4 Pariente B, Cosnes J, Danese S *et al.* Development of the Crohn's disease digestive damage score, the Lémann score. *Inflamm Bowel Dis* 2011; **17**:1415–22.
5 Chiricozzi A, Faleri S, Franceschini C *et al.* AISI: a new disease severity assessment tool for hidradenitis suppurativa. *Wounds* 2015; **27**:258–64.
6 Draaijers LJ, Tempelman FR, Botman YA *et al.* The patient and observer scar assessment scale: a reliable and feasible tool for scar evaluation. *Plast Reconstr Surg* 2004; **113**:1960–5; discussion 6–7.
7 Thorlacius L, Ingram JR, Villumsen B *et al.* A core domain set for hidradenitis suppurativa trial outcomes: an international Delphi process. *Br J Dermatol* 2018; **179**:642–50.

How representative are data from global trials on programmed death-1 blockade in melanoma?

DOI: 10.1111/bjd.21621

Linked Article: Bai *et al.* *Br J Dermatol* 2022; **187**:401–410.

Immune checkpoint inhibition blocking PD-1 (programmed cell death receptor-1) is an efficient and tolerable systemic therapy in advanced melanoma.[1–4] However, it is becoming clearer and clearer that the risks and benefits of therapy are impacted by both external factors such as diet and inborn properties like human leucocyte antigen type.[5,6]

In this issue of the *BJD*, an international group of investigators now adds ethnicity to the list. Bai *et al.*[7] investigated the relationship between ethnicity, melanoma subtypes and clinical outcome after PD-1 immune checkpoint inhibition. The authors report data from 1135 patients with melanoma undergoing anti-PD-1 monotherapy from five independent melanoma centres in Australia, China and the USA. The cohort was then stratified by ethnicity into white (n = 814) and East Asian, Hispanic or African (hereafter referred to as EA/H/A) (n = 321). Of note, the vast majority (93%) of patients in the EA/H/A group were from East Asia. In addition, melanoma subtypes were grouped into nonacral cutaneous (NAC)/unknown primary (UP) [ultraviolet (UV) related, n = 849] and acral/mucosal/uveal (not UV related, n = 286). As expected,[8] white patients presented mostly NAC/UP melanomas (n = 710), whereas > 50% of the EA/H/A patients had non-UV-related melanomas (n = 182).

Within the total cohort, the overall response rate (ORR) for white patients was significantly higher than for EA/H/A patients: 49% [95% confidence interval (CI) 46–53] vs. 17% (95% CI 13–22). In a subgroup analysis according to melanoma subtype, white patients with NAC/UP melanomas also showed a superior ORR of 54% (95% CI 50–57) compared with 20% (95% CI 13–28) for EA/H/A patients. No significant differences could be detected for the ORR when comparing the non-UV-associated subtypes. Moreover, Bai *et al.* performed a multivariate analysis of the response rates of NAC/UP melanomas, the involved primary anatomical site and ethnicity. Here, the ORR remained higher in white patients than EA/H/A patients with NAC/UP. However, the disbalanced numbers of UV-related melanomas between groups must be considered.

Bai *et al.* also analysed the frequency of immune-related adverse events (irAEs) grouped by ethnicity. The overall incidence rate of irAEs was similar between the two groups but differences could be detected in the involved organs systems. While white patients more frequently had gastrointestinal or respiratory irAEs, EA/H/A patients showed a higher incidence of endocrine irAEs.

In conclusion, this retrospective international observational study demonstrates a possible impact of ethnicity on the efficacy and safety of PD-1 blockade. Although it is based mainly on the comparison of East Asian and white patients with advanced melanoma, the study clearly indicates that the worldwide usage of immune checkpoint inhibition warrants careful interpretation of trial data with regards to ethnicity-dependent differences in safety and efficacy.

Patrick Schummer and Bastian Schilling

Department of Dermatology, Venereology and Allergology, University Hospital Würzburg, Würzburg, Germany
Email: *schummer_p@ukw.de*

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

References

1 Ascierto PA, Del Vecchio M, Mandala M *et al.* Adjuvant nivolumab versus ipilimumab in resected stage IIIB-C and stage IV melanoma (CheckMate 238): 4-year results from a multicentre, double-blind, randomised, controlled, phase 3 trial. *Lancet Oncol* 2020; **21**:1465–77.
2 Eggermont AMM, Blank CU, Mandala M *et al.* Adjuvant pembrolizumab versus placebo in resected stage III melanoma (EORTC 1325-MG/KEYNOTE-054): distant metastasis-free survival results from a double-blind, randomised, controlled, phase 3 trial. *Lancet Oncol* 2021; **22**:643–54.
3 Robert C, Long GV, Brady B *et al.* Nivolumab in previously untreated melanoma without *BRAF* mutation. *N Engl J Med* 2015; **372**:320–30.
4 Larkin J, Chiarion-Sileni V, Gonzalez R *et al.* Five-year survival with combined nivolumab and ipilimumab in advanced melanoma. *N Engl J Med* 2019; **381**:1535–46.
5 Naranbhai V, Viard M, Dean M *et al.* HLA-A*03 and response to immune checkpoint blockade in cancer: an epidemiological biomarker study. *Lancet Oncol* 2022; **23**:172–84.
6 Spencer CN, McQuade JL, Gopalakrishnan V *et al.* Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. *Science* 2021; **374**:1632–40.
7 Bai X, Shoushtari AN, Betof Warner A *et al.* Benefit and toxicity of programmed death-1 blockade vary by ethnicity in patients with advanced melanoma: an international multicentre observational study. *Br J Dermatol* 2022; **187**:401–10.

8 Cormier JN, Xing Y, Ding M *et al*. Ethnic differences among patients with cutaneous melanoma. *Arch Intern Med* 2006; **166**:1907–14.

International surveillance of trends in melanoma survival: the impact of morphology

DOI: 10.1111/bjd.21651

Linked Article: Di Carlo *et al*. Br J Dermatol 2022; **187**:364–380.

Melanoma is a growing problem worldwide,[1] but it is a malignancy that shows striking differences in incidence, mortality and survival rates across populations.[2,3] This marked international variability supports the important role of cancer prevention (primary, secondary and tertiary) as a means to reduce future burden. Population-based cancer survival is a key metric used to evaluate the overall effectiveness of melanoma control programmes. In this issue of the *BJD*, Di Carlo and colleagues from the CONCORD Working Group[4] report the findings of the largest analysis to date of melanoma survival (2000–2014), including data from 284 cancer registries across 59 countries from Africa (4) Central and South America (9), North America (2), Asia (13), Europe (29) and Oceania (2), specifically evaluating the prognostic role of morphology. Their findings provide a global perspective on melanoma survival and highlight several important disparities.

The distribution of melanoma morphology varies by continent and country. Nodular and acral lentiginous melanomas are most common in populations with predominantly dark skin; superficial spreading melanomas are most common in populations with predominantly fair skin. Di Carlo *et al*.[4] reported the lowest 5-year net survival for the nodular and acral lentiginous subtypes, contributing to lower overall survival in Asia and in Central and South America where these subtypes are over-represented. As differences in survival between populations may be because of differences in stage of disease at diagnosis, Di Carlo *et al*. performed subgroup analyses using data from registries with complete information on stage and morphology; the lower survival for nodular and acral lentiginous melanoma persisted after adjustment for sex, age and stage of disease at diagnosis. Survival from superficial spreading melanoma was lower in Asia and eastern Europe compared with other regions. The proportion of melanomas of the superficial spreading subtype generally increased over time; however, survival from superficial spreading melanoma improved. The latter observation likely reflects a shift towards the diagnosis of thinner lesions as a result of heightened early detection activities.[5]

Long-term surveillance of global trends in melanoma incidence and mortality rates form the basis of estimates of the cancer burden used to establish priorities for melanoma control programmes. High-quality data from cancer registries is seen as the gold standard for these comparisons; however, variation in cancer registration practices across registries and countries can limit the interpretation of observed trends. Di Carlo and colleagues[4] have highlighted the issue of incomplete pathological reporting of melanoma morphology; a high proportion (overall 43%) of melanomas were registered as morphology 'not otherwise specified'. Although the benefits of pathological reporting of morphology in terms of patient management are debated (as treatment options do not differ between histological subtypes at a given stage at diagnosis),[6] the benefit for population-based research and reporting cannot be disputed.

The work of the CONCORD consortium is a powerful example of synthesized evidence that can highlight differences and provide important insights; the breadth of international collaboration is commendable. The study by Di Carlo and colleagues[4] will provide a baseline against which countries can monitor the progress of their melanoma control efforts.

Acknowledgments: Thanks to Professor David C. Whiteman (Cancer Control Group, QIMR Berghofer Medical Research Institute, Brisbane, Australia) for his critical review of this commentary.

Catherine M. Olsen

Cancer Control Group, QIMR Berghofer Medical Research Institute, Herston, QLD, 4006, Australia
Email: catherine.olsen@qimrberghofer.edu.au

Conflicts of interest: the author declares no conflicts of interest.

References

1 Arnold M, Singh D, Laversanne M *et al*. Global burden of cutaneous melanoma in 2020 and projections to 2040. *JAMA Dermatology* 2022; https://doi.org/10.1001/jamadermatol.2022.0160.
2 Yang DD, Salciccioli JD, Marshall DC *et al*. Trends in malignant melanoma mortality in 31 countries from 1985 to 2015. Br J Dermatol 2020; **183**:1056–64.
3 Whiteman DC, Green AC, Olsen CM. The growing burden of invasive melanoma: projections of incidence rates and numbers of new cases in six susceptible populations through 2031. J Invest Dermatol 2016; **136**:1161–71.
4 Di Carlo V, Stiller CA, Eisemann N *et al*. Does the morphology of cutaneous melanoma help explain the international differences in survival? Results from 1578482 adults diagnosed during 2000–2014 in 59 countries (CONCORD-3). Br J Dermatol 2022; **187**:364–80.
5 Sacchetto L, Zanetti R, Comber H *et al*. Trends in incidence of thick, thin and in situ melanoma in Europe. Eur J Cancer 2018; **92**:108–18.
6 Lattanzi M, Lee Y, Simpson D *et al*. Primary melanoma histologic subtype: impact on survival and response to therapy. J Natl Cancer Inst 2019; **111**:180–8.