Incorporating the patient voice in sarcoma research:

How can we assess health-related quality of life in this heterogeneous patient groep?

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EORTC Quality of Life Group

ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

Radboudumc

- Evaluation (new) treatments and care protocols traditionally focused on **objective outcomes** (e.g. disease-free and overall survival, response rate, adverse events) or centered around **provider's perspective** (e.g. number of complications)

- Assessment of **patient perspective** can provide important additional information to assess the benefits and risks of cancer treatments

Health care professionals and researchers increasingly be aware of how patient perspective may differ from theirs

Patient-reported outcomes (PROs)

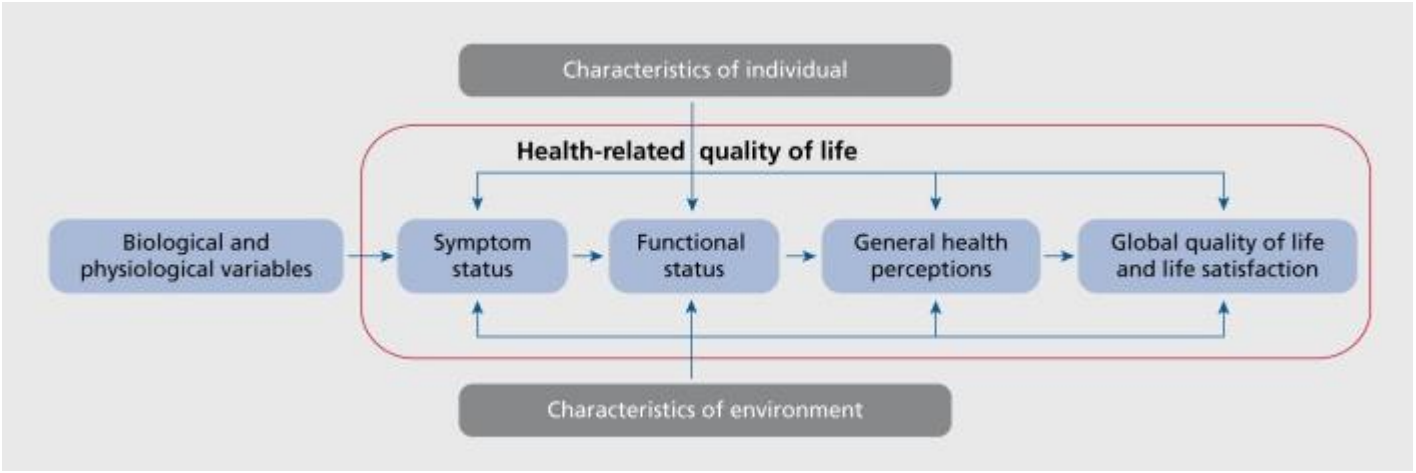
"Refer to a host of outcomes coming directly from patients about how they feel or function in relation to a health condition and its therapy without interpretation by healthcare professionals or anyone else"[1]

- Symptoms (e.g. pain, fatigue)
- Perception of daily functioning (e.g. physically, socially)
- Satisfaction with care
- **Health-related quality of life**

[1] U.S. Department of Health and Human Services, Food and Drug Administration. Guidance for industry: Patient-reported outcomes measures: Use in medical product development to support labeling claims.

Health-related quality of life (HRQoL)

- A multidimensional concept that includes subjective reports of symptoms, side effects, functioning in multiple life domains, and general perceptions of life satisfaction and quality



- Or: The impact of disease and treatment on domains of physical, psychological, and social functioning

1. Wilson IB., Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA.* 1995;273:59–65.; 2.Kluetz et al. Focusing on Core Patient-Reported Outcomes in Cancer Clinical Trials: Symptomatic Adverse Events, Physical Function, and Disease-Related Symptoms. Clinical Cancer Research, 2016.

Why is it important to measure PROs?

EDITORIAL

Missing Patients' Symptoms in Cancer Care Delivery—The Importance of Patient-Reported Outcomes

Ethan Basch, MD

As cancer care professionals, we care deeply about our patients' symptoms. Indeed, symptom management is a cornerstone of oncology practice. Yet, many studies demonstrate that we consistently miss up to half of our patients' symptoms.

Several years ago, a methodologist colleague at Memorial Sloan Kettering demonstrated to me that I do no better detecting symptoms than any other oncologist, despite my belief that I am a relatively "patient-centered" clinician (he did this by analyzing research data sets that include both clinician and patient symptom reports). The implications of our missing this information are profound: undermanagement of symptoms, unnecessary suffering, avoidable emergency department visits and hospitalizations, and treatment interruptions.[1-3] In clinical trials, this phenomenon can lead to underestimation of risk compared with benefit.[4]

Related article page 445

practices to improve symptom detection and management without disrupting efficiency or workflow? Multiple web-based systems have been developed and successfully implemented at individual cancer centers and hospitals for patient self-reporting.[15] Some of the key logistical and technical considerations have been outlined by the International Society for Quality of Life Research.[16] Key considerations include:

1. Thoughtful selection of which symptoms to assess based on the population of interest. The National Cancer Institute (NCI) has recommended "core" symptoms to assess across cancer populations.[17] Physical functioning should also be assessed.
2. Identification of appropriate questionnaires. Good options for symptom assessment include the NCI's Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE), the MD Ander-

As cancer care professionals, we care deeply about our patients' symptoms. Indeed, symptom management is a cornerstone of oncology practice. Yet, many studies demonstrate that we consistently miss up to half of our patients' symptoms.

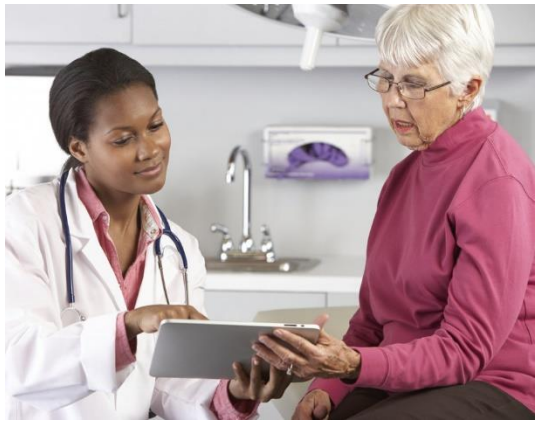
Several years ago, a methodologist colleague at Memorial Sloan Kettering demonstrated to me that I do no better detecting symptoms than any other oncologist, despite my belief that I am a relatively "patient-centered" clinician (he did this by analyzing research data sets that include both clinician and patient symptom reports).

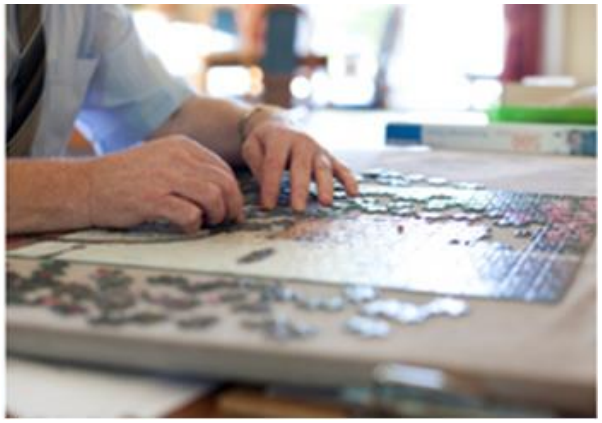
Undetected symptoms can lead to:

- Increased ED visits
- Increased hospital admissions
- Poorer patient satisfaction
- Poorer medication adherence
- Poorer HRQoL
- Poorer (objective) disease outcomes

Pakhomov et al., Am. J. Man. Care, 2008; Basch, NEJM, 2017; Atkinson et al, Qual. Life Res., 2012; Laugsand et al., Health Qual Life Outcomes, 2010; Fromme et al., JCO, 2004

- The use of PROs in clinical practice improves patient-provider communication and can also improve problem detection, management, and outcomes[1,2]





- Several recent studies have even demonstrated improved survival with PRO monitoring[2]

[1] Berry DL et al. Enhancing patient provider communication with the Electronic Self-Report Assessment for Cancer: a randomized trial. J Clin Oncol. 2011;29:1029-1035; [2] Basch E et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. J Clin Oncol. 2016;34:557-565.

Example Basch: PRO monitoring

VOLUME 34 · NUMBER 6 · FEBRUARY 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial

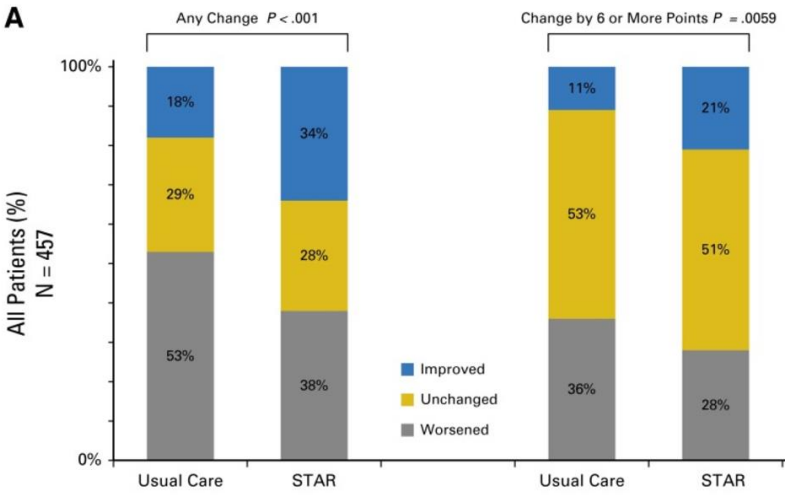
Ethan Basch, Allison M. Deal, Mark G. Kris, Howard I. Scher, Clifford A. Hudis, Paul Sabbatini, Lauren Rogak, Antonia V. Bennett, Amylou C. Dueck, Thomas M. Atkinson, Joanne F. Chou, Dorothy Dulko, Laura Sit, Allison Barz, Paul Novotny, Michael Fruscione, Jeff A. Sloan, and Deborah Schrag

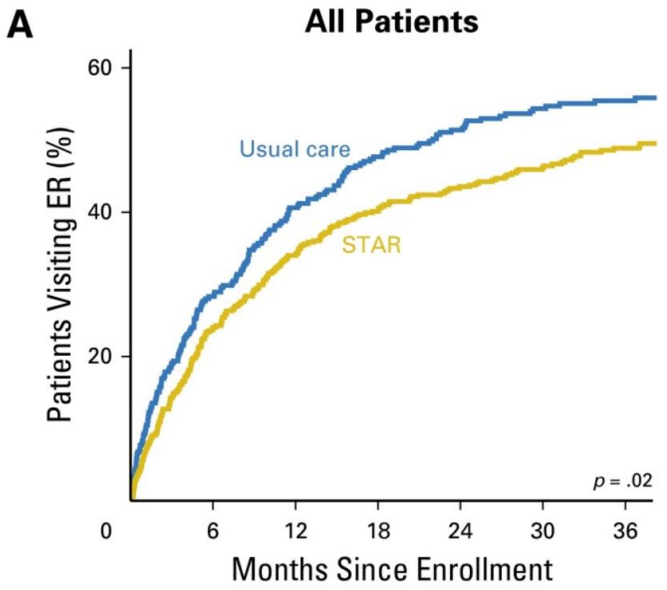
See accompanying editorial on page 527

- 766 patients with advanced solid cancer starting chemo
- Randomised to weekly online report of symptoms (n=441) or standard care (n=325)
- Nurse practitioners receive alerts when severe or worsening symptoms

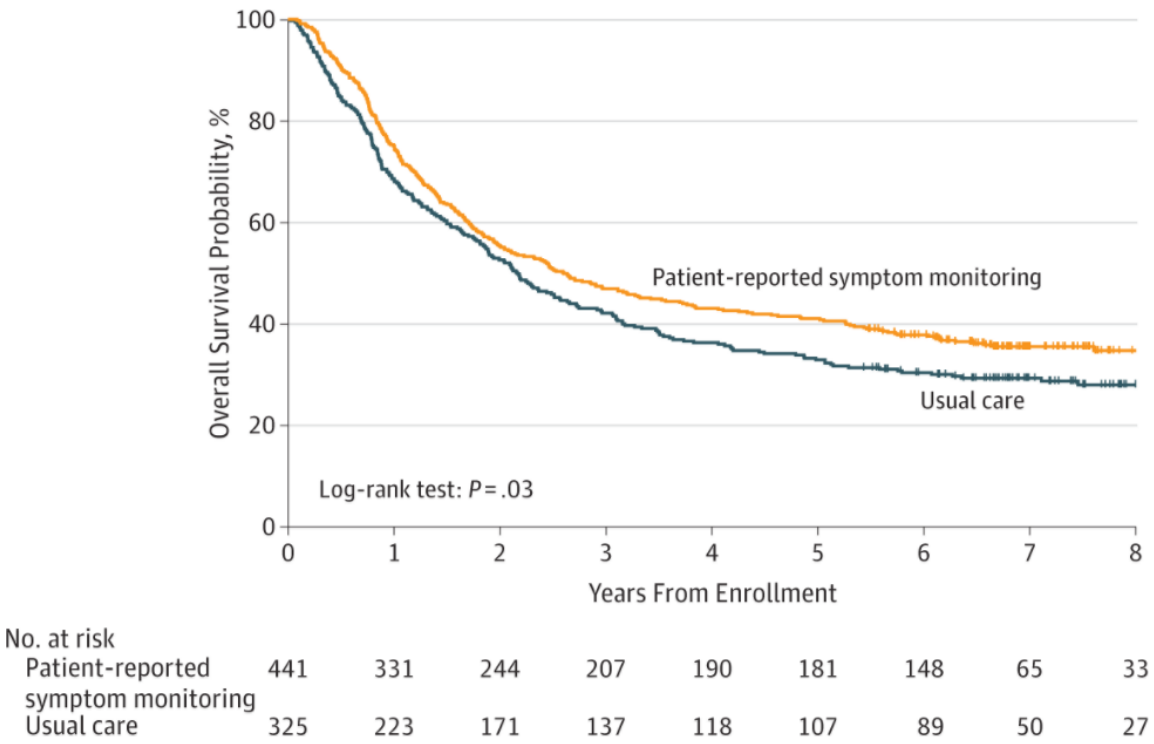
Assessed at 6 months, compared to baseline, pts in intervention group:

- HRQoL improved more and worsened among fewer (34 vs. 41%)
- Less frequently admitted to ER or hospitalized (45 vs. 49%)
- Remained on chemo longer (8.2 v. 6.3 months)





Basch et al. JCO 2016

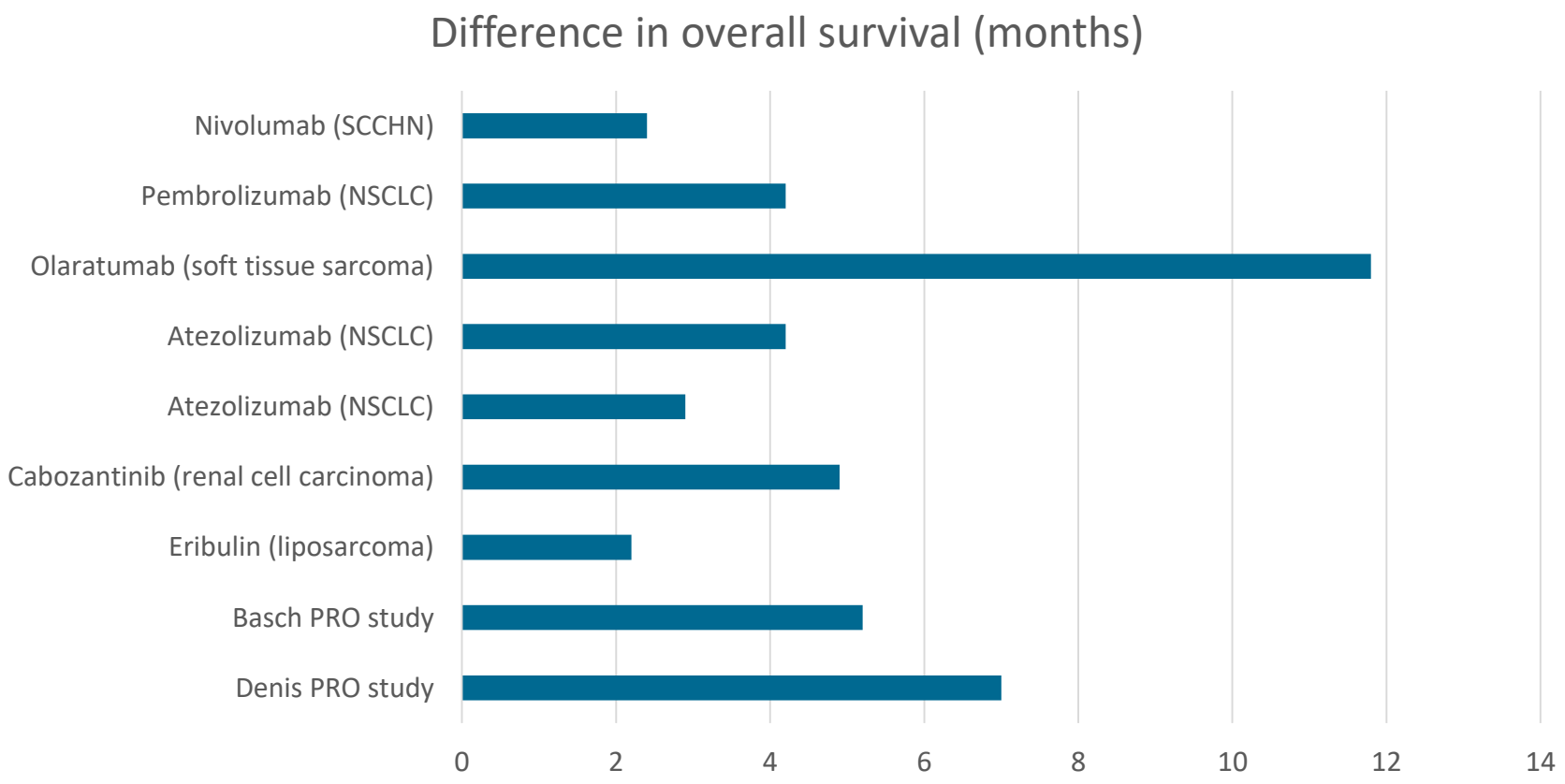


- Median OS for patients in the self-reporting arm was 31.2 months vs 26.0 months in the standard care cohort, which equated to an almost 20% increase in survival time for these patients.

- Remained significant in multivariable analysis (Adjusted HR=0.832)

Basch EM, Deal AM, Dueck AC, et al. Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment [published online first June 4, 2017]. *JAMA.* doi:10.1001/jama.2017.7156.

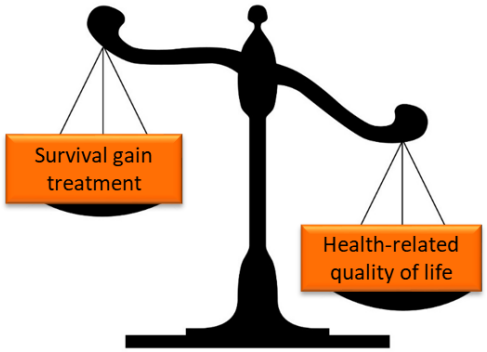
2016 FDA Approvals for metastatic tumors



Adapted from: https://www.fda.gov/drugs/informationondrugs/approveddrugs

Net clinical benefit

- Many sarcoma patients experience a substantial treatment burden of physical and psychosocial symptoms, with an adverse impact on HRQoL.



- Integration of HRQoL with traditional measures of therapeutic response will provide a more comprehensive assessment of efficacy and toxicity of (novel) therapies for sarcoma patients.

Do we assess HRQoL?

JCO special series

JOURNAL OF CLINICAL ONCOLOGY
SPECIAL SERIES

Novel Therapeutic and Diagnostic Advances in Bone and Soft Tissue Sarcomas

Published online December 8, 2017

Sarcoma: The Merging of Science and Clinical Care *Schwartz et al*

Sarcomas are cancers of connective tissues. There will be approximately 15,000 new cases of sarcoma diagnosed in the United States this year, collectively making them a rare form of cancer. The situation is made more complex in that sarcoma is not one diagnosis, any more than lung cancer is. Rather, sarcomas comprise at least 50 different histologic subtypes, each characterized by a unique biology, pathology, and genetics, with the extra complexity of anatomic locations from head to toes. As a result, sarcomas represent a complex family of cancers. Read more »

In this issue

- Contemporary Sarcoma Diagnosis, Genetics, and Genomics *Schaefer et al*
- Local Control of Soft Tissue and Bone Sarcomas *Crompton et al*
- Perioperative Management of Extremity Soft Tissue Sarcomas *Haas et al*
- Emerging Targeted and Immune-Based Therapies in Sarcoma *Pollack et al*
- Gastrointestinal Stromal Tumors *von Mehren et al*
- Soft Tissue and Uterine Leiomyosarcoma *George et al*
- Clinical and Molecular Spectrum of Liposarcoma *Lee et al*
- Biology and Management of Undifferentiated Pleomorphic Sarcoma, Myxofibrosarcoma, and Malignant Peripheral Nerve Sheath Tumors: State of the Art and Perspectives *Widemann et al*
- Rhabdomyosarcoma, Ewing Sarcoma, and Other Round Cell Sarcomas *Pappo et al*
- Synovial Sarcoma: Current Concepts and Future Perspectives *Stacchiotti et al*
- Osteosarcoma, Chondrosarcoma, and Chordoma *Whelan et al*
- Pathologic Angiogenesis of Malignant Vascular Sarcomas: Implications for Treatment *Khan et al*
- Locally Aggressive Connective Tissue Tumors *Gounder et al*
- Carcinosarcomas and Related Cancers: Tumors Caught in the Act of Epithelial-Mesenchymal Transition *Pang et al*

HRQoL data of sarcoma patients are sparse, but suggest that patients suffer from poorer HRQoL

Eur J Cancer Care (Engl). 2017 Jul;26(4). doi: 10.1111/ecc.12603. Epub 2016 Nov 7.

Quality of life after bone sarcoma surgery around the knee: A long-term follow-up study.

Bekkering WP[1,2], van Egmond-van Dam JC[1], Bramer JAM[2], Beishuizen A[3], Fiocco M[4], Dijkstra PDS[1].

Sarcoma. 2017;2017:2372135. doi: 10.1155/2017/2372135. Epub 2017 Apr 23.

Evaluation of Quality of Life at Progression in Patients with Soft Tissue Sarcoma.

Hudgens S[1], Forsythe A[2], Kontoudis I[3], D'Adamo D[2], Bird A[4], Gelderblom H[5].

J Surg Oncol. 2016 Dec;114(7):821-827. doi: 10.1002/jso.24424. Epub 2016 Sep 16.

Health-related quality of life following treatment for extremity soft tissue sarcoma.

Davidson D[1], Barr RD[2], Riad S[3], Griffin AM[3], Chung PW[4], Catton CN[4], O'Sullivan B[4], Ferguson PC[3,5,6], Davis AM[7], Wunder JS[3,5,6].

Author information

Abstract

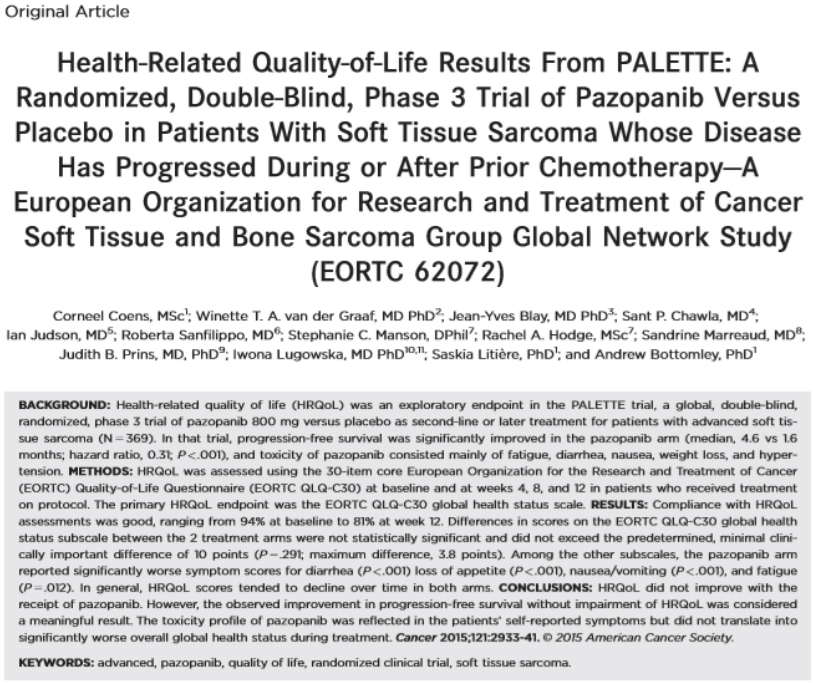
BACKGROUND AND OBJECTIVES: The primary objective of this study was to estimate the change in health-related quality of life (HRQL) 1 year following treatment for extremity soft tissue sarcoma (STS), measured by the EQ-5D. Secondary objectives included determining clinical variables associated with HRQL at 1 year, estimating the proportion with a clinically important difference (CID) in HRQL, and evaluating variability within EQ-5D domains.

METHODS: Patients over the age of 16 years, treated for a localized extremity STS, were included. The EQ-5D change score from pre-treatment to 1-year follow-up was determined. The association of clinical variables with EQ-5D scores was estimated using a linear regression model. The proportion of patients with a CID in HRQL score was determined. A vector analysis of the EQ-5D domains was undertaken.

RESULTS: The mean EQ-5D change score was 0.02. Age, sex, disease status, and initial EQ-5D score were associated with EQ-5D score at 1 year. There was a CID improvement in 32% and a deterioration in 24%. The anxiety and depression domain demonstrated the most change between baseline and 1 year after treatment.

CONCLUSION: Most patients maintain a high level of HRQL following treatment for extremity STS. J. Surg. Oncol. 2016;114:821-827. © 2016

PALETTE study



Original Article

Health-Related Quality-of-Life Results From PALETTE: A Randomized, Double-Blind, Phase 3 Trial of Pazopanib Versus Placebo in Patients With Soft Tissue Sarcoma Whose Disease Has Progressed During or After Prior Chemotherapy—A European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group Global Network Study (EORTC 62072)

Corneel Coens, MSc[1]; Winette T. A. van der Graaf, MD PhD[2]; Jean-Yves Blay, MD PhD[3]; Sant P. Chawla, MD[4]; Ian Judson, MD[5]; Roberta Sanfilippo, MD[6]; Stephanie C. Manson, DPhil[7]; Rachel A. Hodge, MSc[7]; Sandrine Marreaud, MD[8]; Judith B. Prins, MD, PhD[9]; Iwona Lugowska, MD PhD[10,11]; Saskia Litière, PhD[1]; and Andrew Bottomley, PhD[1]

BACKGROUND: Health-related quality of life (HRQoL) was an exploratory endpoint in the PALETTE trial, a global, double-blind, randomized, phase 3 trial of pazopanib 800 mg versus placebo as second-line or later treatment for patients with advanced soft tissue sarcoma (N = 369). In that trial, progression-free survival was significantly improved in the pazopanib arm (median, 4.6 vs 1.6 months; hazard ratio, 0.31; $P < .001$), and toxicity of pazopanib consisted mainly of fatigue, diarrhea, nausea, weight loss, and hypertension. **METHODS:** HRQoL was assessed using the 30-item core European Organization for the Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire (EORTC QLQ-C30) at baseline and at weeks 4, 8, and 12 in patients who received treatment on protocol. The primary HRQoL endpoint was the EORTC QLQ-C30 global health status scale. **RESULTS:** Compliance with HRQoL assessments was good, ranging from 94% at baseline to 81% at week 12. Differences in scores on the EORTC QLQ-C30 global health status subscale between the 2 treatment arms were not statistically significant and did not exceed the predetermined, minimal clinically important difference of 10 points ($P = .291$; maximum difference, 3.8 points). Among the other subscales, the pazopanib arm reported significantly worse symptom scores for diarrhea ($P < .001$) loss of appetite ($P < .001$), nausea/vomiting ($P < .001$), and fatigue ($P = .012$). In general, HRQoL scores tended to decline over time in both arms. **CONCLUSIONS:** HRQoL did not improve with the receipt of pazopanib. However, the observed improvement in progression-free survival without impairment of HRQoL was considered a meaningful result. The toxicity profile of pazopanib was reflected in the patients' self-reported symptoms but did not translate into significantly worse overall global health status during treatment. *Cancer* 2015;121:2933–41. © *2015 American Cancer Society.*

KEYWORDS: advanced, pazopanib, quality of life, randomized clinical trial, soft tissue sarcoma.

- The PALETTE study of pazopanib versus placebo, as 2nd-line or greater treatment for advanced STS, is one of the few clinical trials which reported HRQoL as exploratory endpoint.

- Pazopanib improved progression-free survival without relevant deterioration in **<u>global quality of life</u>** compared with placebo.

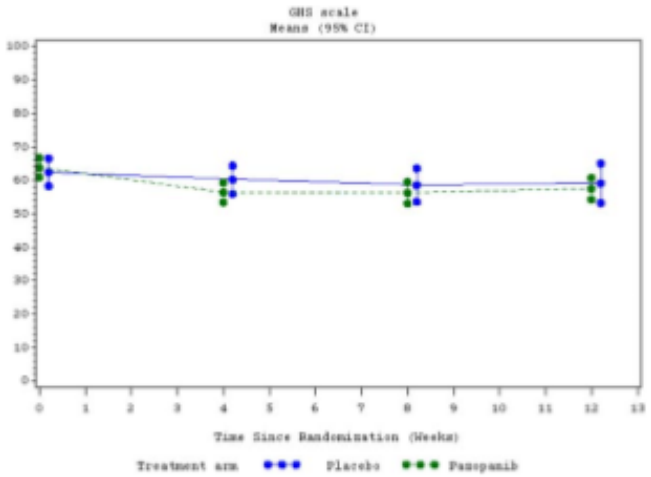


Figure 1. Mean global health status (GHS) scores and corresponding 95% confidence intervals (CIs) were estimated using the model. In both treatment arms, the GHS scores tended to decline over time.

- This demonstrates that combining HRQoL data with clinical data can show overall clinical treatment benefit.

But….

TABLE 3. Summary of the Health-Related Quality-of-Life Results

	QLQ-C30 Scales						
	Primary Scale of Interest	Secondary Scales of Interest					Sensitivity Analysis
	GHS	Diarrhea	Loss of Appetite	Nausea/Vomiting	Fatigue	Role Functioning	Imputed GHS
	P-value for test of overall difference						
	.291	< .001	< .001	< .001	0.012	0.039	0.272
	Difference between treatment arms (95% CI)[a]						
Baseline	1.4 (−3.7, 6.4)	1.9 (−2.1, 5.8)	0.1 (−6.1, 6.3)	−0.2 (−3.2, 2.8)	−1.0 (−6.6, 4.7)	1.4 (−5.7, 8.5)	1.7 (−3.0, 6.3)
Wk 4	−3.8 (−9.0, 1.3)	19.0 (12.4-25.6)	15.3 (7.9-22.6)	8.3 (3.8-12.8)	10.1 (3.9-16.2)	−9.5 (−17.1, −1.9)	−2.9 (−7.6, 1.8)
Wk 8	−2.3 (−8.3, 3.7)	26.4 (18.3-34.6)	17.1 (7.9-26.3)	11.0 (5.1-16.8)	7.6 (1.0-14.3)	−8.1 (−16.8, 0.6)	−3.2 (−8.3, 1.9)
Wk 12	−1.6 (−8.4, 5.1)	20.9 (10.4-31.5)	13.2 (3.3-23.2)	12.3 (5.8-18.9)	4.5 (−3.3, 12.4)	−4.9 (−14.5, 4.6)	−0.7 (−6.3, 4.9)

Abbreviations: GHS, general health status; QLQ-C30, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire core 30.
[a] Estimates for the differences between treatment arms were calculated using linear mixed modelling and are expressed in absolute score points on the scale. For the GHS and role functioning scales, positive numbers indicate a higher value (better quality of life) for pazopanib compared with placebo. For the symptom scales (diarrhea, loss of appetite loss, nausea/vomiting, and fatigue), positive numbers indicate a higher level of symptoms (worse quality of life) for pazopanib compared with placebo.

- There were both statistically and clinically significant differences in scores between the 2 arms for **diarrhea**, **loss of appetite**, **nausea/vomiting**, **fatigue** and **role functioning** in favor of placebo group

Are all aspects of HRQoL assessed?

- Several side-effects or symptoms common to angiogenesis inhibitors were not assessed as they are not part of the cancer-generic HRQoL questionnaire.

- Most notably absent are symptoms related to **hand-foot syndrome** or **skin reactions**.

- These symptoms represent a severe limitation to the patient when performing normal daily activities. Dermatologic problems may be considered more important by patients because of their chronicity, obvious appearance, and social impact, thus affecting daily activities more than might be apparent from a clinical perspective.

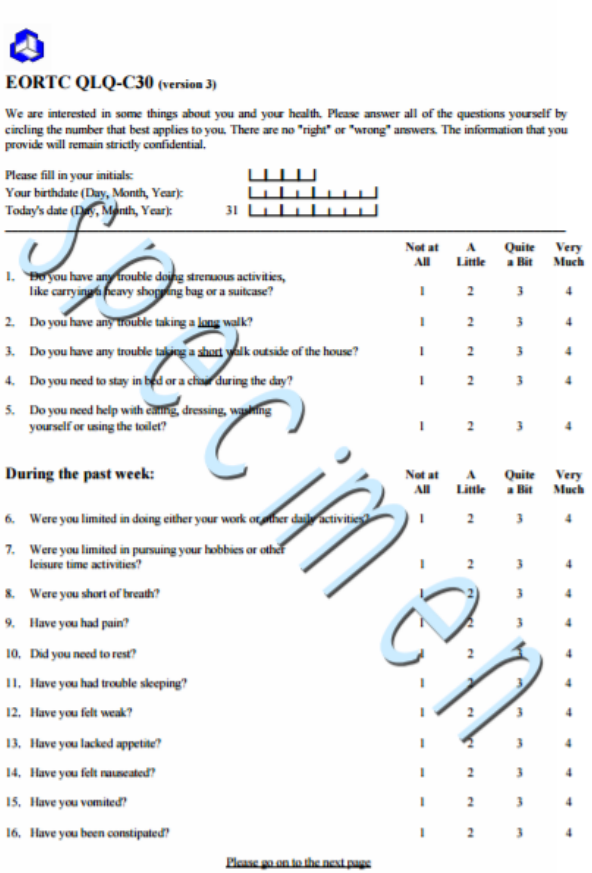
- Disease- and treatment-specific symptoms most of the times strongest predictors of overall HRQoL

How to assess HRQoL?

- One of the biggest challenges in sarcoma is how to assess HRQoL in this heterogeneous patient group.

- Previous studies all used generic HRQoL instruments (e.g. EORTC QLQ-C30; SF36, FACT-G).

Static: EORTC QLQ-C30 & C15-PAL



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ____
Your birthdate (Day, Month, Year): __ __ __ __ __ __
Today's date (Day, Month, Year): 31 __ __ __ __ __ __

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

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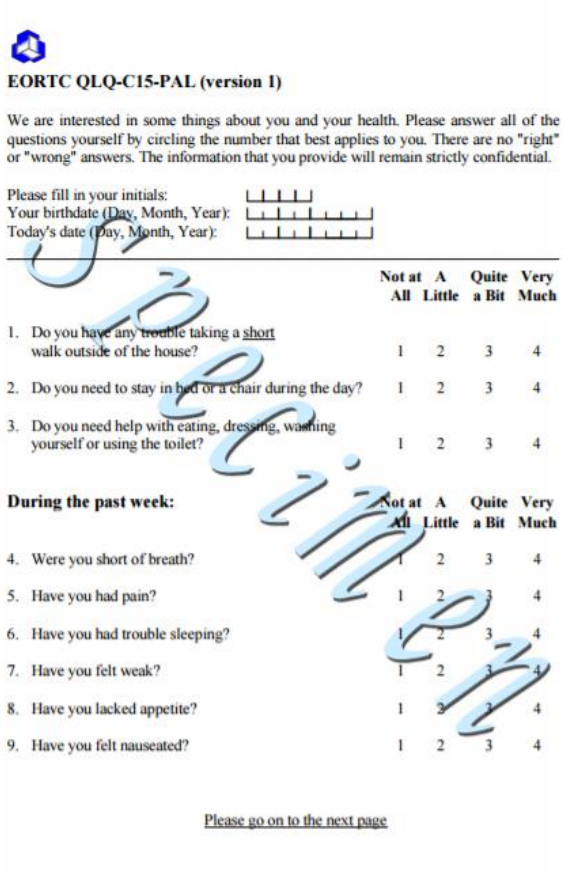


EORTC QLQ-C15-PAL (version 1)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ____
Your birthdate (Day, Month, Year): __ __ __ __ __ __
Today's date (Day, Month, Year): __ __ __ __ __ __

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
2. Do you need to stay in bed or a chair during the day?	1	2	3	4
3. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

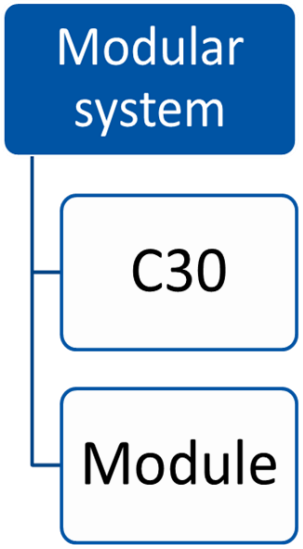
During the past week:

	Not at All	A Little	Quite a Bit	Very Much
4. Were you short of breath?	1	2	3	4
5. Have you had pain?	1	2	3	4
6. Have you had trouble sleeping?	1	2	3	4
7. Have you felt weak?	1	2	3	4
8. Have you lacked appetite?	1	2	3	4
9. Have you felt nauseated?	1	2	3	4

Please go on to the next page

- These generic tools do not efficiently capture the unique experiences of sarcoma patients and thus lack content validity

- Traditionally inadequate content coverage has been addressed using a **tumor-**, **treatment-**, or **domain-specific** module that captures all specific HRQoL issues, in conjunction with generic HRQoL measures.



Validated Modules

QLQ-BIL21	CHOLANGIOCARCINOMA AND GALLBLADDER CANCER
QLQ-BM22	BONE METASTASES
QLQ-BN20	BRAIN
QLQ-BR23	BREAST
QLQ-CR29	COLORECTAL
QLQ-CX24	CERVICAL
QLQ-ELD14	ELDERLY CANCER PATIENTS
QLQ-EN24	ENDOMETRIAL
QLQ-FA12	CANCER-RELATED FATIGUE
QLQ-GI.NET21	NEUROENDOCRINE CARCINOID
QLQ-HCC18	HEPATOCELLULAR CARCINOMA
QLQ-H&N35	HEAD & NECK
QLQ-INFO25	INFORMATION
QLQ-LC13	LUNG
QLQ-LMC21	COLORECTAL LIVER METASTASES
QLQ-MY20	MULTIPLE MYELOMA
QLQ-OES18	OESOPHAGEAL
QLQ-OG25	OESOPHAGO-GASTRIC
QLQ-OH15	ORAL HEALTH
QLQ-OV28	OVARIAN
QLQ-PR25	PROSTATE
QLQ-STO22	GASTRIC

Modules in Phase IV

QLQ-BrR24	BREAST RECONSTRUCTION
QLQ-CAX24	CANCER CACHEXIA AND NUTRITIONAL STATUS
QLQ-CIPN20	PERIPHERAL NEUROPATHY
QLQ-CML24	CHRONIC MYELOID LEUKAEMIA
QLQ-H&N43	UPDATE OF H&N35
QLQ-LC29	UPDATE OF LC13
QLQ-PRT23	RADIATION PROCTITIS
QLQ-SHQ22	SEXUAL HEALTH
QLQ-SWB32	SPIRITUAL WELLBEING
QLQ-TC26	TESTICULAR CANCER

Modules Phase III Completed

QLQ-ANL27	ANAL CANCER
QLQ-BLM30	MUSCLE INVASIVE BLADDER CANCER
QLQ-CLL17	CHRONIC LYMPHOCYTIC LEUKAEMIA - REPLACING QLQ-CLL16
QLQ-CLL16	CHRONIC LYMPHOCYTIC LEUKAEMIA – BEING REPLACED BY QLQ-CLL17
QLQ-COMU26	COMMUNICATION
QLQ-HDC29	HIGH-DOSE CHEMOTHERAPY
QLQ-HL27	HODGKIN LYMPHOMA
QLQ-MEL38	MELANOMA
QLQ-NHL-HG29	HIGH-GRADE NON-HODGKIN LYMPHOMA
QLQ-NHL-LG20	LOW-GRADE NON-HODGKIN LYMPHOMA
QLQ-NMIBC24	NON-MUSCLE INVASIVE BLADDER CANCER
QLQ-OPT30	OPHTHALMIC CANCER
QLQ-PAN26	PANCREATIC CANCER

Modules in Phase III

- Nasopharyngeal Carcinoma
- Outpatient Satisfaction
- Satisfaction with Cancer Care Core
- Symptom-Based Questionnaires
- Thyroid Cancer
- Vulva Cancer

Modules in Phase I–II

- Adolescents and Young Adults
- Breast Cancer (update of BR23)
- Hereditary Cancer Predisposition Syndrome
- IADL in Brain Tumor Patients
- Pancreatic Neuroendocrine Tumor
- Spinal Cord Compression
- Survivorship

-**Tumor-specific** modules (e.g. breast cancer)

-**Domain-specific** questionnaires (e.g. fatigue)

-**Treatment-specific** (e.g. symptoms of new targeted agents)

Module development process – co-creation with patients

- **Phase 1: Generation of HRQoL issues**

Compiling an exhaustive list of relevant HRQoL issues based on three sources: literature, patients and health care professionals

- **Phase 2: Construction of the item list**

Issues is converted into questions with the format and time frame compatible with the EORTC QLQ-C30

- **Phase 3: Pre-testing**

Identify and solve potential problems in its administration (e.g., the phrasing of questions, the sequence of questions) and identify missing or redundant issues.

- **Phase 4: Field-testing**

Determine its acceptability, reliability, validity, responsiveness and cross-cultural applicability

Sarcoma-specific HRQoL?

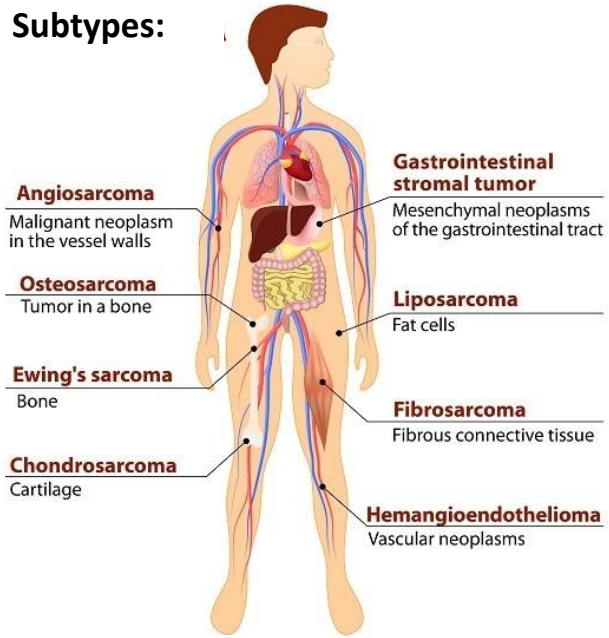
- Sarcoma-specific module is needed to detect, with more sensitivity, HRQoL issues particularly relevant to sarcoma patients

- However, given the heterogeneity of the disease in terms of subtype, presentation, age and treatment, the development of such an instrument may be challenging

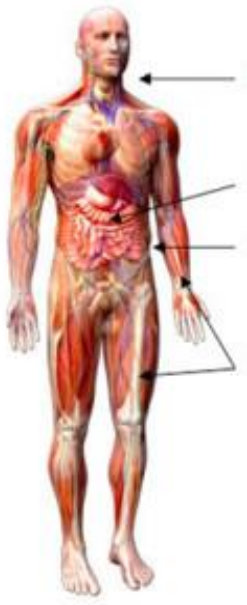
A patient with Ewing sarcoma faces different challenges compared with a patient with undifferentiated pleomorphic sarcoma

Sarcoma - Heterogeneity

Subtypes:



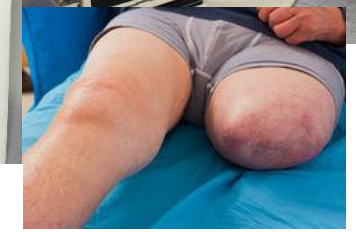
Ages:



Localizations:

-Upper and lower extremities
-Head and neck
-Thorax
-Retroperitoneal / intra-abdominal
-Gynaecological

Stages:



Treatments:

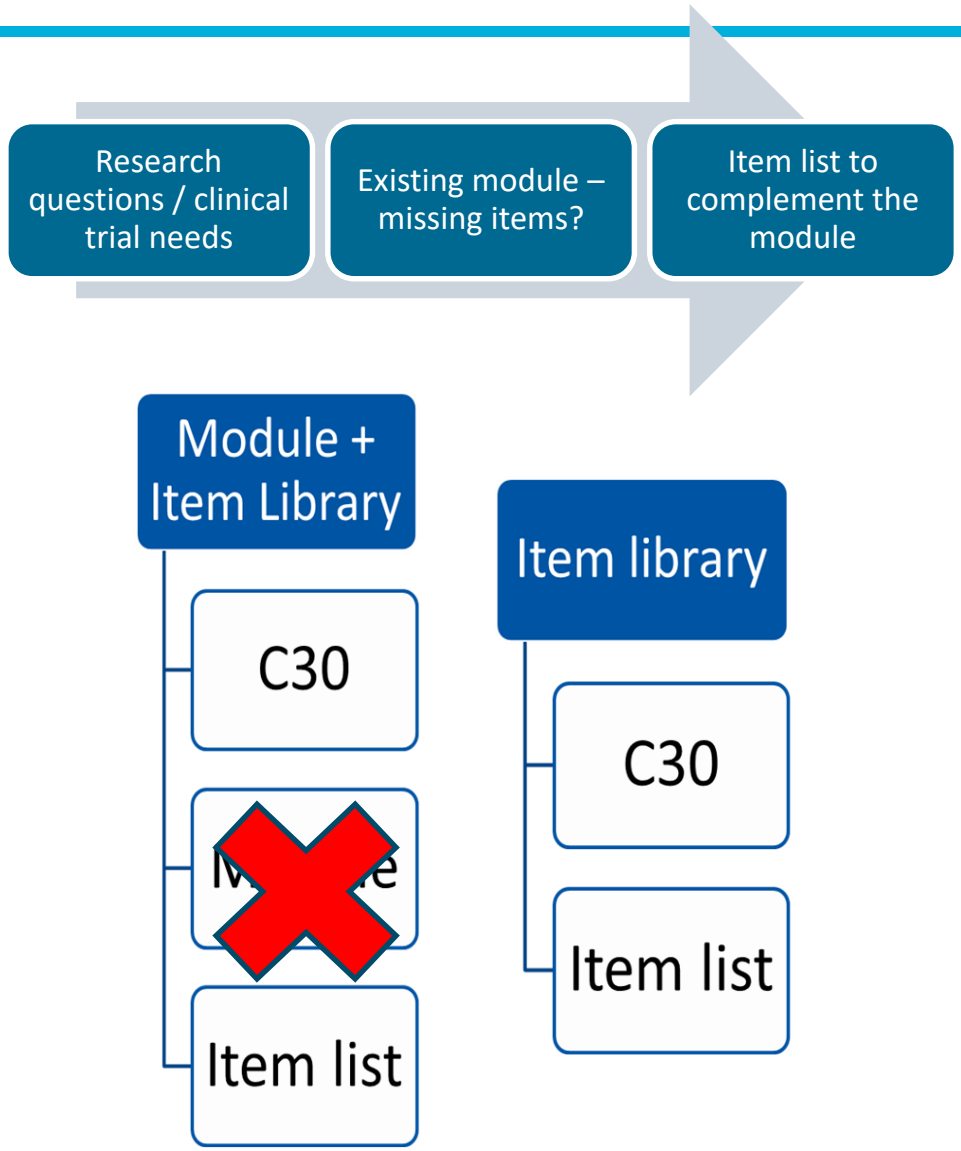
New strategy

- Given the rapid evolution of treatment options, a module may not be the best option to meet the needs of academia and industry to assess the impact of new treatments

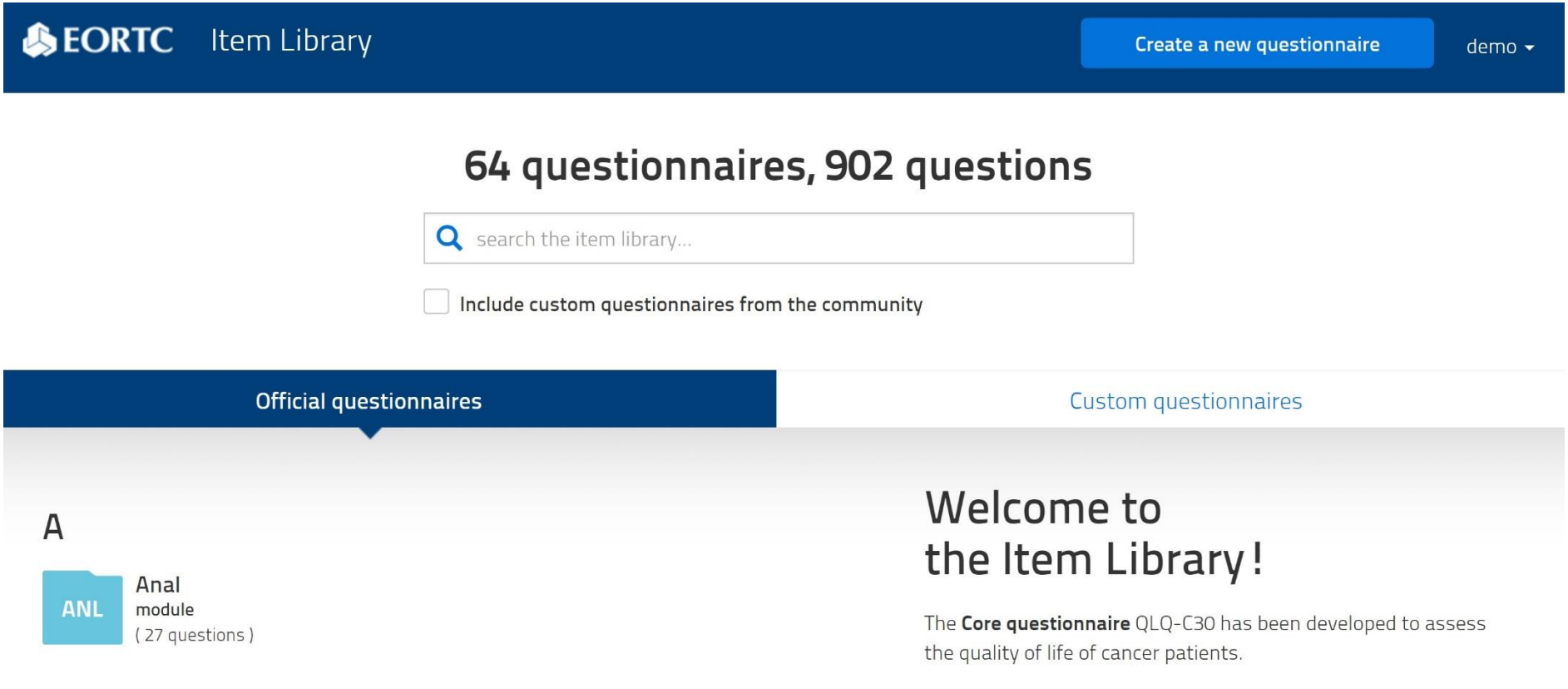
- Standardized or so-called **"static"** questionnaires consisting of a fixed set of items may miss important adverse events.

- The EORTC QLG therefore recently recommended the use of a combination of standardized HRQoL questionnaires and validated items from item libraries: **static plus flexible/dynamic approach**

- This would ensure adequate assessment of not only adverse events of new treatments, but also their impact on common functional health problems reported by patients


Research questions / clinical trial needs
Existing module – missing items?
Item list to complement the module
Module + Item Library
C30
Item list
Item library
C30
Item list

Item Library

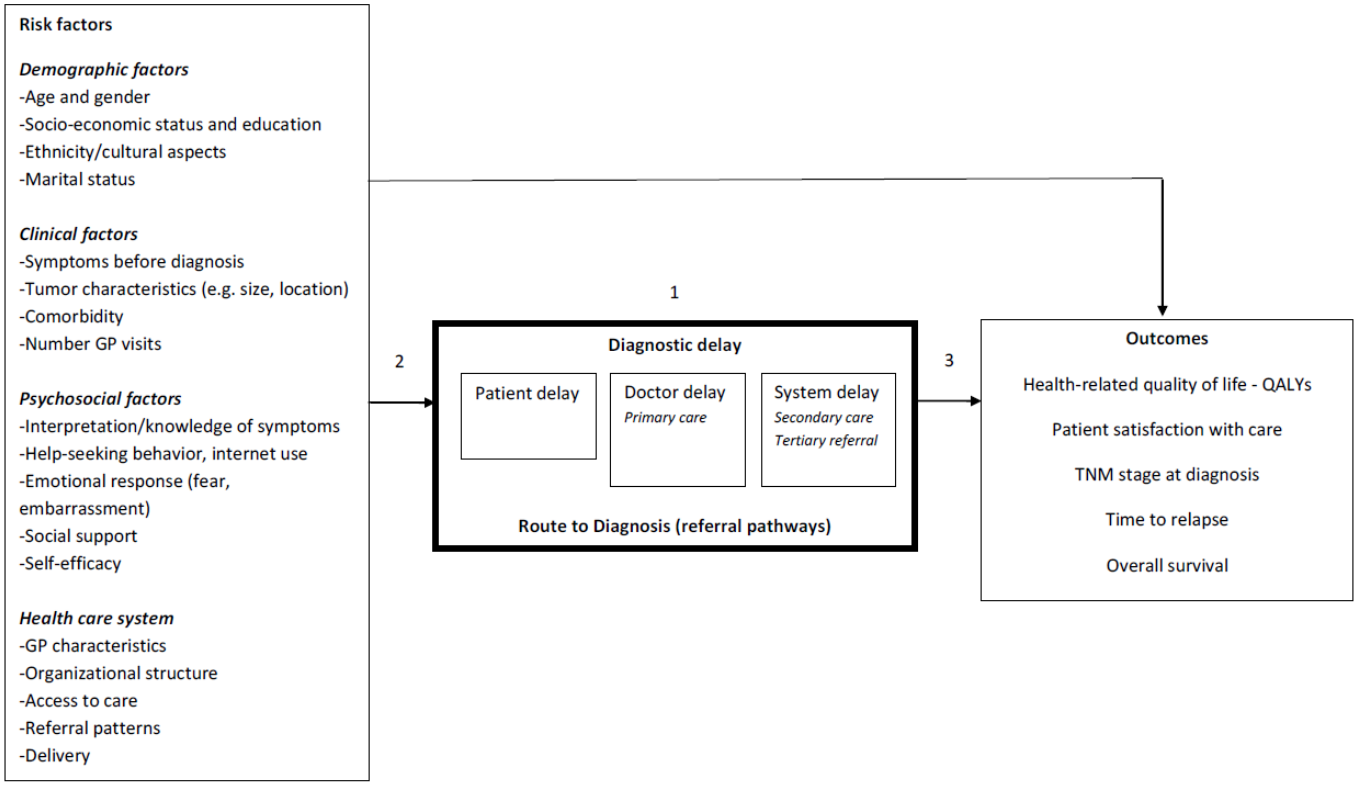


EORTC QLG project starting soon

Is it possible to develop one module covering all sarcoma issues, or are the HRQoL issues surrounding the different subtypes/treatments sufficiently different to warrant the development of separate modules and/or item lists (with items selected from the EORTC item library)?

Other sarcoma PRO studies

Diagnostic pathway and Quality of life in sarcoma patients: QUOTE study



Phd-student: Vicky Soomers

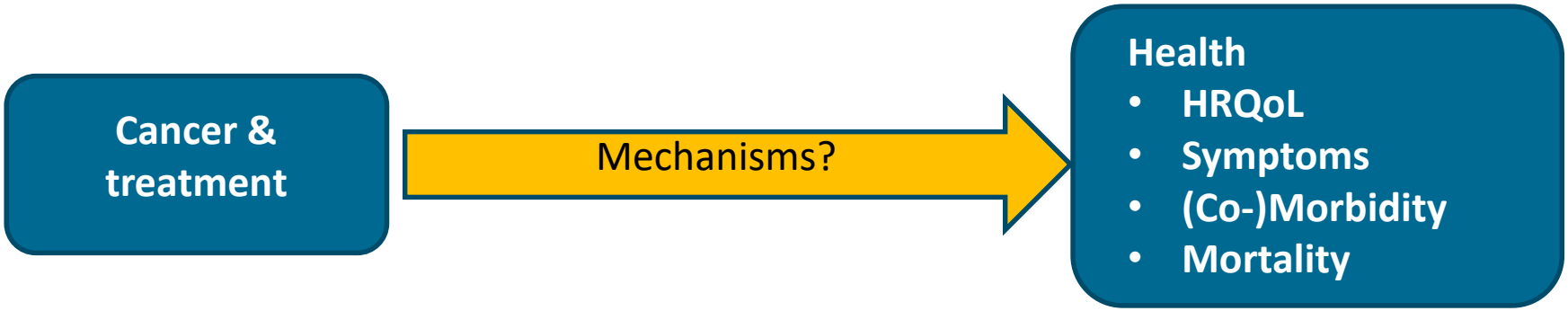
Health-related quality Of Life In patients with advanced Soft TIssue sarcomas treated with Chemotherapy: HOLISTIC study

- Decision making often challenging due to low response rates and marginal survival benefit.
- Analysis of HRQoL trajectories in advanced STS patients treated with chemotherapy
- HRQoL data will provide additional information on the impact chemotherapy and thus aid collaborative decision making.

PhD-student: Eugenie Younger

(Long-term) survivorship issues

Diagnosed between 2008-2016 and still alive in 2018:



- Prevalence of physical and psychosocial problems
- **Who** is at risk for poor outcomes?
- **Why** that person?

PhD-student: Vicky Soomers

Living with desmoid-type fibromatosis

***Title* Identification of health related quality of life issues and measures to assess these in patients with sporadic desmoïd-type fibromatosis: a literature review and focus group study.**

***Running title* Health related quality of life in patients with desmoïd-type fibromatosis**

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Desmoid fibromatosis through the patients' eyes: Time to change the focus and organisation of care?

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This manuscript has been prepared in accordance with the style of the journal, and all authors have approved its content. This manuscript is not being considered for publication elsewhere and the findings of this manuscript have not been previously published.

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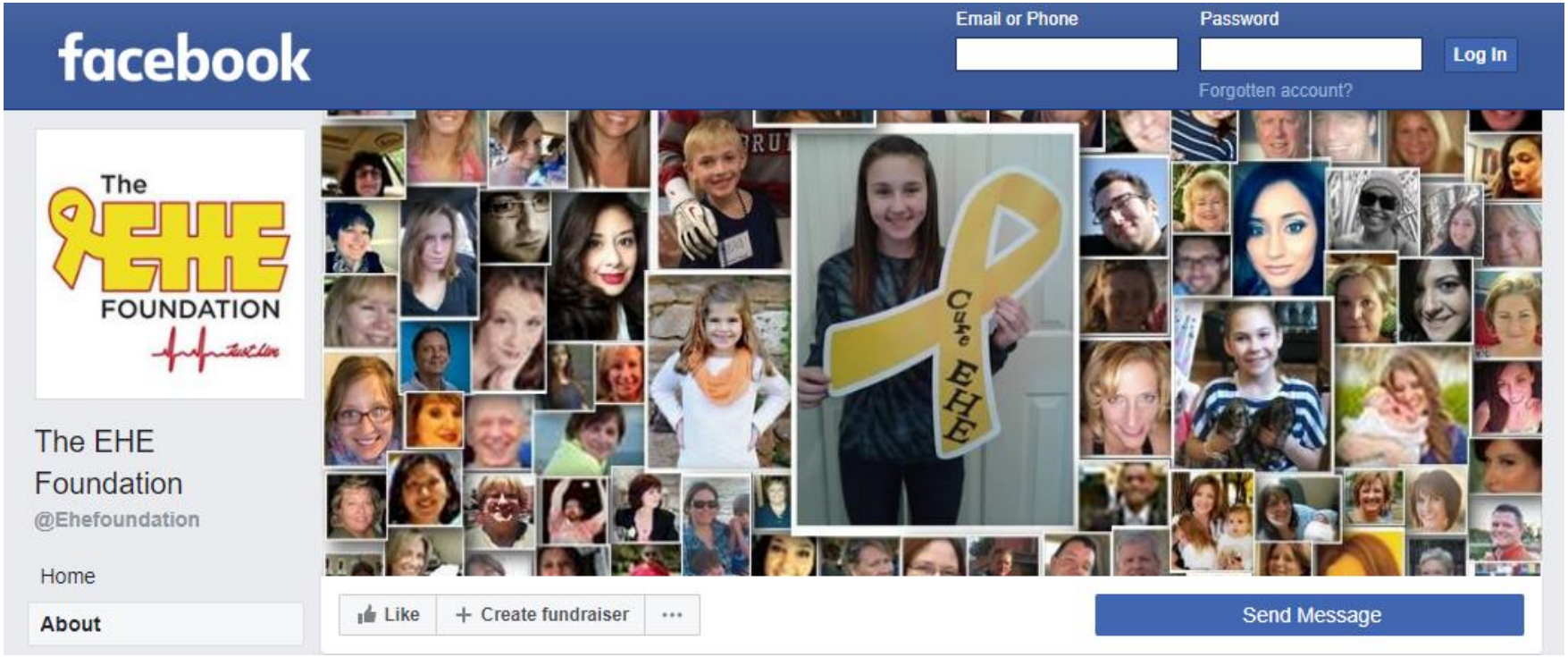
ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

Radboudumc

Living with Epithelioid Hemangioendothelioma (EHE): Facebook study



PhD-student: Marije Weidema

Questions or ideas?

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