NEW PATHWAYS TO SMARTER MEDICINE™

Rezpegaldesleukin (REZPEG)

Corrected Phase 1b Dataset for Studies of REZPEG in Atopic Dermatitis and Psoriasis:

These slides contain corrected data on EASI-related and PASI-related clinical efficacy endpoints as compared to previously reported erroneous data at the 2022 EADV Meeting

2022 EADV Atopic Dermatitis Poster Presentation

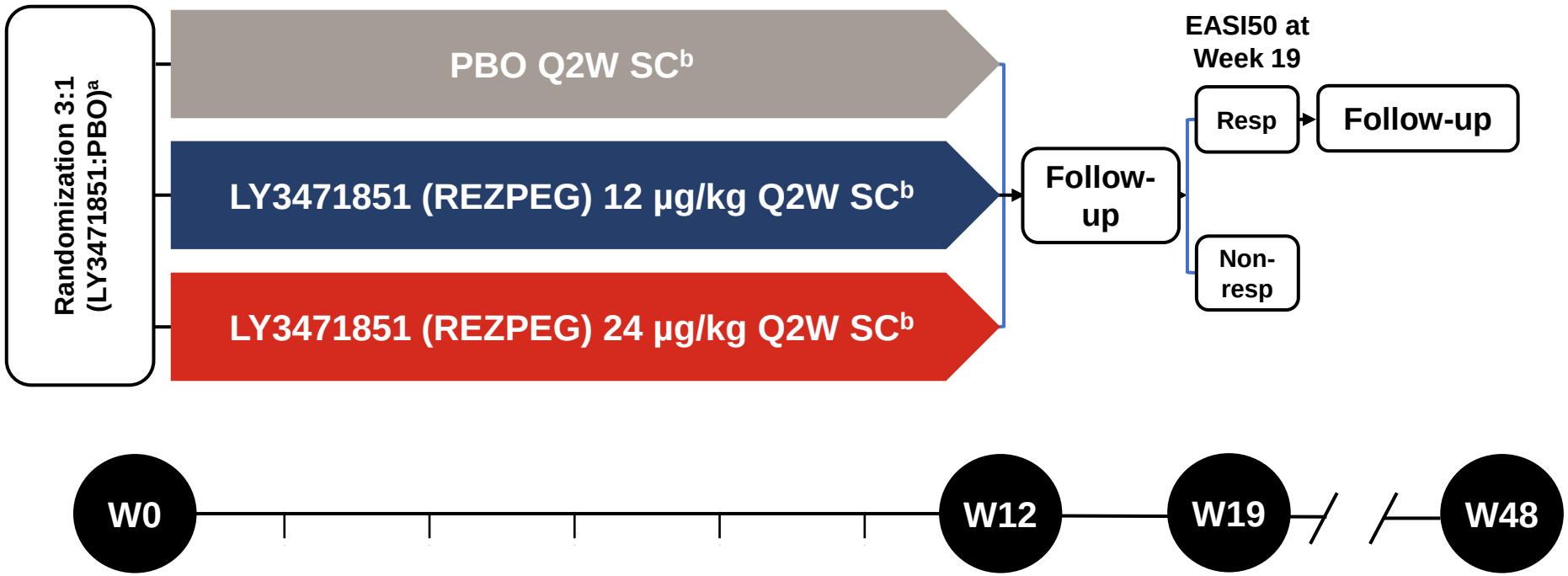
2022 EADV Psoriasis Poster Presentation

August 7, 2023

REZPEG Phase 1b, Double-Blind, Placebo-Controlled Study (NCT04081350) of Patients With Atopic Dermatitis

Key Eligibility Criteria

- Aged 18-70 years
- Moderate-to-severe AD involving ≥10% body surface area in the affected skin
- History of inadequate response or intolerance to topical medications
- vIGA-AD™ ≥3
- Eczema Area and Severity Index (EASI) ≥16



Source: Schleicher et. al.: "*Efficacy and Safety of a Selective Regulatory T-Cell Inducing IL-2 Conjugate (LY3471851) in the Treatment of Atopic Dermatitis: A Phase 1 Randomised Study*"

[a] Full study design is not shown; the LY3471851 10 µg/kg cohort is not included in this analysis

[b] Total of 7 doses/patient

LY3471851 (NKTR-358, Rezpegaldesleukin, Rezpeg); *EASI50=50% improvement from baseline in Eczema Area and Severity Index; PBO=placebo; Q2W=once every 2 weeks; SC=subcutaneous; W=Week*

Phase 1b Study of REZPEG in Atopic Dermatitis: Statistical Methodology and Independent Statistical Audit

Corrected Efficacy Assessments

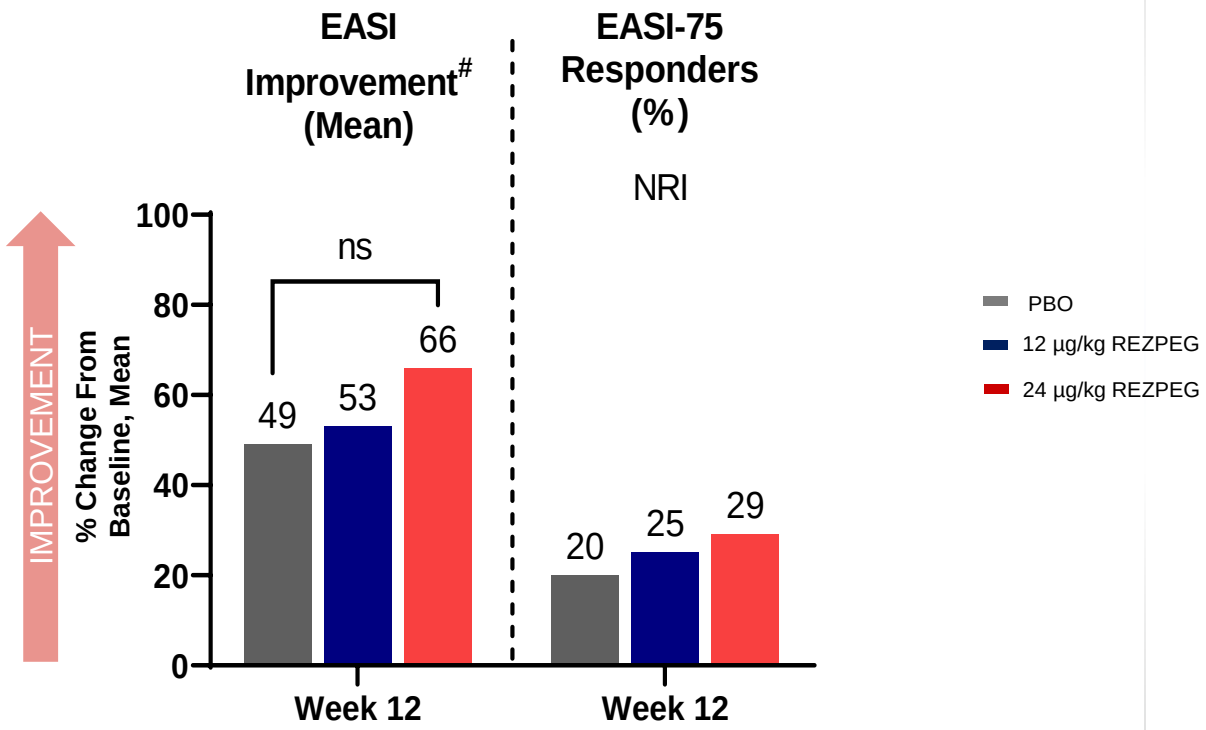
- **Change from baseline in Eczema Area Severity Index (EASI)**
- **Proportion of patients who achieved at least 75% improvement from baseline in EASI score (EASI-75)**

Statistical Analyses

- EADV 2022 presentation and the independent statistical audit were from interim data cutoff of May 10, 2022.
- EASI-75 response rates are calculated using non-responder imputation (NRI) methodology for missing data **and also** as a proportion of patients who had a disease assessment observed at 12 weeks (as observed).
- Independent statistical verification was conducted on EASI Score and EASI-derived parameters. Continuous endpoint of EASI percent change from baseline was calculated by an independent statistical audit from observed data using a mixed model for repeated measures (MMRM) to generate LS means and the p value, as specified in the statistical analysis plan (SAP) defined in the protocol.
- Data was corrected by an independent statistical audit with the 72-point EASI Score and included data from three patients in the database that were previously excluded from the EADV 2022 analyses.

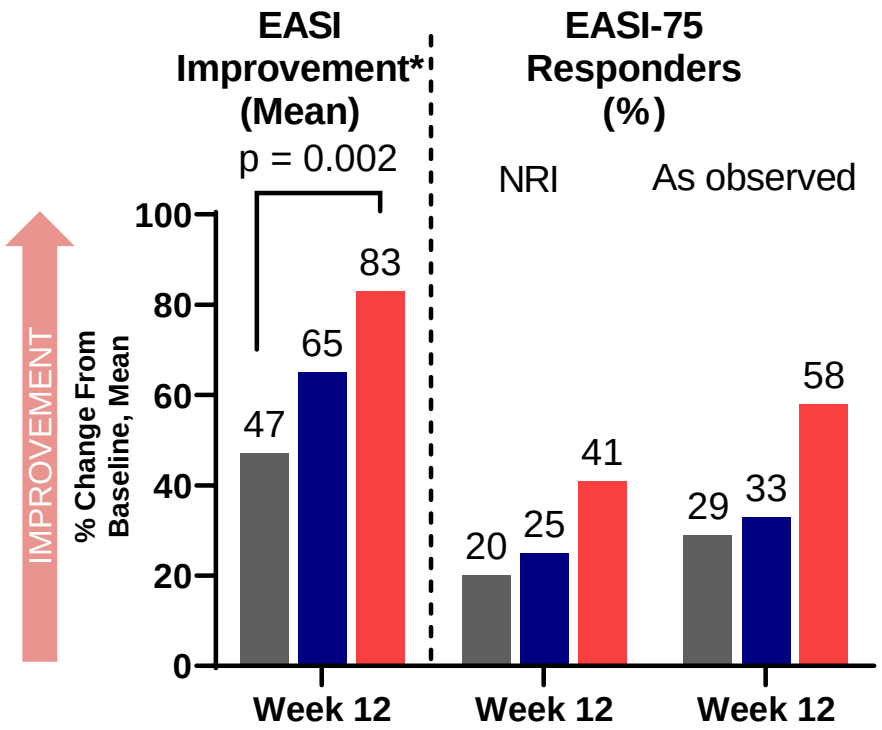
Phase 1b Study of REZPEG in Atopic Dermatitis: Mean % Improvement in EASI Score and EASI-75 Responder Rate at Week 12

Erroneous Data
Schleicher et. al., EADV 2022



#EASI Improvement results at EADV 2022 were presented as observed mean percent change from baseline

Corrected Data from Independent Statistical Audit
August 7, 2023



- 72-point EASI score utilized
- All patients in the database included in the analysis
- *EASI Improvement results are least squares (LS) mean percent change from baseline obtained from MMRM as specified in the statistical analysis plan (SAP) defined in the protocol

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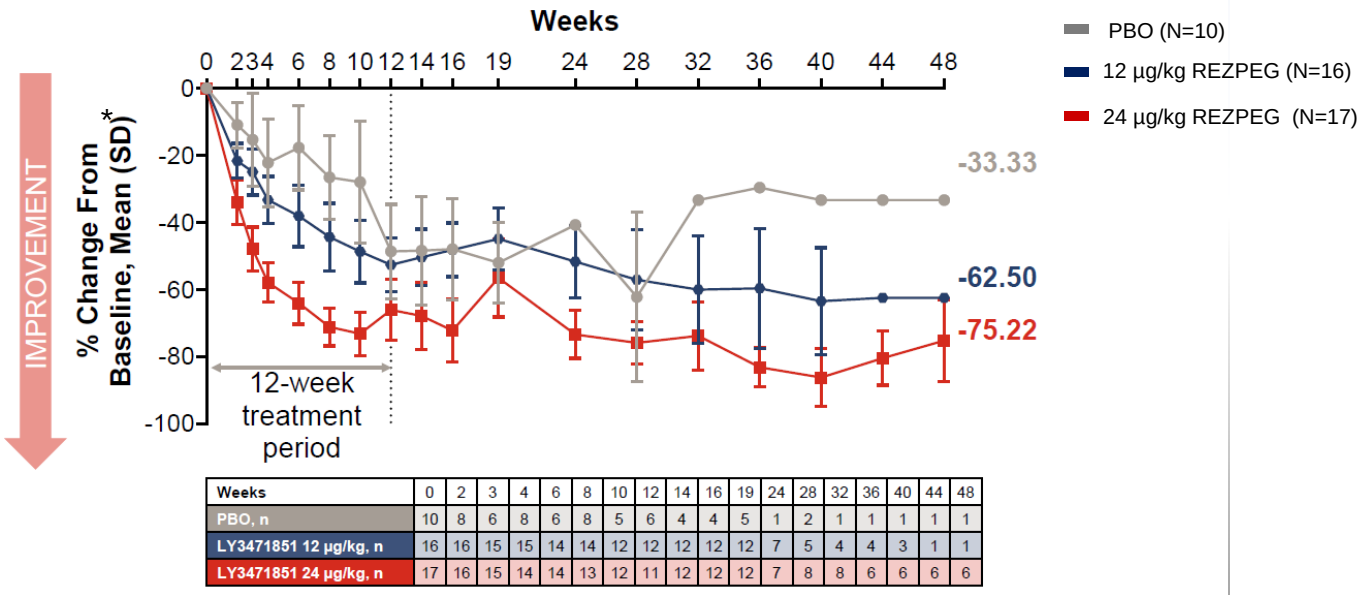
Phase 1b Study of REZPEG in Atopic Dermatitis: Percent Change From Baseline of Observed EASI Score

Erroneous Data
Schleicher et. al., EADV 2022

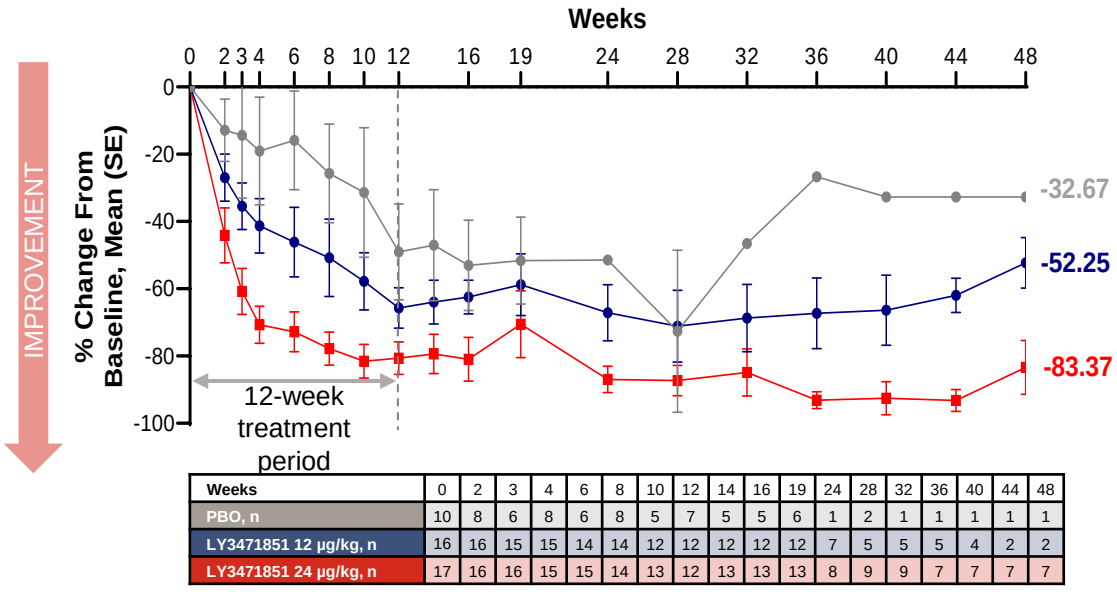


Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
PBO, n	10	8	6	8	6	8	5	6	4	4	5	1	2	1	1	1	1	1
LY3471851 12 µg/kg, n	16	16	15	15	14	14	12	12	12	12	12	7	5	4	4	3	1	1
LY3471851 24 µg/kg, n	17	16	15	14	14	13	12	11	12	12	12	7	8	8	6	6	6	6

Note: n=number of patients with assessments at the visit

**EADV 2022 chart was labeled as Mean (SD), however the labeling was incorrect and should have been Mean (SE)*

Corrected Data from Independent Statistical Audit
August 7, 2023



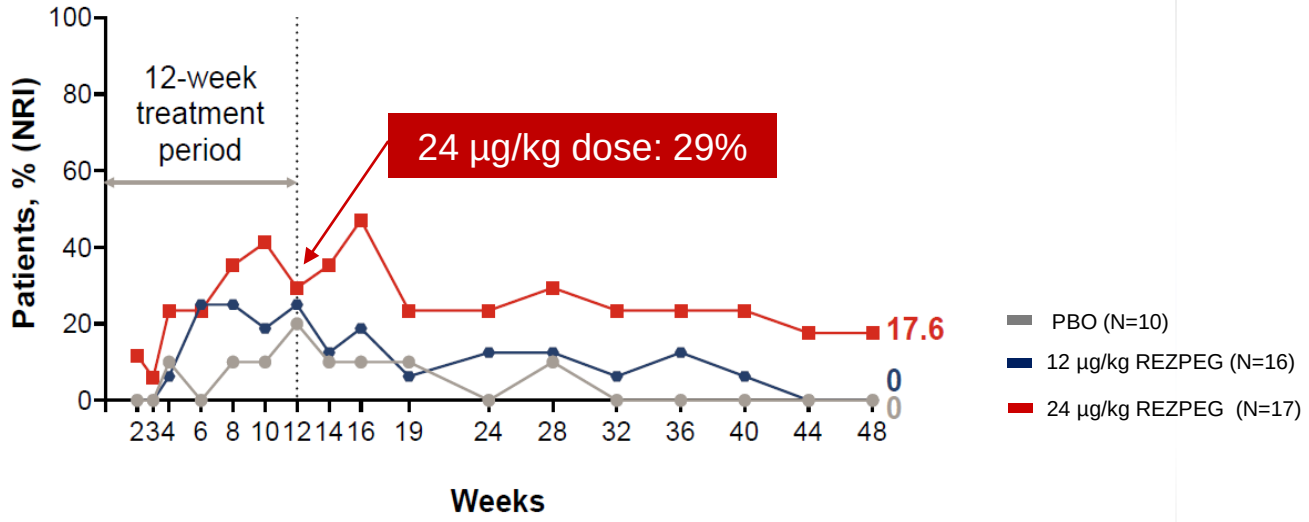
Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
PBO, n	10	8	6	8	6	8	5	7	5	5	6	1	2	1	1	1	1	1
LY3471851 12 µg/kg, n	16	16	15	15	14	14	12	12	12	12	12	7	5	5	5	4	2	2
LY3471851 24 µg/kg, n	17	16	16	15	15	14	13	12	13	13	13	8	9	9	7	7	7	7

Note: n=number of patients with assessments at the visit

- 72-point EASI score utilized
- All patients in the database included in the analysis

Phase 1b Study of REZPEG in Atopic Dermatitis: EASI-75 Responders

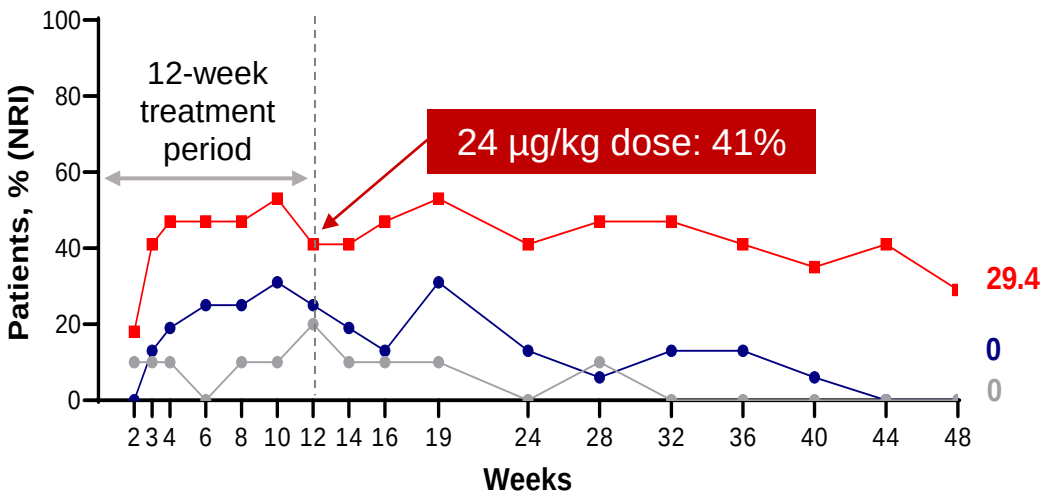
Erroneous Data
Schleicher et. al., EADV 2022



Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
PBO, n	10	0	0	1	0	1	1	2	1	1	1	0	1	0	0	0	0	0
LY3471851 12 µg/kg, n	16	0	0	1	4	4	3	4	2	3	1	2	2	1	2	1	0	0
LY3471851 24 µg/kg, n	17	2	1	4	4	6	7	5	6	8	4	4	5	4	4	4	3	3

Note: n=number of responders

Corrected Data from Independent Statistical Audit
August 7, 2023



Weeks	0	2	3	4	6	8	10	12	14	16	19	24	28	32	36	40	44	48
PBO, n	10	1	1	1	0	1	1	2	1	1	1	0	1	0	0	0	0	0
LY3471851 12 µg/kg, n	16	0	2	3	4	4	5	4	3	2	5	2	1	2	2	1	0	0
LY3471851 24 µg/kg, n	17	3	7	8	8	8	9	7	7	8	9	7	8	8	7	6	7	5

Note: n=number of responders

- 72-point EASI score utilized
- All patients in the database included in the analysis

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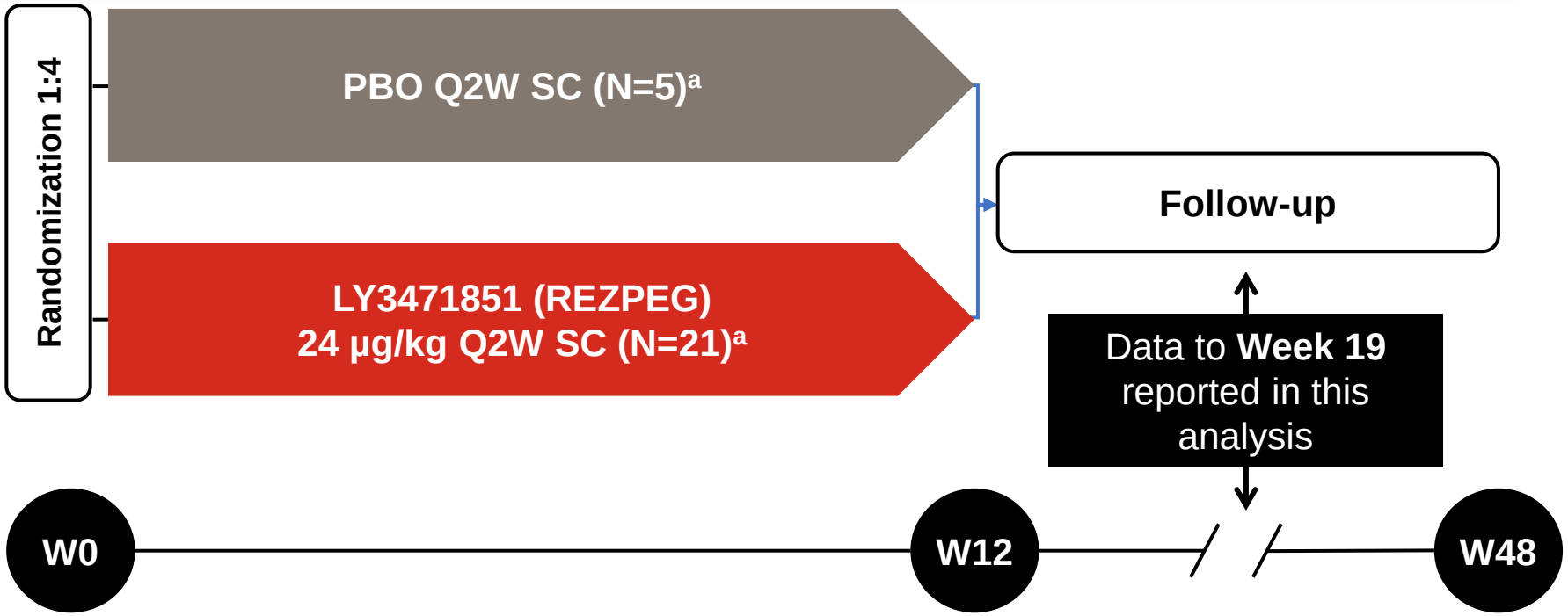
REZPEG Phase 1b, Double-Blind, Placebo-Controlled Study (NCT04081350) of Patients with Psoriasis

Key Eligibility Criteria

- Aged 18-70 years
- Plaque psoriasis involving ≥10% body surface area in the affected skin[a]
- Candidates for systemic therapy or phototherapy
- At least 2 similar and evaluable lesions
- Static Physician's Global Assessment (sPGA) score ≥3
- Psoriasis Area and Severity Index (PASI) ≥12



Source: Forman et. al: *"Efficacy and Safety of a Selective Regulatory T-Cell Inducing IL-2 Conjugate (LY3471851) in the Treatment of Psoriasis: A Phase 1 Randomised Study"*

[a] Total of 7 doses/patient

LY3471851 (NKTR-358, Rezpegaldesleukin, Rezpeg); *PBO=placebo; Q2W=once every 2 weeks; SC=subcutaneous; W=Week*

Phase 1b Study of REZPEG in Psoriasis: Statistical Methodology and Independent Statistical Audit

Corrected Efficacy Assessments

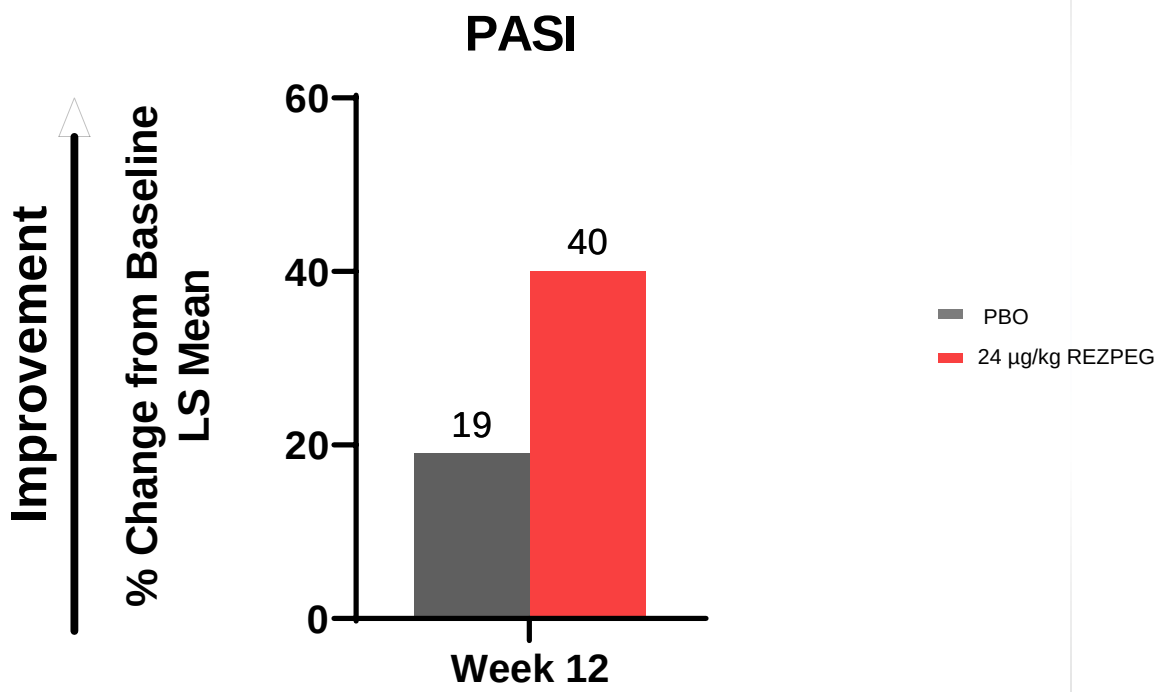
- **Change from Baseline in Psoriasis Area and Severity Index (PASI)**
- **Proportion of patients who achieved at least 50% improvement from baseline in PASI score (PASI-50)**
- **Proportion of patients who achieved at least 75% improvement from baseline in PASI score (PASI-75)**

Statistical Analyses

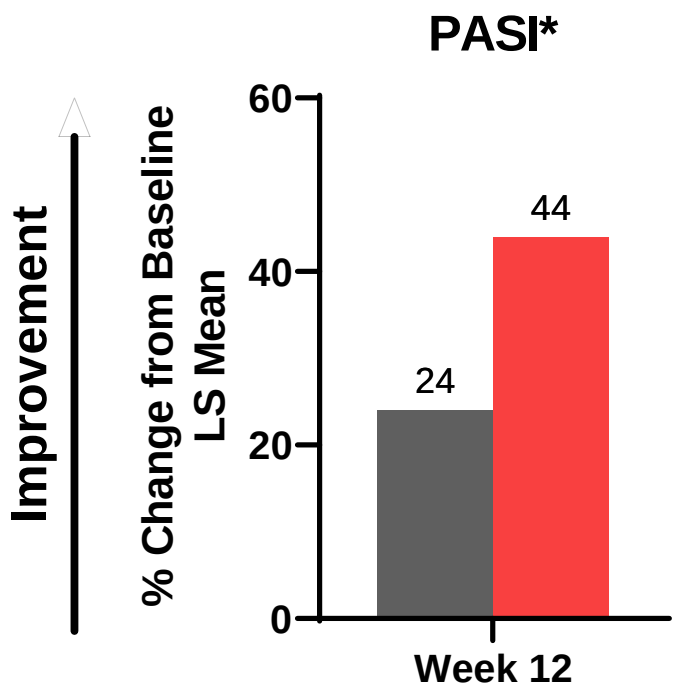
- EADV 2022 presentation and the independent statistical audit were from the final study dataset.
- PASI-50 or PASI-75 response rates are presented using non-responder imputation (NRI) methodology (NRI) for missing data **and also** as a proportion of patients who had a disease assessment observed at 12 weeks (as observed).
  - Response rates for PASI-50 & PASI-75 were calculated using an adjusted intent to treat (ITT) population with placebo (n=5) and Rezpeg (n=19) at Week 12 (Forman et al. EADV2022).
- Independent statistical verification was conducted on PASI Score and PASI-derived parameters. Continuous endpoint of PASI percent change from baseline was calculated by an independent statistical audit from observed data using a mixed model for repeated measures (MMRM) to generate LS means, as specified in the statistical analysis plan (SAP) defined in the protocol.
- Data was corrected by an independent statistical audit with the 72-point PASI Score.

Phase 1b Study of REZPEG in Psoriasis:
PASI Percent Change From Baseline at Week 12

Erroneous Data
Forman et. al., EADV 2022



Corrected Data from Independent Statistical Audit
August 7, 2023



- 72-point EASI score utilized
- All patients in the database included in the analysis
- *PASI Improvement results are least squares (LS) mean percent change from baseline obtained from MMRM as specified in the statistical analysis plan (SAP) defined in the protocol

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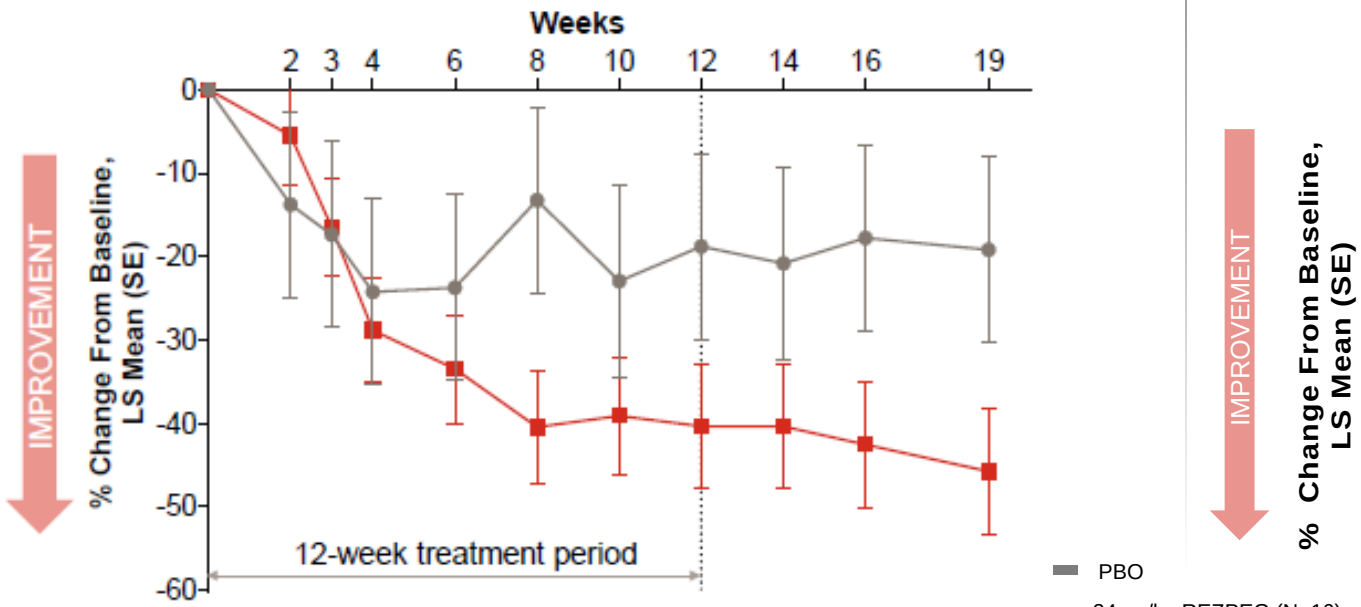
Percent change from baseline PASI (LS Mean) results were obtained from MMRM as specified in the statistical analysis plan (SAP) defined in the protocol

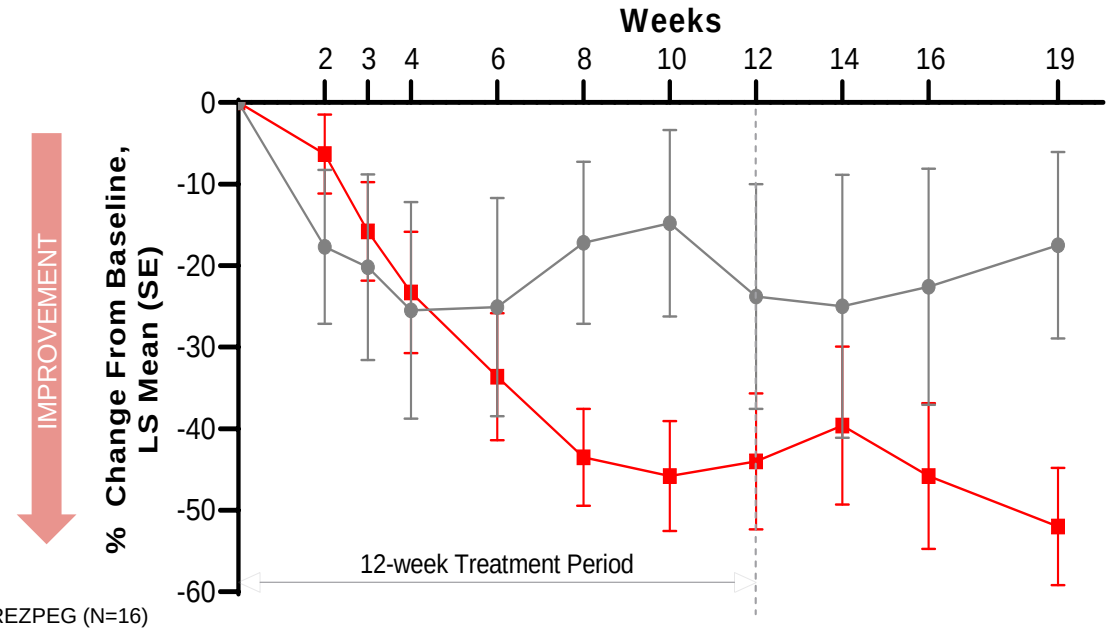
Phase 1b Study of REZPEG in Psoriasis:
PASI LS Mean Percent Change From Baseline

Erroneous Data
Forman et. al., EADV 2022



Weeks	2	3	4	6	8	10	12	14	16	19
PBO, n/N	5/5	5/5	5/5	5/5	5/5	4/5	5/5	4/5	5/5	5/5
LY3471851 24 µg/kg, n/N	18/21	17/21	14/21	13/21	12/21	11/21	11/21	11/21	11/21	11/21

Corrected Data from Independent Statistical Audit
August 7, 2023

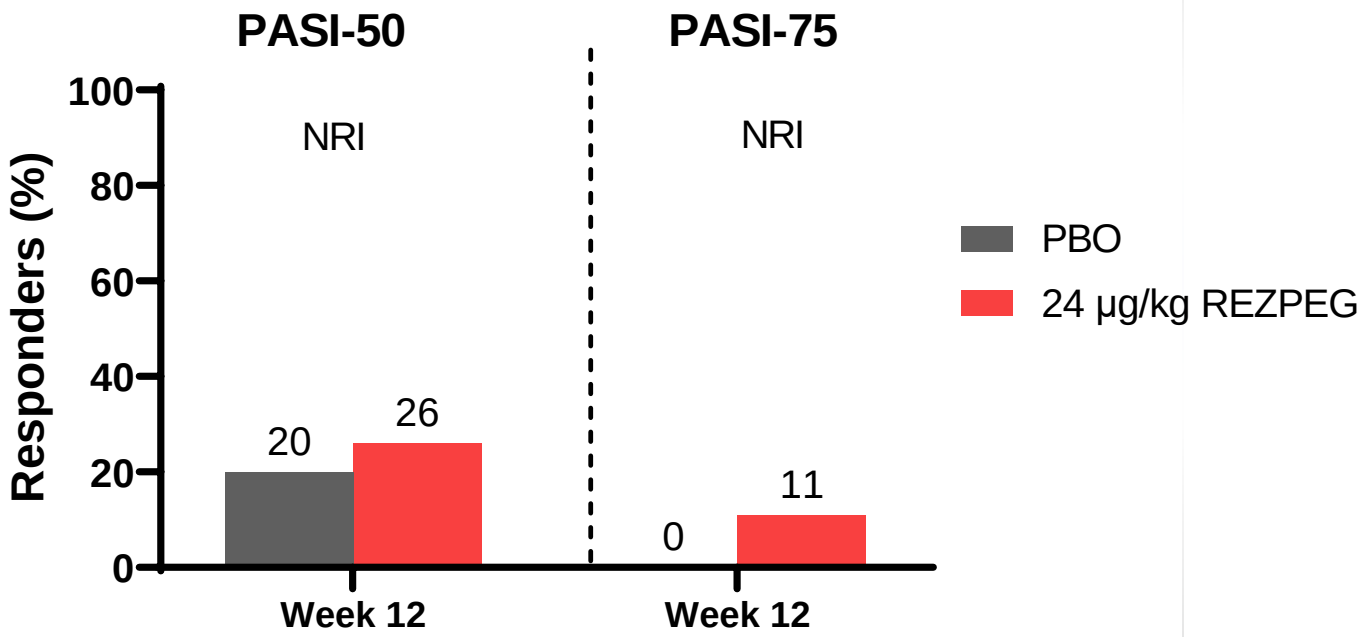


Weeks	2	3	4	6	8	10	12	14	16	19
PBO, n/N	5/5	5/5	5/5	5/5	5/5	4/5	5/5	4/5	5/5	5/5
LY3471851 24 µg/kg, n/N	18/21	17/21	14/21	13/21	12/21	11/21	11/21	11/21	11/21	11/21

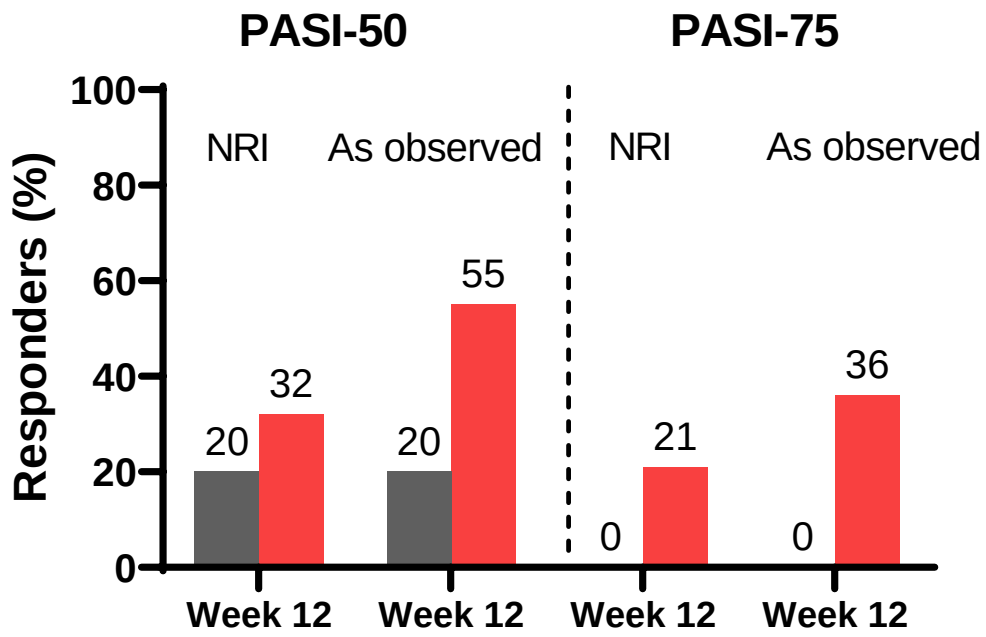
- 72-point PASI score utilized
- All patients in the database included in the analysis

Phase 1b Study of REZPEG in Psoriasis: PASI-50 and PASI-75 Responders at Week 12

Erroneous Data
Forman et. al., EADV 2022



Corrected Data from Independent Statistical Audit
August 7, 2023



- 72-point PASI score utilized

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APPENDIX

Calculating Eczema Area and Severity Index (EASI)

Severity Score
Grade each sign on a scale: 0=clear/none 1=mild 2=moderate 3=severe

Area Score							
% Involvement	0	1-9%	10-29%	30-49%	50-69%	70-89%	90-100%
Area Score	0	1	2	3	4	5	6

EASI Calculator (Adults)

Body Region	Erythema (0-3)	Edema/ Papulation (0-3)	Excoriation (0-3)	Lichenification (0-3)	Area Score (0-6)	Multiplier	Score
Head/Neck	(+	+	+	)	x	x 0.1	
Trunk	(+	+	+	)	x	x 0.3	
Upper Extremities	(+	+	+	)	x	x 0.2	
Lower Extremities	(+	+	+	)	x	x 0.4	
The final EASI score is the sum of the 4 region scores (0-72):							_____

- **Eczema Area and Severity Index (EASI) is a composite score that measures disease severity in patients with atopic dermatitis**
- The extent of body area involvement is incorporated into EASI via the “Area Score” for each body region
- The Area Score is further modified by a “multiplier” to account for the body surface area represented by that region

Source: Hanifin JM, Baghoomian W, Grinich E, et al. The Eczema Area and Severity Index-A Practical Guide. Dermatitis : Contact, Atopic, Occupational, Drug. 2022 May-Jun 01;33(3):187-192. DOI: 10.1097/der.0000000000000895. PMID: 35594457; PMCID: PMC9154300.

Calculating Psoriasis Area and Severity Index (PASI)

Plaque characteristic	Lesion score	Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None 1 = Slight 2 = Moderate 3 = Severe 4 = Very severe				
Induration/Thickness					
Scaling					
Add together each of the 3 scores for each body region to give 4 separate sums (A).					
Lesion Score Sum (A)					

Percentage area affected	Area score	Head	Upper Limbs	Trunk	Lower Limbs
Area Score (B) *Degree of involvement as a percentage for each body region affected (score each region with score between 0-6)*	0 = 0% 1 = 1% - 9% 2 = 10% - 29% 3 = 30% - 49% 4 = 50% - 69% 5 = 70% - 89% 6 = 90% - 100%				
Multiply Lesion Score Sum (A) by Area Score (B), for each body region, to give 4 individual subtotals (C).					
Subtotals (C)					
Multiply each of the Subtotals (C) by amount of body surface area represented by that region, i.e. x 0.1 for head, x 0.2 for upper body, x 0.3 for trunk, and x 0.4 for lower limbs.					
Body Surface Area		**x 0.1**	**x 0.2**	**x 0.3**	**x 0.4**
Totals (D)					
Add together each of the scores for each body region to give the final PASI Score.					

PASI Score = ☐

- **Psoriasis Area and Severity Index (PASI) is a composite score that measures disease severity in patients with psoriasis**
- The extent of body area involvement is incorporated into PASI via the “Area Score” for each body section
- The Area Score is further modified by a “multiplier” to account for the body surface area represented by that region

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Source: British Association of Dermatologists: “Dermatology Handbook for Registrars” (2020)