

# Excimer laser treatment for vitiligo

Luigi Naldi

USC Dermatologia, A.O. Papa Giovanni XXIII, Bergamo  
Centro Studi GISED, Bergamo



Azienda Ospedaliera  
Papa Giovanni XXIII  
Bergamo



**CENTROSTUDI** *Gised*

## **Conflict of Interests Disclosure**

I was an author in a RCT of excimer laser combined with topical steroids

- **Some definitions**
- The concept of targeted repigmentation
- Excimer laser treatment of vitiligo: the evidence
- Future perspectives

# Definition of a “laser”

- The term "laser" originated as an **acronym** for Light Amplification by Stimulated Emission of Radiation
- A laser is a device that emits light through a process of **optical amplification** based on the stimulated emission of electromagnetic radiation

# Characteristics of a laser light

- **Monochromatic:** it consists of one single color or wavelength. The light is extremely pure and consists of a very narrow spectral range.
- **Directional:** the beam is well collimated (very parallel) and travels over long distances with very little spread.
- **Coherent:** means that all the individual waves of light are moving precisely together through time and space, i.e. they are in phase.

# Excimer laser vs lamp

- An **excimer laser** typically uses a combination of a noble gas (argon, krypton, or xenon) and a reactive gas (fluorine or chlorine).
- Under the appropriate conditions of electrical stimulation and high pressure, a pseudo-molecule called an excimer (or in the case of noble gas halides, exciplex) is created, which can only exist in an energized state and can give rise to laser light in the ultraviolet range
- Emission of excimer molecules is also used as a source of spontaneous ultraviolet light (**excimer lamp**)



Xenon, pulsed light laser  
308 nm monochromatic light

Spot 2x2cm

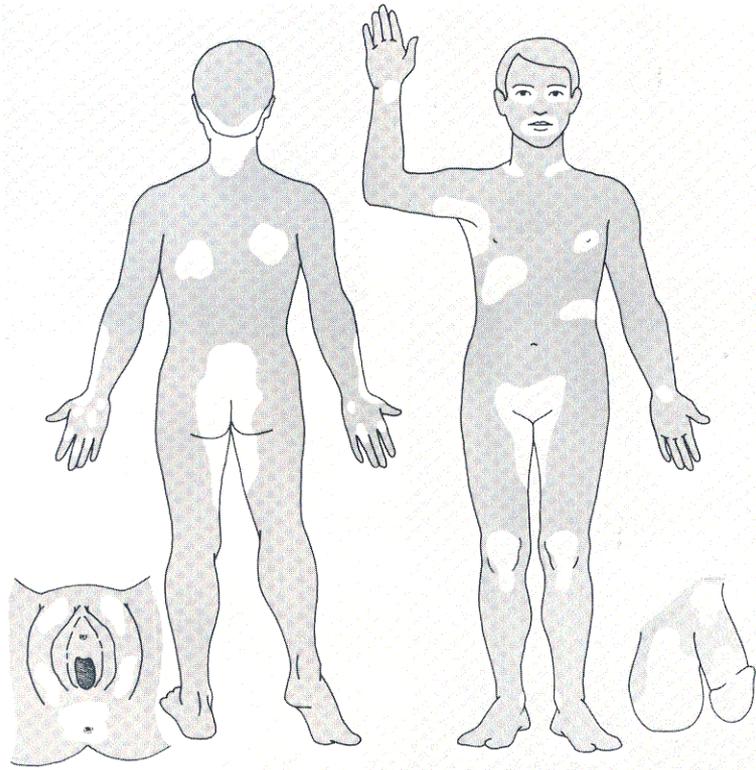
Pulse energy 2-3 mj/cm<sup>2</sup>  
Duration of pulse 30 nsec

- Some definitions
- **The concept of targeted repigmentation**
- Excimer laser treatment of vitiligo: the evidence
- Future perspectives

# Repigmentation

- Vitiligo repigmentation depends on a **viable melanocyte reservoir**
- In many patients with vitiligo repigmentation is possible when pigment cells are **stimulated** with appropriate treatment
- Melanocytes for repigmentation by medical methods arise **from three main sources**: (a) the hair follicle unit; (b) unaffected melanocytes within areas of depigmented epidermis, and (c) melanocytes located at the edge of vitiligo lesions

# Vitiligo



## Generalized

Depigmented patches on the hands, neck, genitalia, limbs, and face

## Segmental

Unilateral distribution (Blascko lines)

## Focal vitiligo

# Stigma

(After E. Goffman, 1963)

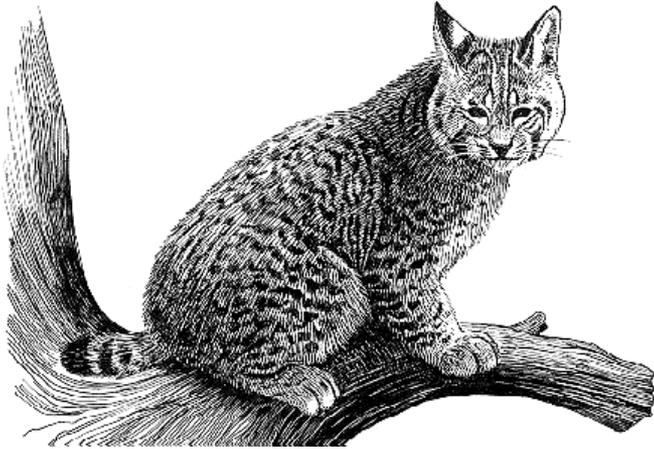
A **physical mark** that would be placed on a person to signify them as **deviant**, such as branding of slaves.

Today stigma refers to the **social marks** that are defined as undesirable and deviant. They range from physical disability to perceived weaknesses

Intrinsic in the discussion of stigma is the issue of deviance.

“Veste quae ex duobus texta est, non indueris” (Leviticus, 19,19)

*“Clothes which are made of two different materials are not allowed”*



**Ed ecco quasi al cominciar dell'erta  
una lonza leggera e presta molto  
che di pel maculato era coperta...**

**(Dante, Divina Commedia, canto 1)**

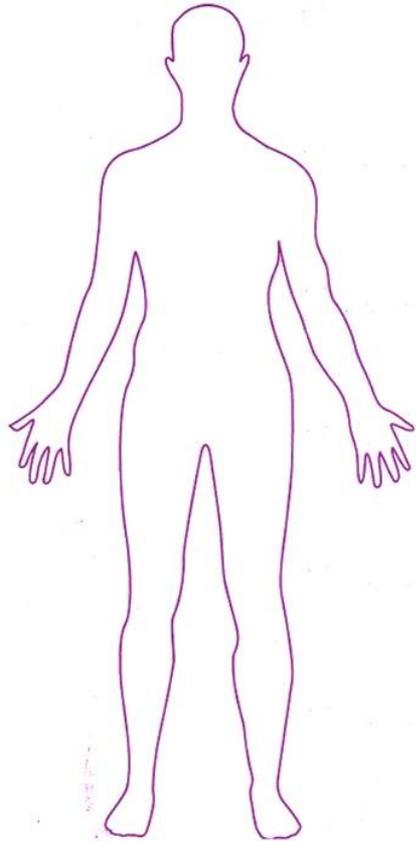


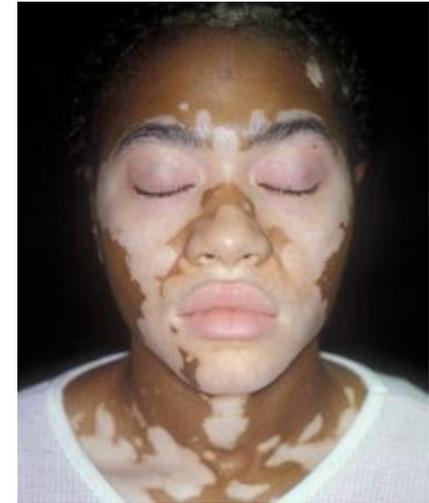
Spotted surfaces or animal coats, has been associated since Medioeval age, in Western countries, with the idea of impurity or disease

(M. Pastoreau, 1991)









Xenon, pulsed light laser

Targeting vitiligo areas

Avoiding tanning  
nonaffected areas

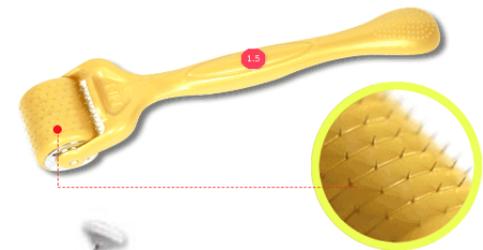
# ORS melanocyte transferral

Extraction of outer-roototh sheet (ORS) melanocytes

Suspension in isotonic saline solution

Pre-treatment of target site by microneedling

Transferral of ORS melanocyte suspension to target site



---

# **Repigmentation by Outer-Root-Sheath-Derived Melanocytes: Proof of Concept in Vitiligo and Leucoderma**

Wolfgang Vanscheidt<sup>a</sup> Thomas Hunziker<sup>b</sup>

<sup>a</sup>Dermatologische Gemeinschaftspraxis, Freiburg, Germany; <sup>b</sup>Department of Dermatology, University of Bern, Bern, Switzerland

# Guideline for the diagnosis and management of vitiligo

D.J. Gawkrödger, A.D. Ormerod, L. Shaw, I. Mauri-Sole, M.E. Whitton,\*† M.J. Watts, A.V. Anstey, J. Ingham‡ and K. Young‡

British Association of Dermatologists, 4 Fitzroy Square, London W1T 5HQ, U.K.

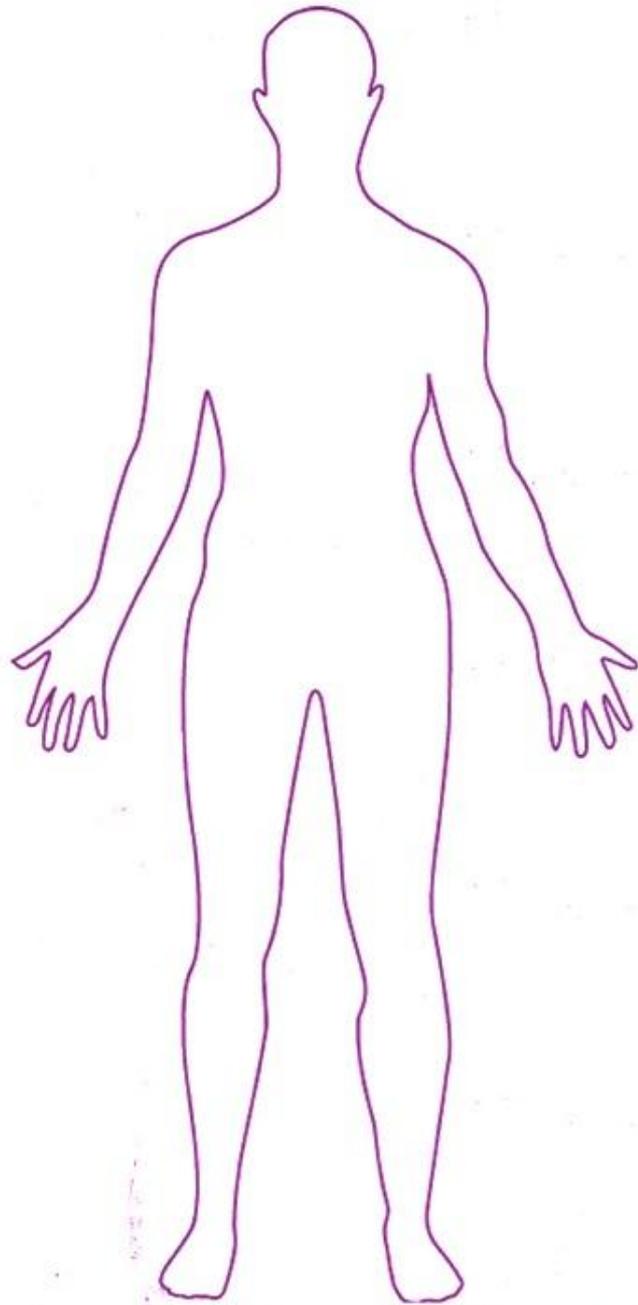
\*Vitiligo Society, 125 Kennington Road, London SE11 6SF, U.K.

†Cochrane Skin Group, Centre of Evidence Based Dermatology, King's Meadow Campus, University of Nottingham NG7 2NR, U.K.

‡Royal College of Physicians, St Andrew's Place, Regent's Park, London NW1 4LE, U.K.

# Recommended treatments

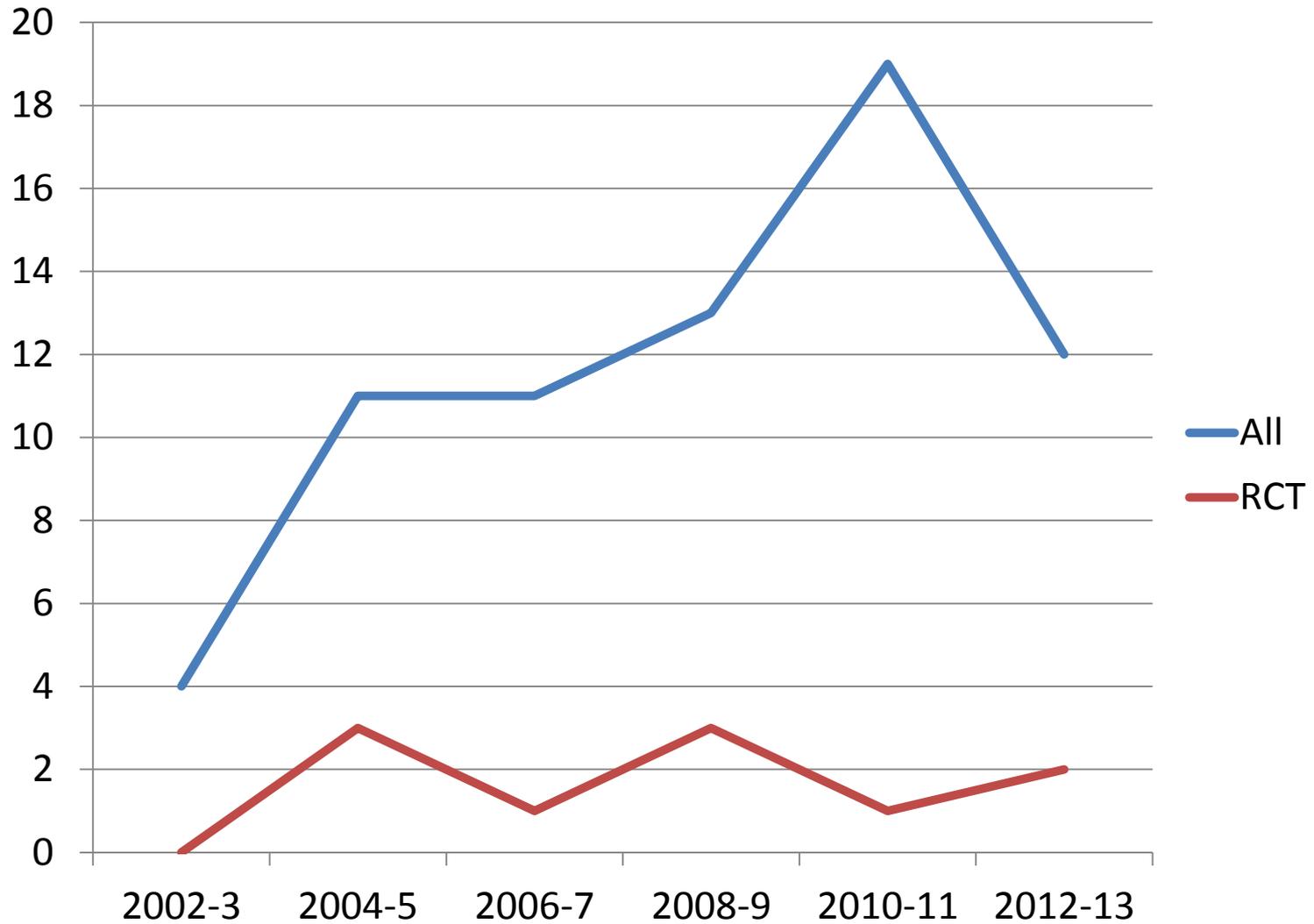
- Topical corticosteroids or topical calcineurin inhibitors
- Narrow-band UVB better than PUVA



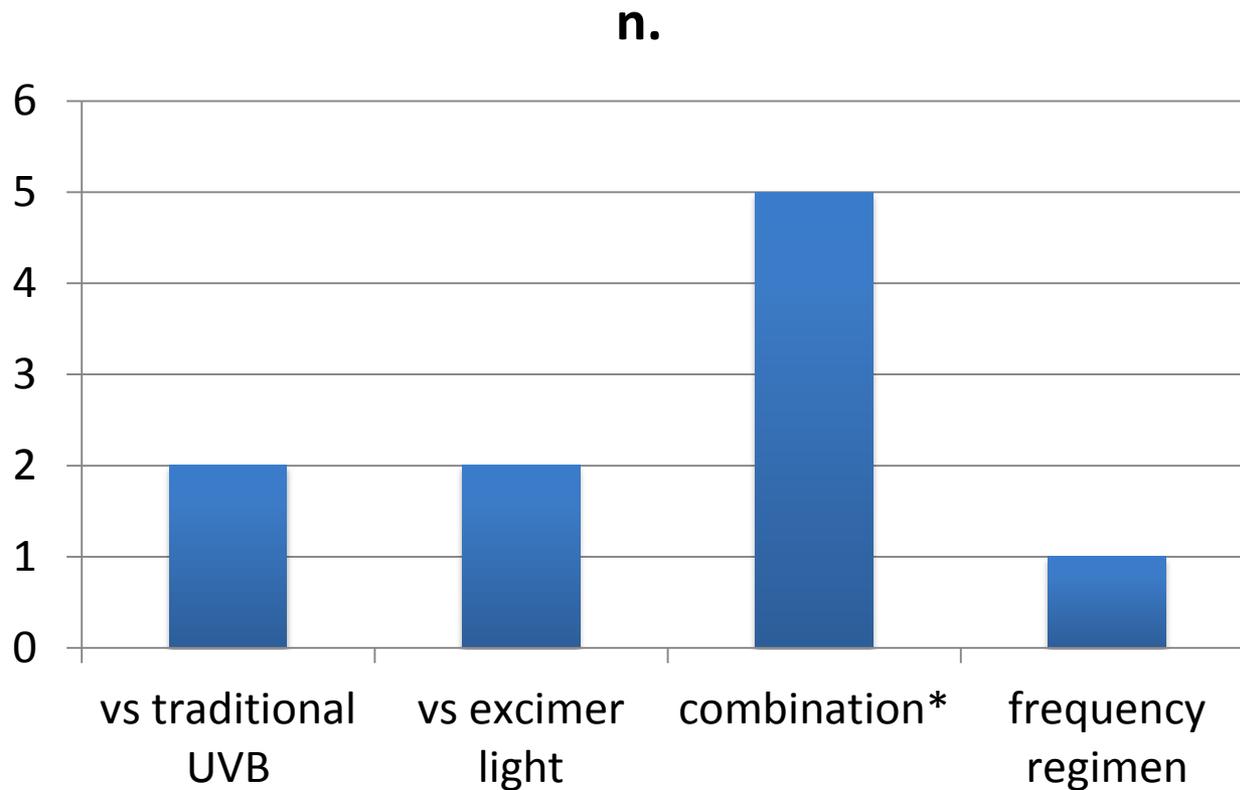


- Some definitions
- The concept of targeted repigmentation
- **Excimer laser treatment of vitiligo: the evidence**
- Future perspectives

# Clinical studies on excimer laser in vitiligo (PubMed search 2001-2013)



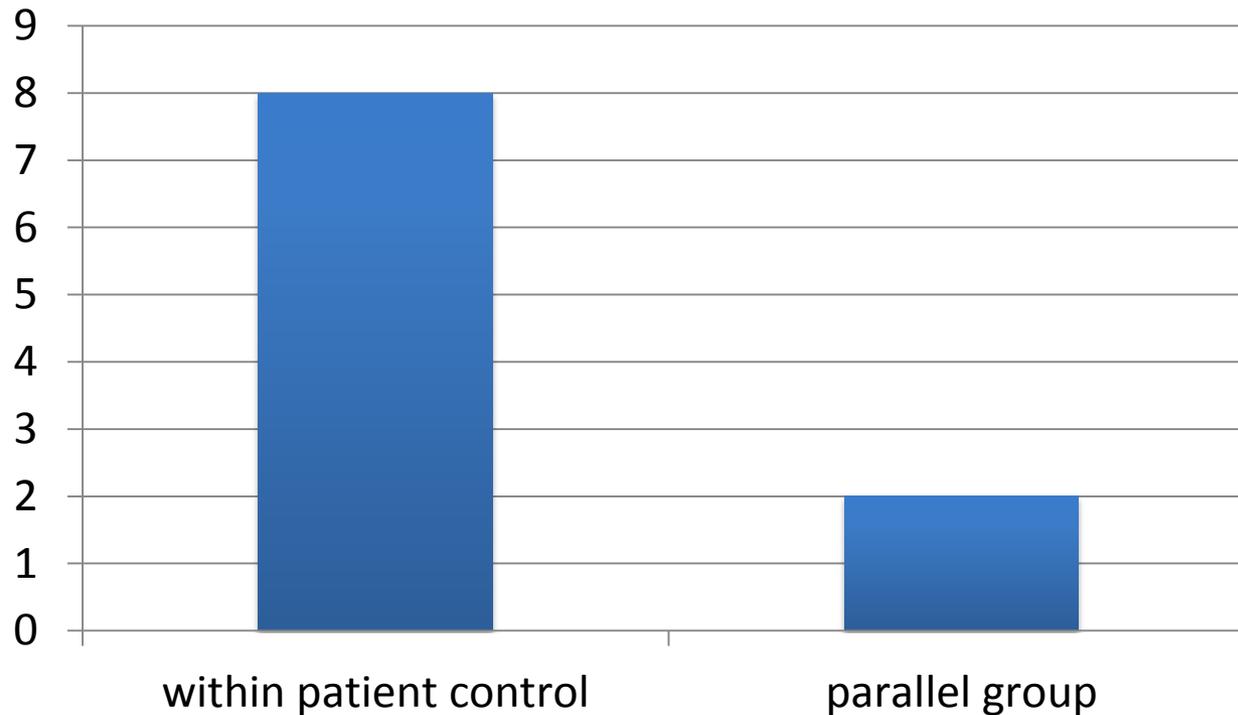
# Distribution of RCTs on excimer laser in vitiligo by study focus (PubMed search 2001-2013)



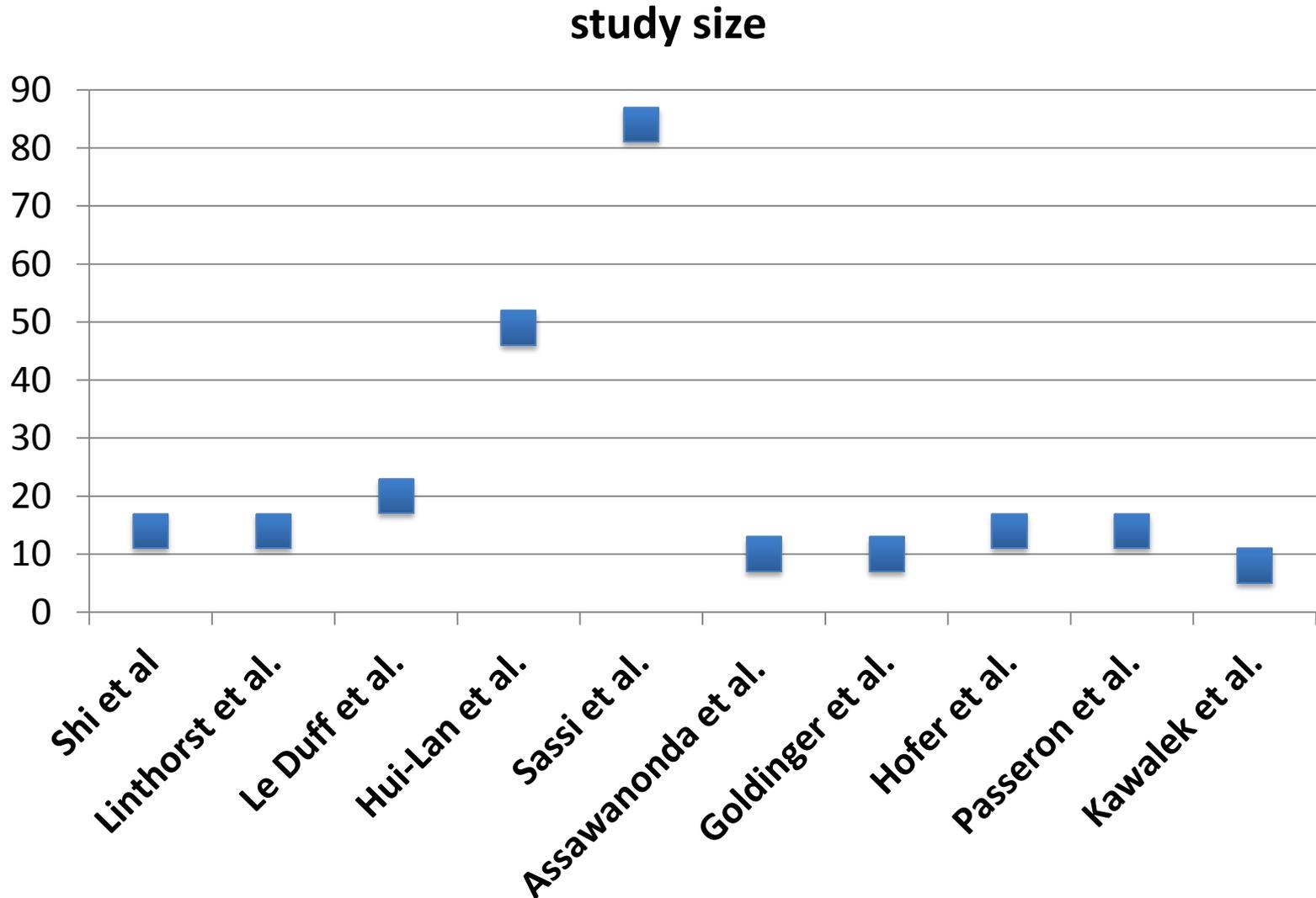
\* Combination regimens included: topical steroid (1), tacrolimus (2), pimecrolimus (1), calcipotriol (1)

# Distribution of RCTs on excimer laser in vitiligo by study design (PubMed search 2001-2013)

**n.**



# Sample size in the RCTs analysed (PubMed search 2001-2013)



# Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck

F. Sassi,\* S. Cazzaniga,\*† G. Tessari,‡ L. Chatenoud,§ A. Reseghetti,¶ L. Marchesi,¶ G. Girolomoni‡ and L. Naldi\*¶

\*Centro Studi GISED and ¶Department of Dermatology, Ospedali Riuniti, 24100 Bergamo, Italy

†Department of Mathematics, University of Milan, Italy

‡Department of Dermatology, University of Verona, Italy

§Unit of Analytic Epidemiology, Mario Negri Institute for Pharmacological Research, Milan, Italy

British Journal of Dermatology 2008 **159**, pp1186–1191

# Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck

F. Sassi,\* S. Cazzaniga,\*† G. Tessari,‡ L. Chatenoud,§ A. Reseghetti,¶ L. Marchesi,¶ G. Girolomoni‡ and L. Naldi\*¶

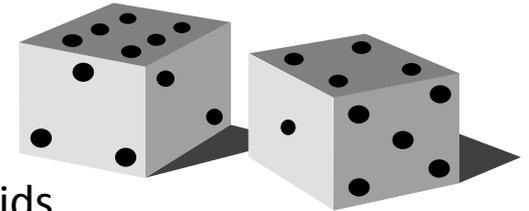
**Study design:** parallel group randomised trial

**Treatment arms:** excimer laser vs excimer laser plus topical steroids

**Inclusion criteria:** stable vitiligo on the face or neck

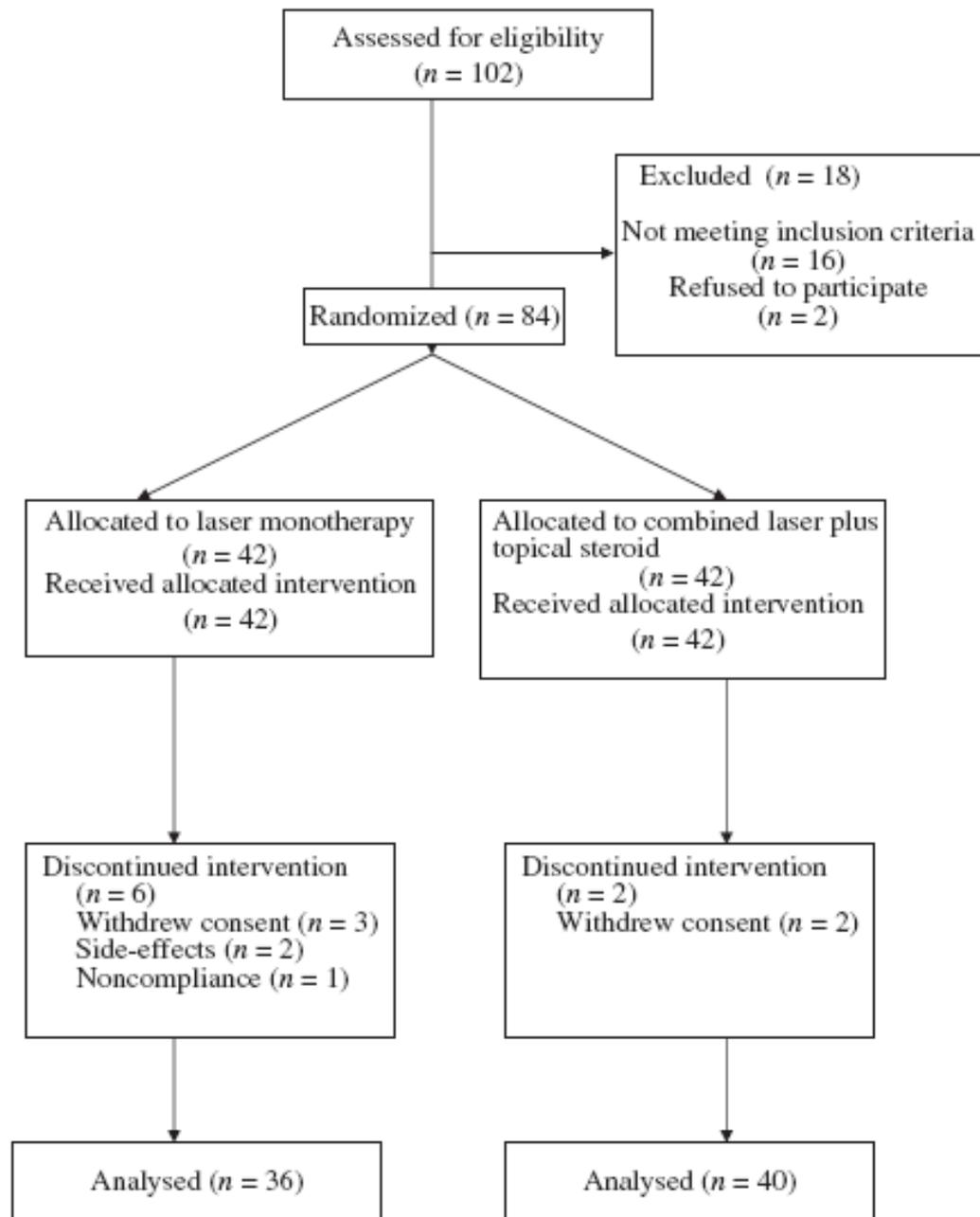
**Sample size:** 84 patients

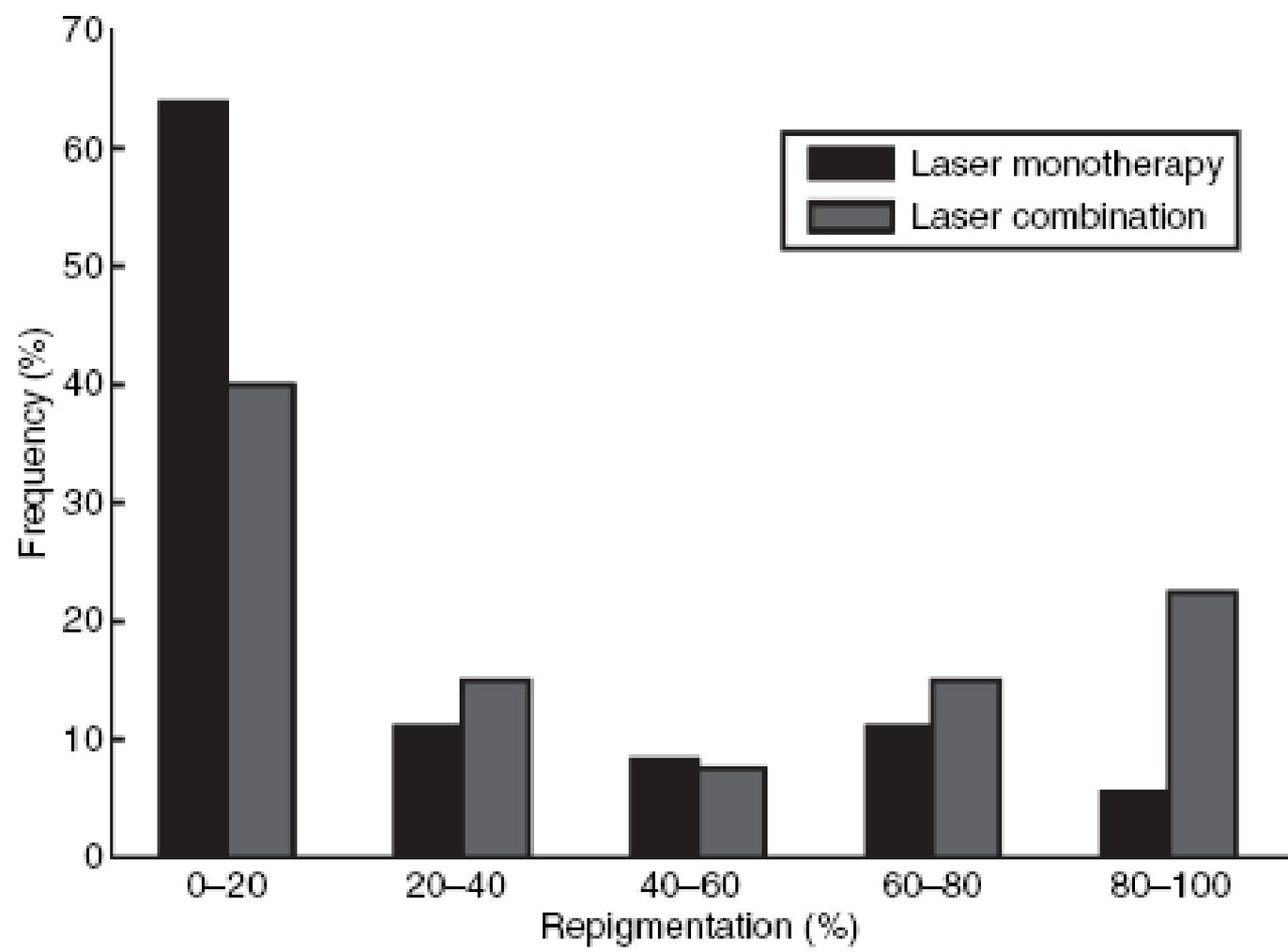
**Outcome measures:** repigmentation as assessed on UV-light reflected photographs  
Physician's Global Assessment (PGA)  
Skindex-29 scores variations



# Entry criteria

- Age 18-75 years
- Vitiligo present since at least 6 months
- Lesions on the face and/or neck, exclusion of segmental vitiligo
- Lack of response to UVB or PUVA (at least 16 weeks of continuous treatment)
- Withdrawal of any topical agent since at least 15 days





## Quality of life

Quality of life indices improved to a similar extent in the two treatment groups. The values of the composite score at entry were 19.4 (SEM 2.53) in the laser monotherapy group and 23.1 (SEM 2.8) in the combination group. At the end of the treatment course, values decreased to 14.2 (SEM 2.5) and 18.7 (SEM 2.5), respectively (Mann–Whitney U-test for between-group comparison,  $P = 0.27$ ).

No significant differences were found between groups for any of the Skindex-29 subscales. Overall, variations were ) 0.50 (SEM 1.2) for symptoms, ) 7.5 (SEM 1.1) for emotion, and ) 2.08 (SEM 0.7) for social functioning subscales.

---

# **Prediction of Clinical Response to Excimer Laser Treatment in Vitiligo by Using Neural Network Models**

Simone Cazzaniga<sup>a</sup> Fabrizia Sassi<sup>a</sup> Santo Raffaele Mercuri<sup>b</sup> Luigi Naldi<sup>a,c</sup>

**Parametri clinici**

Dimensione lesione [3% 17%] ▾

Sede Lati viso ▾

Trattamento con cortisone Sì ▾

Sesso M ▾

Età 30

Altezza (cm) 175

Colore occhi Scuri ▾

Colore capelli Scuri ▾

Fototipo abbastanz... ▾

Consumo alcolici No ▾

Fumatore No ▾

Parenti con vitiligine No ▾

N° anni insorgenza generale 15

N° anni insorgenza sede 10

Tipologia vitiligine Generalizz... ▾

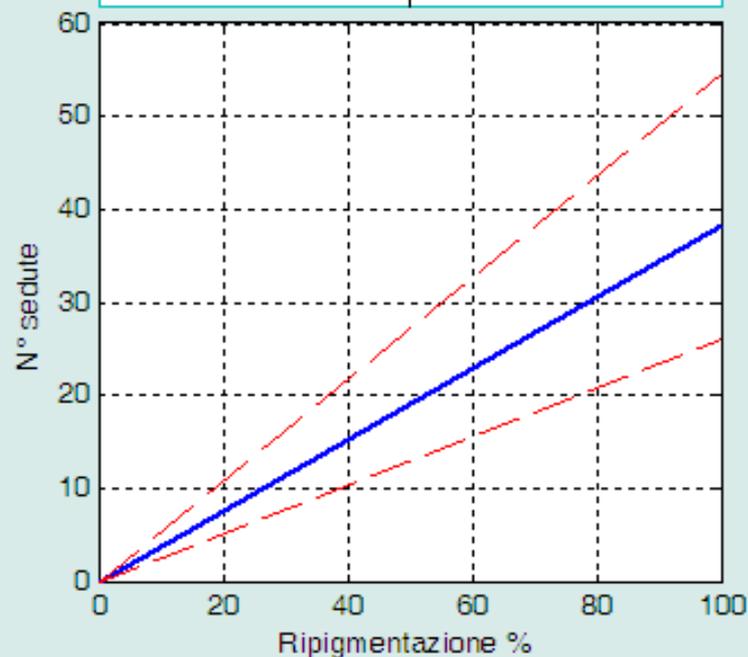
Malattie autoimmuni No ▾

**Calcola**

**Stampa**

Nome paziente

Ripigmentazione %	N° sedute	
25	10	[7 - 14]
50	19	[13 - 27]
75	29	[20 - 41]
100	38	[26 - 55]



Hui-Lan Y, et al. Combination of 308-nm excimer laser with topical pimecrolimus for the treatment of childhood vitiligo.

Pediatr Dermatol. 2009;26:354-6.

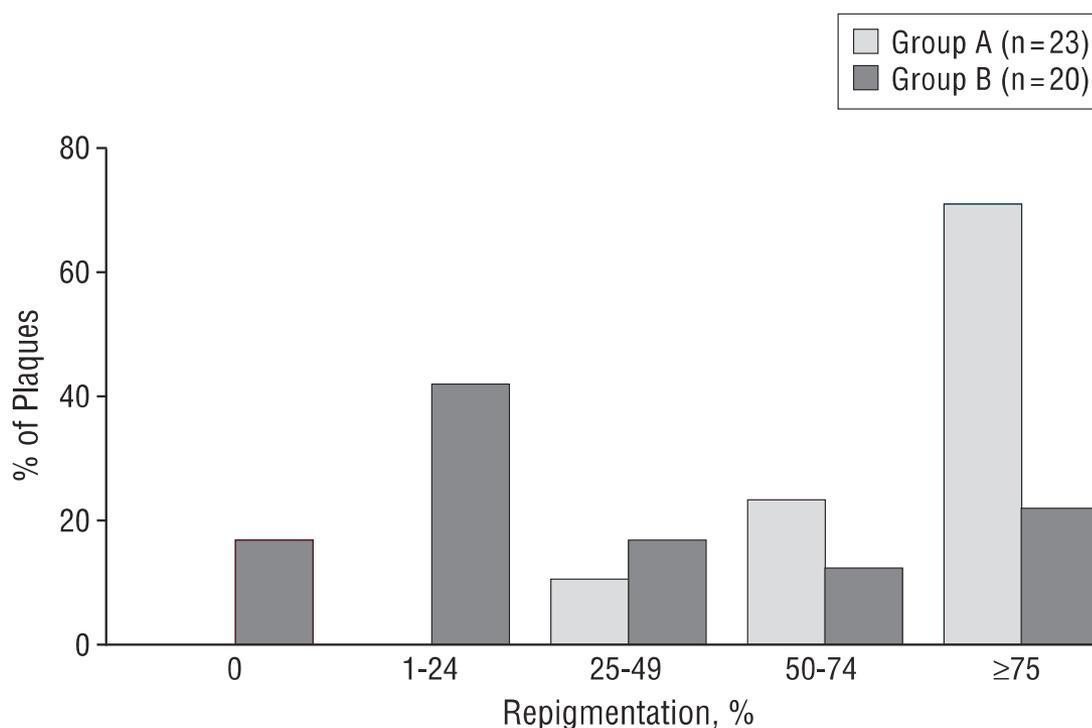
- Single-blinded, randomized trial
- 308-nm excimer laser therapy plus topical 1% pimecrolimus cream twice daily (group A) vs excimer laser therapy twice per week alone (group B)
- Forty-nine patients enrolled, and 48 patients evaluated
- After 30 weeks of treatment, 71% of patients from group A achieved Grade 3 or 4 repigmentation compared with 50% in group B ( $p = 0.001$ ).

# Topical Tacrolimus and the 308-nm Excimer Laser

## *A Synergistic Combination for the Treatment of Vitiligo*

Thierry Passeron, MD; Nima Ostovari, MD; Wassim Zakaria, MD; Eric Fontas, MD;  
Jean-Claude Larrouy, MD; Jean-Philippe Lacour, MD; Jean-Paul Ortonne, MD

*Arch Dermatol.* 2004;140:1065-1069



**Forteen patients  
4-10 target lesions per  
patient**

**Within patient control**

**Group A:** combination of  
308-nm excimer laser and  
0.1% tacrolimus

**Group B:** 308-nm excimer  
laser monotherapy.

Goldinger SM, et al. Combination of 308-nm xenon chloride excimer laser and topical calcipotriol in vitiligo. J Eur Acad Dermatol Venereol. 2007;21:504-8.

- Within patient control study
- Ten patients with vitiligo with bilateral symmetrical lesions
- All patients received 308-nm XeCl excimer laser therapy three times weekly. Calcipotriol ointment was applied to lesions on one side of the body twice daily.
- After 24 treatments (8 weeks), nine patients were evaluated. Eight patients showed evidence of repigmentation on both body sides, with no significant difference

ORIGINAL ARTICLE

# **A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients**

M.W. Linthorst Homan,<sup>†,‡</sup> Ph. I. Spuls,<sup>‡</sup> L. Nieuweboer-Krobotova,<sup>†,‡</sup> J. de Korte,<sup>‡</sup> M.A.G. Sprangers,<sup>§</sup> J.D. Bos,<sup>‡</sup> A. Wolkerstorfer,<sup>†,‡</sup> J.P.W. van der Veen<sup>†,‡,\*</sup>

*JEADV* 2012, 26, 690–695

ORIGINAL ARTICLE

# **A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients**

M.W. Linthorst Homan,<sup>†,‡</sup> Ph. I. Spuls,<sup>‡</sup> L. Nieuweboer-Krobotova,<sup>†,‡</sup> J. de Korte,<sup>‡</sup> M.A.G. Sprangers,<sup>§</sup> J.D. Bos,<sup>‡</sup> A. Wolkerstorfer,<sup>†,‡</sup> J.P.W. van der Veen<sup>†,‡,\*</sup>

**Study design:** within patient control study

**Treatment arms:** excimer laser vs NB UVB after skin grafting

**Inclusion criteria:** symmetrical vitiligo patches on extremities

**Sample size:** 16 (lost to follow-up 2)

**Outcome measures:** repigmentation as assessed on photographs by image analysis  
patient satisfaction and patient preferences

## ORIGINAL ARTICLE

# A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients

M.W. Linthorst Homan,<sup>†,‡</sup> Ph. I. Spuls,<sup>‡</sup> L. Nieuweboer-Krobotova,<sup>†,‡</sup> J. de Korte,<sup>‡</sup> M.A.G. Sprangers,<sup>§</sup> J.D. Bos,<sup>‡</sup> A. Wolkerstorfer,<sup>†,‡</sup> J.P.W. van der Veen<sup>†,‡,\*</sup>

	Gender M/F	Age	Treated lesion	Skin type (I–VI)	Repigmentation after excimer laser (%)	Repigmentation after NB-UVB (%)	Cumulative doses EL (J/cm <sup>2</sup> )	Cumulative doses NB-UVB (J/cm <sup>2</sup> )	Difference in cumulative doses (J/cm <sup>2</sup> )	Patient satisfaction EL	Patient satisfaction NB-UVB	Treatment preference
1	F	18, 5	Arms	V	84	95	9.45	29.47	20.02	Very good	Very good	Excimer
2*	F	18, 8	Trunk	IV	82	95	5.69	16.73	11.04	Rather good	Very good	None
3	F	48, 9	Arms	IV	56	53	2.30	8.52	6.22	Rather good	Very good	NB-UVB
4	F	52, 9	Arms	IV	11	17	3.29	14.41	11.12	Not good – Not bad	Good	None
5	M	37, 9	Feet	IV	1	5	13.97	49.31	35.34	Bad	Rather good	NB-UVB
6†	F	63, 8	Legs	IV	65	93	10.67	33.24	22.57	Rather good	Good	NB-UVB
7	F	42, 7	Legs	II	2	44	8.91	37.75	28.84	Bad	Good	NB-UVB
8	M	54, 1	Trunk	V	59	51	2.94	13.23	10.29	Very good	Very good	None
9	M	45, 5	Feet	IV	6	4	10.50	36.17	25.67	Bad	Bad	None
10	F	62, 1	Trunk	III	22	39	4.41	14.11	9.70	Good	Good	None
11	F	27, 1	Trunk	II	15	12	5.20	23.68	18.48	Not good – Not bad	Not good – Not bad	NB-UVB
12	M	69, 1	Legs	II	17	19	10.25	34.05	23.80	Good	Good	Excimer
13	M	50, 0	Legs	IV	5	7	6.56	23.83	17.27	Rather bad	Rather good	NB-UVB
14	F	27, 0	Feet	IV	5	4	8.40	23.90	15.50	Not good – not bad	Not good – not bad	NB-UVB
Mean (SD)							7.32 (3.50)	25.60 (11.62)	18.27 (8.34)			

ORIGINAL ARTICLE

## **Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study**

Qiong Shi\*, Kai Li\*, Jun Fu, Yanchun Wang, Cuiling Ma, Qiang Li, Chunying Li & Tianwen Gao

*Photodermatol Photoimmunol Photomed* 2013; 29: 27–33

A randomized within patient control trial

Fourteen subjects with 48 symmetrical vitiligo lesions were enrolled

One lesion was treated with the 308-nm excimer laser, and its counterpart was treated with the 308-nm excimer lamp.

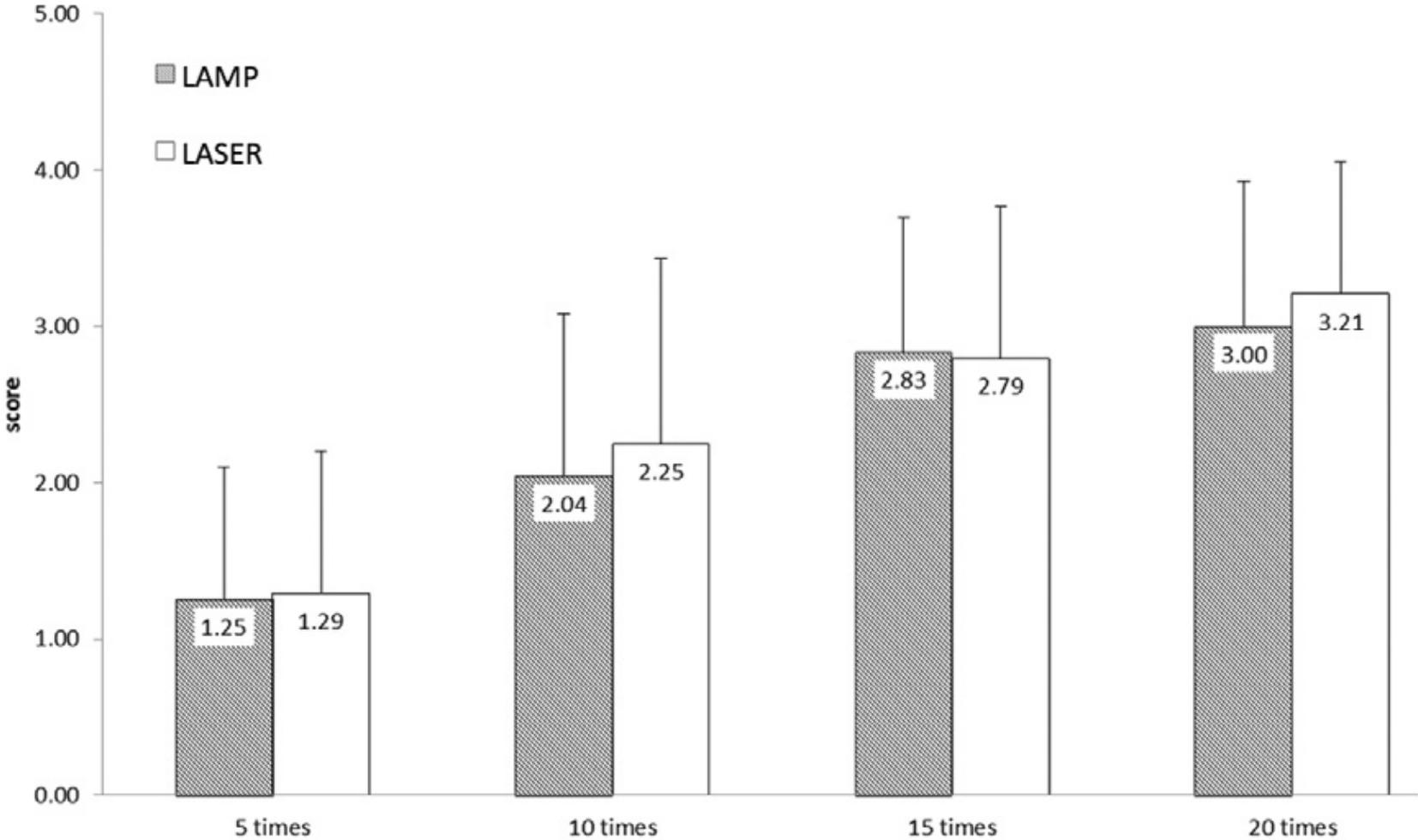
Lesions were treated three times a week with the same dose on both sides for a total of 20 sessions.

# Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study

**Table 2.** Treatment response

ID	Site	Repigmentation grade							
		308-nm excimer laser				308-nm excimer lamp			
		×5	×10	×15	×20	×5	×10	×15	×20
001	Breast	3	4	4	4	1	2	3	4
001	Perineum	1	2	3	4	0	2	3	4
002	Face	1	1	3	4	1	2	3	4
002	Neck	1	2	2	3	1	1	3	4
003	Neck	3	3	4	4	1	2	3	4
004	Chest	0	1	2	3	1	1	3	4
005	Breast	1	1	2	2	1	1	3	4
006	Chest	4	4	4	4	2	4	4	4
006	Back	1	4	4	4	4	4	4	4
006	Ear	2	4	4	4	2	2	3	3
007	Face	1	2	2	2	1	1	2	2
007	Arm	1	2	2	3	1	2	2	3
008	Face	1	2	4	4	1	2	4	4
009	Abdomen	1	2	3	3	1	2	3	4
010	Neck	1	2	2	3	1	2	2	3
010	Wrist	0	1	1	1	0	1	1	1
011	Neck	1	4	4	4	2	3	4	4
011	Lip	1	2	2	2	1	2	2	2
012	Breast	1	4	4	4	1	4	4	4
013	Perineum	2	3	3	4	3	4	4	4
014	Chest	1	1	2	2	1	1	2	3
014	Neck	1	1	2	3	1	1	2	3
014	Abdomen	1	1	2	3	1	2	2	3
014	Axilla	1	1	2	3	1	1	2	3

# Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study



# Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients

A. Hofer,\*† A.S. Hassan,\* F.J. Legat,\*† H. Kerl\*† and P. Wolf\*†

Departments of \*Photodermatology and †Dermatology, Medical University Graz, Auenbruggerplatz 8, A-8036 Graz, Austria

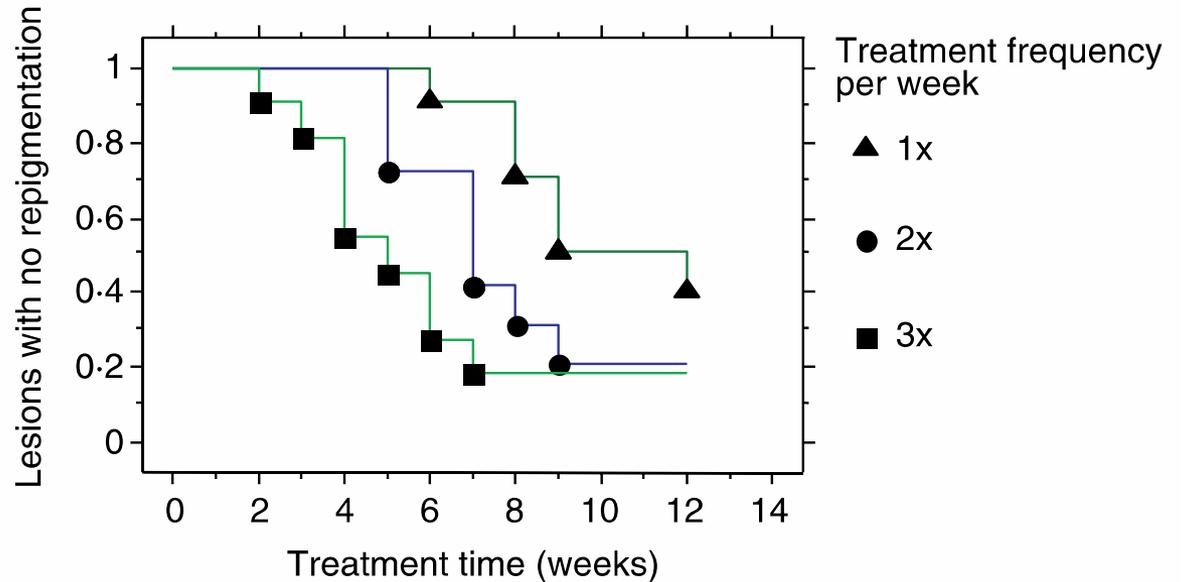
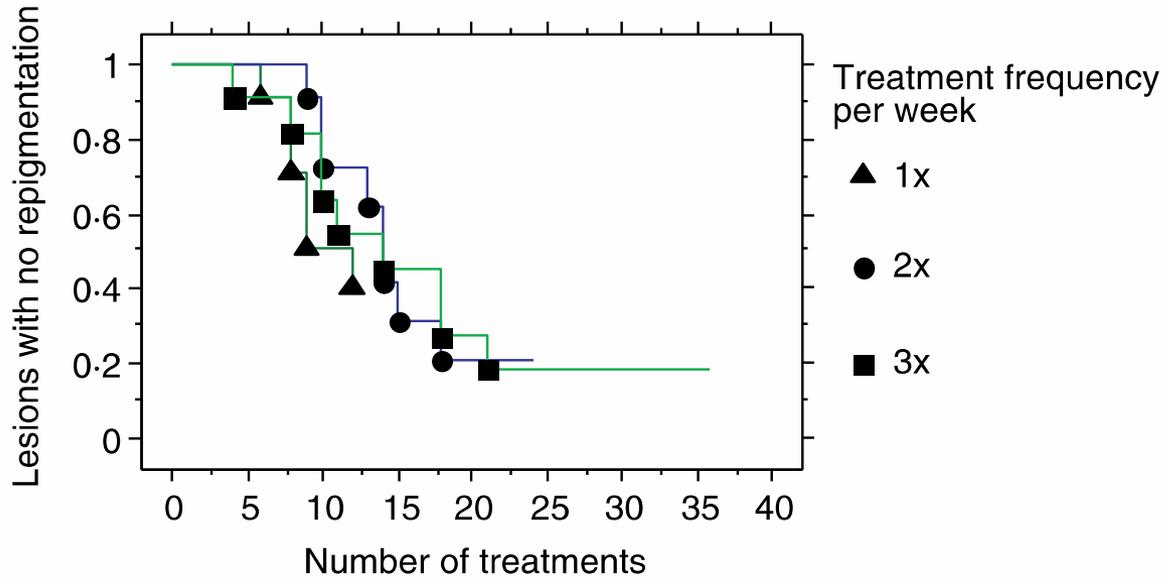
## Within patient control study of 14 patients

Each patient had **at least three stable vitiligo lesions** in the same body area. The three stable vitiligo lesions in each subject were randomly assigned to receive excimer laser treatment once, twice, and three times weekly

The initial ultraviolet (UV) dose was 50 mJ per square centimeter. The UV dose was increased at each treatment session according to the erythematous response to the previous treatment

**Thirteen** subjects were treated **for at least 6 weeks**; **seven** were treated **for all 12 weeks**.

# Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients





## Summary of the evidence

- Excimer laser may represent an option as a targeted therapy of vitiligo in photosensitive areas (face, neck)
- There is no indication that excimer laser is superior to targeted NB-UVB or excimer lamp
- Combination with topical steroids (or calcineurin inhibitors) offers better results than excimer laser alone
- Excimer laser achieves clinical response with less cumulative UV dose than NB-UVB
- There is an obvious need to improve study quality



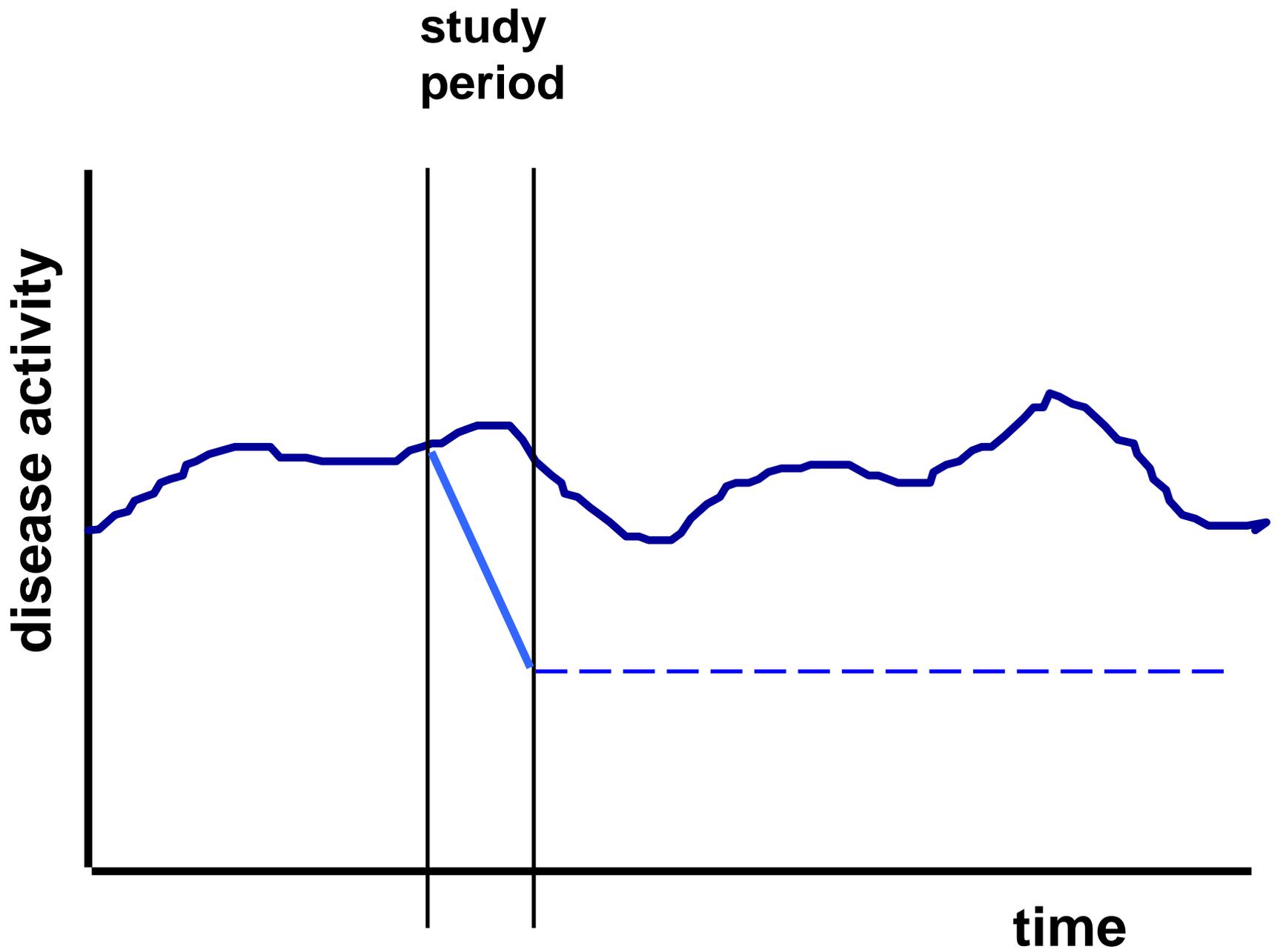
- Some definitions
- The concept of targeted repigmentation
- Excimer laser treatment of vitiligo: the evidence
- **Future perspectives**

# Pragmatic trials (1)

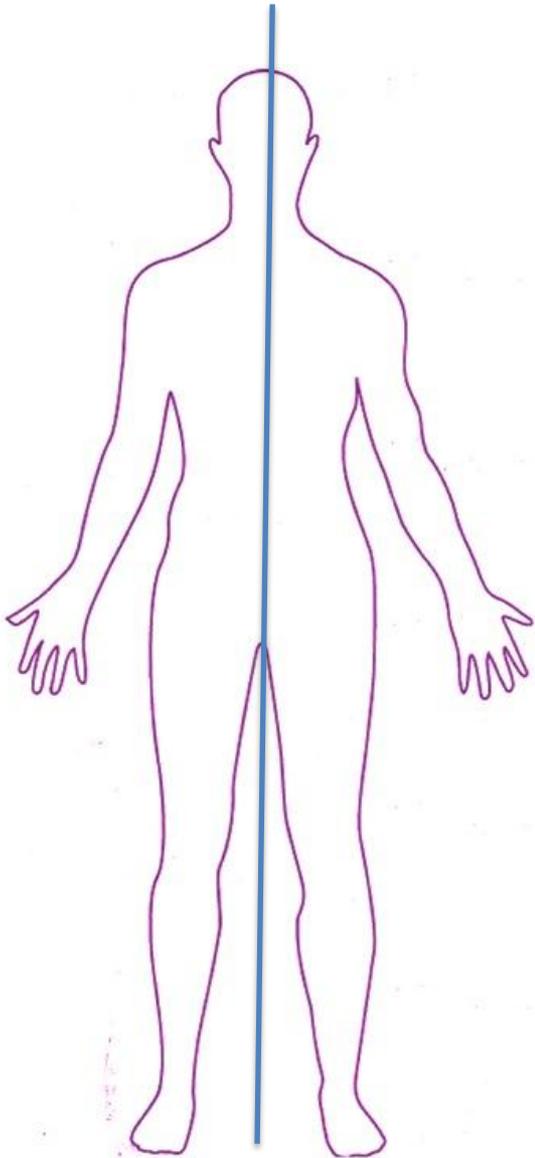
- Targeted therapy vs nontargeted therapy (total body NB-UVB vs excimer laser on limited areas)
- Combination therapies (topical steroids, ORS melanocytes)
- Home therapy vs hospital-based therapies (with excimer lamp)
- Early treatment

# Pragmatic trials (2)

- Adequate time frame to assess persistence of response and relapse rates
- Outcome: patient preferences and quality of life
- Sample size issue and negative results
- Combination with epidemiologic approaches: assessment of predictors of response



## Drawbacks of within patient control studies



- Cumbersome
- Not realistic manouuvres, artificial conditions
- Problems with withdrawals
- Only short term assessment

# Vitiligo Care *concept*

- **Census** of therapeutic offer in the country
- Definition of **standards of care**
- Establishment of a **disease network** with **reference centres**
- Development of **RCTs**, **outcome studies** and **monitoring of quality of care**



# UNITED COLORS OF VITILIGO