

Table 8: In all patients with vitiligo, what is the efficacy of a course of narrow-band UVB including high intensity light sources compared to placebo in terms of condition progression, area reduction and QOL score? AV Anstey

| Bibliographic citation | Study type | Ev lev | No of patients | Intervention | Comparison | Length follow-up | Outcomes measured and result | Patient characteristics | Additional comments |
|------------------------|--|--------|----------------|---|--|---------------------------|---|---|---|
| Spencer 2002 | Intervention study | 3 | 18 | Excimer laser | Within patient controls (untreated vitiligo) | 4/52 | Arbitrary scoring method | | Pilot study |
| Hofer A. 2006 | Intervention study, single arm, before and after | 3 | 25 | Excimer laser | Within patient controls (untreated vitiligo) | 12/12 | Arbitrary scoring method + photos. No stats No stats | White patients | Benefit depends on body site. |
| Hamzavi I. 2004 | RCT | 1- | 22 | NB-UVB vs no treatment | L vs R | 6/12 | VASI scores compared to baseline. 42.9% repigmentation on treated side versus 3.3% on untreated side ($p < 0.001$) 50% or more | 15 white, 6 indo-Pakistan, 1 Chinese | Odds ratios for response according to body region. Greatest response on trunk and nonacral extremities |
| Menchini G. 2003 | Open study | 3 | 734 | Filtered Xenon arc lamp with fibre optic cable | Response compared to baseline | Unclear | Photograph planimetry. No statistics | Ages 6-78. All had stable or active disease | "Highly effective with no side effects" No controls |
| Westerhof. 1997 | 2 arm before and after study | 2- | 175 | PUVA vs TL01 for first study; TL01 alone for second study | Response compared to baseline | up to 12 months | Arbitrary scoring system. No statistics. 67% of TL01 group showed repigmentation after 4 months | Mainly Skin Type III | No controls. No adverse effects with TL01. TL01 is "as efficient as topical PUVA with fewer side effects" |
| Yones 2007 | Double-blind randomize | 1+ | 56 | PUVA Vs TL01 | Change in area affected, | Up to 12 months after end | Colour photographs, clinical assessment of affected skin using rule of nines, DLQI | Non-segmental vitiligo. | Both PUVA and NBUVB produced a significant improvement. Improvement |

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| | d study | | | | and colour match afet 48 treatments, end of course and after 12 months after end of course | of course | | Exclusions: age less than 18 or greater than 70, previous failure of PUVA | was greater for NBUVB but this was not significant. |
| Hartmann A 2005 | Intervention study | 2- | 10 | Within patient comparison of TL01 vs Broad-band UVB | Response compared to baseline | up to 12 months | Photography, planimetry, VIDA score and DLQI 6/9 showed response to TL01, 0/6 responded to BB UVB at 6 months | | Conclusion: TL01 was effective in treating vitiligo, whereas broad-band had no effect. Combination with calcipotriol was not superior to TL01 monotherapy |
| Hong SB 2005 | Open, intervention study | 2- | 8 | Excimer laser vs TL01 | No controls. One intervention was compared with the other | 10 weeks | Arbitrary score of photographs. At 20 treatments, the score for treated areas showed better scores for Excimer laser than TL01 (p<0.05) | | Authors state that Excimer produced more rapid and more profound repigmentation |
| Njoo M. J 2000 | Open study in children | 3 | 51 | NB-UVB | No controls | 1 year max | Arbitrary score + VIDA. 53% of patients had more than 75% repigmentation. There was "stabilisation" of disease in 80% | | All patients were children |

Table 9: In all patients with vitiligo, what is the efficacy of a course of **PUVA** or **PUVASol** compared to **placebo** in terms of condition progression, area reduction and QOL score? AV Anstey

| Bibliographic citation | Study type | Ev lev | No of patients | Intervention | Comparison | Length follow-up | Outcomes measured and result | Effect size | Patient characteristics | Additional comments |
|------------------------|------------------------------|--------|----------------|----------------------------------|-------------------------|------------------|----------------------------------|-------------|-----------------------------|--|
| Barman KD 2004 | | | | | | | | | | Not relevant to question |
| Czajkowski 2004 | | | | | | | | | | Not relevant to question |
| Valkova 2004 | | | | | | | | | | Not relevant to question |
| Baysal 2003 | | | | | | | | | | Not relevant to question |
| Cherif 2003 | | | | | | | | | | Not relevant to question |
| Ameen 2001 | | | | | | | | | | Not relevant to question |
| Ermis 2001 | | | | | | | | | | Not relevant to question |
| Mofty 2001 | | | | | | | | | | Not relevant to question |
| Parsad 1999 | | | | | | | | | | Not relevant to question |
| Westerhof 1997 | "Before and after study" | 3 | 28 | Topical PUVA compared with TL01 | Before and after study! | 4 months | Arbitrary assessment of response | No stats | Predominantly Skin Type III | 46% of PUVA group showed repigmentation |
| Khalid 1995 | Clinical trial, cohort study | 2- | 366 | Clobetasone vs PUVASOL | Global response | 26 months | Photographs | No stats | East Indian patients | Mostly not relevant to question |
| Sehgal ???? | Three limb non-randomis | 2- | 89 | Three psoralen products compared | Clinical response | | Arbitrary assessment | No stats | | Trimethyl Psoralen and Psoralen were better than 8-MOP |

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| | ed clinical study | | | (Trimethyl Psoralen, psoralen and 8-MOP) | | | | | | |
| Farah 1997 | Open study of psoralens and triamcinolone by mouth | 3 | | | | | | | | Not relevant to question |
| Pathak MA. 1994 | Randomised, double-blind prospective study | 2- | 366 | 8 treatment groups. Various concentrations of Psoralen vs placebo | With placebo | up to 2 years | Arbitrary assessment of photographs | No statistics | Indian | Small differences between different psoralens in terms of rate of responses |
| Yones SS <i>et al.</i> 2007 | Double-blind randomized study | 1+ | 56 | PUVA vs TL01 | Patients with other treatment, and response compared to baseline status | 1 year study, 1 year follow-up | Rule of nines. Photographs. DLQI. VAS self-assessment | yes, exact χ^2 , exact Mann-Whitney and Wilcoxon signed rank correlation coefficient | Non-segmental vitiligo affecting 2-70% of skin. Skin types I-IV | 16 of 25 patients (64%) in TL01 group showed greater than 50% improvement compared to 9 out of 25 patients in the PUVA group (36%). Colour match was good for TL01 but less good for PUVA. Loss of pigmentation was more significant in the PUVA than the TL01 group |

Table 10: In all patients with vitiligo, what is the efficacy of a course of **khellin** with sunlight, UVA or UVB compared to **PUVA** or **PUVAso1** in terms of condition progression, area reduction and QOL score? AV Anstey

| Bibliographic citation | Study type | Ev level | No pats | Intervention | Comparison | Length of FU | Outcomes measured and result | Additional comments |
|------------------------|---------------------------------|----------|---------|--|--|--------------|---|---|
| Valkova S. 2004 | Pilot study | 3 | 33 | Khellin + UVA | Within patient, before and after study | Not stated | Arbitrary. KUVA achieved better results in younger patients. No stats | KUVA: no side effects PUVA: Erythema, itching, GI-upset in some patients. Repigmentation for both treatments was "comparable" |
| Orrecchia. J 1999 | L vs R study | 2- | 36 | Khellin gel + UVA versus UVA monotherapy | Within patient L Vs R | Not stated | Repigmentation of >10% of the combination therapy (86%) compared to 66% for the UVA monotherapy side $p < 0.01$ | Young patients with short duration of disease showed better response. Authors state: "Khellin gel + UVA significantly improves outcome of patients with vitiligo" |
| Procaccini. J 1995 | L vs R placebo-controlled study | 2- | 72 | Khellin + UVA vs vehicle alone | L vs R | 5 months | Clinically and with photographs. No randomisation. No statistics | Topical application of Khellin did not induce repigmentation; responders seem to respond to UVA <u>not</u> khellin. No adverse effects noted. |
| Orecchia. 1992 | L vs R study | 3 | 41 | Khellin + sun vs vehicle + sun | L vs R | 4 months | Arbitrary | No difference was found between the 2 groups |
| Abdel-Fattah. 1992 | Double-blind | 3 | 60 | Oral khellin | Double-blind | 4 months | Arbitrary. No statistics. Control patients showed no response. Khellin + sunlight patients included 12 out of 30 with greater than 50% repigmentation | "The achieved pigmentation was stable for 1 year after drug cessation" |

Table 11: What is the evidence for the risk of long-term complications of precancerous change or skin cancer with PUVA or narrow-band UVB in the treatment of vitiligo? AV Anstey

| Author, citation | Evidence level | Number of patients | Intervention | Comparison | Length of follow-up | Outcome measured and result | Additional comments |
|--------------------|----------------|--|--|--|---------------------------------|---|--|
| Harrist TJ. 1984 | 3 | 596 enrolled in prospective study 230 followed-up for 55 months | PUVA | Within patient controls (ie unaffected skin) | 4 years | 29 (13%) developed skin lesions within areas of vitiligo. Skin lesions were biopsied: no malignancy. Some actinic keratoses, lichenoid keratoses. | No tumours identified. Follow-up too short to have excluded future risk of skin cancers. Conclusion: No increased risk of carcinoma was apparent during the follow-up period |
| Abdel Nasser. 2004 | 3 | 1 | PUVA for 3 years, cumulative dose ~1750J/cm ² | Within patient | | Skin lesions biopsied | No evidence of skin malignancy was observed clinically or histologically |
| Takeda H. 1998 | 4 | 1 | PUVA | No control | 9 years of PUVA. 360 treatments | Multiple SCCs in situ were diagnosed within vitiligo areas. | Overall dose of UVA was low (392 J/cm ²) |
| Halder RM. 1995 | 4 | 326 | PUVA | No controls | 4 years + | 264 adults in study. No actinic keratoses or malignancies were observed in any of the patients | Power of the study to detect increased risk of malignancy was "quite limited" |

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| Calanchini- Postizzi E. 1987 | | | PUVA | Case control study | | No significant increase in skin cancer compared to controls | |
| Westerhof W. 1996 | 4 | 2500 | PUVA | Open observation (not a true study) | | No skin cancer in any patient | |
| Buckley DA. 1996 | 4 | 1 | PUVA | Case report | | Multiple SCC and keratoses in vitiligo with prolonged PUVA | 271 PUVA exposures and 451 J/cm ² UVA. |