

## Development of a patient decision aid for superficial basal cell carcinoma

DOI: 10.1111/bjd.19662

DEAR EDITOR, Patients with superficial basal cell carcinoma (sBCC) may be offered several treatment options including surgery, imiquimod, 5-fluorouracil (5-FU) or photodynamic therapy (PDT).<sup>1,2</sup> Patient decision aids (PDAs) are tools to assist patients and physicians in shared decision making; a recent study showed that patients with BCC would like to participate in decision making.<sup>3</sup> Stacey *et al.* provided evidence showing that PDAs helped patients improve knowledge of their disease and possible treatments, and perform risk assessment.<sup>4</sup> Junn *et al.* recently described the development of a paper-based PDA for patients with sBCC with limited life expectancy that weighs the benefits and risks of treatments vs. watchful waiting.<sup>5</sup> We describe the development of a digital PDA for all patients with sBCC. The PDA was developed in line with the International Patient Decision Aid Standards.<sup>6</sup>

Phase 1: content development. The Dutch Association for Dermatology and Venereology approved the PDA development. A literature review was performed to obtain evidence for the PDA's content: (i) effectiveness (recurrence rates) of surgery, 5-FU, imiquimod and PDT; (ii) side-effects and complications; (iii) cosmetic outcomes; (iv) treatment regimen (at home vs. in hospital, frequency, duration); and (v) patient preferences and values (qualitative research). Information on cryotherapy and electrodesiccation and curettage was not included, because these treatments are reserved for patients who desire quick treatment. It was assumed that these patients will not benefit from a PDA. To evaluate which values Dutch patients deemed important, our research group conducted a survey.<sup>7</sup> The part on 'value and preference elicitation' was based on the literature search (international) and the survey (national).

Phase 2: alpha testing with focus groups. Alpha testing is an umbrella term for gathering feedback on the content, graphics and usability of the PDA from patients and professionals. A first draft of the PDA was designed as a mock-up version with a set of images that look and work like actual but simplistic websites. We organized a semistructured patient focus group to evaluate this draft and explore whether all topics were covered.

From the dermatology department of a university hospital (MUMC+), 21 patients (minimum 18 years old) with a history of sBCC were invited for the focus group; eight patients were included (three men and five women). The mean age was 63.5 years (range 50–77) and six patients had a high education level. The discussion was audio recorded, transcribed verbatim, analysed and coded using the qualitative data software package NVivo 11a (QSR International, Doncaster, Australia). Patients

provided feedback on three topics: (i) photographs of sBCCs should be optional, (ii) information concerning the metastatic potential of BCC could cause worry, and (iii) information on Mohs surgery was lacking.

The PDA was adapted according to the feedback and an interactive web app was developed and tested in a second focus group. A noninteractive version of the PDA is available via Figshare (10.6084/m9.figshare.13117598). The second focus group consisted of five dermatologists with 1–14 years of experience. Their discussion points were similar to the patients' with regard to the photographs and information on metastatic potential, although they advised not to include information on Mohs surgery because it is not a standard treatment for sBCC in the Netherlands. The results of both focus groups and the changes made to the PDA are summarized in Table 1. After testing the PDA the text was rewritten by a Dutch publishing agency to improve comprehensibility for people of all levels of education.

Phase 3: project team and patient interviews. The PDA was evaluated by a project team consisting of dermatologists from academic and general hospitals (with or without dermatology interest), a dermatology resident, patient representatives, a physician assistant, an epidemiologist, a software developer, a technical physician and a health technology assessment researcher. The project team gave written feedback on the final content of the PDA, which was analysed, prioritized and discussed in the research team (L.C.J.v.D., N.W.J.K.-S., B.A.B.E.). Next, interviews were performed with patients by telephone or in person. Usability, workflow, interaction of patients with the PDA, and comprehensibility were evaluated using a think-aloud method (to find out how a device is used in a simulated real-life situation). Interviews were performed until sampling saturation, and then audio recorded, transcribed and analysed. During the interviews with five patients, we evaluated all changes made in phase 2. Only minor details and final 'bugs' were adapted. All considerations including references were documented in a background document (available on request from the authors).



In conclusion, there is sufficient evidence that dermatology patients would like to be involved in decision making. Consequently, shared decision making in dermatology has been gaining interest fast. This article shows that the input of patients and physicians improved the comprehensibility and usability of the PDA. Testing this PDA in patients with newly diagnosed sBCC is essential to evaluate whether the PDA results in better knowledge, decreased decisional conflict, and more contentment with their decision.

Acknowledgments: we would like to thank all participants of the survey, focus groups and interviews. Special thanks goes out to our software developer, and all members of the project team, including Dr. W. Savelberg, who shared her experience on developing a PDA.

Table 1 Outcomes of alpha testing a patient decision aid (PDA) for superficial basal cell carcinoma (sBCC)

| Topic                       | Patients   | Adaptions  | Professionals  | Adaptations  |
|-----------------------------|--|--|--|--|
| General                     | Attractive layout  | NC   | Attractive layout  | NC   |
|                             | The PDA should be open access, available to all patients                   | NC   | Strive for national use. In order to do so give all treatment options attention (also less effective, less frequently used treatments) | Cryosurgery and curettage and electrodesiccation were excluded; both patients and professionals agreed |
| Images and visual display   | Opinions on showing pictures of sBCCs were divided                         | Link to optional photo page with examples of sBCCs                 | The image on incidence of sBCC is unclear<br>Improve quality of photographs  | Changed the image to 100 'persons', 20 highlighted<br>Uploaded new sBCC photographs<br>Changed         |
| Pros and cons of treatments | Positive and negative explanation of results adds to the comprehensibility | NC   | Change pros and cons to treatment characteristics  | Changed  |
| Value clarification         | Every patient will state that all statements are very important            | Patients have to prioritize statements                             | No comment   | NC   |
| Content of information      | Information on different subtypes of BCC is necessary                      | Added information on subtypes in general information section       | Wondered if all BCC subtypes should be discussed   | Removed this section and checked with patients during interviews                                       |
|                             | Statement on metastases is worrying  | Nuanced statement  | Change sentence to clarify that BCC very rarely metastasizes   | Changed sentence to 'BCC very rarely metastasizes'   |
|                             | Mohs surgery is not an included treatment option; it should be             | Did not include extra section, but added statement on Mohs surgery | Concerned about patients without indication asking for Mohs  | Removed statement saying patients with indication for Mohs will not get PDA                            |
|                             | Add statement on what happens if treatment does not work                   | Added statement  | Add information for use of creams  | Added information  |
|                             | Inform about timely cessation of noninvasive treatment                     | Under treatment duration changed '6 weeks' to 'maximum 6 weeks'    | Add preventing ultraviolet exposure after PDT  | Added information  |
| Sequence of PDA sections    | Logical order  | NC   | Specify control after 'several months'   | Specified information  |
|                             | Personal information at the end  | Moved personal information   | Logical order<br>No comment  | NC<br>NC   |
| Comprehensibility           | Minor textual changes in different sections                                | Changed text where appropriate                                     | Minor textual changes  | Changed text where appropriate   |
|                             | Work with bullets for numerations  | Added bullets  | No comment   | NC   |
| References                  | No scientific articles. Show guidelines and pamphlets                      | Altered reference list   | Refer to patient information provided by NVDV  | The patient information of the NVDV will be used   |

The results were analysed and coded using a qualitative data software package, QSR NVivo 11a. NC, no changes; NVDV, Dutch Association for Dermatology and Venereology; PDT, photodynamic therapy.

L.C.J. van Delft <sup>1,2</sup>, B.A.B. Essers <sup>3</sup>, P.J. Nelemans,<sup>4</sup>  
K. Mosterd<sup>1,2</sup> and N.W.J. Kelleners-Smeets<sup>1,2</sup>

<sup>1</sup>Department of Dermatology and <sup>3</sup>Department of Clinical Epidemiology & Medical Technology Assessment, Maastricht University Medical Center+,

Maastricht, the Netherlands; <sup>2</sup>GROW Research Institute for Oncology and Developmental Biology and <sup>4</sup>Department of Epidemiology, Maastricht University, Maastricht, the Netherlands  
Email: [lieke.van.delft@mumc.nl](mailto:lieke.van.delft@mumc.nl)

## References

- 1 Peris K, Fagnoli MC, Garbe C et al. Diagnosis and treatment of basal cell carcinoma: European consensus-based interdisciplinary guidelines. *Eur J Cancer* 2019; **118**:10–34.
- 2 Kim JYS, Kozlow JH, Mittal B et al. Guidelines of care for the management of cutaneous squamous cell carcinoma. *J Am Acad Dermatol* 2018; **78**:560–78.
- 3 van Egmond S, Wakkee M, Droger M et al. Needs and preferences of patients regarding basal cell carcinoma and cutaneous squamous cell carcinoma care: a qualitative focus group study. *Br J Dermatol* 2019; **180**:122–9.
- 4 Stacey D, Legare F, Lewis K et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2017; **4**:CD001431.
- 5 Junn A, Shukla NR, Morrison L et al. Development of a patient decision aid for the management of superficial basal cell carcinoma (BCC) in adults with a limited life expectancy. *BMC Med Inform Decis Mak* 2020; **20**:81.
- 6 Coulter A, Stilwell D, Kryworuchko J et al. A systematic development process for patient decision aids. *BMC Med Inform Decis Mak* 2013; **13** (Suppl. 2):S2.
- 7 van Delft LCJ, Essers BAB, Harnas S, Kelleners-Smeets NWJ. Quantitative survey into value clarification of discussed treatment options among patients treated for basal cell carcinoma. *Br J Dermatol* 2019; **180**:1256–7.

Funding sources: the study was funded by a grant (€3000) from Health Foundation Limburg (Stichting Akkermans). This is a private foundation that supports scientific research in Limburg, the Netherlands. The grant was used for printing costs and distribution (e.g. of questionnaires and letters), to cover the website (developing and maintenance) and to organize focus groups.

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

## Second primary cutaneous melanoma in patients with advanced melanoma treated with anti-programmed-death-receptor-1 monoclonal antibodies

DOI: 10.1111/bjd.19629

DEAR EDITOR, Cases of second primary cutaneous melanoma (SPCM), which were mostly BRAF-wildtype, have been reported in patients with BRAF-inhibitor-treated advanced cutaneous melanoma.<sup>1</sup> Anti-programmed-death-receptor-1 (anti-PD-1) monoclonal antibodies (mAbs) nivolumab and pembrolizumab have also revolutionized the prognosis of these patients, but 10–15% of them experience grade 3–4 adverse events according to common terminology criteria for adverse events. The risk of developing a SPCM in this population has not been reported and could be reduced by anti-PD-1 treatment.

We investigated for the first time the occurrence of SPCM in patients with advanced melanoma treated with anti-PD-1 mAbs. A retrospective study was conducted in two French dermatology referral centres. We included all consecutive patients with advanced melanoma treated with anti-PD-1

mAb ± ipilimumab (retrieved from Pharmacy databases) who had a SPCM diagnosed after anti-PD-1 mAb initiation, between September 2010 and May 2019 (retrieved from Pathology databases). BRAF or NRAS mutational status was assessed by targeted next-generation sequencing panels, real-time polymerase chain reaction or immunochemistry with anti-BRAF<sup>pV600E</sup> (VE1) antibody. All patients had a full-body skin examination (± dermoscopy) at the hospital every 3 months. Among 498 patients (242 in Ambroise-Paré and 256 in Cochin Hospitals) treated with nivolumab (± ipilimumab, n = 46, 9.2%) or pembrolizumab, we identified four patients [mean age 66.5 (14.6) years] with a SPCM, for an overall incidence proportion of SPCM of 0.8% [95% confidence interval (CI) 0.3–2.0%] and an incidence of 640 new cases per 100 000 person-years (95% CI 240.9–1699.8). Table 1 summarizes SPCM and first primary melanomas characteristics. All four patients had received first- or second-line (after progression on BRAF + MEK inhibitors) nivolumab for a median duration of 15.5 (range 10–24) months. The median follow-up from the first anti-PD-1 infusion was 29 (range 18–41) months. Two patients had also received radiosurgery for brain metastases. The median time between first primary melanoma diagnosis or first nivolumab infusion and SPCM diagnosis was 34 (24–129) months and 17.5 (5–21) months, respectively. All patients had their SPCM diagnosed after having achieved complete response (CR), including one patient for whom nivolumab was discontinued for 4 months. Finally, nivolumab treatment was discontinued in all patients, and no relapse was observed after a median 11.5 (1–18) months off therapy.

SPCM specimen analysis by dermato-pathologists revealed four superficial spreading melanomas, including one invasive (Breslow thickness 0.3 mm) and three intraepidermal melanomas, which were subsequently surgically re-excised with lateral safety margins of 5 mm (for intraepidermal melanomas) or 10 mm (invasive melanoma). After a median follow-up of 11.5 (range 1–12) months after SPCM excision, no recurrence was observed. Paradoxically, all SPCMs occurred in patients who had achieved CR to anti-PD-1 mAb. One might speculate that the immune actions of the treatment should have prevented SPCM development. Furthermore, two patients experienced vitiligo-like depigmentation, an immune-related side-effect shown to correlate with a better efficacy of anti-PD-1 mAb in patients with melanoma, suggesting enhanced melanocyte-specific immunity.<sup>2,3</sup> However, no pathological sign of regression was found on any SPCM specimens. We speculate that the tumour burden of these SPCMs was too low to induce sufficient antigenic stimulation to elicit an immune response against SPCM melanocytes despite concurrent anti-PD-1 therapy.

A recent study reported pembrolizumab-associated 'paradoxical' eruptive keratoacanthomas and suggested an immune mechanism.<sup>4</sup> The risk of developing a SPCM is estimated to be 5–10%.<sup>5,6</sup> In a recent prospective Greek cohort study of 977 patients with melanoma, the risk of developing a second primary melanoma within the first 5 years was 8.0%.<sup>7</sup> We cannot conclude from our observational study that anti-PD-1 mAb treatment could decrease this risk.