et al. *Br J Dermatol* 2005; 152: 176–198


T0


T0


T24


T24

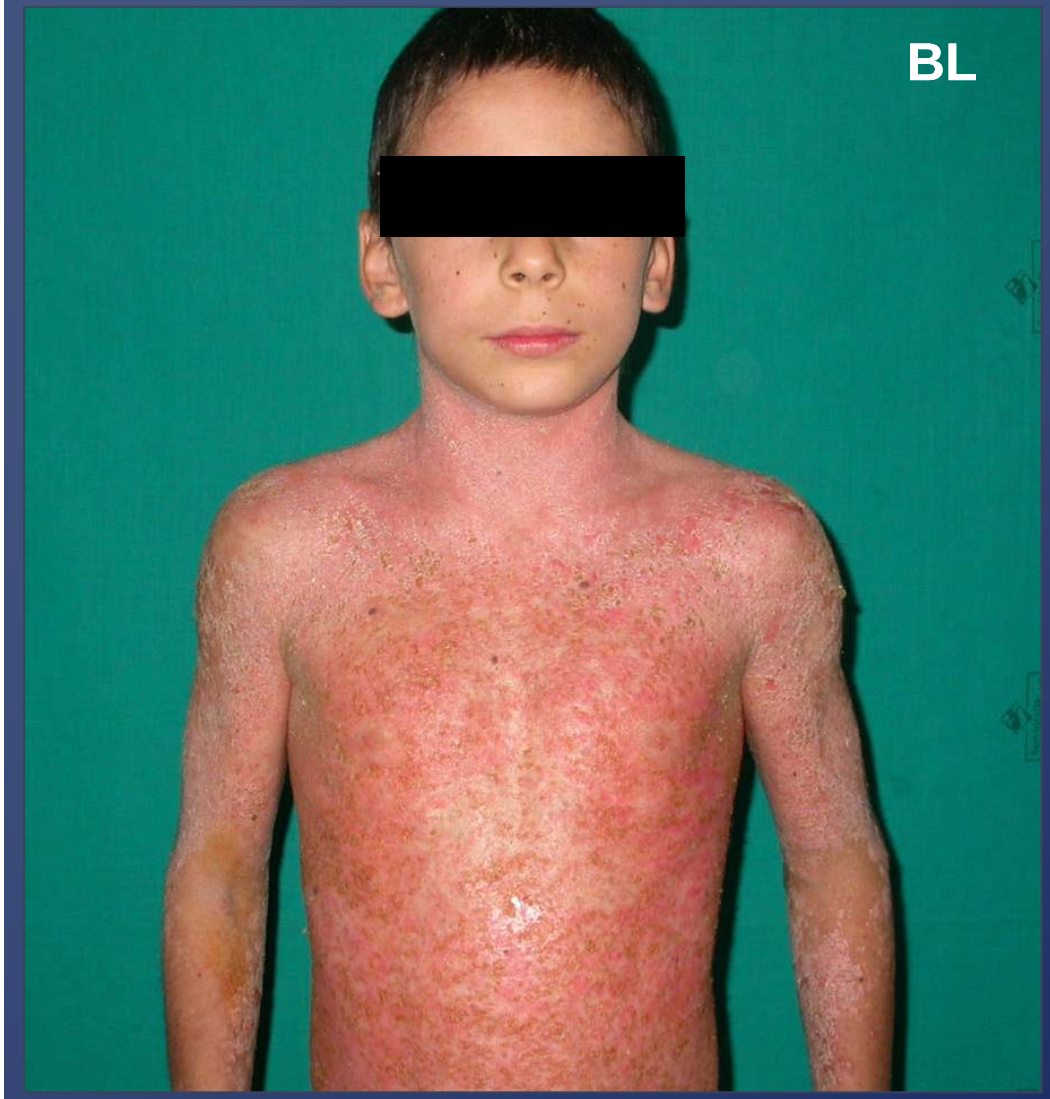
Br J Dermatol, 2006;155(1):156-9

THERAPEUTICS

Treatment of erythrodermic psoriasis with etanercept

M. Esposito, A. Mazzotta, C. de Felice, M. Papoutsaki and S. Chimenti

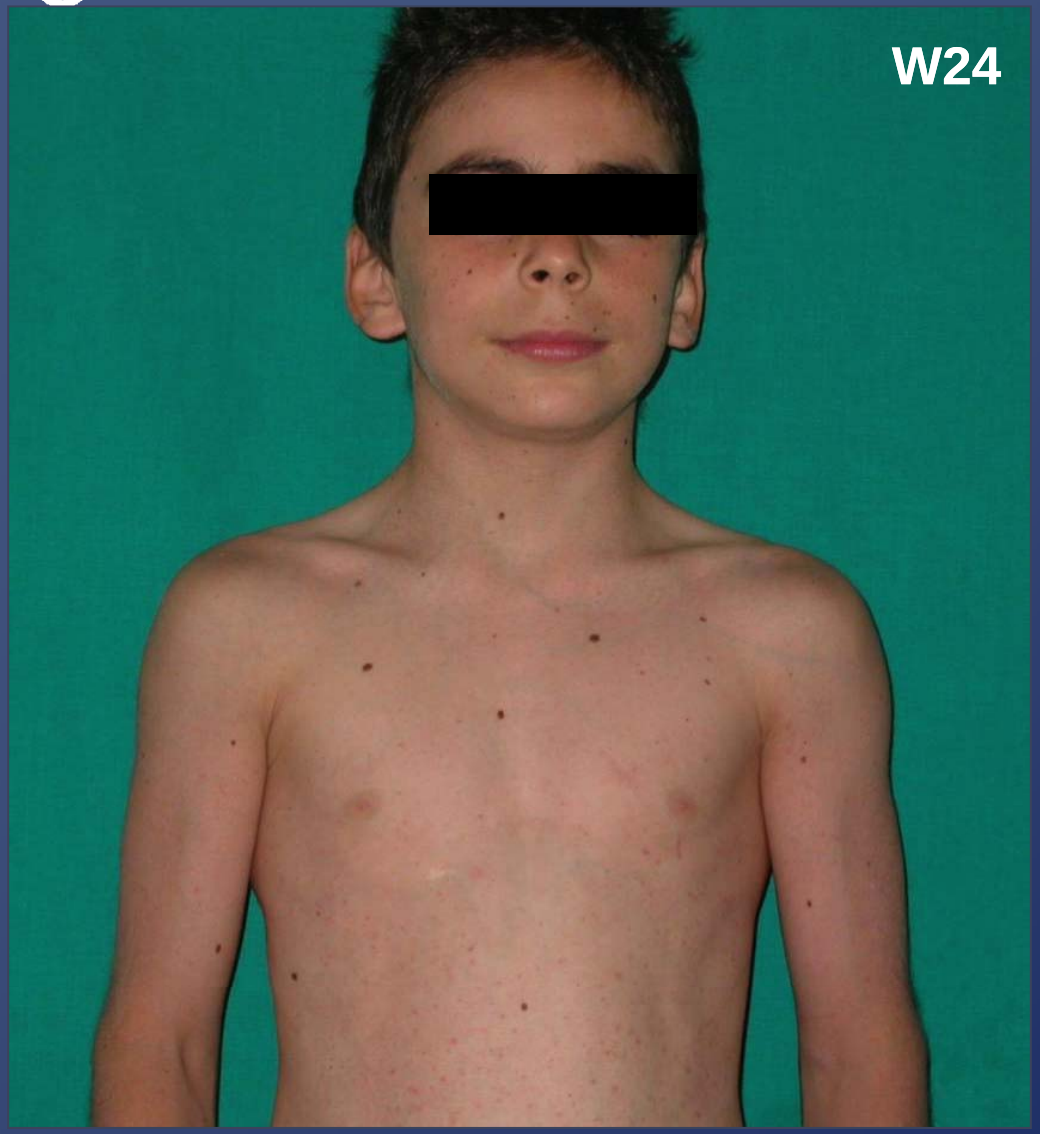
Department of Dermatology, University of Rome 'Tor Vergata', Viale Oxford 81, 00133 Rome, Italy


BL


BL


BL

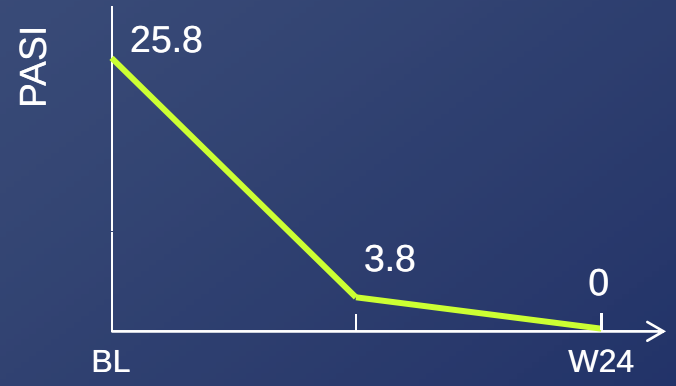

BL


W24


W24


W24


W24


PASI
25.8
3.8
0
BL
W24

© 2005 British Association of Dermatologists • British Journal of Dermatology 2006 154, pp177–204

Etanercept for the treatment of severe childhood psoriasis

Department of Dermatology,
University of Rome 'Tor Vergata',
Viale Oxford 81,
00133 Rome, Italy

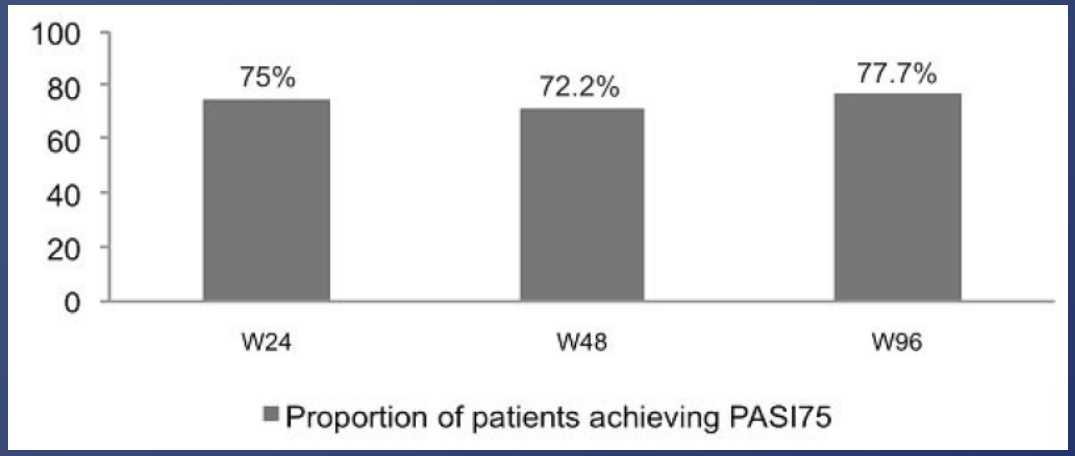
M. Papoutsaki
A. Costanzo
A. Mazzotta
T. Gramiccia
R. Soda
S. Chimenti

Br J Dermatol, 2006; 154: 181-2

INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 23, no. 2, 0-0 (2010)

CONTINUOUS TREATMENT OF PLAQUE-TYPE PSORIASIS WITH ETANERCEPT: AN OBSERVATIONAL LONG-TERM EXPERIENCE

M. ESPOSITO, A. GIUNTA, A. MAZZOTTA, G. BABINO, M. TALAMONTI, M.S. CHIMENTI[1] and S. CHIMENTI



	BL	W24	W48	W96
Primary outcome				
Mean PASI score	17.05	2.38	2.95	2.83
Mean of differences		*14.67*	*14.10*	*14.21*
Standard deviation of differences		*10.51*	*12.30*	*11.66*
Significance (p<0.0001)		+	+	+
QoL outcomes				
Mean DLQI score	11.36	2.09	0.72	0.72
Mean of differences		*9.27*	*10.63*	*10.63*
Standard deviation of differences		*6.85*	*7.39*	*7.43*
Significance (p<0.0001)		+	+	+
Mean PDI score	23.41	2.5	1.86	1.13
Mean of differences		*20.91*	*21.54*	*22.27*
Standard deviation of differences		*15.90*	*16.69*	*16.57*
Significance (p<0.0001)		+	+	+

I farmaci biologici in Dermatologia

- Agenti anti CD20
  - Rituximab
- Agenti anti-Tumor Necrosis Factor (TNF) alfa
  - Adalimumab
  - Etanercept
  - Infliximab
- Agenti anti-interleuchine
  - Ustekinumab

Agenti anti-TNF-alfa

Infliximab

- Anticorpo monoclonale chimerico anti-TNF-alfa

Esperienza personale:

- 325 pazienti (160 affetti da psoriasi volgare e 165 da psoriasi artropatica)
  - 30 pazienti hanno raggiunto il 5° anno di trattamento
  - 1 paziente è in trattamento da 8,5 anni

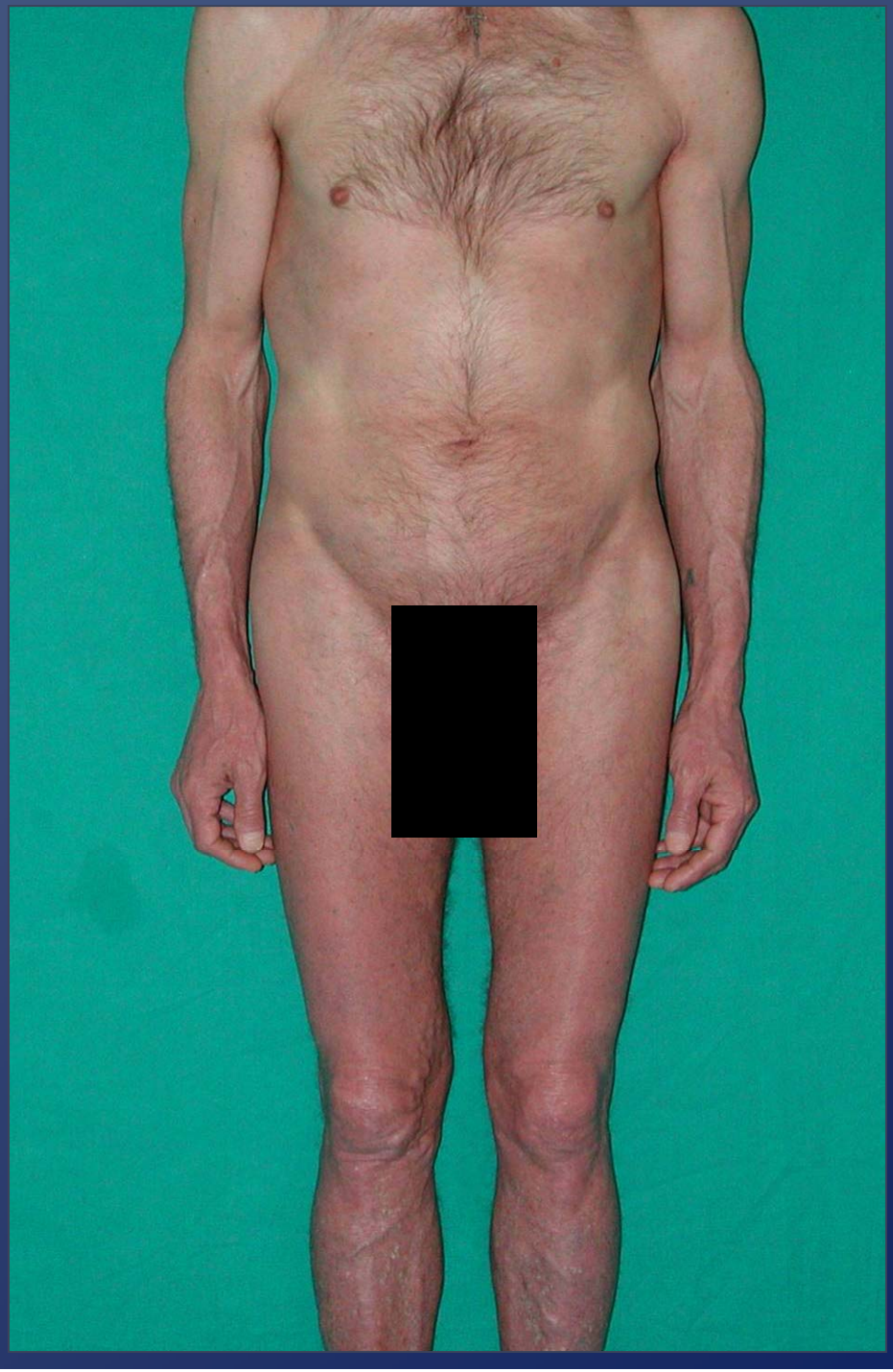


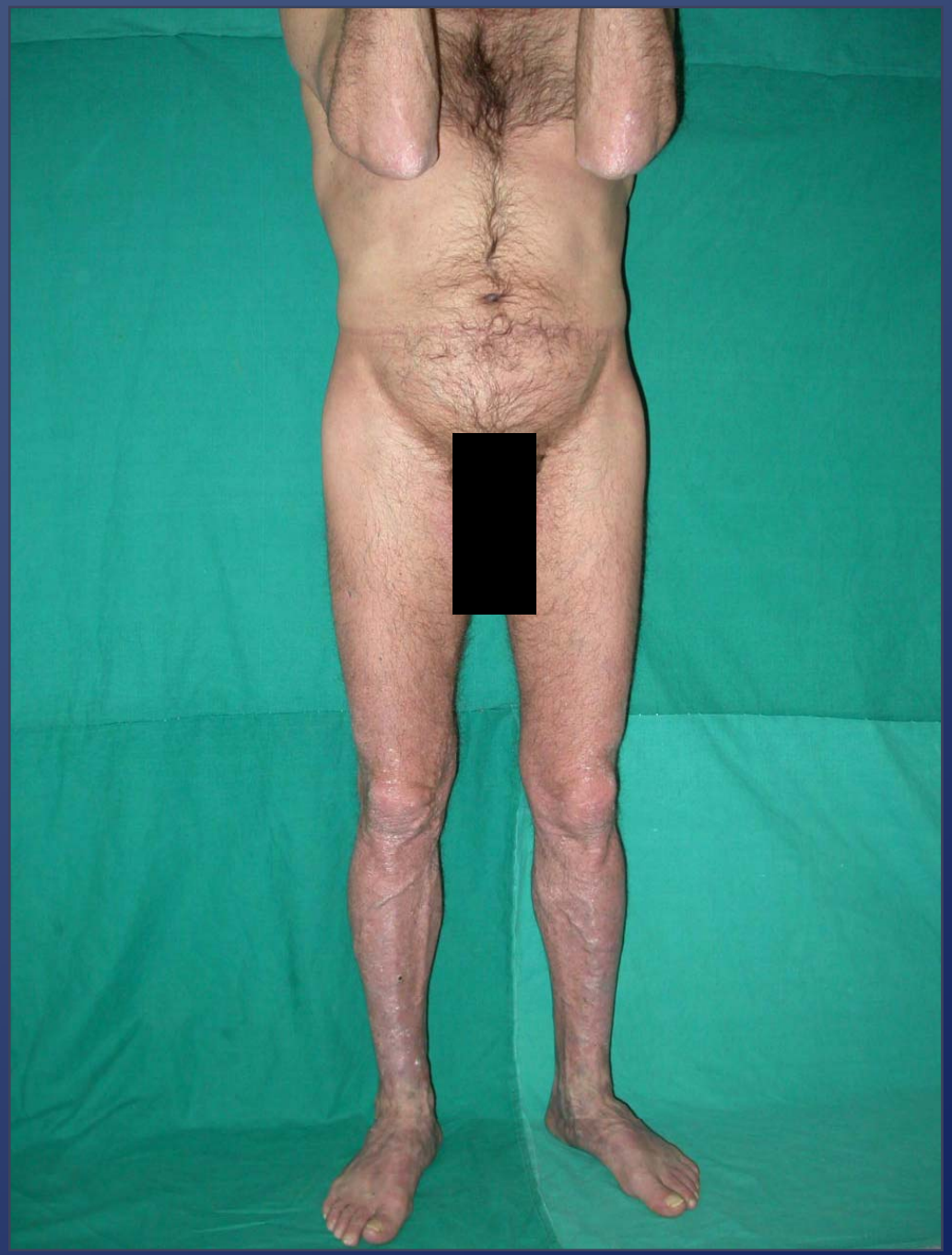
BL

PASI: 35

Week 22

PASI: 0





1 year

PASI: 0

2 years

PASI: 0.8





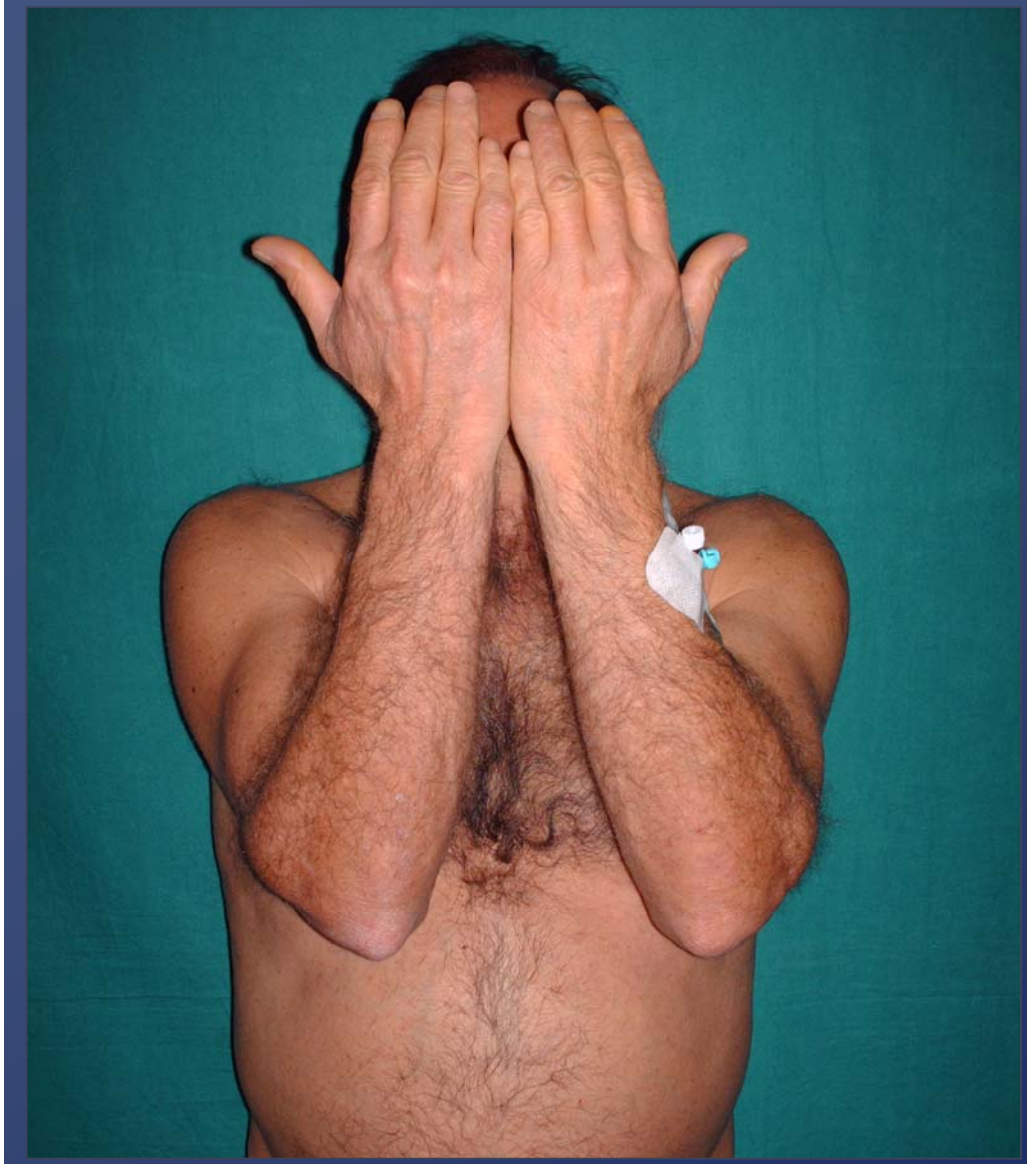


3 years

PASI: 0.2

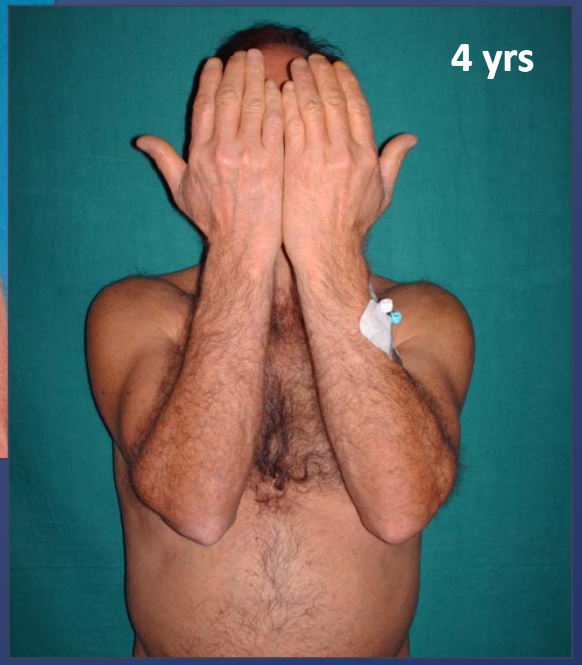
4 years

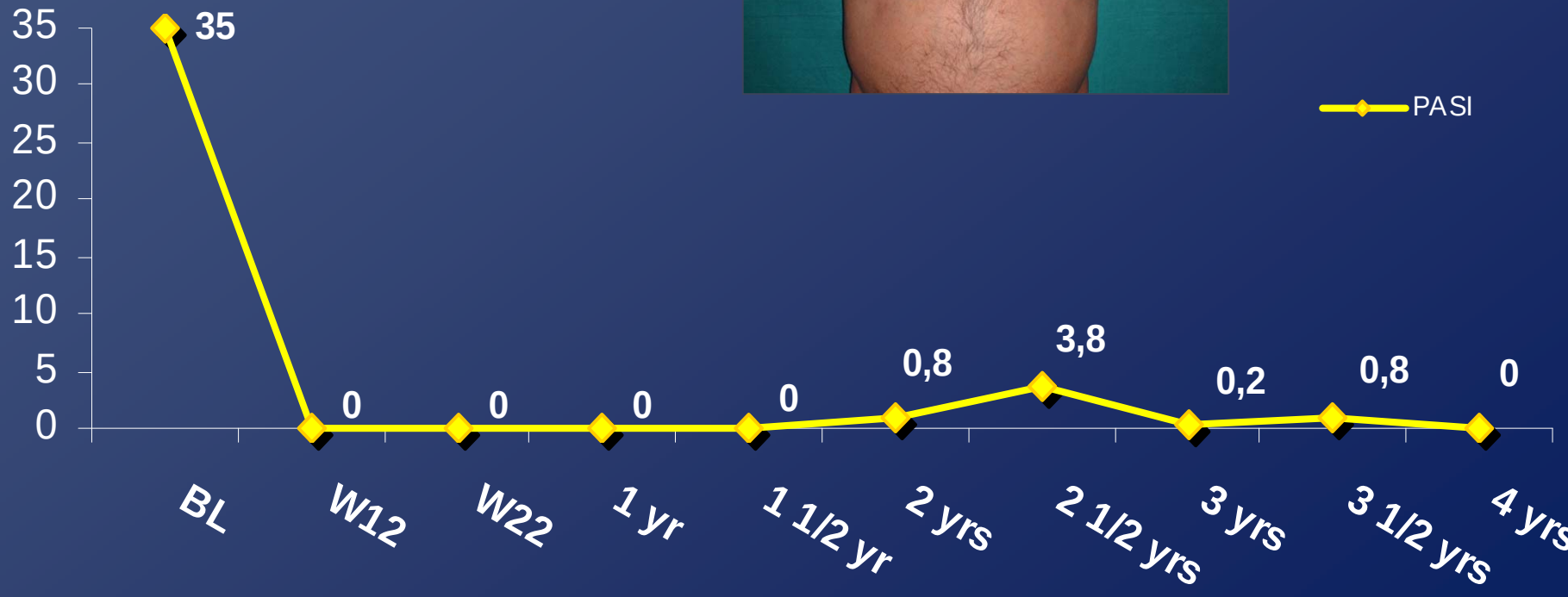
PASI: 0






BL


4 yrs


35
30
25
20
15
10
5
0
35
0
0
0
0
0,8
3,8
0,2
0,8
0
PASI
BL
W12
W22
1 yr
1 1/2 yr
2 yrs
2 1/2 yrs
3 yrs
3 1/2 yrs
4 yrs

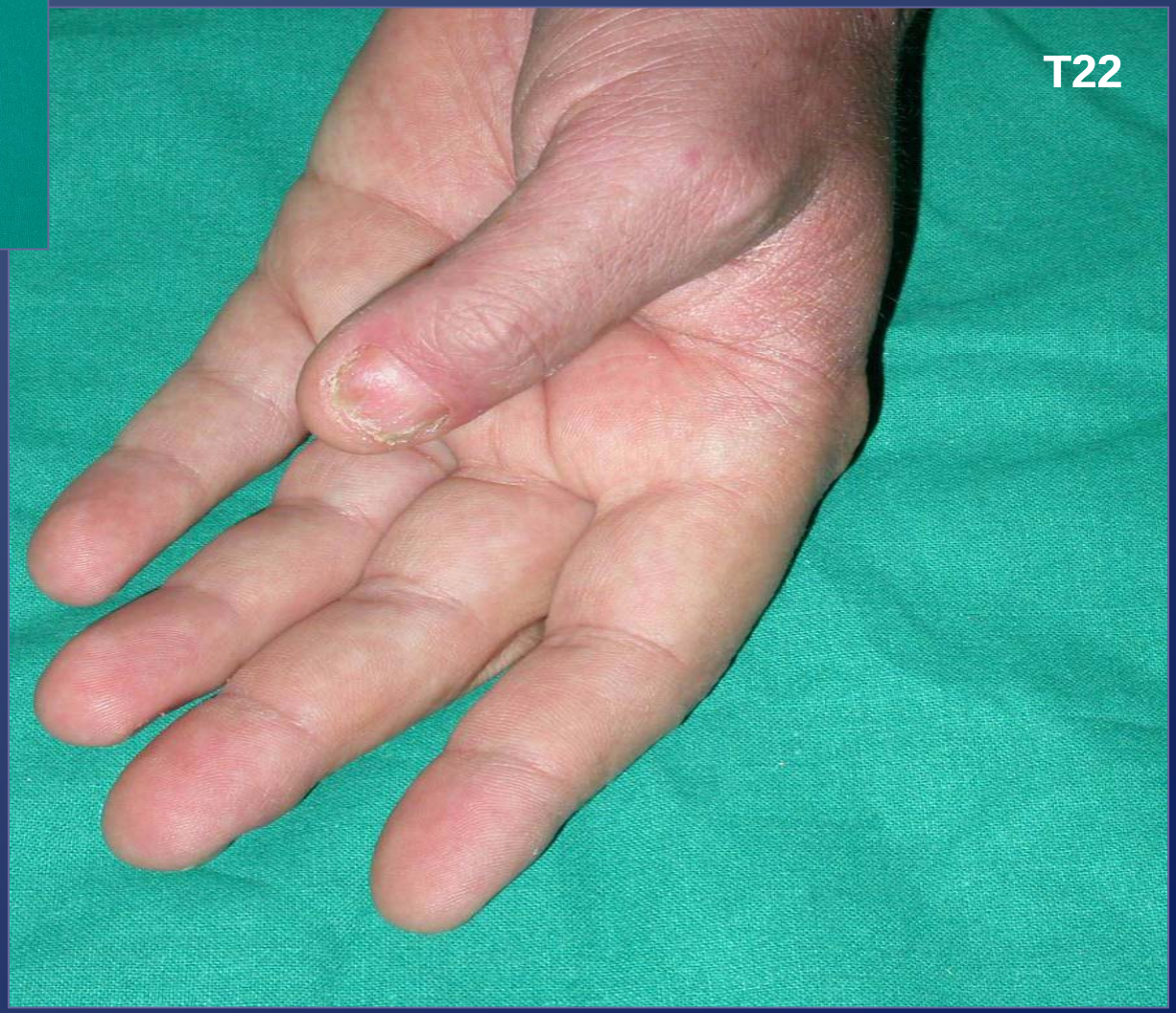


Bianchi L, Bergamin A, DeFelice C, Capriotti E, Chimenti S

Remission and time resolution of nail psoriasis during infliximab therapy.

J Am Acad Dermatol. 2005; 52 (4): 736-7





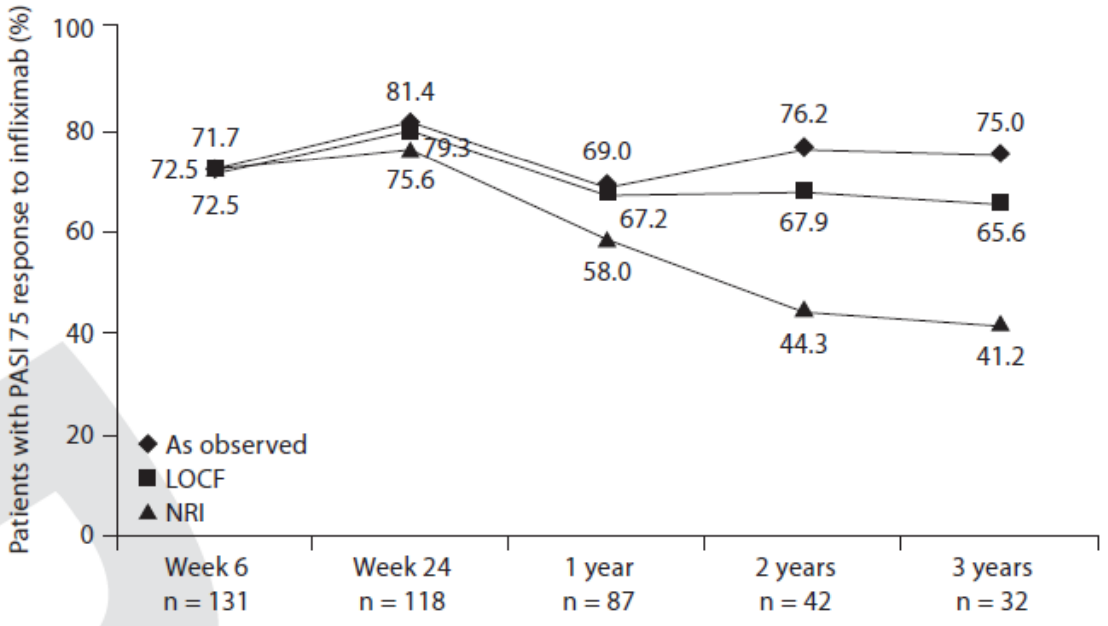
Dermatology

Dermatology 2010;221(suppl 1):43–47
DOI: 10.1159/000316184

Published

The Impact of Methodological Approaches for Presenting Long-Term Clinical Data on Estimates of Efficacy in Psoriasis Illustrated by Three-Year Treatment Data on Infliximab

M. Papoutsaki[a] M. Talamonti[b] A. Giunta[b] A. Costanzo[b] M. Ruzzetti[b]
M. Teoli[b] S. Chimenti[b]



Agenti anti-interleuchine

Ustekinumab

- Anticorpo monoclonale umanizzato che lega la subunità p40 dalle interleuchine 12 (IL-12) e 23 (IL-23)

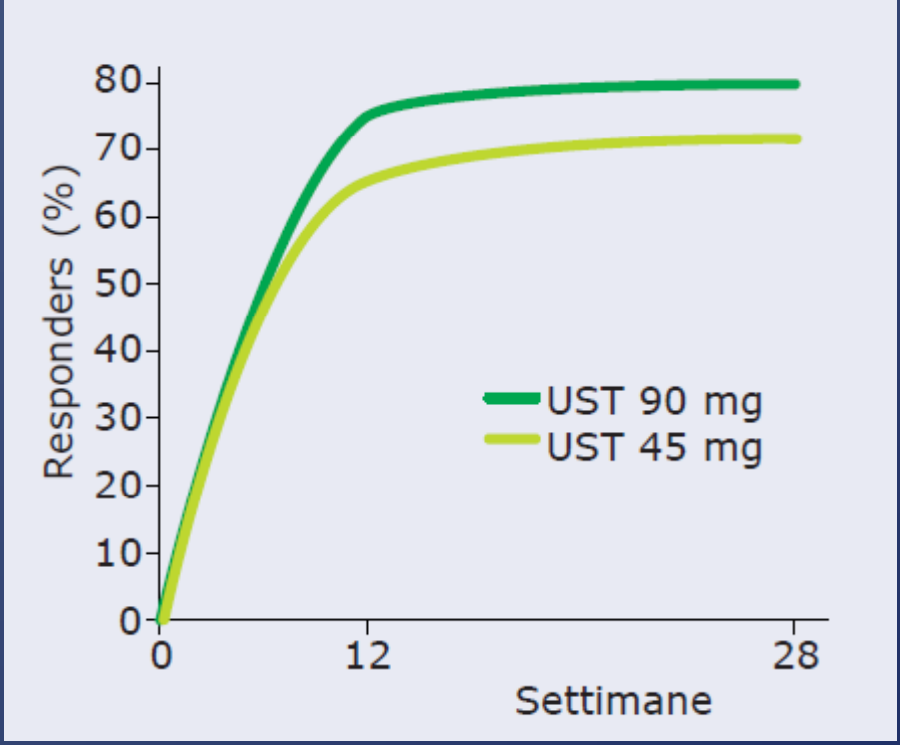
Esperienza personale:

- Studio CNTO-1275PSO-4004: 21 pazienti (16 M e 5 F)
- 15 pazienti (9 M e 6 F) arruolati dopo l'indicazione AIFA

Review

Target therapy della psoriasi: ustekinumab

Giunta A, Esposito M, Saraceno R, et al. Psoriasis target therapy: ustekinumab. Trends Med 2010; 10(3):157-163.



Conclusioni

L’introduzione nella pratica clinica dei farmaci biologici, ha rappresentato una vera e propria rivoluzione per la Dermatologia e per la Medicina in generale, permettendo di raggiungere risultati un tempo solo ipotizzabili nel trattamento di numerose patologie


L'ADIPSO
(Associazione per la Difesa degli Psoriasici)
è lieta di presentare
LA SERATA DI BENEFICENZA
PER SOSTENERE
LA RICERCA GENETICA
SULLA PSORIASI
assisterete alla rappresentazione teatrale
"Esercizi di Stile"
di Raymond Queneau
nel libero adattamento di Anna Chiara Giordani
recitano i Dermatologi della Clinica Dermatologica
dell'Università degli Studi di Roma
"Tor Vergata"
Regia di
Anna Chiara Giordani
con la partecipazione straordinaria del Prof. Sergio Chimenti
24 marzo 2009 ore 20:30
AUDITORIUM DELLA CONCILIAZIONE
auditorium conciliazione
Via della Conciliazione, 4
Roma
Saranno presenti Autorità e Rappresentanti delle Istituzioni
A.DI.PSO. Associazione per la Difesa degli Psoriasici - tel. 06 3211545 - www.adipso.org
INGRESSO LIBERO







