Taking the burden out of symptom reporting in patients with melanoma using a digital real-world evidence platform

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BACKGROUND

Melanoma

Melanoma is an aggressive form of skin cancer that originates from melanocytes in the basal layer of the epidermis.

Although melanoma most frequently occurs on the skin[1], it can also arise in the mucous membranes of the mouth and genitalia, the respiratory, gastrointestinal, and uveal tracts and the leptomeninges.

Melanoma is the fifth most common cancer in the UK, with 14,509 new cases registered across the UK in 2014[2].

New treatments in melanoma are gradually transforming the disease into a chronic condition:

- For advanced disease stages, the median survival has significantly increased (from 9 months in stage 4 patients with limited treatment options, to a 3-year survival rate of up to 58%[3], with a proportion of them living to 5–10 years).
- In the early setting, adjuvant therapy is taking a prominent place in the therapeutic landscape, with many patients with normal life expectancies being exposed to treatments with potential side effects (some long term or irreversible).

The value of real-world data

Real-world data are vital to understand the impact of a chronic condition such as melanoma, and its treatments, on patients' lives, symptoms, functioning, work and other forms of productivity and daily activities, such as caring for a family.

The NICE methods guide[4] recommends collection of real-world data as a condition of entry into the revised Cancer Drugs Fund (CDF), to address uncertainty in technology appraisal.

In the real-world setting, data can be collected from a broader range of patients than is encountered in clinical trials, including those with co-morbidities and across all age ranges.

In the UK, melanoma patients are registered at the population level by one of the four National Cancer Registries and numerous regional melanoma registries; however, none of the existing UK registries collect health-related quality of life (HRQL) or patient reported outcomes (PRO) data. Furthermore, the CDF requires data collection over 24 months, which is often insufficient time to develop and extract data from a de novo registry, particularly using paper-based data capture.

The value of patient reported outcomes

Treatment is becoming increasingly patient-centred; regulators, HTA agencies and other healthcare decision-makers are increasingly interested in patients' experience of living with a condition and being treated for it, using measures which ask the patient directly.

PRO data, including HRQL, symptoms and daily functioning, are becoming increasingly important to provide an overall view of the burden of a disease and context to the potential value of treatment.

In many instances, PROs provide the most accurate and precise description of disease burden and the impact of treatment.

PROs are typically measured using instruments that have been developed for this purpose. These include disease-specific instruments designed to be used to measure outcomes in a specific indication such as the EORTC QLQ-C30, a measure of quality of life in cancer patients.

Whilst PROs are increasingly evaluated in clinical trials in some disease areas, they are considered less often in the real-world setting. Collection of PROs in the real-world has significant additional value compared with PROs measured within clinical trials. The data:

- are collected in "real-time"
- include different cohorts of patients, with co-morbidities that are not included in RCTs
- provide increased opportunity for patients to report symptoms difficult to capture on trial visits, such as daily burden of disease, diet and exercise
- demonstrate how a condition such as melanoma and its treatments affects patients in the long term.

The MyRealWorld™ melanoma registry

The Melanoma Registry has been developed in collaboration with the Patient Advocacy Organisation (PAO) Melanoma UK and the Royal Marsden NHS Foundation Trust (London).

The Registry records patient demographics, treatment patterns, AEs, ECOG performance status, diet and exercise, as well as monthly PRO data:

Using the study app on their mobile devices ("bring your own device" [BYOD] technology), patients complete EQ-5D-5L, EORTC QLQ-C30, and a melanoma-focused subset of the PRO-CTCAE. In response to patient consultation, a "symptom diary" tracking headache, abdominal pain, general pain, bodyweight, blood pressure and body temperature was also developed to enable daily tracking of most important symptoms.

Development of the app was informed by feedback from patients and Melanoma UK.

Patients with any type or stage of melanoma are recruited in collaboration with Melanoma UK.

The registry was launched at the end of October 2017.

Ethics approval has been obtained.

Informed consent is obtained electronically via the study app.

The study is fully GDPR compliant.

The study protocol has been registered with clinicaltrials.gov:

- ID NCT03379454
- Study title: The impact of melanoma and drug treatment in the real-world

MyRealWorld™ BYOD RWE platform

The MyRealWorld™ (MRW) platform combines the state-of-the-art digital technology with HTA and PRO expertise.

RIGOUR	SPEED	GRANULARITY	CO-CREATION
Ethics approval GDPR/HIPAA SABs ISO certification Valid PRO instruments	Community-based recruitment Close to real-time data access Built-in stats	International Any language Not just clinic visits	Patient advocacy partnerships Gamification

Patient recruitment & inclusion criteria

Patients are recruited in collaboration with Melanoma UK.

The patient inclusion criteria are broad to ensure that a wide selection of people is recruited:

- resident in UK; with NHS (or CHI) number
- current or previous diagnosis of melanoma
- age ≥18 years
- willing to use their own smartphone or tablet.

Study objective

The aim of the present study was to conduct an analysis of the symptom burden data recorded in the registry in order to understand:

- the everyday experience of living with melanoma
- and the impact of participants using an electronic application to report their symptoms within their real-life context rather than within clinical surroundings.

METHODS

Our methodology consisted of two steps:

- Analysis of the quantitative data collected through the app on patient demographics, disease symptoms and adverse events
- Analysis of qualitative feedback received via the conduct of pre- and post-launch surveys to elucidate the value of:
- the BYOD app
- patient-recorded data at medical consultation and its impact on anxiety relating to recall-based pain reporting
- the burden of recall over extended periods.

Quantitative data

Two sets of data are recorded through the app:

- Patient demographics
  - background questionnaire completed at baseline
  - collects demographic data, data relating to the diagnosis and treatment of their melanoma, and data relating to lifestyle (e.g. diet, exercise, alcohol intake, smoking)
  - patients are asked to update their information every 6 months
  - patients are reminded to complete their profile with in-app notifications
- Monthly PROs:
  - patients are asked to complete three PRO questionnaires (the EQ- 5D-5L, EORTC QLQ-C30 and a melanoma-focused subset of the PRO-CTCAE) on a monthly basis
  - the present analysis is based on symptom burden recorded via the EORTC QLQ-C30
- Daily symptom tracker
  - During development, patients requested a symptom tracker to enable daily recording of key symptoms – headache, abdominal pain, general pain, body weight, blood pressure, body temperature. Where possible, questions were based on validated items.

The EORTC QLQ-C30

The present study analysed symptom data collected via the MRW app with the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30, a cancer specific instrument widely used in oncology across different types of cancers.

A melanoma-specific module of the EORTC QLQ-C30 (QLQ-MEL38) is in development (not fully validated at the time of registry launch, thus was not included in the study).

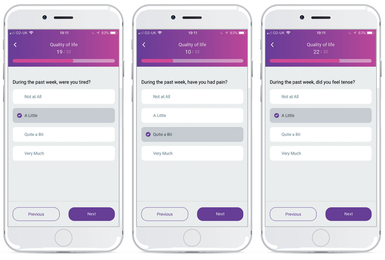
The EORTC QLQ-C30 incorporates[5]:

1. five functional scales (physical, role, cognitive, emotional, and social)
2. a global health status / HRQL scale
3. three symptom scales (fatigue, pain, and nausea and vomiting)
4. a number of single items assessing additional symptoms commonly reported by cancer patients (dyspnoea, loss of appetite, insomnia, constipation and diarrhoea) and perceived financial impact of the disease.

In the present study we focused on the analysis of (3) and (4).

Response categories for the symptom scales in the EORTC QLQ-C30 are as follows:

"Not at all"; "A little"; "Quite a bit"; "Very much"



Qualitative feedback

The following qualitative surveys were conducted:

- a patient focus group held in October 2016, at the Royal Marsden, during which feedback was collected on the key aspects of the plans for the digital melanoma registry
  - via a structured discussion guide
  - from a group of 11 patients (aged between 23–72 years, representation of both sexes and all stages of disease)
  - participants were recruited by Melanoma UK and the Royal Marsden NHS Foundation Trust
  - collaborative workshop at the Melanoma UK Patient Conference (June 2017)
- a series of patient testing consultation WebEx feedback sessions (throughout 2017)
- patient feedback sessions, consisting of 1:1 interviews with patients (April 2018)

RESULTS

Note: The results presented here are based on 73 registry participants who provided symptom burden and disease stage data from a total sample of 145 participants recruited at the time of the data cut.

309 participants are currently registered.

Patient demographics

Figure 1: Patient sample by stage

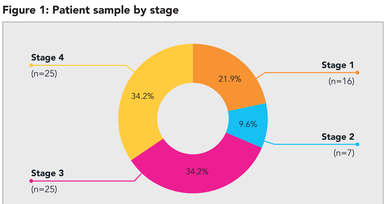
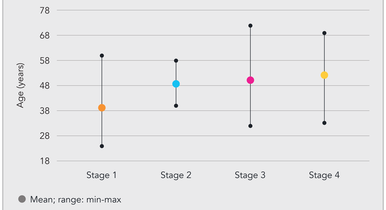
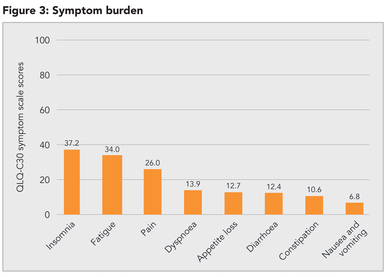


Figure 2: Mean age by stage



Note: The registry includes only adult patients, thus age of recruitment was 18

Figure 3: Symptom burden



All of the scales and single-item measures range in score from 0 to 100. Higher scores indicate greater symptom burden. Of the symptoms measured by the QLQ-C30, insomnia, fatigue and pain are the most burdensome (Figure 3). Melanoma patients also report that dyspnoea, appetite loss, diarrhoea, constipation, and nausea/ vomit symptoms affect their everyday activity and quality of life.

Figure 4: Insomnia scores by disease stage

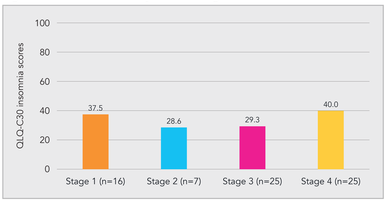


Figure 5: Fatigue scores by disease stage

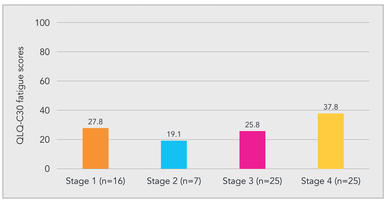


Figure 6: Pain scores by disease stage

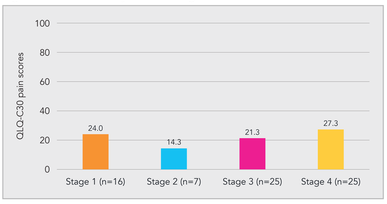
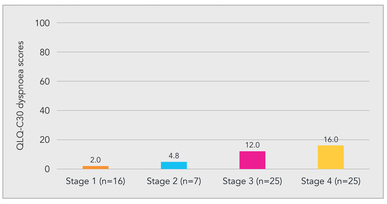


Figure 7: Dyspnoea scores by disease stage



The analysis showed that symptom burden varies across disease stages, with more patients at more advanced stages reporting higher symptom scores. (Figures 4–7) In particular, stage 4 patients have the highest scores across all disease symptoms. It is worth noting that stage 1 patients report the second highest symptom score for insomnia, fatigue and pain, indicating that these three symptoms have a high impact on patients' everyday activities and quality of life even at the early stages of the disease.

Results of the qualitative study

The benefits of the app were highlighted by patients:

- flexible and intuitive reporting
- immediacy of reporting
- level of detail of the questions, which enables accurate, granular reporting
- usefulness of instant access to data during consultations
- a reduction in participant anxiety and burden related to verbal recall, which led to an increased satisfaction in interactions with their healthcare professional.

There were also benefits identified for carers, clinicians and other external stakeholders, who can utilise instant access to accurate and granular self-reported pain data in order to offer improved treatment options and care.

CONCLUSIONS

Melanoma symptoms mostly affecting patients' everyday activities and quality of life are insomnia, fatigue and pain.

Symptom burden is higher for patients with more advanced disease.

These findings are based on real-world data collected via the MRW app which

- allows patients to record symptoms in real time
- reduces patient anxiety and burden related to verbal recall, and leads to an increased satisfaction in interactions with their healthcare professional
- provides access to accurate and granular symptom data helping clinicians to improve treatment and care

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