



Health-related quality of life in men with oligometastatic prostate cancer following metastases-directed stereotactic body radiotherapy: Real-world data from the E²-RADIatE OligoCare cohort

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ABSTRACT

Objective: To evaluate the impact of metastases-directed stereotactic body radiotherapy (SBRT) on health-related quality of life (HRQoL) in men with oligometastatic prostate cancer (PCa) using real-world data from the OligoCare cohort.

Materials and methods: OligoCare is a pragmatic, observational cohort designed to assess the impact of metastases-directed SBRT on patients with oligometastatic disease (OMD). We report an interim analyses of the secondary endpoint HRQoL, assessed using the EORTC QLQ-C30, within six months of metastases-directed SBRT for oligometastatic disease in men with PCa among the first 1600 registered patients. HRQoL data collection was optional within the OligoCare cohort. To compare HRQoL between baseline and first follow-up assessment, a Wilcoxon signed-rank test was used. A multiple linear regression model was used to explore the HRQoL associations with predefined factors.

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Results: Out of the 1600 registered patients, 658 were treated for oligometastatic PCa, of which 233 had baseline QoL data and 132 patients had both baseline and follow-up HRQoL data. At baseline, most patients had a WHO performance status of 0 or 1 (87 %), were de-novo oligometastatic (79 %), had one metastasis (90 %), and had a good overall global health status (mean 80.81, SD16.11, IQR 75–92). 51 % received hormonal therapy as concomitant systemic treatment. Patients with comorbidities as assessed by the Charlson Comorbidity index had a worse global health status at baseline (-4.88, 95 % CI: -9.35, -0.42). No clinically meaningful significant difference in global health status was observed at first assessment following SBRT (median 3.0 months) compared with baseline (mean difference 2.27, 95 % CI: -1.54, 6.08). Upon evaluating the proportions, meaningful clinically important differences (a 10-point or more difference) was observed in, 17 % and 11 % of the patients reporting deterioration and improvement of global health status, respectively.

Conclusion: Metastases-directed stereotactic body radiotherapy had no negative impact on global HRQoL within the first six months after treatment.

Introduction

The use of metastases-directed stereotactic body radiotherapy (SBRT) in combination with standard of care systemic therapy has shown promising results in small randomized phase II trials [1–3] and is recommended in international practice guidelines [4,5]. Understanding how SBRT affects health-related quality of life (HRQoL) is pivotal for providing patient-centered care [6]. The EORTC QLQ-C30 has a prognostic value for overall survival in a real-world setting [7,8] and patient-reported outcome measurements (PROMs) can assist in clinical shared-decision making process on treatment options and improve patient empowerment [9]. Moreover, the European Society for Radiotherapy – Advisory Committee for Radiation Oncology Practice (ESTRO-ACROP) Delphi consensus statement regarding recommendations for radiation therapy in oligometastatic prostate cancer (PCa) has highlighted that among the most critical endpoints for metastasis-directed radiotherapy strategies are patient-reported outcomes and quality of life [10]. Nonetheless, little is known regarding the impact of SBRT on the quality of life (QoL) within the context of oligometastatic disease [11,12]. The low toxicity profile of SBRT suggests its favorable impact on patients' quality of life, despite previous studies [13] having indicated discrepancies between the toxicities reported by clinicians and those reported by patients. This underscores the need for a proper assessment of HRQoL through PROMs.

In light of this, the OligoCare registration study was established, seeking to assess the impact of metastases-directed SBRT on patients with oligometastatic disease.

OligoCare is a cohort within the E2-RADIaTE study, which stands for the EORTC-ESTRO RADiotherapy InfrAstrucTure for Europe. E2-RADIaTE is a prospective non-interventional non-therapeutic multi-cohort study or platform. It is a collaboration between the European Organization for Research and Treatment of Cancer (EORTC) and the ESTRO. The overall aim of OligoCare is to identify patient, tumour, staging, and treatment characteristics impacting overall survival after radical radiation treatment of oligometastatic disease in patients with oligometastatic disease of breast, non-small cell lung, prostate, and colorectal cancers. One of the secondary objectives of OligoCare is assessing HRQoL in the context of oligometastatic disease.

Hereafter, we report the HRQoL data for PCa at first follow-up to six months after the start of SBRT derived from the OligoCare cohort.

Materials and methods

Study design and participants

OligoCare is a pragmatic, observational cohort to evaluate the impact of metastases-directed SBRT for patients with oligometastatic disease. OligoCare is a cohort within E2-RADIaTE (NCT03818503). The primary endpoint of OligoCare is overall survival and HRQoL is a secondary endpoint. Inclusion eligibility for the current analyses focused on PCa patients within the SBRT population with HRQoL data among the first 1600 registered patients. The clinical cut-off date of 28th February 2023 was determined as last date of radiotherapy plus six months, and the database for these analyses was locked on 6th of April 2023.

Outcome measures

HRQoL was measured with the EORTC Quality of Life Questionnaire Core 30 items (QLQ-C30) version 3.0 [14,15]. The QLQ-C30 evaluates five functional domains (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea/vomiting), a global health status/QoL scale, and six single items assessing other symptoms/difficulties commonly associated with cancer (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Most questions ($n = 28$) are based on a four-point scale (1 = not at all, to 4 = very much) and two questions are using a seven-point scale (1 = very poor to 7 = excellent), with most items referring to the period of the previous week.

HRQoL data was collected before radiotherapy, at the end of radiotherapy and at each subsequent follow-up time point, as derived from real-life practice within the OligoCare cohort, using a self-completion paper questionnaire. Data collection was suggested at six months, twelve months and annually thereafter, and whenever a primary or secondary endpoint occurs i.e., death, relapse or toxicity. HRQoL data collection was optional within the OligoCare cohort, therefore not all sites collected this outcome measure, and not all patients consented for HRQoL data collection (Supplementary data 1).

Data handling and statistical analysis

The scales and single-items of the EORTC QLQ-C30 were scored and linearly transformed to 0–100 scales according to the EORTC guidelines [16]. A higher score of a symptom scale or item indicates a high level of symptomatology/problems; a higher score of a functional scale or global health status/QoL indicates a high level of functioning/QoL. HRQoL data was considered missing if at least half of the items of the EORTC QLQ-C30 questionnaire were missing. A minimal clinical important difference (MCID) was defined as a score of difference of at least 10 points within a patient between two different time points (i.e., deterioration < 10 points, stable between ± 10 points and improvement > 10 points) [17]. A five-point difference was used for the sensitivity analysis. The primary HRQoL endpoint for this cohort study, as described per protocol, is global QoL. Exploratory analyses were performed for other HRQoL domains.

Descriptive statistics were used to describe patients' sociodemographic, disease, and treatment characteristics, as well as HRQoL scores. Wilcoxon signed-rank test was used to compare HRQoL scores between the baseline and the first follow-up assessment. The first follow-up assessment was defined as the HRQoL assessment within 6 months of SBRT treatment, occurring at least two weeks after the end of SBRT. A multiple linear regression model was used to explore the association: (a) of baseline patients' characteristics with baseline global health status, and (b) patients' characteristics with the change in global health status from baseline to the first follow-up assessment within six months from start of SBRT. The patients' characteristics included oligometastatic disease (OMD) (defined by the ESTRO/EORTC classification [4] as de-novo, induced, or repeat), WHO performance status (0, >0, not done), age, comorbidity (comorbidities assessed using the Charlson Comorbidity Index) [18], prior treatments, number of oligometastases (1, >1), basic disease (e.g. months since diagnosis of primary cancer) and

treatment related (e.g. prior treatments), and concomitant systemic treatment. All tests were two sided, and p values < 0.05 were considered significant. SAS version 9.4 (2002–2012 per SAS Institute Inc., Cary, NC) was used for the statistical analysis. The CONSORT PRO extension was used as guidance for reporting of the PRO results [19].

Results

Between 14/08/2019 and 13/07/2022, 1600 patients were registered in OligoCare cohort, with 659 of patients in the analysis population having prostate cancer. Among them, 233 (35 %) patients had

baseline HRQoL data, and 132 (20 %) patients had both baseline and follow-up HRQoL data (Fig. 1). An overview of the timing of HRQoL assessment at baseline and within the six month time period can be found in [Supplementary figure 1](#).

Median months from start of SBRT to first follow-up HRQoL assessment was 3.0 (IQR 1.3–5.3, n = 132). An overview of the included patients per country can be found in [Supplementary data 1](#). At baseline (n = 132), most patients had a WHO performance status of 0 or 1 (87 %), a median age of 71 years, were de-novo oligometastatic (79 %), and had a single lesion treated with SBRT (90 %). Concomitant therapy, in the form of hormonal therapy, was administered to half of the patients (51

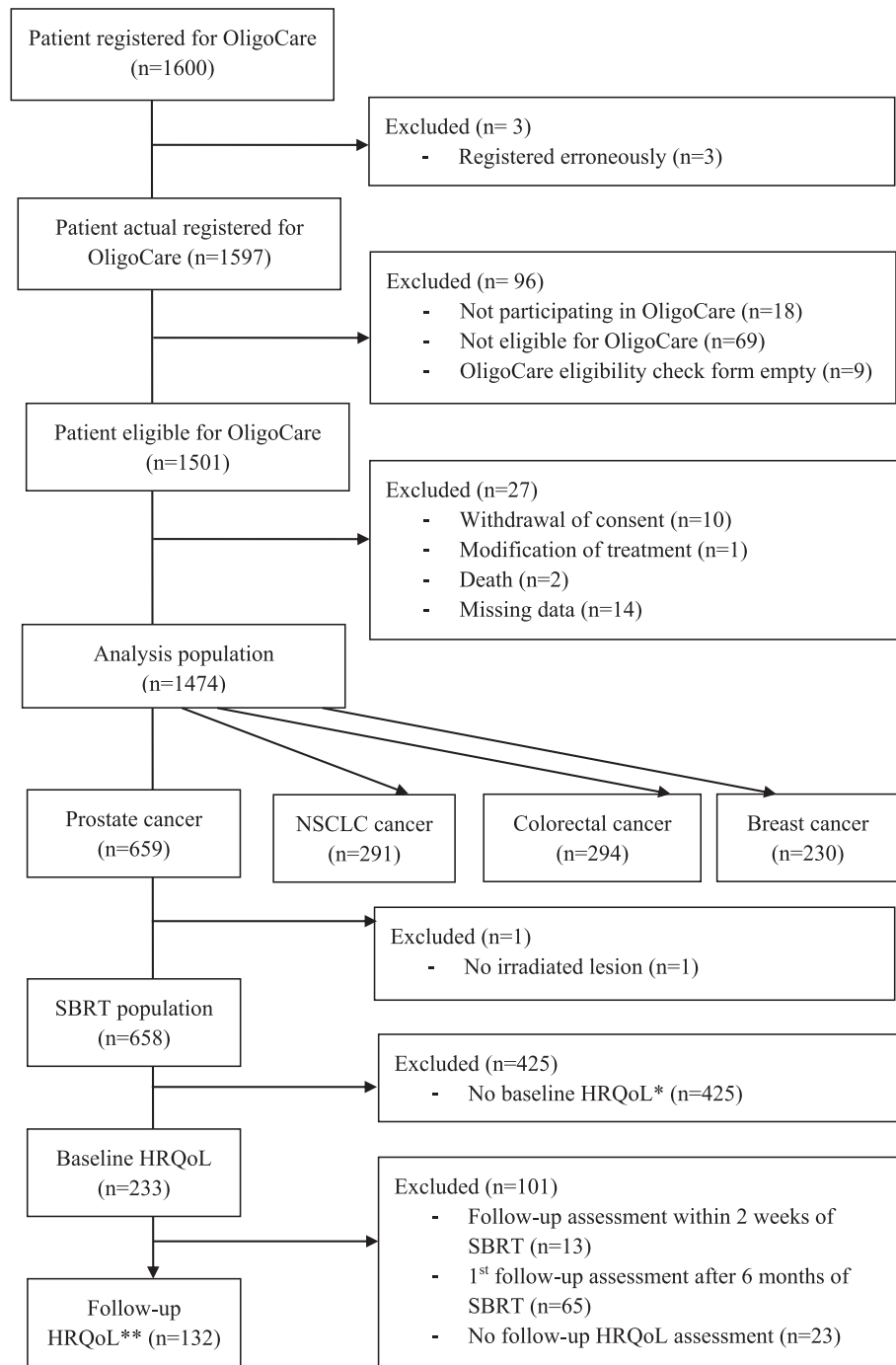


Fig. 1. CONSORT flow diagram. Legend: *Patient-reported outcome collection was optional within OligoCare cohort. ** HRQoL assessment within six months of SBRT treatment, and at least two weeks after the end of SBRT. Abbreviations: HRQoL, health-related quality of life; NSCLC, non-small cell lung cancer; SBRT, stereotactic body radiation therapy.

%). **Table 1** provides an overview of baseline characteristics, and supplementary characteristics are shown in **Supplementary data 2**, including the groups of all patients with available HRQoL data at baseline, $n = 233$ and no available HRQoL data, $n = 425$. There are no noteworthy differences observed between the patients' characteristics of those having both baseline and follow-up data ($n = 132$) and the complete group with available HRQoL data ($n = 233$). All patients included in the analysis were alive 6 months from the start of SBRT.

Table 1
Baseline patient sociodemographic, disease and treatment characteristics.

| Characteristic | N (%) |
|---|------------|
| Age categorised (years) | |
| 45–55 | 3 (2.3) |
| 55–65 | 25 (18.9) |
| 65–75 | 73 (55.3) |
| >75 | 31 (23.5) |
| WHO performance status | |
| 0 | 97 (73.5) |
| 1 | 18 (13.6) |
| Not done | 17 (12.9) |
| Relevant comorbidities* | |
| No | 70 (53.0) |
| Yes | 62 (47.0) |
| Months since diagnosis of primary cancer | |
| Median | 55.4 |
| Range | 1.5–243.1 |
| Q1–Q3 | 23.8–104.1 |
| N obs | 132 |
| Months since diagnosis of first metastatic disease | |
| Median | 1.7 |
| Range | 0.2–129.3 |
| Q1–Q3 | 1.1–3.0 |
| N obs | 130 |
| Number of metastatic lesions | |
| 1 | 97 (73.5) |
| 2 | 19 (14.4) |
| 3 | 10 (7.6) |
| 4 | 2 (1.5) |
| 5 | 3 (2.3) |
| 6 | 1 (0.8) |
| New ESTRO/EORTC classification** of OMD state | |
| De-novo | 104 (78.8) |
| Repeat | 26 (19.7) |
| Induced | 2 (1.5) |
| Number of OMD sites | |
| 1 | 119 (90.2) |
| 2 | 12 (9.1) |
| 3 | 1 (0.8) |
| OMD site | |
| Non-regional lymph nodes | 26 (17.8) |
| Non-vertebral bones | 64 (43.8) |
| Spine | 32 (21.9) |
| Regional lymph nodes | 22 (15.1) |
| Other | 2 (1.4) |
| Any prior treatment ° | |
| No | 7 (5.3) |
| Yes | 125 (94.7) |
| Concomitant systemic treatment | |
| No | 65 (49.2) |
| Yes, hormonal therapy | 67 (50.8) |

*Included comorbidities are those assessed in the Charlson Comorbidity index (i.e., Myocardial infarction, Congestive heart failure, Peripheral vascular disease, Cerebrovascular disease, Dementia, Chronic pulmonary disease, Rheumatic disease, Peptic ulcer disease, Liver disease, Diabetes with/without chronic complication, Hemiplegia or paraplegia, renal disease and AIDS (excluded asymptomatic infection)).

**OMD; de-novo, repeat and induced was defined by the ESTRO/EORTC classification (4).

°Any other treatment includes surgery of primary tumor, lymph node resection, radiotherapy to primary tumor or loco-regional lymph nodes or systemic treatment.

Abbreviations: OMD, oligometastatic disease; WHO performance score: World Health Organization classification score for performance.

Prior to SBRT, the average overall global health status was 80.81 (SD 16.11, $n = 132$), functioning scores ranged on average from 82.89 to 91.97 ($n = 132$) and symptoms scores from 1.52 to 20.96 ($n = 132$). A complete overview can be found in **Fig. 2** and **Supplementary data 3**.

HRQoL over time

No clinically meaningful significant difference was observed in global health status at baseline compared to the first assessment from the start of SBRT (mean difference 2.27, 95 % CI = -1.54–6.08). Also, for the functioning scores and symptoms no clinically meaningful significant difference was found (MCID < 10-point difference) (**Table 2**).

When considering the proportion of patients experiencing an individual MCID, most patients remained stable in overall HRQoL, functional and symptom scales (**Fig. 3**). Global health status improved in 11 % and deteriorated in 17 % of the patients over time. Furthermore, improvements over time were primarily observed in emotional functioning (21 %), while deterioration over time was seen for fatigue (38 %), pain (27 %), role functioning (22 %) and cognitive functioning (21 %). Sensitivity analyses, using a 5-points difference, showed similar results except for deterioration in global health status (34 %), physical functioning (35 %), and emotional functioning (28 %) and emotional functioning improved in 36 % of the patients (**Supplementary figure 2**). An additional post-hoc analysis was performed to differentiate between deterioration, stability and improvement in pain based on anatomical location of SBRT (bone lesions versus other). These results were comparable as 77.8 % and 72.2 % of patients with improvement and deterioration respectively were treated with bone lesions. A second post-hoc categorization was performed for the domains/symptoms in which ≥ 20 % of patients reported deterioration, as defined per MCID, to compare these outcomes between those receiving concomitant systemic therapy or those who did not (i.e., only receiving SBRT). It was observed that more patients who reported deterioration in their global health status (65 % versus 35 %) and pain (61 % versus 39 %) also received concomitant systemic treatment (**Fig. 4**).

HRQoL regression models

The multiple linear regression model showed, among the variables included, a significant association only for the presence of comorbidities a significant association with worse baseline global health status (**Table 3**). Patients with comorbidities had significantly lower global health status at baseline compared to those with no comorbidities (-4.88, 95 % CI = -9.35; -0.42, $p = 0.032$). The multiple linear regression model for change in global health status from baseline to first follow-up within 6 months from start of SBRT showed no significant associations with the included patient characteristics explored, including OMD, WHO performance status, age, comorbidity, prior treatment, number of oligometastases, and concomitant systemic treatment.

Discussion

To our knowledge, this is the first study to report HRQoL data in men with oligometastatic PCa, being treated with metastases-directed radical radiotherapy, using real-world data.

The main early finding of this study indicates that men with oligometastatic PCa had a good overall global health prior to commencing treatment (mean 80.81, SD 16.11, $n = 132$), and this remained stable within the first six months after treatment (mean 78.54, SD 15.31, $n = 132$). Comparatively, reference values of PCa [20] (data set including 23 % recurrent/metastatic patients, age group ≥ 70 years) had a mean global health status of 67.4 (SD 22.2) and general population normative data [21] (data set including, 13 European countries, Canada and USA) showed a mean global health status of 69.6 (age group ≥ 70 , SD 20.3) and 67.0 (age group 60–69 years, SD 20.8). Functioning scores were also

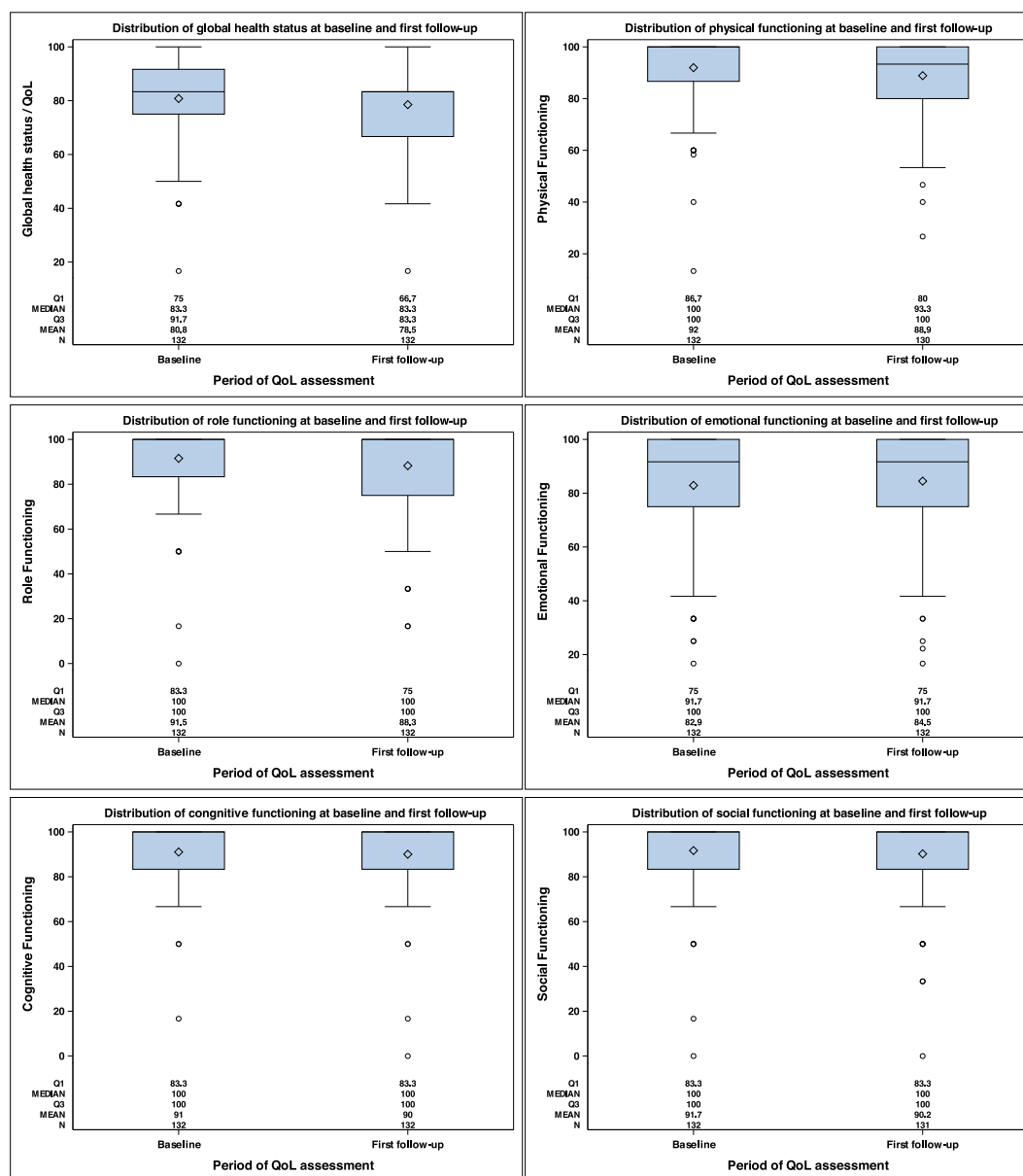


Fig. 2. Distribution of HRQoL scores at baseline and first follow-up following SBRT. Abbreviations: HRQoL, health-related quality of life; SBRT, stereotactic body radiation therapy.

higher in our patient cohort compared to the reference for PCa, and symptoms scores were lower, indicating less symptomatology [20]. The systematic review of Lehrer et al. [22] showed that the toxicity profile of SBRT for oligometastatic disease is favorable, with < 2 % risk of acute and late grade 3 + toxicity. This favorable profile may elucidate the minimal or absent negative impact of SBRT on HRQoL, particularly when assessed through a general instrument such as EORT QLQ-C30.

This finding, using real-world data, is consistent with results from several small phase I and II trials. The STOMP trial, a phase II RCT study, using EORTC QLQ-C30, showed HRQoL scores remained stable over time at 3 months and 1 year [1]. Another, phase II trial, OLIGOPELVIS GETUG P07, showed no change in global health status over time (assessed by EORTC QLQ-C30 at 18 months) [23]. A prospective phase I trial, the POPSTAR trial, also showed that HRQoL, assessed with EORTC QLQ-C30 and QLQ-BM-22, was maintained after SBRT in oligometastatic PCa [24]. The SABR-COMET study, using FACT-G (Functional Assessment of Cancer Therapy – General; a 27-item questionnaire

designed to measure physical, social, emotional, and functional domain of HRQoL in cancer patients), showed that average QoL declines slowly over time, however, this study included different primary tumour types in their analyses, encompassing breast, lung, colorectal and prostate cancers [11]. Another phase II study using mixed tumour types, found no significant change in HRQoL up to 9 months [25]. Maintenance of HRQoL after SBRT also aligns with the low incidence of SBRT toxicities reported in studies evaluating SBRT in oligometastatic PCa [1,2].

Several trials: including STORM (NCT03569241), POSTCARD (NCT03795207), PCS IX (NCT02685397), CORE (NCT02759783), STEREO-OS (NCT03143322), are further investigating the impact of SBRT in oligometastatic PCa including HRQoL as secondary outcome, which might be helpful to enhance our understanding of SBRT's impact on HRQoL in oligometastatic PCa. However, the PROMs used in these ongoing trials are diverse and are using different time frames, making comparison challenging.

Furthermore, there were no clinically meaningful significant

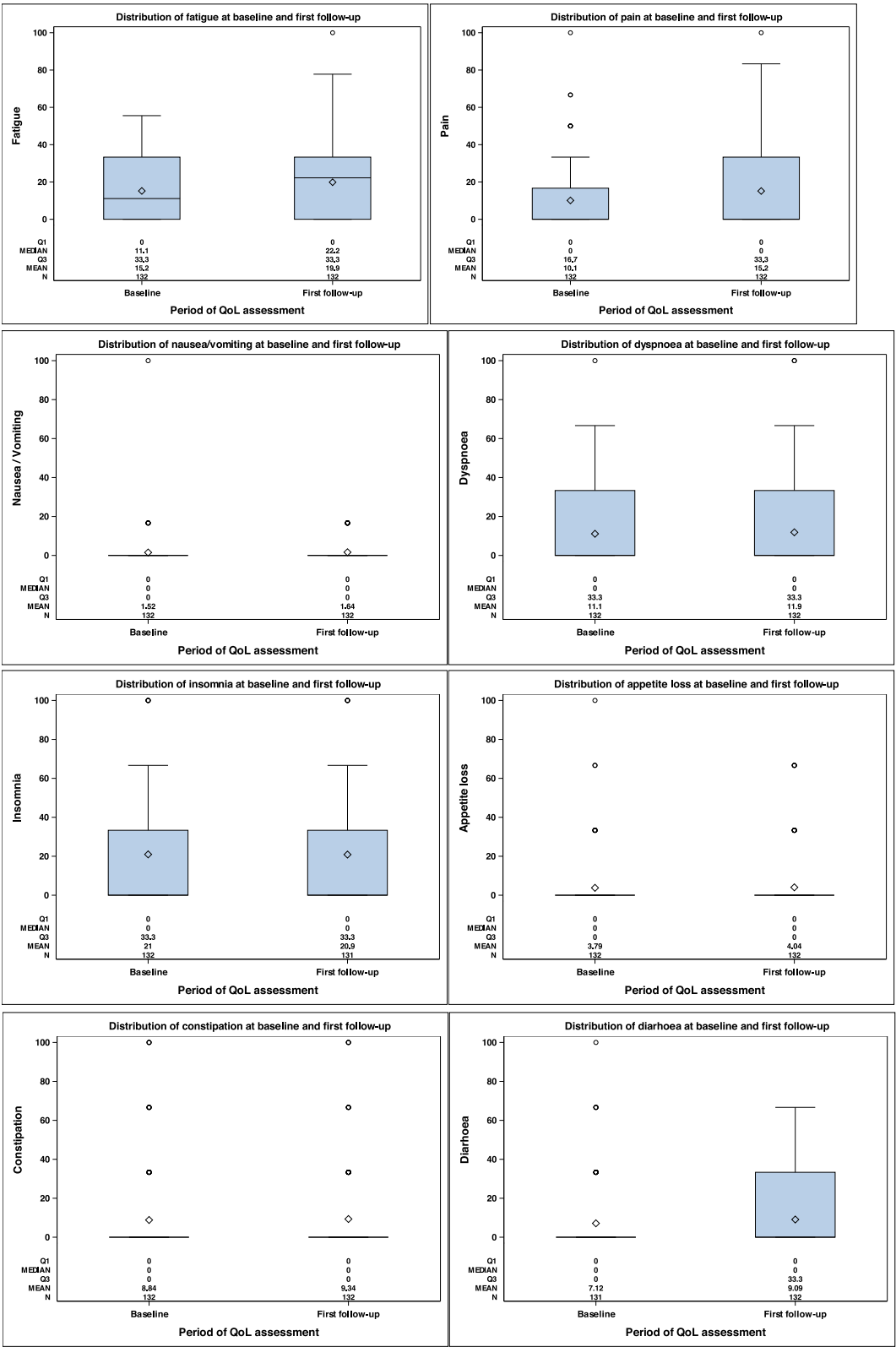


Fig. 2. (continued).

differences over time (i.e., within six months) observed in functional and symptom scales. This result is consistent with other studies reporting no clinically meaningful difference in the functional and symptom scales [1,24,26]. Also, individual patient functional and symptom scores were evaluated using MCIDs. The most notable observations were

deterioration over time in fatigue (38 %), pain (27 %), role functioning (22 %) and cognitive functioning (21 %). However, drawing conclusions about these individual proportions of MCIDs is difficult due to the absence of a control group and the exploratory nature of the subdomain analyses. Moreover, 51 % of the patients received concomitant

Table 2
Difference in mean HRQoL score between baseline and first follow-up assessment.

| QoL scale | Baseline assessment (B) | | | First follow-up assessment (F) | | | Difference (B-F) | |
|-----------------------|-------------------------|-------|--------------|--------------------------------|-------|--------------|------------------|--------------|
| | N | Mean | 95 % CI | N | Mean | 95 % CI | Mean | 95 % CI |
| Global health status | 132 | 80.81 | 78.03, 83.58 | 132 | 78.54 | 75.90, 81.17 | 2.27 | −1.54, 6.08 |
| Physical Functioning | 132 | 91.97 | 89.69, 94.25 | 130 | 88.87 | 86.33, 91.41 | 3.10 | −0.30, 6.50 |
| Role Functioning | 132 | 91.54 | 88.58, 94.50 | 132 | 88.26 | 84.94, 91.58 | 3.28 | −1.14, 7.71 |
| Emotional Functioning | 132 | 82.89 | 79.50, 86.28 | 132 | 84.49 | 81.32, 87.66 | −1.60 | −6.22, 3.02 |
| Cognitive Functioning | 132 | 91.04 | 88.65, 93.42 | 132 | 90.03 | 87.21, 92.84 | 1.01 | −2.66, 4.68 |
| Social Functioning | 132 | 91.67 | 88.82, 94.51 | 131 | 90.20 | 87.11, 93.30 | 1.46 | −2.72, 5.65 |
| Fatigue | 132 | 15.19 | 12.38, 18.00 | 132 | 19.87 | 16.52, 23.21 | −4.67 | −9.02, −0.32 |
| Pain | 132 | 10.10 | 7.04, 13.17 | 132 | 15.15 | 11.71, 18.60 | −5.05 | −9.64, −0.46 |
| Nausea / Vomiting | 132 | 1.52 | −0.09, 3.12 | 132 | 1.64 | 0.78, 2.50 | −0.13 | −1.94, 1.69 |
| Dyspnoea | 132 | 11.11 | 7.66, 14.56 | 132 | 11.87 | 8.38, 15.35 | −0.76 | −5.64, 4.12 |
| Insomnia | 132 | 20.96 | 16.34, 25.58 | 131 | 20.87 | 16.38, 25.35 | 0.09 | −6.31, 6.50 |
| Appetite loss | 132 | 3.79 | 1.37, 6.21 | 132 | 4.04 | 1.69, 6.40 | −0.25 | −3.61, 3.11 |
| Constipation | 132 | 8.84 | 5.10, 12.58 | 132 | 9.34 | 5.64, 13.05 | −0.51 | −5.75, 4.74 |
| Diarrhoea | 131 | 7.12 | 4.09, 10.16 | 131 | 8.91 | 6.15, 11.66 | −1.7 | −5.86, 2.29 |

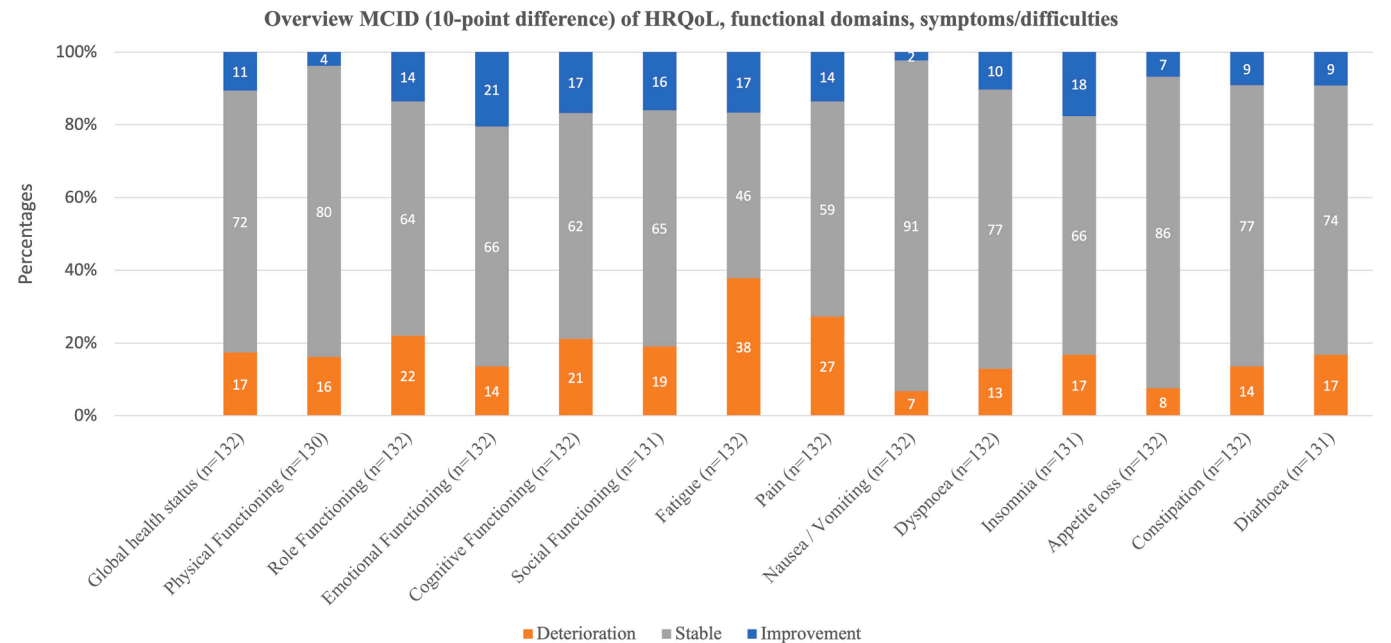


Fig. 3. Overview of MCID (10-point difference) HRQoL and its domains. Legend: median months from start of SBRT to first follow-up HRQoL assessment was 3.0 months (IQR 1.3–5.3, n = 132). Median months from end of SBRT to first follow-up HRQoL assessment was 2.8 months (IQR 1.1–5.2, n = 132).

hormonal therapy, leading us to hypothesize that these deteriorations are mainly attributed to the hormonal therapy. This hypothesis is also supported by the post-hoc categorization, which revealed differences in global health status (65 % versus 35 %) and pain (61 % versus 39 %) in the proportions of patients receiving concomitant systemic therapy or those receiving only SBRT. This hypothesis is further supported by the results of the systematic review of Barry et al. showing that there was no difference in patients with OMD receiving SBRT and those that did not [12]. Of note, pain measured in the EORTC QLQ-C30 is based on two items, which means a patient can only change by 16.5 points, whereas multi-item scales have more intermediate values and thus more continuous change scores, therefore caution is indicated using this MCIDs at individual level with scales that have a low number of items, such as pain [27,28].

Finally, exploratory regression models were performed. Our study results suggest that the presence of comorbidities before start of treatment is associated with worse baseline global health status, which should be taken into consideration analyzing HRQoL data over time and in the management of PCa patients in routine practice with multiple comorbidities [29]. No significant associations were found with

patients' characteristics and change in health status within six months. However, we want to highlight the potential role of concomitant systemic treatment (p = 0.0731) in our results, which should be further investigated in future trials.

Whilst this is a large and unique cohort of patients, there are some limitations that need to be mentioned. Firstly, it is important to note that the collection of HRQoL data was optional within this cohort trial, leading to only 35 % of patients having available PRO data at baseline. Because data collection was voluntary at both the site and patient levels, a portion of the baseline data may be considered as missing-at-random (at the site level). However, it cannot be excluded with certainty that patients with worse HRQoL were either unable or unwilling to complete questionnaires from the beginning. Missingness at our follow-up time-point (n = 101), occurring within six months after the start of SBRT, is mainly (77 %) attributed to first follow-up data collection at different time points. Among these cases, 13 % had follow-up within 2 weeks of SBRT and 64 % had follow-up after six months of SBRT, which differs from the time frame used in our analyses. In future longitudinal cohorts, effort should be directed towards addressing the barriers to initiate PRO data collection [30,31] and strategies should be implemented to

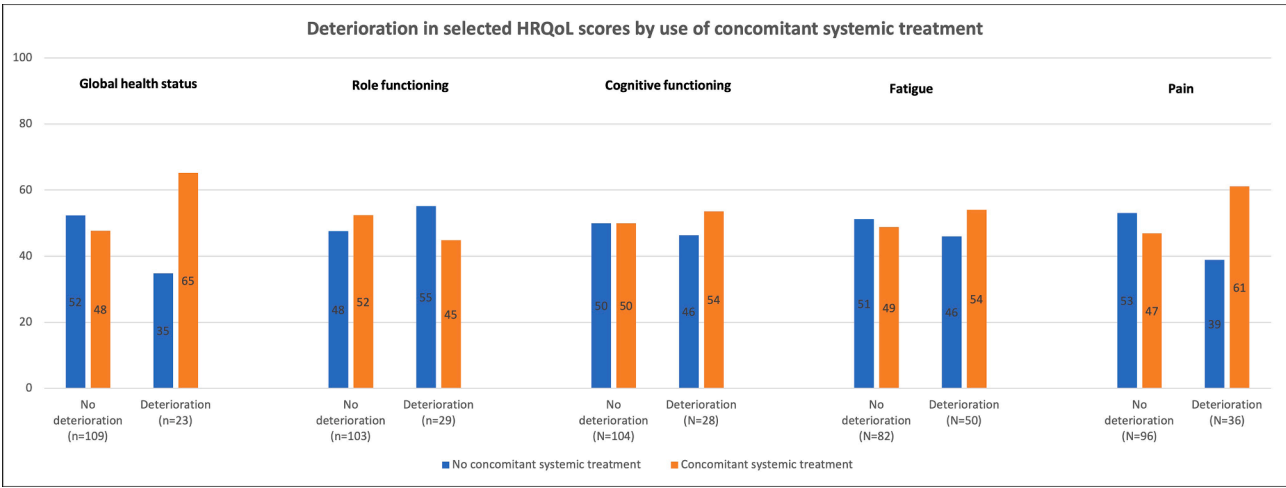


Fig. 4. Deterioration in selected HRQoL scores by use of concomitant systemic treatment. Legend: Deterioration was defined as a score of a negative difference of at least 10 points within a patient between two different time points. Concomitant systemic treatment was defined as receiving concomitant treatment alongside SBRT. In this analysis, all patients received hormonal therapy as systemic treatment. Abbreviations: HRQoL, health-related quality of life.

Table 3
Association of patients' baseline characteristics with baseline global health status and with the change in global health status from baseline to first follow-up following SBRT.

| | Baseline | | | p-value ^{°°} | First FU within 6 months from start SBRT | | | p-value ^{°°} |
|--|----------|------------------------|-------|-----------------------|--|------------------------|-------|-----------------------|
| Variable | Estimate | 95 % Confidence Limits | | | Estimate | 95 % Confidence Limits | | |
| New ESTRO/EORTC classification of OMD** | | | | | | | | |
| De-novo | Ref | | | 0.2557 | Ref | | | 0.4097 |
| Induced | −5.33 | −19.63 | 8.98 | | 1.78 | −20.42 | 23.97 | |
| Repeat | −4.21 | −9.67 | 1.24 | | 4.59 | −2.23 | 11.41 | |
| WHO Performance status | | | | | | | | |
| 0 | Ref | | | 0.0857 | Ref | | | 0.5396 |
| >0 | −6.40 | −12.55 | −0.24 | | −4.33 | −12.22 | 3.57 | |
| Not done | 2.42 | −5.37 | 10.21 | | −1.58 | −9.63 | 6.48 | |
| Age | | | | | | | | |
| 45–55 | Ref | | | 0.9601 | Ref | | | 0.8370 |
| 55–65 | 3.05 | −11.42 | 17.53 | | −7.48 | −25.91 | 10.95 | |
| 65–75 | 1.72 | −12.25 | 15.70 | | −5.15 | −22.88 | 12.57 | |
| >75 | 2.16 | −12.09 | 16.41 | | −5.97 | −24.12 | 12.18 | |
| Comorbidity* | | | | | | | | |
| No | Ref | | | 0.0323 | Ref | | | 0.6655 |
| Yes | −4.88 | −9.35 | −0.42 | | −1.18 | −6.57 | 4.21 | |
| prior treatment[°] | | | | | | | | |
| No | Ref | | | 0.1422 | Ref | | | 0.8325 |
| Yes | 6.36 | −2.15 | 14.86 | | −1.30 | −13.44 | 10.84 | |
| Number of oligometastases | | | | | | | | |
| 1 | Ref | | | 0.6885 | Ref | | | 0.2594 |
| >1 | 0.98 | −3.83 | | | 3.37 | −2.52 | 9.26 | |
| Concomitant Systemic treatment | | | | | | | | |
| No | | | | | Ref | | | 0.0731 |
| Yes | | | | | −4.77 | −10.00 | 0.45 | |

*Included comorbidities are those assessed in the Charlson Comorbidity index (i.e., Myocardial infarction, Congestive heart failure, Peripheral vascular disease, Cerebrovascular disease, Dementia, Chronic pulmonary disease, Rheumatic disease, Peptic ulcer disease, Liver disease, Diabetes with/without chronic complication, Hemiplegia or paraplegia, renal disease and AIDS (excluded asymptomatic infection)).

**OMD; de-novo, repeat and induced was defined by the ESTRO/EORTC classification(4).

°Any other treatment includes surgery of primary tumor, lymph node resection, radiotherapy to primary tumor or loco-regional lymph nodes or systemic treatment.

°° Multiple linear regression model.

Abbreviations: OMD, oligometastatic disease; SBRT, stereotactic body radiation therapy; WHO performance score: World Health Organization classification score for performance;

increase PRO compliance rates [32], especially if patients are willing in principle to complete PRO assessments [33]. Although we did experience a notable loss of HRQoL data due to the optional collection, this cohort is still the largest cohort examining HRQoL in real-world circumstances among men with oligometastatic PCa. Secondly, 59 % of the patients came from Western European countries (including Belgium, The Netherlands and Switzerland) and 34 % from Southern European

countries (including Italy and Spain), thus potentially limiting the generalizability of the results. Thirdly, when interpreting HRQoL data, especially in advanced stages, the response shift theory (i.e. the change in an individual's internal standards, values or conceptualizations that occur in response to a particular catalyst, such as ill health), may play a role, possibly resulting in overestimating their QoL [34,35]. Finally, the results must be interpreted with the caution, given that 51 % of the

included patients also received concomitant hormonal therapy, which influences the impact on HRQoL.

Conclusions

Patients with oligometastatic PCa had a good overall global health prior to treatment initiation. The presence of comorbidities at baseline was statistically significantly associated with worse global health. The use of metastases-directed SBRT was not associated with global QoL differences in the first six months after treatment. To increase the number of available HRQoL data, strategies should be directed towards addressing the barriers to initiate PRO data collection at the site level and strategies should be implemented to increase PRO compliance rates at the patient level in standard clinical practice.

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CRedit authorship contribution statement

Renée Bultijnck: Conceptualization, Formal analysis, Visualization, Writing – original draft, Writing – review & editing, Methodology. **Mieke Van Hemelrijck:** Conceptualization, Methodology, Supervision, Writing – review & editing, Formal analysis. **Valérie Fonteyne:** Resources, Writing – review & editing. **Lorenzo Livi:** Writing – review & editing, Resources. **Barbara Alicja Jereczek-Fossa:** Resources, Writing – review & editing. **Hossein Hemmatzad:** Resources, Writing – review & editing. **Michael Mayinger:** Resources, Writing – review & editing. **Heike Peulen:** Resources, Writing – review & editing. **Luc Verbeke:** Resources, Writing – review & editing, Resources, Writing – review & editing. **Sara Ramella:** Resources, Writing – review & editing. **Pablo Castro:** Resources, Writing – review & editing. **Pelagia Tsoutsou:** Resources, Writing – review & editing. **Karin Stellamans:** Resources, Writing – review & editing. **Adnan Shaikat:** Resources, Writing – review & editing. **Miha Orazem:** Resources, Writing – review & editing. **Paul Jeene:** Resources, Writing – review & editing. **Pètra Braam:** Resources, Writing – review & editing. **Helena Verkooijen:** Resources, Writing – review & editing. **Inga-Malin Simek:** Resources, Writing – review & editing. **Filippo Alongi:** Resources, Writing – review & editing. **Enrico Clementel:** Data curation, Resources, Writing – review & editing. **Catherine Fortpied:** Data curation, Formal analysis, Resources, Writing – review & editing, Methodology. **Abigail Machingura:** Writing – review & editing, Methodology. **Felix Boakye Oppong:** Data curation, Formal analysis, Methodology, Resources, Writing – review & editing, Visualization. **Matthias Guckenberger:** Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Writing – review & editing. **Piet Ost:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- Matthias Guckenberger and Piet Ost are PIs of the ESTRO-EORTC 1811-E2-RADIaE OligoCare trial.
- Matthias Guckenberger is president-elect of ESTRO.
- Mieke Van Hemelrijck is board member of the EORTC.
- Piet Ost reports a relationship with Janssen, Advanced Accelerator Applications, Curium, Bayer and MSD that includes: consulting or advisory. Piet Ost reports a relationship with Bayer and Varian that includes: funding grants

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ctro.2023.100715>.

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