achieving HiSCR-75 and HiSCR-100 at weeks 12 and 24 (Figure 1a).

Brodalumab administration weekly over 24 weeks in a pilot cohort of 10 participants with HS did not identify significant safety concerns. A 100% HiSCR response was observed at week 4. In contrast to E2W dosing, no cyclical disease suppression or recurrence was observed. Weekly dosing has a more rapid onset of disease suppression as measured by HiSCR; however, these differences were largely negligible by week 24 (Figure 1a).

Limitations include the small cohort (n = 10), lack of a placebo arm and limited timeframe of assessments (24 weeks). Given that other studies have excluded participants with more than 20 draining tunnels, this cohort gives a unique insight into the effect of brodalumab on a largely excluded patient population. Given the uncertainty regarding the natural variation in disease activity in HS, further placebo-controlled studies are necessary to validate the observed improvements.

J.W. Frew 1, K. Navrazhina 1, M. Sullivan-Whalen 1, P. Gilleaudeau 1, S. Garce 1 and J.G. Krueger 1

1Laboratory of Investigative Dermatology, The Rockefeller University, New York, NY, USA and 2Weill Cornell/Rockefeller/Sloan Kettering Tri-Institutional MD-PhD Program, New York, NY, USA

Email: jfw@rockefeller.edu

References

1 Papp K, Reich K, Paul C et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. Br J Dermatol 2016; 175: 273–86.

2 Frew JW, Navrazhina K, Grand D et al. The effect of subcutaneous brodalumab upon disease activity in hidradenitis suppurativa: an open-label cohort study. J Am Acad Dermatol 2020; https://doi.org/10.1016/j.jaad.2020.05.007.

3 Kimball AB, Sobell JM, Zouboulis CC et al. HiSCR (Hidradenitis Suppurativa Clinical Response): a novel clinical endpoint to evaluate therapeutic outcomes in patients with hidradenitis suppurativa from the placebo-controlled portion of a phase 2 adalimumab study. J Eur Acad Dermatol Venereol 2016; 30: 989–94.

4 Zouboulis CC, Tzellos T, Kyrigidis A et al. Development and validation of the International Hidradenitis Suppurativa Severity Score System (IHS4), a novel dynamic scoring system to assess HS severity. Br J Dermatol 2017; 177: 1401–9.

Funding sources: J.W.F. was supported in part by grant UL1 TR001866 from the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH) Clinical and Translational Science Award (CTSA) programme. K.N. was supported by an MSTP grant from the National Institute of General Medical Sciences of the NIH under award number T32GM007739 to the Weill Cornell/Rockefeller/Sloan Kettering Tri-Institutional MD-PhD Program.

Conflicts of interest: J.G.K. has received research support (grants paid to institution) from AbbVie, Amgen, BMS, Boehringer, EMD Serono, Innovaderm, Kineta, LEO Pharma, Novan, Novartis, Paraxel, Pfizer, Regeneron and Vitea; and personal fees from AbbVie, Acrros, Allergan, Aurigene, Biogenidec, Boehringer, Escalier, Janssen, Lilly, Novartis, Pfizer, Roche and Valeant. The other authors declare they have no relevant conflicts of interest.

Quantification of skin sensitivity to ultraviolet radiation using ultrawideband optoacoustic mesoscopy

DOI: 10.1111/bjd.19463

Dear Editor, Phototesting is used to assess individual sensitivity to ultraviolet (UV) radiation in order to determine adequate UV dosage for phototherapy. Under the standard procedure, small skin areas are exposed to increasing doses of UV radiation. The lowest UV dose that induces a delineated erythema at 24 ± 2 h after UV exposure defines the minimal erythema dose (MED).2 Visual assessment is the gold standard for MED determination; however, this is prone to observer variability.3 Optical methods have been considered to quantify the magnitude of erythema response. However, these methods are limited by light scattering and therefore high-resolution imaging is restricted to depths of < 200 μm, resulting in unreliable measurements.4,5

Ideally, a quantitative method should offer a comprehensive observation of the skin and its microvascular structure, the latter exhibiting considerable inter- and intraindividual variations likely influencing the visual appearance of erythema formation.6 In addition, it would ensure that precisely the same skin region of interest (ROI) is measured before and after UV-induced erythema development. Also, this method should disentangle the effect of the melanin layer from the effect of the haemoglobin.

Optoacoustic techniques enable high-resolution imaging at a deeper level than purely optical methods by resolving optical contrast at ultrasonic resolutions. They work by illuminating the ROI with short laser pulses, stimulating the tissue to emit acoustic waves, which are detected by an ultrasound detector. Mathematical processing of the detected waves yields threedimensional imaging of light-absorbing structures, such as blood vessels. Ultrawideband raster scan optoacoustic mesoscopy (UWB-RSOM) in particular, is an optoacoustic imaging modality that allows visualization of skin structures and dermal microvasculature at depths of up to 1–5 mm, reaching resolutions of up to 7 μm (axial) and 30 μm (lateral).7,8 This process allows for the detection and quantification of microvascular features typical of inflammatory skin diseases, such as psoriasis and eczema, which are inaccessible using other methods. We wanted to investigate whether UWB-RSOM could provide high-resolution objective assessments of standard phototesting through comprehensive analysis of shallow and deep microvascular responses.

Seven healthy volunteers participated in the study, one of whom was treated as a nonirradiated control. Six skin areas measuring 2.8 × 2.5 cm in each of the six participants (one woman, five men; age range 27–66 years; Fitzpatrick skin types II–III) were exposed to increasing doses of UVB-rich radiation (wavelength 275–365 nm). The control participant did not receive UV radiation. After 24 ± 2 h an experienced
clinician determined the MED of each volunteer based on visual assessment. Before UV irradiation and at the time of clinical evaluation, the same sections of dermal microvasculature were assessed with UWB-RSOM by means of a protocol based on ink fiducial markers (Figure 1a, b). UV-induced changes in dermal total blood volume (dermal blood fraction) were quantified from identical parts of the dermal microvasculature. The ROIs were defined using microvascular bifurcations as reference from the en face cross-sectional images. Six nonirradiated skin areas in the control participant were imaged and quantified likewise at 0 h and 24 h.

UWB-RSOM cross-sectional views reveal the effect of the erythematous skin reaction on the whole microvascular structure after exposure to the MED (Figure 1a). As expected, the effect is more pronounced for higher doses (Figure 1a). UWB-RSOM shows UV-induced recruitment of vessels that were not previously perfused. The images also reveal vasodilation, visible as an increase in vessel diameter at different depths. Smaller microvessels and capillaries, which emit higher-frequency ultrasound signals, are shown in green; larger microvessels emitting lower-frequency signals are shown in red.

Figure 1(c) shows that the blood fraction, as measured by UWB-RSOM, increased approximately linearly as a function of UV dose. The UV dose of 25 mJ cm\(^{-2}\) below the visual MED triggered an average increase in blood fraction of 5.1% (± 5.3%) and the highest dose produced an average increase of 49.6% (± 25.4%). The control measurement showed a negligible average change in blood fraction of −1.6% (± 5.6%).

---

**Figure 1** (a) The same section of the dermal vasculature before and 24 h after ultraviolet (UV) irradiation using the minimal erythema dose (MED). Vasodilation (blue arrows) and vessel recruitment (red arrows) can be observed. Clinical images are shown in the insets. (b) The same process as described in (a) with exposure increased to 2.5-fold MED. (c) Change in blood fraction corresponding to all participants irradiated with UV radiation and the nonirradiated control participant after 24 h. Doses are expressed relative to the individual MED. EP, epidermis; SP, subepidermal plexus; CV, connecting vessels; IF, ink fiducial marker.
Individual vessel diameters show a similar trend (data not shown).

Our results demonstrate that UWB-RSOM allows direct monitoring and quantification of UV-induced erythema in phototesting with unprecedented spatial precision. We imaged and quantified the effect of increasing doses of UV radiation on identical microvascular regions through the entire depth of the skin, directly observing vasodilation and vessel recruitment as a function of macroscopic erythema. Moreover, the results indicate that UWB-RSOM could be a useful tool to detect the suberythemal response of the skin to UV radiation, which may increase the sensitivity of phototesting. The UWB-RSOM prototype has certain technical limitations including motion artefacts and slight variations in laser energy, which may explain changes in blood volume in only five of six phototested skin areas exposed to the MED. However, our findings suggest that UWB-RSOM holds potential to improve the accuracy of phototesting.

Acknowledgments: the authors would like to thank Robert J. Wilson for invaluable help editing the paper. Open access funding enabled and organized by Projekt DEAL.

B. Hindelang,1,2,3 J. Aguirre,2,3 A. Berezhnoi,2,3 T. Biedermann,1, U. Darsow,1 B. Eberlein1 and V. Ntziachristos2,3

1 Clinic for Dermatology and Allergology at Biederstein; 2 Chair of Biological Imaging, School of Medicine, Technical University of Munich, Munich, Germany; and 3 Institute of Biological and Medical Imaging, Helmholtz Zentrum München, Neuherberg, Germany

Correspondence: Vasilis Ntziachristos.
Email: v.ntziachristos@tum.de

References

1. Lim HW, Honigsmann H, Hawk J. Photodermatology. Boca Raton, FL: CRC Press, 2013.
2. Singer S, Schwarz T, Berneburg M. Grundlagen zur phototherapie. In: Phototherapie (Singer S, Schwarz T, Berneburg M, eds). Wiesbaden: Springer Fachmedien Wiesbaden, 2016; 1–7 (in German).
3. Lock-Andersen J, Wulf HC. Threshold level for measurement of UV sensitivity: reproducibility of phototest. Photodermaux Photoimmunol Photomed 1996; 12:154–61.
4. Humbert P, Fanian F, Maibach HI, Agache P. Agache’s Measuring the Skin: Non-invasive Investigations, Physiology, Normal Constants, 2nd edn. Cham: Springer International Publishing, 2017.
5. Huang M-W, Lo P-Y, Cheng K-S. Objective assessment of sunburn and minimal erythema dose: comparison of noninvasive in vivo measuring techniques after UVB irradiation. EURASIP J Adv Signal Process 2010; 2010:483562.
6. Simonen P, O’Brien M, Hamilton C et al. Normal variation in cutaneous blood content and red blood cell velocity in humans. Physiol Meas 1997; 18:155–70.
7. Aguirre J, Schwarz M, Garzorz N et al. Precision assessment of label-free psoriasis biomarkers with ultra-broadband optoacoustic mesoscopy. Nat Biomed Eng 2017; 1:68.
8. Omar M, Schwarz M, Soliman D et al. Pushing the optical imaging limits of cancer with multi-frequency-band raster-scan optoacoustic mesoscopy (RSOM). Noplneu 2015; 17:208–14.

Funding sources: this project received funding from the EU’s Horizon 2020 research and innovation programme [grant agreement number 687866 (INNODERM)], from the European Research Council under the EU’s Horizon 2020 research and innovation programme [grant agreement number 694968 (PREMSOT)] and from Deutsche Forschungsgemeinschaft [grant agreement number SFB 824, project B10].

Conflicts of interest: V.N. has a financial interest in iThera Medical GmbH, Munich, Germany, which was not involved in this work.

Intralesional rituximab in the treatment of indolent primary cutaneous B-cell lymphoma

DOI: 10.1111/bjd.19490

Dear Editor, Primary cutaneous B-cell lymphomas (PCBCLs) are a heterogeneous group of extranodal lymphomas.1 Primary cutaneous marginal zone lymphoma (MZL) and follicle centre lymphoma (FCL), the most prevalent PCBCLs, are typically indolent.

Various treatments are available for MZL and FCL, including intralesional (IL) rituximab, a chimeric monoclonal IgG antibody against CD20, a major B-cell marker.2 However, there remain few reports of IL rituximab in PCBCL, and its ideal administration schedule remains undefined.3–5 In this study, we evaluated the efficacy, safety and tolerability of IL rituximab in PCBCL, including the use of weekly injections – a schedule not previously described.

We reviewed the charts of adult patients diagnosed with MZL/FCL and treated with IL rituximab at McGill University’s Jewish General Hospital between January 2014 and December 2018. Rituximab was prepared daily as a 3-mL aliquot of the stock 10 mg mL−1 solution. It was injected intralesionally until the lesion blanched, for a maximum of 30 mg per session, without premedication. In the case of relapse, salvage therapy was determined accounting for patient preference of repeat IL rituximab vs. radiotherapy. We noted: age, sex, PCBCL type, tumour–nodes–metastasis stage,2 previous treatments, number and location of lesions, rituximab dose, frequency and number of injections, treatment response, toxicity, and patient satisfaction. Treatment efficacy was evaluated by assessing clinical response according to the standardized cutaneous lymphoma criteria.6 Response was used to compute objective response rates, i.e. the proportion of patients with either complete or partial response. This review was approved by the institutional research ethics committee.

Twelve patients were included in this series (Table 1). None had extracutaneous involvement. The median patient age was 49 years (range 19–80). Patients had local/regional disease on scalp/face, trunk, and/or extremities. Median duration of follow-up was 3.2 years (range 1.9–6.1). The median number of prior treatments was one (range 0–2). Radiotherapy was the most common prior treatment (n = 7). Only one