tildrakizumab treatment during pregnancy. Female patients with psoriasis of childbearing age and/or their partners should continue to follow local practice recommendations for contraceptive use while taking tildrakizumab and avoid pregnancy.

Acknowledgments: we thank the patients for their participation. Editorial support was provided by AlphaBioCom, LLC, and was funded by Sun Pharmaceutical Industries, Inc.

K. Haycraft,[1] D. DiRuggiero,[2] S.J. Rozzo,[3] A.M. Mendelsohn[3] and T. Bhutani[4]

[1]*Riverside Dermatology & Spa, Hannibal, MO, USA;* [2]*Skin Cancer & Cosmetic Dermatology Center, Rome, GA, USA;* [3]*Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA; and* [4]*UCSF Medical Center, San Francisco, CA, USA*

E-mail: *kathleenhaycraft@yahoo.com*

References

1 Tauscher AE, Fleischer AB Jr, Phelps KC *et al.* Psoriasis and pregnancy. *J Cutan Med Surg* 2002; **6**:561–70.
2 Papp K, Thaçi D, Reich K *et al.* Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. *Br J Dermatol* 2015; **173**:930–9.
3 Reich K, Papp KA, Blauvelt A *et al.* Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. *Lancet* 2017; **390**:276–88.
4 Palmeira P, Quinello C, Silveira-Lessa AL *et al.* IgG placental transfer in healthy and pathological pregnancies. *Clin Dev Immunol* 2012; **2012**:985646.
5 Khalilieh S, Hodsman P, Xu C *et al.* Pharmacokinetics of tildrakizumab (MK-3222), an anti-IL-23 monoclonal antibody, after intravenous or subcutaneous administration in healthy subjects. *Basic Clin Pharmacol Toxicol* 2018; **123**:294–300.
6 Ilumya™ (tildrakizumab-asmn) injection, for subcutaneous use [full prescribing information]. Sharjah, U.A.E.: Sun Pharma Global FZE, Inc., 2018.
7 Kopp T, Riedl E, Bangert C *et al.* Clinical improvement in psoriasis with specific targeting of interleukin-23. *Nature* 2015; **521**:222–6.
8 Garcia-Enguidanos A, Calle ME, Valero J *et al.* Risk factors in miscarriage: a review. *Eur J Obstet Gynecol Reprod Biol* 2002; **102**:111–19.

Funding sources: these studies were funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA Analyses were funded by Sun Pharmaceutical Industries, Inc.

Conflicts of interest: K.H. has been a member of advisory committees for Celgene, Lilly, Novartis, Ortho Dermatologics, Pfizer, Sun Pharmaceutical Industries, Inc., AbbVie and Valeant; and has served as a speaker for Celgene and Lilly. D.D. has been a member of advisory committees for Novartis, Celgene and Ortho Dermatologics. S.J.R. and A.M.M. are employees of Sun Pharmaceutical Industries, Inc. T.B. has served as an investigator for Janssen, Merck, Lilly and Strata Life Sciences.

Incidences of different cancer types in dermatomyositis, polymyositis and dermatopolymyositis: results of a registry analysis

DOI: 10.1111/bjd.18948

Dear Editor, Studies confirming dermatomyositis/polymyositis/dermatopolymyositis (DM/PM/DPM) as a paraneoplastic disease have found cancer incidence rates elevated at the time-point of diagnosis and remaining elevated over time.[1] Guidelines promote cancer screening in patients with newly diagnosed myositis.[2] Data on the incidence of cancer types in patients with DM and PM are insufficient to guide targeted screening.[3–5]

We conducted a retrospective registry analysis using data from the Danish National Patient Register (NPR). The NPR, established in 1977, is an administrative registry that provides individual-level linkage. Cancers that were diagnosed before and after the onset of myositis were studied. Patients with DM/PM/DPM were identified by their first outpatient or inpatient consultation for DM/PM/DPM using the International Classification of Diseases 8th Revision (ICD-8) codes 716·00 and 716·10, and ICD-10 codes M33·0, M33·1, M33·2 and M33·9. The primary endpoint was the development of any type of cancer (ICD-8: 140–209; ICD-10: C00–97, B21). Secondary endpoints were the occurrence of the most frequent cancer types during the predefined time period (colon–rectum–anus, ICD-8: 153–4; ICD-10: C18–21), lung (ICD-8: 162; ICD-10: C33–34), bladder (ICD-8: 188; ICD-10: C67), female breast (ICD-8: 174; ICD-10: C50), ovary (ICD-8: 183; ICD-10: C56) and prostate cancer (ICD-8: 185; ICD-10: C61), as well as non-Hodgkin lymphoma (NHL) (ICD-8: 200, 202; ICD-10: C82–86, C96) and multiple myeloma (MM) (ICD-8: 203; ICD-10: C88, C90).

We calculated the cancer incidence rates (IRs) of these individuals and compared them with general-population values (matched for age and sex). The general population was sampled using the Civil Registration System (for detailed information see Schmidt *et al.*).[6] To assess the cancer risk after diagnosis of DM/PM/DPM we calculated IRs for four periods: 0–1, 1–2, 2–5 and ≥ 5 years. Individuals were followed up until death from any cause, migration or occurrence of another type of cancer, whichever happened first. To assess the cancer risk before diagnosis of DM/PM/DPM we calculated IRs for three periods: ≤ 2, 2–5 and ≥ 5 years.

The initial cohort of patients with DM/PM/DPM, aged ≥ 18 years, identified from 1 January 1977 to 31 December 2017, comprised 2825 individuals. In total, 249 had a cancer diagnosis prior to DM, PM and/or DPM (n = 96, 108 and 45, respectively).

Table 1 Incidence rates (IRs) and 95% confidence intervals (CIs) per 100 person-years for any type of cancer after diagnosis of dermatomyositis (DM), polymyositis (PM) and/or dermatopolymyositis (DPM), stratified by time after diagnosis

	DM	PM	DPM	DM/DPM	DM/PM/DPM	(Matched) general population
0–1 years						
Cancers	53	37	19	72	109	227
IR (95% CI)	153 (117–200)	51·8 (37·5–71·5)	85·6 (54·6–134)	127 (101–160)	85·0 (70·4–103)	24·9 (21·9–28·4)
P-value[a]	< 0·001	0·0047	< 0·001	< 0·001	< 0·001	–
1–2 years						
Cancers	8	18	6	14	32	224
IR (95% CI)	14·4 (7·2–28·8)	11·3 (7·1–17·9)	13·1 (5·9–29·1)	13·8 (8·2–23·3)	12·3 (8·7–17·3)	9·8 (8·6–11·2)
P-value[a]	0·27	0·61	0·49	0·21	0·25	–
2–5 years						
Cancers	11	43	11	22	65	604
IR (95% CI)	3·4 (1·9–6·2)	4·3 (3·2–5·8)	4·7 (2·6–8·6)	4·0 (2·6–6·0)	4·2 (3·3–5·3)	3·9 (3·6–4·3)
P-value[a]	0·66	0·58	0·55	0·96	0·64	–
≥ 5 years						
Cancers	55	120	21	76	196	2298
IR (95% CI)	0·7 (0·5–0·9)	0·8 (0·7–1·0)	0·9 (0·6–1·4)	0·72 (0·57–0·90)	0·8 (0·7–0·9)	0·7 (0·7–0·8)
P-value[a]	0·71	0·65	0·82	0·67	0·94	–

[a]P-values were calculated for the incidence rate ratio using the matched general population as the reference.

Table 1 illustrates cancers after diagnosis of DM, PM and DPM (n = 127, 218 and 57, respectively). In the first year after diagnosis, the risk of any type of cancer was significantly higher for DM/DPM [IR 126·6 per 100 person-years, 95% confidence interval (CI) 100·5–159·5; P < 0·001] than for the general population. After that the effects were not sustained. The adjusted level of significance was P ≤ 0·0019. PM did not reach statistical significance at any point in time. With regard to cancers arising before DM, the majority (57·3%) preceded DM and one-third preceded PM by > 2 years before diagnosis. In contrast, most diagnoses of DPM (60·0%) and PM (38·3%) were made ≥ 5 years before cancer.

Analysis by type of cancer in patients with DM/DPM showed a significantly higher risk of diagnosis of lung cancer (incidence rate ratio (IRR) 8·93, 95% CI 5·24–15·2; P < 0·001) and ovarian cancer (IRR 27·1, 95% CI 8·49–86·3; P < 0·001) than in the general population during the first year after diagnosis. In the same period, patients with PM had higher incidences of NHL (IRR 3·18, 95% CI 1·81–5·60; P < 0·001) and MM (IRR 4·50, 95% CI 1·93–10·5; P < 0·001) in comparison with general-population values (IR per 100 person-years 0·7, 95% CI 0·3–1·5 for NHL; IR 0·2, 95% CI 0·1–0·9 for MM). The different rates in terms of cancer type and extent for all cancer types 1 year after diagnosis of DM/DPM and PM emphasize the differences in pathophysiology of these diseases. We did not identify significantly elevated risks for specific cancer types over time to justify specific screening recommendations.

This study has several limitations. Firstly, although statistical testing was performed, it remains controversial whether or not to adjust for multiple comparisons.[7] Secondly, the clinical validity of the diagnostic codes was not addressed in this study. Hence, it remains unclear which characteristics were used to assigned patients to DPM in the ICD-10 classification. An additional coding validation study may further strengthen the validity of the results. Thirdly, the IRRs were adjusted only for age and sex. Other confounders (e.g. deprivation) were not adjusted for.

In line with previous work, we found an increased risk of malignancy, with strong emphasis on the first year after diagnosis. This close temporal association is consistent with a paraneoplastic mechanism. In contrast to Hill *et al.*,[1] we were not able to detect an effect that persisted more than 1 year after DM diagnosis. Detection bias due to cancer screening at the timepoint of diagnosis of DM/PM/DPM, and possibly ascertainment bias need to be taken into consideration as a cause of the elevated rate of cancer diagnosis during the first year, rather than an increased propensity for malignancy in patients with autoimmune disease.

Diagnosis of DM/PM/DPM often leads to high patient concerns due to its described paraneoplastic nature. Specific autoantibodies like anti-p155/14M may assist in differentiating between paraneoplastic and nonparaneoplastic DM/PM/DPM. Analyses linking anti-p155/140 antibodies and a routine myositis panel to cancer incidence rates may help to investigate further the paraneoplastic nature of DM/PM/DPM and to consult patients with regard to their cancer risk and provide appropriate screening and follow-up measures.

M. Zidane,[1,2] C. Dressler,[1,2] A. Nast[1,2] and A. Egeberg[3]

[1]*Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin, Germany;* [2]*Berlin Institute of Health, Department of Dermatology, Venerology and Allergy, Division of Evidence-Based Medicine (dEBM), Berlin, Germany and* [3]*Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, Denmark*

Correspondence: Alexander Nast.

Email: alexander.nast@charite.de

References

1 Hill CL, Zhang Y, Sigurgeirsson B *et al*. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet* 2001; **357**:96–100.
2 Trallero-Araguas E, Rodrigo-Pendas JA, Selva-O'Callaghan A *et al*. Usefulness of anti-p155 autoantibody for diagnosing cancer-associated dermatomyositis: a systematic review and meta-analysis. *Arthritis Rheum* 2012; **64**:523–32.
3 Callen JP. Relation between dermatomyositis and polymyositis and cancer. *Lancet* 2001; **357**:85–6.
4 Gallais V, Crickx B, Belaich S. [Prognostic factors and predictive signs of malignancy in adult dermatomyositis]. *Ann Dermatol Venereol* 1996; **123**:722–6 (in French).
5 Olazagasti JM, Baez PJ, Wetter DA *et al*. Cancer risk in dermatomyositis: a meta-analysis of cohort studies. *Am J Clin Dermatol* 2015; **16**:89–98.
6 Schmidt M, Pedersen L, Sorensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol* 2014; **29**:541–9.
7 Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology* 1990; **1**:43–6.

Funding sources: none.

Conflicts of interest: the authors declare they have no conflicts of interest.

Results from the *BJD* survey on readership views towards clinical practice guidelines

DOI: 10.1111/bjd.18960

Linked Editorial: Yiu et al. *Br J Dermatol* 2020; **183**:1–2.

Dear Editor, The *BJD* has been publishing clinical practice guidelines (CPGs) in dermatology for more than 20 years.[1–3] With the increasing adoption of gold-standard guideline development methodology and reporting checklists, such as the GRADE[4] approach and the AGREE II[5] toolkit, recent CPGs published in the *BJD* are of high quality and are highly accessed, with CPGs making up half of the top 10 downloaded *BJD* articles in 2019. As a group of guideline developers and journal editors associated with the *BJD*, we were interested in how the readership perceives and uses CPGs. The objective of this study was to survey the demographics of the *BJD* CPG readership, and the utility of and attitudes towards CPGs.

An anonymous, cross-sectional electronic survey for healthcare professionals was conducted between May 2019 and January 2020. The survey was distributed to 7000 people listed as an *BJD* author through email via the *BJD* submission system. The survey was promoted on social media through the *BJD* Facebook and Twitter pages, on the Wiley online library *BJD* website, and to the British Association of Dermatologists membership through newsletters.

The questionnaire consisted of two sections and 21 questions. We selected eligible participants, namely healthcare practitioners, with an introductory question. In the first section we also collected information about participants' age, sex, number of years' experience within dermatology, country of practice, frequency of access to the *BJD* for CPGs, and the preference of CPG type. Free-text sections were included for the final two questions. The second section consisted of 13 statements to which the respondents indicated their agreement or disagreement on a five-point Likert scale (from 1, strongly disagree to 5, strongly agree). These statements identified the attitudes to CPGs, barriers to the use of CPGs and perceived reliability of CPGs, based on a previous study[6] and the 'Attitudes Towards Guidelines' scale.[7] A final question elicited an overall suggestion for making CPGs more useful for daily clinical practice. We performed descriptive analyses of the data, and thematic analysis of the overall suggestions in the final question.

There were 1043 questionnaire responses (~14·9% response rate), out of which 758 participants were eligible healthcare professionals. Most of the respondents were between 35 and 64 years of age (n = 542, 71·5%) and over half were male (n = 432, 57·0%). The participants had a median of 18·0 years of clinical dermatology experience (interquartile range 10·0–27·0). There were respondents from 68 different countries, and there were nine countries of origin that had more than 20 respondents: the Netherlands (n = 21), India (n = 24), France (n = 30), Japan (n = 38), Taiwan (n = 40), Italy (n = 47), Germany (n = 48), the USA (n = 80) and the UK (n = 142).

Most respondents (n = 552, 72·8%) had accessed the *BJD* for a CPG within 6 months of the survey. In total 33 respondents gave reasons for not accessing the *BJD* for CPGs, including getting CPGs from other sources, CPGs being behind the paywall and CPGs not being applicable to the local population. The majority of respondents (n = 614, 81·0%) found disease-based guidelines the most useful, compared with 14·1% (n = 107) for drug-utility guidelines. The remaining respondents found that both guideline types were equally helpful, that neither were useful, or that diagnostic and procedure-based guidelines were favourable instead (n = 37, 4·9%).

There was an agreement with most statements assessing attitudes towards guidelines posed in section 2, with the mean Likert score above 4 or below 2 in seven questions (Figure 1). There was a variety of opinion for two statements that related to attitudes towards CPGs – 'guidelines oversimplify medical practice' (mean ± SD score 3·0 ± 1·2) and 'guidelines challenge the autonomy of care providers' (3·1 ± 1·2) – and for one barrier-of-use statement: 'guidelines are difficult to find if needed' (2·6 ± 1·2). Four main themes were identified from the final question, namely succinctness of guidelines, better accessibility, more considerations for implementation, and more updates.

These results indicate that the global readership has a broadly positive attitude towards the reliability and utility of CPGs published in the *BJD*. The two statements with the highest divergence of opinion are indicative of the debate on and art of guideline implementation in medicine, with the mantra 'guidelines, not tramlines'[8] elegantly summarizing the balance needed between adherence to guideline recommendations and clinical judgement for real-world implementation. The overall

