SUPPLEMENTARY MATERIAL

Appendix S1

Summary of the Guidelines for Management of Cutaneous Events in DECIDE

Guidelines for the management of patients with cutaneous adverse events (AEs) were provided to the study investigators. The guidelines recommended that patients who experienced a clinically significant cutaneous AE in the opinion of the investigator should be evaluated by a dermatologist to document the event, take photographs, and perform a skin biopsy, if appropriate. Localized or highly circumscribed cutaneous AEs were to be managed according to standard local medical practices and systemic corticosteroids were allowed, as indicated. The guidelines indicated that patients with any diffuse cutaneous AE were to be seen by a dermatologist within 72 h after the onset of the event to assess, photograph, and perform a skin biopsy, if appropriate. In patients with a diffuse or severe cutaneous AE, study treatment was to be withheld until the AE resolved. If an allergic hypersensitivity reaction was suspected, study treatment was to be permanently discontinued. For all other cutaneous AEs, permanent discontinuation of study treatment was at the discretion of the investigator in consultation with the dermatologist. Patients with diffuse rash that was highly inflammatory at presentation, or worsened over time (e.g., increased body surface area, more lesions, mucosal involvement), or persisted for more than 1 week without improvement were to be evaluated for appropriateness for corticosteroid treatment. If corticosteroid treatment was not contraindicated, the patient was to be treated with high-dose systemic corticosteroids (equivalent to prednisone 60 mg or intravenous methylprednisolone 1 g/day) for approximately 5 days followed by gradual taper if the AE had stabilized, or treated with alternate therapies if the AE had not improved. Other treatments were to be considered for patients in whom corticosteroids were contraindicated.

Table S1 Protocol guidance for AE severity rating and classification of serious AEs

Investigators rated the severity of each AE using the following guidance:	
Mild	Symptom(s) barely noticeable by the patient or did not make them uncomfortable; did not influence performance or functioning; prescription drug not ordinarily needed for relief of symptom(s), but could be given based on patient personality
Moderate	Symptom(s) of a sufficient severity to make the patient uncomfortable; performance of daily activity influenced; patient was able to continue in study; treatment for symptom(s) could be needed
Severe	Symptom(s) caused severe discomfort, incapacitation or significant impact on patient's daily life; severity could cause cessation of study treatment; treatment for symptom(s) could be given and/or patient hospitalized
An AE was deemed serious if it met the following criteria:	
Serious AE	AE that required hospitalization or a prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity, congenital anomaly/birth defect or death; life-threatening event in the opinion of the investigator; medically important event in the opinion of the investigator that could have jeopardized the patient or required intervention to prevent one of the previously listed outcomes

AE adverse event

Table S2 Topical corticosteroids: relative potency of various formulations

Class	Drug	Dosage Form(s)	Strength (%)
I. Very high potency	Augmented betamethasone dipropionate	Ointment	0.05
	Clobetasol propionate	Cream, foam, ointment	0.05
	Diflorasone diacetate	Ointment	0.05
	Halobetasol propionate	Cream, ointment	0.05
II. High potency	Amcinonide	Cream, lotion, ointment	0.1
	Augmented betamethasone dipropionate	Cream	0.05
	Betamethasone dipropionate	Cream, foam, ointment, solution	0.05
	Desoximetasone	Cream, ointment	0.25
	Desoximetasone	Gel	0.05
	Diflorasone diacetate	Cream	0.05
	Fluocinonide	Cream, gel, ointment, solution	0.05
	Halcinonide	Cream, ointment	0.1
	Mometasone furoate	Ointment	0.1
	Triamcinolone acetonide	Cream, ointment	0.5
III–IV. Medium potency	Betamethasone valerate	Cream, foam, lotion, ointment	0.1
	Clocortolone pivalate	Cream	0.1
	Desoximetasone	Cream	0.05
	Fluocinolone acetonide	Cream, ointment	0.025
	Flurandrenolide	Cream, ointment	0.05
	Fluticasone propionate	Cream	0.05
	Fluticasone propionate	Ointment	0.005
	Mometasone furoate	Cream	0.1
	Triamcinolone acetonide	Cream, ointment	0.1
V. Lower-medium potency	Hydrocortisone butyrate	Cream, ointment, solution	0.1
	Hydrocortisone probutate	Cream	0.1
	Hydrocortisone valerate	Cream, ointment	0.2
	Prednicarbate	Cream	0.1
VI. Low potency	Alclometasone dipropionate	Cream, ointment	0.05
	Desonide	Cream, gel, foam, ointment	0.05
	Fluocinolone acetonide	Cream, solution	0.01
VII. Lowest potency	Dexamethasone	Cream	0.1
	Hydrocortisone	Cream, lotion, ointment, solution	0.25, 0.5, 1
	Hydrocortisone acetate	Cream, ointment	0.5–1

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Includes representative examples and not all available agents

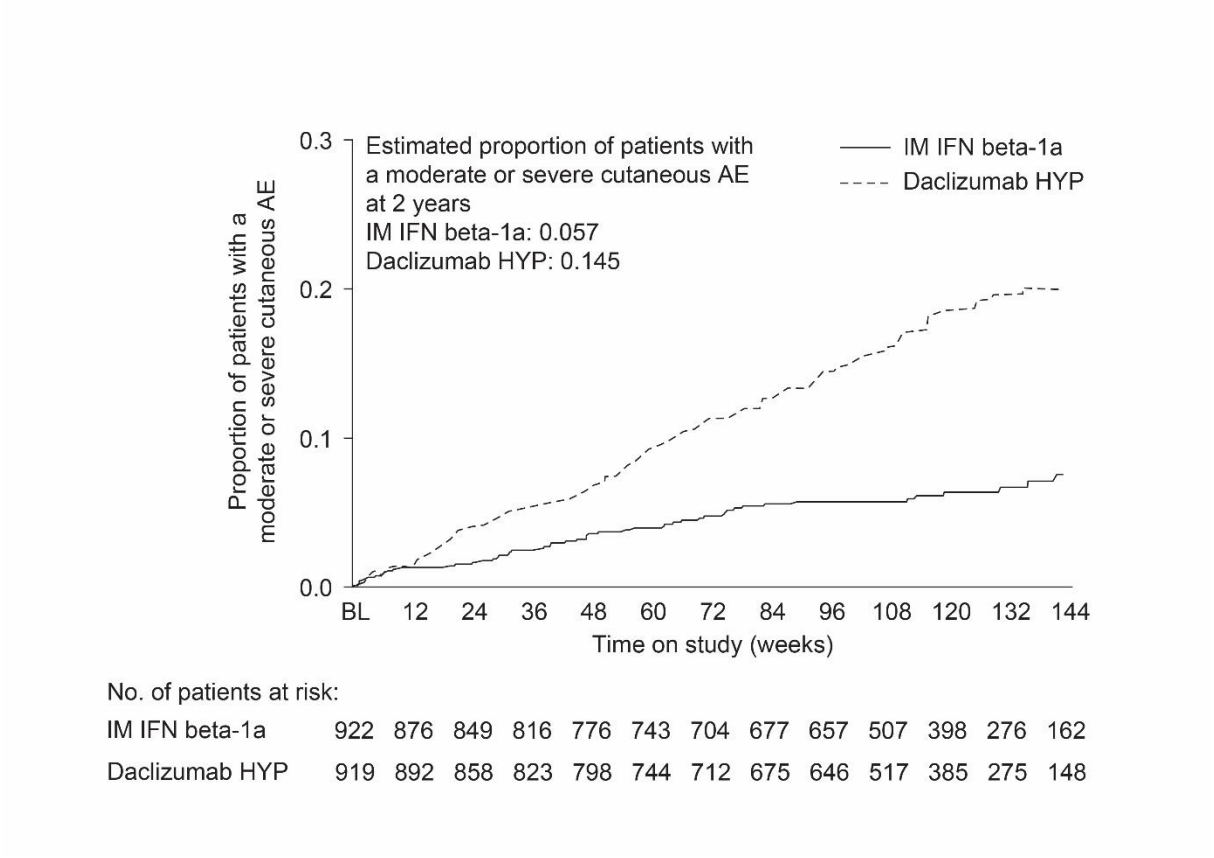


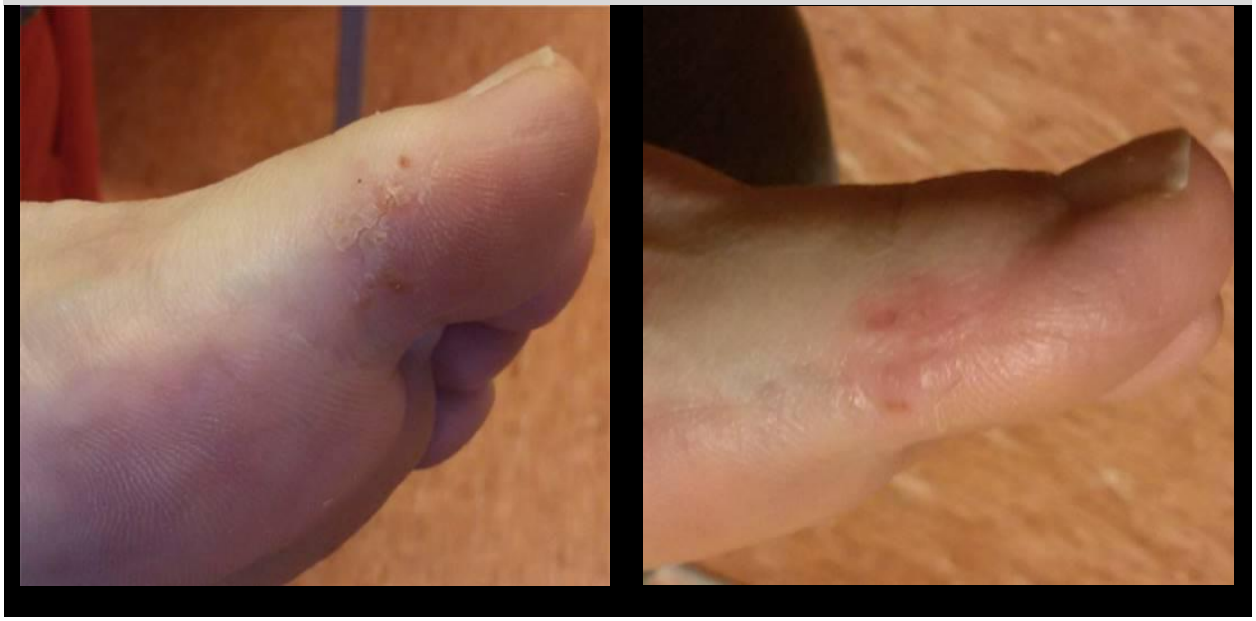
Figure S1 Kaplan–Meier plot of time to first moderate or severe cutaneous AE. *AE* adverse event, *BL* baseline, *HYP* high-yield process, *IFN* interferon, *IM* intramuscular

Figure S2 Examples of mild (**a**), moderate (**b**), and severe (**c**) cutaneous AEs reported in daclizumab HYP-treated patients. Individual pictures of the same event differ only because of magnification. *AE* adverse event, *HYP* high-yield process

a Examples of mild cutaneous AEs reported in daclizumab HYP-treated patients

Mild event example 1

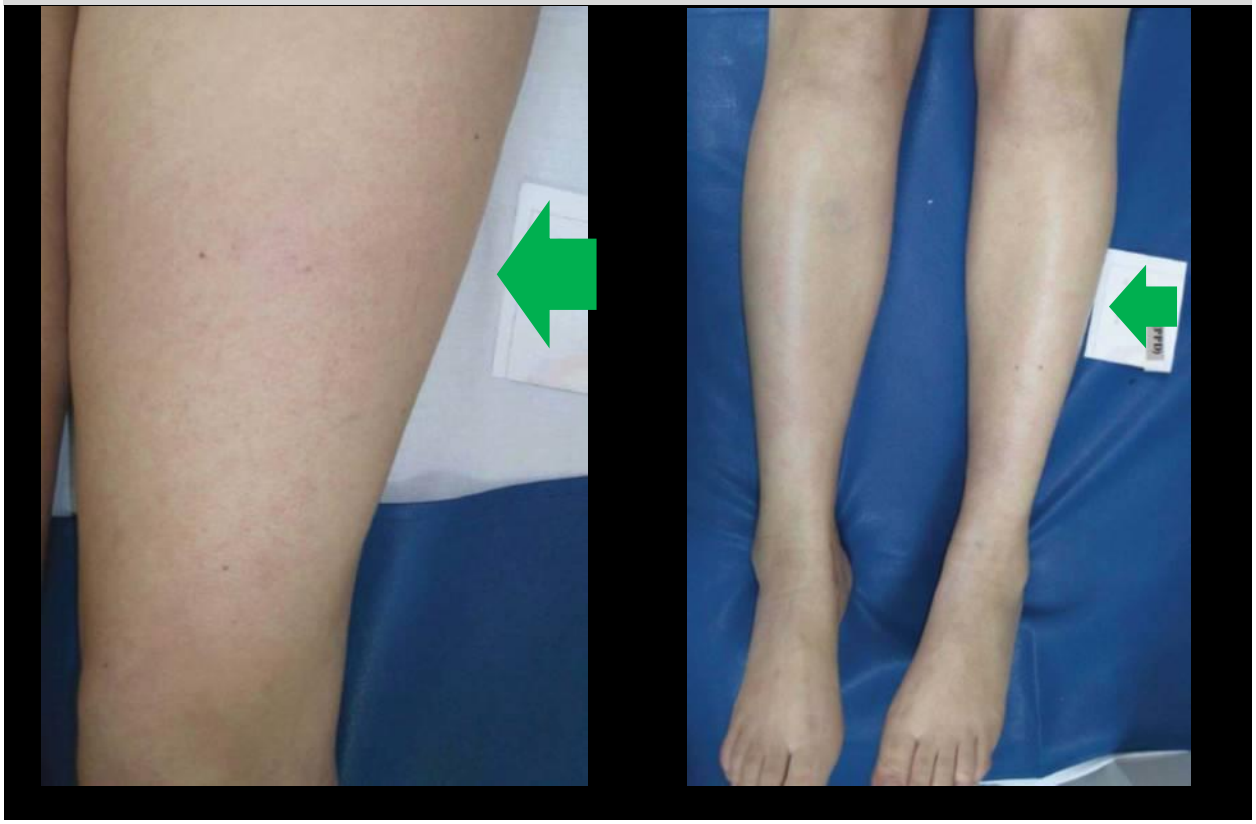
Central dermatologist's description of the cutaneous AE: "These lesions are deep seated vesicles arising from spongiosis or a process that is part of the eczema spectrum of diseases. Hand and foot dermatitis was a common diagnosis in DECIDE. This particular lesion is a pattern termed pompholyx (pompholyx eczema)."



Mild event example 2

Central dermatologist's description of the cutaneous AE: "This is an example of a very mild eczema.

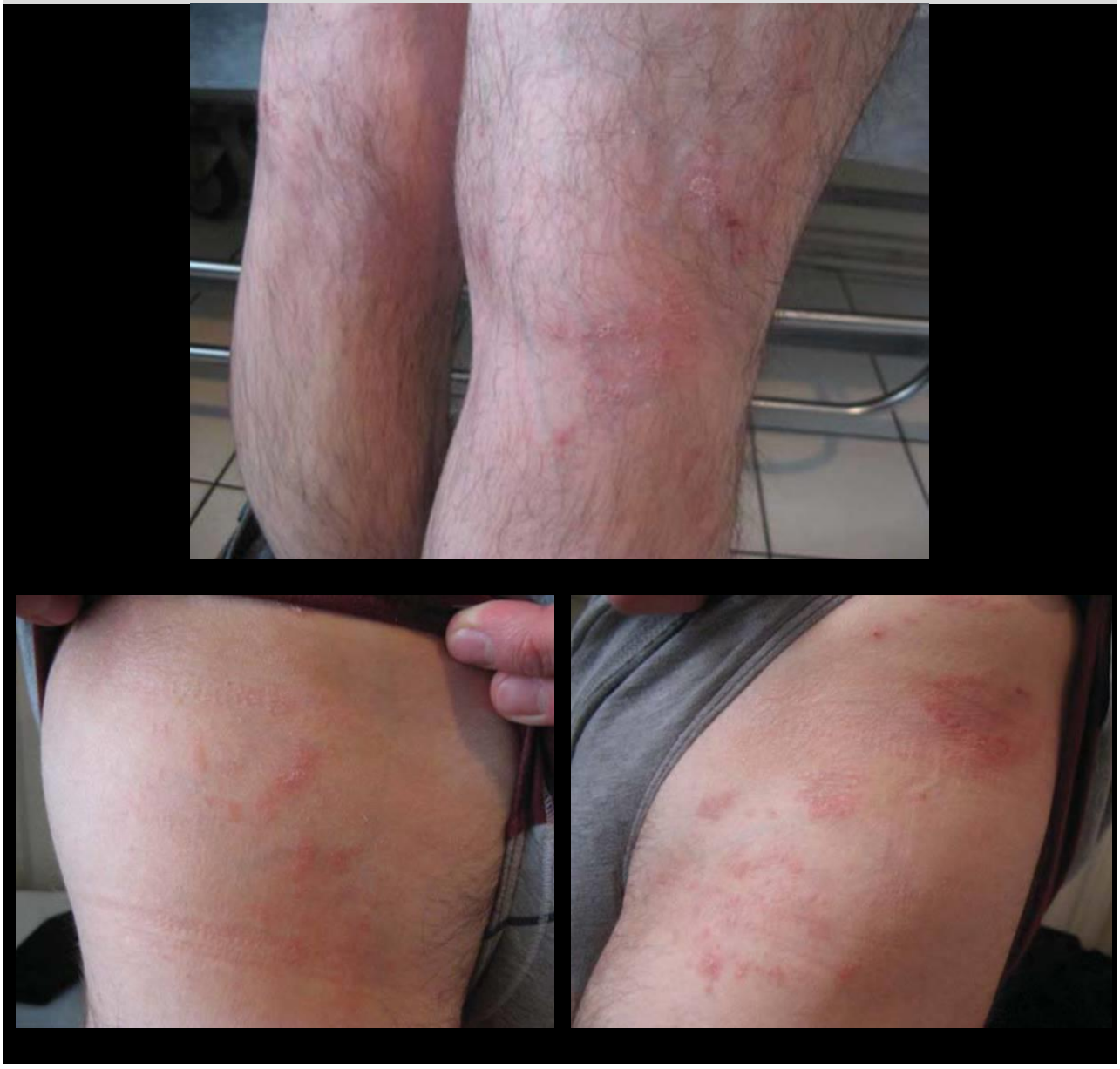
The rash is quite subtle."



b Examples of moderate cutaneous AEs reported in daclizumab HYP-treated patients

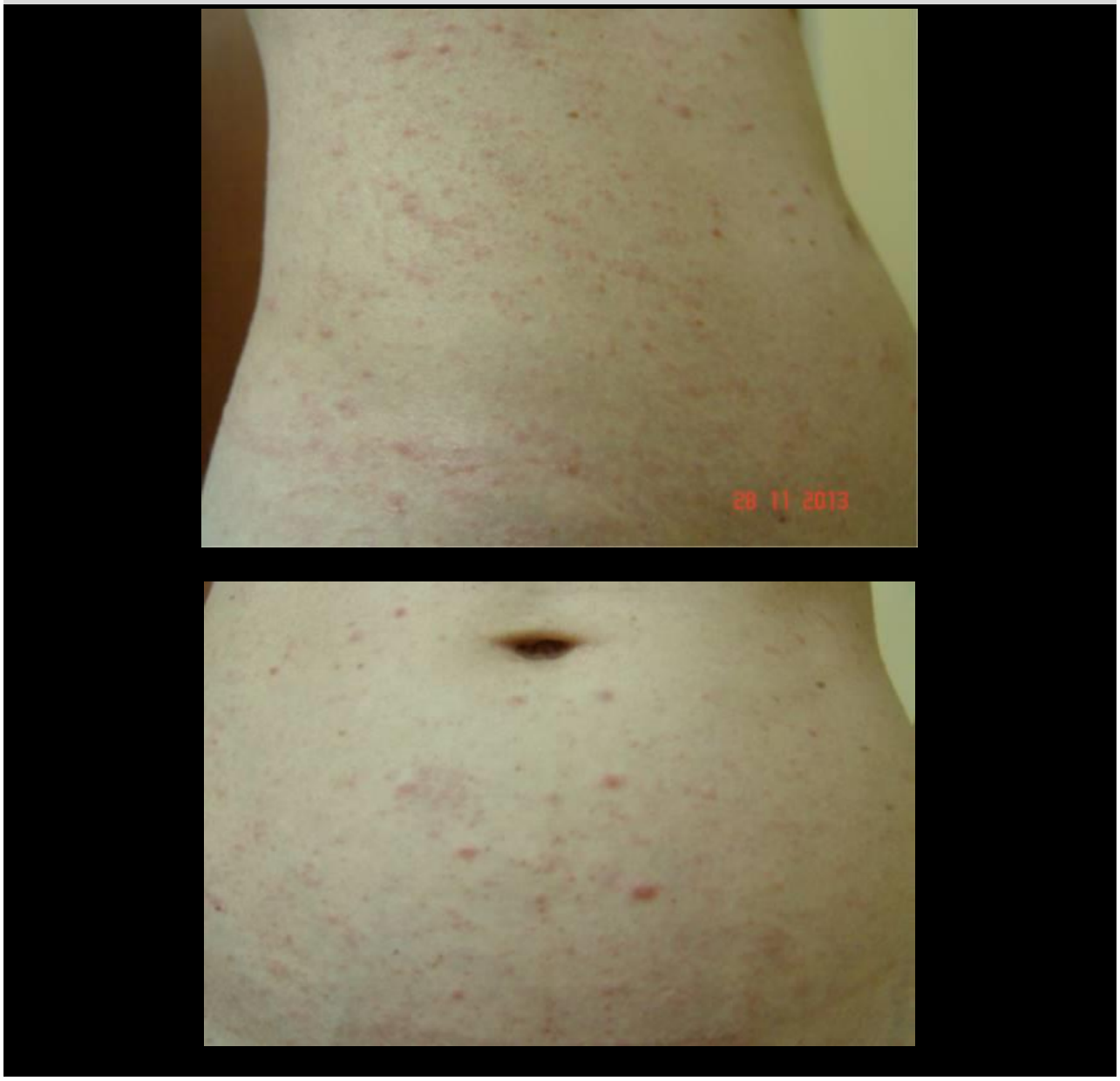
Moderate event example 1

Central dermatologist's description of the cutaneous AE: "These are eczema lesions. In the study, both 'allergic dermatitis' and 'eczema' were used to describe these type of cutaneous AEs depending on the country of origin of the patient."



Moderate event example 2

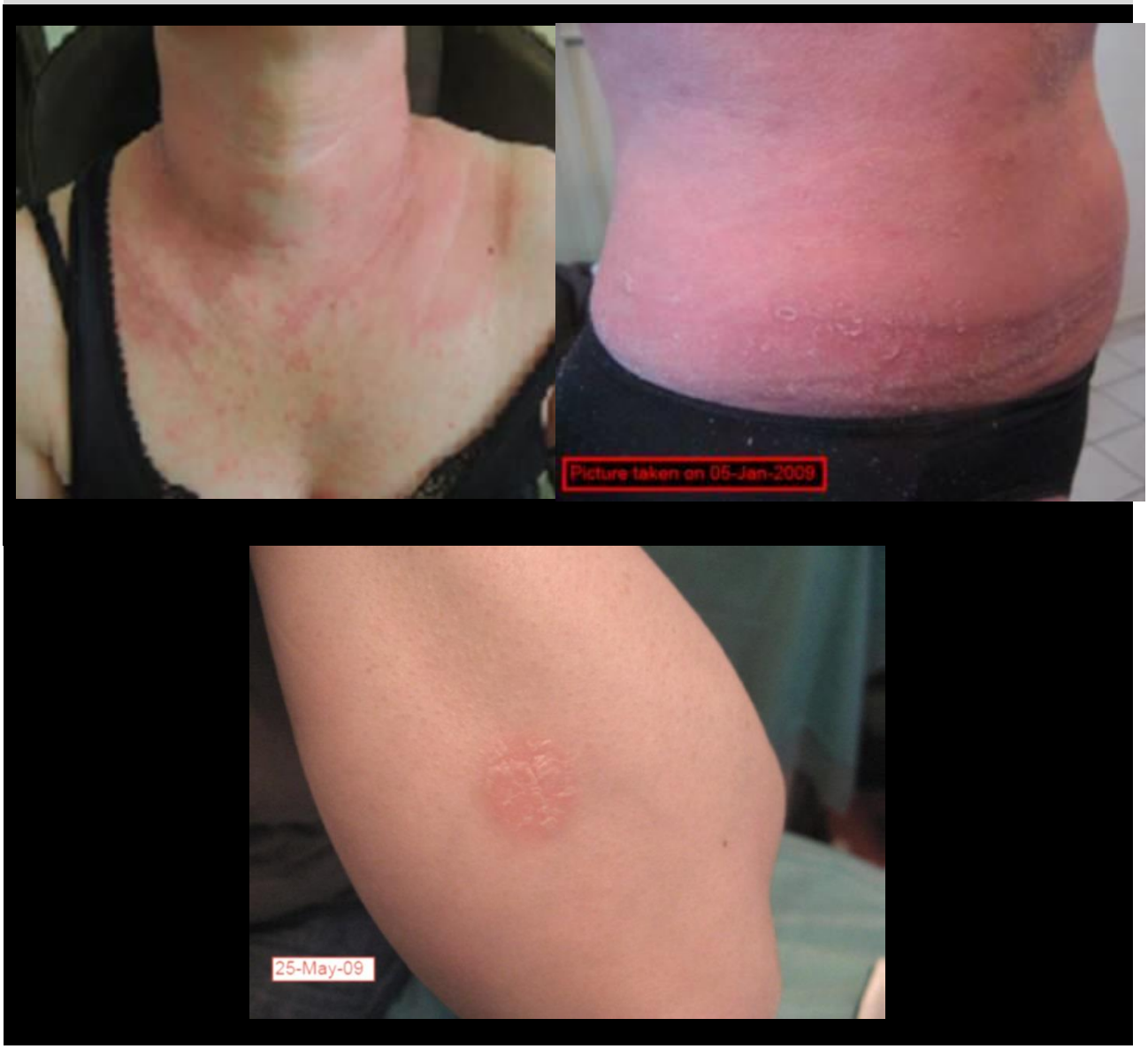
Central dermatologist's description of the cutaneous AE: "This case shows a follicular pattern. It could be follicular eczema or just folliculitis."



c Examples of severe cutaneous AEs reported in daclizumab HYP-treated patients

Severe event example 1

Central dermatologist's description of the cutaneous AE: "There are small to large areas of erythema (macules and patches of erythema) and some dermatographism caused by scratching, but the upper chest is clear. The abdomen is diffusely red with some focal scaling or superficial exfoliation. There is a scaly plaque on the forearm that is red colored. The cutaneous AE is a likely delayed-type hypersensitivity reaction to a systemic antigen and it could be a 'drug' reaction to daclizumab."



Severe event example 2

Central dermatologist's description of the cutaneous AE: "This is a drug-type hypersensitivity rash pattern with the side of face and neck being more typical maculopapular lesions with some confluence to larger lesions (a macule or papule is <1 cm in size). Exfoliation is a superficial process of loss of corneocytes. The reaction of the skin involves some degree of mucositis with involvement of the lips and tongue, as seen in the pictures."