308 nm Excimer laser and lamp phototherapy in Vitiligo and new indications

Klaus Fritz, MD, PHD
Dermatology and Laser Centers Landau (D)
President European Society of Laser dermatology
Associate Professor (inv.). University Bukarest (Ro)
Consultant and lecturer at universities Bern (CH) and Osnabrueck (D)
Assoc. Visiting Prof. University hospital Tokuda, Sofia (BG)
Excimer Xtrac laser
monochromatic

Broad band light sources:
Waldmann UV 21 and UV lamp

290–320 nm with peak
Excimer Laser

X Trac laser “Ultra”

308nm, 30 nsec, XeCl Gas:
Spot Size: 4 cm²
Fiberoptic Laser Delivery:

V Trac lamp
Excimer laser compared to broad band light sources

Less erythema,
less hyperpigmentation,
better improvement
with monochromatic laser wavelength

Excimer MED  Same Joules  Light source MED

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<table>
<thead>
<tr>
<th></th>
<th>XTRAC® (Laser)</th>
<th>VTRAC™ (Lamp)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wavelength</strong></td>
<td>308nm</td>
<td>Same ± 2nm</td>
</tr>
<tr>
<td><strong>Output</strong></td>
<td>Pulsed laser</td>
<td>Continuous lamp</td>
</tr>
<tr>
<td><strong>Minimal Erythema Dose</strong></td>
<td>Erythema at 18-27% lower dose with VTRAC than with XTRAC</td>
<td></td>
</tr>
<tr>
<td><strong>Psoriasis Expected Tx to get 75-100% clear</strong></td>
<td>6-10</td>
<td>8-13*</td>
</tr>
</tbody>
</table>
Laser assisted therapy of **vitiligo**
with and without melanocyte transplantation

Skin type 3: before and after 16 sessions,
starting 100 mJ – end 700 mJ
Vitiligo Therapy according to guidelines

- Potent topical steroid
- Camouflaging cosmetics
- Topical pimecrolimus or tacrolimus
- Depigmentation with p-(benzyloxy)phenol (MBEH)

Psoralen with ultraviolet A (PUVA) therapy
Narrowband UVB phototherapy

Skin-grafting
- Autologous epidermal suspension applied to laser-abraded lesions
- Expanding the autologous cells in tissue culture prior to grafting
- Transfer of suction blisters

Guideline for the diagnosis and management of vitiligo.


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Modern therapeutic options include treatment with topical immunomodulators (tacrolimus, pimecrolimus), analogues of vitamin D3, excimer laser and surgery/transplantation.
UV in Vitiligo - Mechanism of action

not completely elucidated
active melanocytes in epidermis are destroyed,
inactive (dopanegative) melanocytes in the outer root sheaths of hair follicles are not affected.

Repigmentation is initiated by activation, proliferation and migration of these
UV Increases fibroblast growth factor and endothelin-1 from keratinocytes
Migration stimulated by increased expression of matrix metalloproteinase-2 activity from melanocytes
Immunosuppressive activity

Klaus FRITZ - Germany
• UV B 308 nm targets T-cell infiltrates in the epidermis and dermis is more effective than UV B 311nm
• Penetrates as deep as PUVA

308 nm Laser

CD3+ T Cells
CD3+ T Cells
CD8+ T Cells

psoriatic skin after monochromatic excimer light therapy is associated with significant T-cell depletion and alterations of apoptosis-related molecules.
psoriatic skin after monochromatic excimer light therapy is associated with significant T-cell depletion and alterations of apoptosis-related molecules

Expression of Ki-67 before and after Excimer

Klaus FRITZ - Germany
<table>
<thead>
<tr>
<th>Starting Dosage for</th>
<th>Mj / cm² MED Multiplier Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periocular</td>
<td>100mj or (1-1)</td>
</tr>
<tr>
<td>Face, Scalp, Ear, Neck, Axilla Bikini</td>
<td>150mj or (2-1)</td>
</tr>
<tr>
<td>Arm, Leg, Trunk</td>
<td>200mj or (3-1)</td>
</tr>
<tr>
<td>Wrist</td>
<td>250mj or (4-1)</td>
</tr>
<tr>
<td>Elbow</td>
<td>300mj or (5-1)</td>
</tr>
<tr>
<td>Knee</td>
<td>350mj or (6-1)</td>
</tr>
<tr>
<td>Hands, Feet</td>
<td>400mj or (3-2)</td>
</tr>
<tr>
<td>Finger, Toes</td>
<td>600mj or (5-2)</td>
</tr>
</tbody>
</table>
Friedman Tx Protocol for Vitiligo

Protocol

Erythema <24 hour increase by 50mj

**Erythema 24-48 hours** = This is the “Optimum” Treatment fluence should be kept at same fluence as previous treatment

Erythema 48-60 hours decrease by 50 mj

Erythema 60-72 hours Treatment should be postponed

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Excimer in Vitiligo

Sessions are performed 2 - 3 times/week a week for 4 - 36 weeks.

Repigmentation faster with 3x/week

Rate of repigmentation depends on total numbers of sessions

Repigmentation > 75% usually in 15% - 50%
Results of excimer laser and lamp in vitiligo - according to clinical studies -

Most of the studies use a four score system to evaluate repigmentation

<table>
<thead>
<tr>
<th>Score 1</th>
<th>1-25% repigmentation</th>
<th>Score 2</th>
<th>26-50% repigmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 3</td>
<td>51-75% repigmentation</td>
<td>Score 3</td>
<td>76-100% repigmentation</td>
</tr>
</tbody>
</table>
Excimer results

63 Patients, 2x/week, 30 tx,

61.4% achieved >75% Repigmentation,
9.1% 51–75% Repigmentation,
22.7% 26–50% Repigmentation,
6.8% 1–25% Repigmentation.

Repigmentation and duration of vitiligo ≤ 2 years : 100.0%
>2 years : 46.2% (P<0.05).
Repigmentation in korean patients skin type 3 or 4

- 50% of lesions 51-75% = score 3,
- 12.5% show >75% = score 4

80% of improving lesions are located on the face
best result after
- 6 months for head and neck
- 8 months for extremities.
>75% repigmentation in

- 20.7%  (Alotaibi et al)
- 29%    (Esposito et al)
- 33%    (Atul et al)
- 61.4%  (Xiu-Yung et al)
Complete repigmentation in

- 7% (Suhyun et al)
- 25% (Suhail Hadi et al)
The result of vitiligo treatment with 308nm Excimer Laser - Face

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The result of vitiligo treatment with 308nm Excimer Laser - Neck
The result of vitiligo treatment with 308nm Excimer Laser - Trunk

Courtesy Kwang Ho Choi, Seoul, Korea
The result of vitiligo treatment with 308nm Excimer Laser - Neck
The result of vitiligo treatment with 308nm Excimer Laser - Trunk

Courtesy Kwang Ho Choi, Seoul, Korea
Excimer result and skin type

better outcome in patients with darker skin (type III-VI vs I-II)
Before

After 5 Treatments

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After 18 Treatments

After 29 Treatments

Courtesy David Friedman
Jerusalem
Before

After 5 Treatments

After 18 Treatments

After 29 Treatments

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Courtesy David Friedman Jerusalem
Repigmentation responding to Phototherapy in general and Excimer Laser

- **Location**
  Face does best, hands and feet worst

- **Skin type:**
  dark skin reacts better than light skin

- **Plaque size**
  Small react better than large

- **Patients history**
  New spots respond better than old ones

- **age:**
  children better than adults
### 32 Patients after 30 treatments

<table>
<thead>
<tr>
<th>location</th>
<th>number</th>
<th>More than 50 %</th>
<th>More than 75 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>face</td>
<td>24</td>
<td>76</td>
<td>72</td>
</tr>
<tr>
<td>Head/neck</td>
<td>5</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>Genital</td>
<td>4</td>
<td>75</td>
<td>50</td>
</tr>
<tr>
<td>legs</td>
<td>15</td>
<td>60</td>
<td>46</td>
</tr>
<tr>
<td>Body</td>
<td>5</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Hand/Foot</td>
<td>5</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

James M. Spencer, Robert Nossa
"Treatment of vitiligo with the 308-nm excimer laser: A pilot study" *JAAD June 2002*
Excimer results and location

Significantly better in **UV sensitive areas** face, neck, back, breast, and arm compared with **UV-resistant areas** knees, elbows, wrists, hands, ankles, and feet.

Among UV-resistant areas, knees, elbows, and wrists do better than hands, ankles, and feet.
The result of vitiligo treatment with 308nm Excimer Laser – Hands/Forearm
more frequent treatments show better results.

75% repigmentation (187 patients) in

- 0% treated every 14 days:
- 26% treated 2 times/week:
- 32% treated 3 times/week:
Structure of Repigmentation

Similar in both: NB-UVB and excimer laser-treated Groups. Most frequent repigmentation pattern: **perifollicular type**, followed by marginal, diffuse, and combined, in that order.
Vitiligo, resistant to tx since 25 years, skin type 2:
after 32 sessions of Excimer Laser
400 mJ 1x / Week

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Klaus Fritz Laserdermatologie
The result of vitiligo treatment with 308nm Excimer Laser - Trunk

Skin type 2 : 26 sessions

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- Vitiligo in childhood -

30 patients: 2x/week, 100 – 2100 mJ, 7,7 months (Pharos)

56 % improvement > 50 %
12,5 % improvement > 75 %
Best: face, neck, trunk

The 308-nm excimer laser:
- a promising device for the treatment of childhood vitiligo -.
Side effects

Minimal, usually erythema blisters and pruritus occasionally. Generally well tolerated and side
NB UVB versus Excimer laser 308 nm in vitiligo

15 patients, split body NB vs. Excimer 308 nm, 6 months 2x/week

308-nm Excimer laser more effective in Vitiligo than NB-UVB

Laser induces repigmentation earlier
Excimer laser vs Excimer lamp in vitiligo

The 308-nm excimer lamp and laser showed a similar efficacy in treating vitiligo. For the same fluence, the lamp induced more erythema suggesting photobiological differences between the two devices.
Relapse in Vitiligo
little data

- In 1 out of 9 – however data not reliable because:
- Relapse started soon after Excimer therapy was discontinued

Probably no relapse, but stop of treatment in progressive vitiligo
Combinations in Vitiligo

**Hydrocortisone:** Recalcitrant vitiligo of the face and neck may benefit from the combination (84 patients)

*In vitiligo:*
Calcipotriol + UV B no significant effects
Combination excimer laser and pimecrolimus: better

- 48 vitiligo patients, randomized, comparing
- (group A) 308-nm excimer laser + topical 1% pimecrolimus cream 2x/day with
- (group B) excimer laser therapy 2x/week
- after 30 weeks Grade 3 or 4 repigmentation achieved
- group A 71% of patients
- Group B 50% in (p = 0.001).
Combination excimer laser and tacrolimus: much better

- 0.1% tacrolimus plus 308-nm excimer laser is superior to 308-nm laser mono (P<.002).

UV sensitive > 75 % Repigmentation in 77% vs 57 % patients

In UV not sensitive:
- Excimer+tacrolimus = in 60 %
- Excimer only 0 %

The efficacy of the 308-nm excimer laser monotherapy in vitiligo also confirmed, for UV-sensitive areas.
RESULTS:

- 20 vitiliginous patches, 6 subjects

- 50% of patches 75% repigmentation

- Compared to 20% for the placebo.

- Subjects repigmented faster (19%) with combination therapy
Excimer and Khellin

Excimer 308 nm, alone and/or combined with Khellin 4% offered encouraging results and it may be considered
Stretch marks

- 10 women age 20–45 Fitzpatrick skin type 1–4 hypopigmented Striae
- 6–9 sessions: 100% showed initial repigmentation, in 70%

Repigmentation due to an increase in melanin pigment, hypertrophy of melanocytes and an increase in melanocytes.
Halo Nävus

308-nm Excimer laser can treat Halo Nevi, effectively esp. on the face

21 sessions, 80 % repigmentation, > 400 mJ
Scar management:

1. Ablation of hypertrophic areas with Er:Yag laser

2. Pulsed dye 2 tx for erythema and antiproliferation

3. Xtrac 306 nm Excimer for repigmentation
   18 tx at 300 – 400 mJ

4. Silicone gel

Courtesy KLaus Fritz (D)
postinflammatory hypopigmentations after mollusca contagiosa
Post Face Lift Scar

- 50 – 75% improvement in 10 treatments

Friedman PM, Geronemus RG, Use of 308 nm excimer laser for postresurfacing leucoderma. Arch Derm 2001;137:824-825
melanocyte transplantation +
308 nm Excimer Laser Photherpay

Needs 3 procedures
Isolation
cultivation
application
Isolation - ways of grafting

- Punch biopsy grafting
- Ultra thin skin grafting
- Excisions
- Suction blisters
- Isolation from outer root hair shafts
Our procedure anagen scalp hair follicles are plucked fermented and centrifuged in solution without cultivation onsite

5 hairs/ 1 cm \(^2\) needed

\textbf{ORS-Mc} = outer root sheath melanocytes;
1. Ablation

2. Autologous ORS epidermal melanocyte suspension applied to laser-ablated lesions
Implantation on receiving site

- Punch implants = minimal surgery
- Complete ablation bei CO2
- Suspension of cultured melanocytes
- Mesh applied cultured melanocytes
311 nm Excimer laser UV – stimulation post melanocyte transplantation

After re-epithelisation, treated areas of Vitiligo were irradiated with suberythematogenous doses of 311 nm resp 308 nm UVB 2-3 times weekly.
Maintenance: combination therapy

- Potent topical steroid
- Topical pimecrolimus or tacrolimus
- Narrowband UVB phototherapy + excimer laser
  (less effective: Psoralen with ultraviolet A (PUVA) therapy)
- Psychological interventions

Diseases reported to respond to these treatments include, but are not limited to, the following:

<table>
<thead>
<tr>
<th>Phototherapy</th>
<th>Photochemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Psoriasis</td>
<td>a) Psoriasis</td>
</tr>
<tr>
<td>b) Eczema</td>
<td>b) Mycosis fungoides</td>
</tr>
<tr>
<td>c) Photodermatoses</td>
<td>c) Vitiligo</td>
</tr>
<tr>
<td>d) Pruritus</td>
<td>d) Eczema</td>
</tr>
<tr>
<td>e) Pityriasis rosea</td>
<td>e) Photodermatoses</td>
</tr>
<tr>
<td>f) Lichen planus</td>
<td>f) Lichen planus</td>
</tr>
<tr>
<td>g) Pityriasis lichenoides</td>
<td>g) Pityriasis lichenoides</td>
</tr>
<tr>
<td>h) Acne</td>
<td>h) Parapsoriasis</td>
</tr>
<tr>
<td>i) Parapsoriasis</td>
<td>i) Pruritic eruptions of HIV infection</td>
</tr>
<tr>
<td>j) Pruritic eruptions of HIV infection</td>
<td>j) Pruritus, other causes</td>
</tr>
<tr>
<td>k) Other</td>
<td>k) Alopecia areata</td>
</tr>
<tr>
<td></td>
<td>l) Other</td>
</tr>
</tbody>
</table>

J AM ACAD DERMATOL 1994;31:643-8
Reynolds NJ, Franklin V, Gray JC, Diffey BL, Farr PM:

severe atopic eczema, well tolerated.”
308 nm excimer laser treatment of Chronic Eczema

- No improvement after topical corticosteroids
- Since 10 years

- 8 sessions of excimer laser starting with 300 mJ, end 1200 mJ
- Cumulative dose 4500 mJ

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Courtesy KLaus Fritz (D)
Seborrheic Eczema

4 sessions

200-300-300-300 mJ

Courtesy Klaus Fritz (D)
Scrotal eczema

8 sessions, 200 to 600 mJ, cumulative 3200 mJ

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Courtesy Klaus Fritz (D)
Seborrheic Eczema

Cleared after 3 sessions: 200 -300 -500 mJ

Courtesy KLaus Fritz (D)
Spezial location retroauricular

6 sessions 200 to 800 mJ/session, cumulative 2900 mJ

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Lid

5 times 200 mJ

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Courtesy Dr Mueller Steinmann
Prurigo
12 sessions, 300 to 1200 mJ, cumulative 6 J
Pruritus renalis undergoing dialysis 4 years

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Courtesy Klaus Fritz (D)
Severe inflammatory acne
week 8 of pregnancy

post 3 sessions of Xtrac Excimer Laser 350 mJ/cm² per session

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Courtesy KLaus Fritz (D)
Severe inflammatory acne
week 8 of pregnancy

post 8 sessions of Xtrac Excimer Laser 350

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Courtesy KLaus Fritz (D)
Guide lines of the DDG = German Dermatologic Society
Acne and subtypes

1st line factors
- Hyperceratosis of follicle
- Genetics

2nd line factors
- Hyperplasia of sebaceous gland
- External influence
- Psyche
- Inflammation and immune response
- Effect of excimer 308 nm UV

Microbiological factors
Fluhr JW, Gloor M
The antimicrobial effect of narrow-band UVB (313 nm) and UVA1 (345-440 nm) radiation in vitro.

Two new UV lamps were investigated with respect to their antibacterial effectiveness in vitro. **Propioni** (n = 20 strains) and **Micrococcaceae** (n = 16 strains) bacteria extracted from acne patients were applied to RCM and sheep blood agar plates and irradiated with a narrow-band UVB lamp (TL 100W/10R) at a wavelength of 313 nm and a UVA1 lamp (TL 01) at a wavelength of 345-440 nm. The precisely defined energy levels were, in the case of narrow-band UVB, 0.00, 0.30, 0.50, 1.00, 2.00 and 3.00 J/cm² and, in the case of UVA1, 0.00, 2.50, 5.00, 7.50, 10.00 and 20.00 J/cm². **UVA1 inhibited neither** the growth of **Propioni** nor **Micrococcaceae** bacteria. In contrast, the growth of **Micrococcaceae was inhibited** already at a dosage of 0.30 J/cm² of narrow-band UVB (P < 0.05), **highly significant** from 0.50 J/cm² (P < 0.01) and to a maximum of 2.2 powers of 10 at 3.00 J/cm² compared with non-radiated control plates. **Propioni bacteria were significantly inhibited** at the minimum dosage of 0.30 J/cm² of narrow-band **UVB** (P < 0.01) and to a maximum of 2.8 powers of 10 at 3.00 J/cm².
inflammatory acne

Pre tx

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post 5 sessions 200 –300 mJ

Courtesy KLaus Fritz (D)
inflammatory acne
inflammatory acne

Courtesy Klaus Fritz (D)
Rosacea papulosa

"off label use"

Pre

post 3 tx 400/500/600 mJ

Courtesy Dr Mueller Steinmann
Perioral dermatitis.

Pre

nm eximer laser 2 weeks

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post 4 tx 200/300/300/300 mJ 308

Courtesy Dr Mueller Steinmann

„ off label use“
3 Sessions at 200 – 300 mJ

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Courtesy Klaus Fritz
Folliculitis sclerotisans nuchae

Pre
nm eximer laser 2.5 weeks
Before resistant to various therapeutic approaches
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post 7 tx 300 - 800 mJ 308

Courtesy KLaus Fritz
Folliculitis capitis

Pre nm eximer laser 2 weeks

post 3 tx 400/500/600 mJ 308

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Lichen ruber planus

308 nm EXCIMER LASER  
200 – 800 mJ

12 sessions

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Courtesy KLaus Fritz
Lichen ruber planus

308 nm EXCIMER LASER
200 – 800 mJ

12 sessions of

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Alopecia areata

Post 12 tx with 500 mJ/session excimer laser 1x/week

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Courtesy KLaus Fritz
... regrowth in „trichoscan fotofinder“
Alopecia areata

Post 26 tx with 350 - 800mJ/session
excimer laser 2x / week

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Fast relief from pruritus

Wollenschläger I, Ockenfels HM: Targeted UVB-308 therapy with excimer laser in the treatment of atopic dermatitis and other inflammatory dermatoses
Hautarzt 2009, 60 (11): 898 -906

<table>
<thead>
<tr>
<th>Diagnose</th>
<th>Mittlere MEDI (J/cm²)</th>
<th>Mittlere kumulierte Dosis (J/cm²)</th>
<th>Durchschnittliche Anzahl von Behandlungen</th>
<th>Sitzungen pro Woche</th>
<th>Maximaler Behandlungszeitraum</th>
<th>Drop-outs</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Atopische Dermatitis</td>
<td>0,4</td>
<td>8,21</td>
<td>9,6</td>
<td>1–2</td>
<td>6–8 Wochen</td>
<td>0</td>
<td>CR 84,2% (48/57), PR 16,8% (9/57)</td>
</tr>
<tr>
<td>2. Lichen Vidal</td>
<td>0,85</td>
<td>15,13</td>
<td>16,8</td>
<td>2</td>
<td>8–10 Wochen</td>
<td>4</td>
<td>CR 16% (1/6), PR 84% (5/6)</td>
</tr>
<tr>
<td>3. Prurigo nodularis</td>
<td>0,92</td>
<td>9,83</td>
<td>14,3</td>
<td>2</td>
<td>8–10 Wochen</td>
<td>0</td>
<td>CR 20% (1/5), PR 80% (4/5)</td>
</tr>
<tr>
<td>4. Granuloma anulare</td>
<td>0,84</td>
<td>30,16</td>
<td>15,8</td>
<td>2</td>
<td>8–10 Wochen</td>
<td>1</td>
<td>PR 100%</td>
</tr>
<tr>
<td>5. Alopecia areata</td>
<td>0,36</td>
<td>5,97</td>
<td>10,1</td>
<td>1–2</td>
<td>8–10 Wochen</td>
<td>0</td>
<td>CR 40% (6/15), PR 53,3% (8/15), NR 6,6% (1/15)</td>
</tr>
<tr>
<td>6. Lichen ruber disseminatus</td>
<td>0,71</td>
<td>10,2</td>
<td>10,3</td>
<td>1–2</td>
<td>6–8 Wochen</td>
<td>0</td>
<td>CR bei 100% mit PUVA und Excimer</td>
</tr>
</tbody>
</table>

CR komplette Remission („complete response“), PR Teilremission („partial response“ ≥50 bis ≤90%), NR Nichtansprechen („non-responder“)
Dyshidrotic dermatitis: 500mJ/cm²

Before 48 hrs after 7 days after induction start maintenance

Photographs: Dr. Gröne, Germany
Lichen simplex chronicus: 400 mJ/cm²

Photographs: Dr. Gröne, Germany
Morbus Grover: < 800 mJ/cm²

Before 48 hrs after 7 days after induction start maintenance

Photographs: Dr. Gröne, Germany
REM = reticular erythematous mucinosis

Case report: 73 J, 100 - 500 mJ, 1x/week, - 1 month improvement, 3 months clearing
Lymphomatoid Papulosis

308-nm excimer laser can be considered

3x/week, 14 sessions, up to 450 mJ
Mycosis Fungoides

10 lesions / 5 patients, up to a maximum of 10 applications
cumulative dose 600 – 1500 mJ

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Summary

- 308nm Excimer laser provides an effective and safe UVB therapy
- Combination therapies improve results and reduce dosage of UV B and systemic medication
- Excimer laser therapy will be applied to an increasing number of dermatoses that respond to phototherapy or photochemotherapy

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