

University of Groningen

Priorities and preferences of advanced soft tissue sarcoma patients starting palliative chemotherapy

Younger, E.; Jones, R. L.; den Hollander, D.; Soomers, V. L.M.N.; Desar, I. M.E.; Benson, C.; Young, R. J.; Oosten, A. W.; de Haan, J. J.; Miah, A.

Published in:
ESMO Open

DOI:
[10.1016/j.esmoop.2021.100258](https://doi.org/10.1016/j.esmoop.2021.100258)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Younger, E., Jones, R. L., den Hollander, D., Soomers, V. L. M. N., Desar, I. M. E., Benson, C., Young, R. J., Oosten, A. W., de Haan, J. J., Miah, A., Zaidi, S., Gelderblom, H., Steeghs, N., Husson, O., & van der Graaf, W. T. A. (2021). Priorities and preferences of advanced soft tissue sarcoma patients starting palliative chemotherapy: baseline results from the HOLISTIC study. *ESMO Open*, 6(5), [100258]. <https://doi.org/10.1016/j.esmoop.2021.100258>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

ORIGINAL RESEARCH

Priorities and preferences of advanced soft tissue sarcoma patients starting palliative chemotherapy: baseline results from the HOLISTIC study

E. Younger^{1,2}, R. L. Jones^{1,3}, D. den Hollander^{2,4}, V. L. M. N. Soomers², I. M. E. Desar², C. Benson¹, R. J. Young⁵, A. W. Oosten⁶, J. J. de Haan⁷, A. Miah^{1,3}, S. Zaidi¹, H. Gelderblom⁸, N. Steeghs⁴, O. Husson^{3,4†*} & W. T. A. van der Graaf^{1,2,4†}

¹Sarcoma Unit, Royal Marsden NHS Foundation Trust, London, UK; ²Department of Medical Oncology, Radboud University Medical Centre, Nijmegen, The Netherlands; ³Division of Clinical Studies, Institute of Cancer Research, London, UK; ⁴Department of Medical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands; ⁵Academic Unit of Clinical Oncology, The University of Sheffield, Sheffield, UK; ⁶Department of Medical Oncology, Erasmus MC Cancer Institute, Rotterdam; ⁷Department of Medical Oncology, University Medical Center Groningen, Groningen; ⁸Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands



Available online 9 September 2021

Introduction: Palliative chemotherapy is the principal treatment of patients with advanced soft tissue sarcomas (STS); however prognosis is limited (median overall survival 12-19 months). In this setting, patient values and priorities are central to personalised treatment decisions.

Patients and methods: The prospective HOLISTIC study was conducted in the UK and the Netherlands assessing health-related quality of life in STS patients receiving palliative chemotherapy. Participants completed a questionnaire before starting chemotherapy, including attitudes towards quality of life (QoL) versus length of life (LoL), decisional control preferences, and decisional conflict. Chi-square and Fisher's exact tests were used to evaluate associations between patient characteristics and preferences.

Results: One hundred and thirty-seven patients with advanced STS participated (UK: $n = 72$, the Netherlands: $n = 65$). Median age was 62 (27-79) years. Preference for extended LoL ($n = 66$, 48%) was slightly more common than preference for QoL ($n = 56$, 41%); 12 patients (9%) valued LoL and QoL equally (missing: $n = 3$). Younger patients (age <40 years) prioritised LoL, whereas two-thirds of older patients (aged ≥ 65 years) felt that QoL was equally or more important than LoL ($P = 0.020$). Decisional conflict was most common in patients who prioritised QoL ($P = 0.024$). Most patients preferred an active ($n = 45$, 33%) or collaborative ($n = 59$, 44%) role in treatment decisions. Gender, performance status, and country were significantly associated with preferred role. Concordance between preferred and actual role in chemotherapy decision was high ($n = 104$, 76%).

Conclusions: Heterogeneous priorities and preferences among advanced STS patients support personalised decisions about palliative treatment. Considering individual differences during treatment discussions may enhance communication and optimise patient-centred care.

Key words: sarcoma, preferences, priorities, quality of life

INTRODUCTION

Soft tissue sarcomas (STS) are a group of rare, heterogeneous neoplasms of mesenchymal origin. Approximately 10% of patients present with synchronous metastases, and around half of those with localised high-risk tumours will develop metastases after primary treatment.^{1,2} Patients with advanced STS often have a substantial burden of

physical and psychological symptoms, which have a negative impact on health-related quality of life (HRQoL).^{3,4} Quality of life (QoL) is a wide concept including 'non-health' factors. QoL is defined as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns.'⁵

In the setting of advanced STS, principal treatment goals are to alleviate disease-related symptoms, maintain or improve QoL and to prolong survival (median overall survival 12-19 months). Anthracycline-based chemotherapy is standard first-line treatment of most histological subtypes, however, such schedules can have considerable toxicity.^{6,7} Furthermore, chemotherapy may improve certain symptoms, such as pain and discomfort, but may cause (initial)

*Correspondence to: Dr. Olga Husson, Division of Clinical Studies, Institute of Cancer Research, 15 Cotswold Road, Sutton SM2 5NG, UK. Tel: +44 207 352 8133

E-mail: olga.husson@icr.ac.uk (O. Husson).

†Joint contribution as last author.

2059-7029/© 2021 The Authors. Published by Elsevier Ltd on behalf of European Society for Medical Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

deterioration in other symptoms, such as fatigue, and overall QoL.^{8,9}

Patients with advanced STS are therefore faced with a challenging trade-off between possible beneficial outcomes and almost inevitable chemotherapy-related morbidity.¹⁰ Consequently, patients may experience decisional conflict, representing 'personal uncertainty about which course of action to take when choice among competing options involves risk, regret, or challenge to personal life values.'¹¹ Decisional conflict is influenced by personal values, understanding information, degree of support, and perception that a decision was poor or ineffective.¹¹

Previous studies have demonstrated that patients' beliefs and attitudes are strongly influenced by their current health status, previous experiences, family, friends, health care professionals, and media.¹² Treatment preferences in seriously unwell patients are also related to the perceived burden of treatment, the likelihood of the outcome, and the outcome itself (e.g. survival or functional improvement).¹³ Shared decision making is a method to support patients in treatment decisions, and is acknowledged to be a central component of patient-centred care.¹⁴ Clinicians should provide information on the anticipated benefits of treatment, potential adverse effects, alternative management approaches (including best supportive care), while considering individual values and preferences.^{12,15} Acknowledging clinical uncertainty and encouraging patients to discuss their preferences may enhance shared decision making.¹⁶ Conversely, not all patients want to participate in decision making, and eliciting preferences for involvement in treatment decisions can improve communication, satisfaction, and quality of care.^{17,18} The Control Preferences Scale is the most widely used tool to assess patient preferences for involvement in decisions about medical treatment, measuring the degree of control an individual wants to assume during decisions about their health.¹⁹ Understanding control preferences can enhance patient satisfaction and high-quality care.^{17,18,20}

In order to provide high-quality, patient-centred care, a clear understanding of patient priorities is needed. The primary objectives of this analysis are to explore priorities towards quality versus length of life (LoL), decisional control preferences, and decisional conflict in advanced STS patients starting first-line palliative chemotherapy in sarcoma centres in the United Kingdom (UK) and the Netherlands (NL).

MATERIALS AND METHODS

HOLISTIC (Health-related quality Of Life In patients with advanced Soft Tissue sarcomas treated with Chemotherapy) is a prospective cohort study for patients aged ≥ 18 years, treated with chemotherapy for advanced STS in the UK and the NL (NCT03621332).²¹ Ethical approval was obtained in the UK (REC 17/NI/1097) and at all participating sites in the NL. Data were collected in the PROFILES registry; an established international registry for collection of cancer patient-reported outcomes.²²

The study was carried out in accordance with the Declaration of Helsinki.

Patients

Patients were recruited from two sarcoma reference centres in the UK and five in the NL. All patients had a histologically-confirmed diagnosis of STS. Advanced disease was defined as metastatic disease, or locally advanced disease not amenable to curative surgical resection. Patients with advanced Ewing's sarcoma, rhabdomyosarcoma, desmoplastic small round cell sarcoma, and gastrointestinal stromal tumours were excluded. After providing informed consent, participants completed a baseline questionnaire (online or paper/English or Dutch) before starting first-line chemotherapy. Participants then completed a questionnaire after each cycle of chemotherapy and 3-monthly during follow-up. The primary endpoint of the HOLISTIC study was change in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC-QLQ-C30) global QoL score from baseline to post cycle 4 of chemotherapy (mean number of cycles completed); final results are awaited (follow-up 2 years). Exploratory endpoints included baseline attitudes towards QoL versus LoL, decisional control preferences, decisional conflict; reported here. We also assessed baseline expectations of treatment, and these results will be reported separately. Full details of the protocol are published elsewhere.²¹

Measures

Participant characteristics. Sociodemographic characteristics such as age, gender, ethnicity, religious beliefs, relationship status, and education were assessed in the baseline patient questionnaire. Clinical characteristics were collected in case report forms, including disease extent, histological subtype, and baseline Eastern Cooperative Oncology Group (ECOG) performance status (PS). We did not collect details on primary surgery or local recurrence as this was beyond the scope of the study.

Questionnaires. The EORTC-QLQ-C30 was used to measure global QoL.²³ The Quality-Quantity Questionnaire, was used to explore attitudes towards the trade-off between QoL or LoL.¹⁰ Four items are related to preference for QoL and four related to quantity (length) of life (LoL). Patients are asked how strongly they agree or disagree with these items on a five-point Likert scale. Higher total score for QoL or LoL items demonstrates inclination towards QoL or LoL, respectively.¹⁰

The Control Preference Scale is a widely used measure to assess patient preferences for role in treatment decisions.¹⁹ Patients were asked to select from five options, the phrase that best describes their preferred role in decisions about their cancer diagnosis and treatment, and the role they have actually taken in treatment decisions.¹⁹ Roles are classified as fully active ('I prefer to make the decision about what treatment I receive'), active-collaborative role ('I prefer to make the decision about my treatment after seriously considering my doctor's opinion'), collaborative

role ('I prefer that my doctor and I share responsibility in deciding which treatment is best for me'), passive-collaborative ('I prefer that the doctor makes the final decision about what treatment will be used, but seriously considers my opinion'), or fully passive ('I prefer to leave all decisions regarding treatment to my doctor').

The four-item Decisional Conflict Scale ('SURE') was used to measure the level of uncertainty over the decision to receive chemotherapy.²⁴ The 'SURE' acronym represents the four items; 'Sure of myself', 'Understand information', 'Risk-benefit ratio' and 'Encouragement', with two answer categories ('yes' or 'no').²⁴

Statistical analysis

Patient characteristics were summarised using descriptive statistics. The chi-square test was used to compare characteristics of patients recruited in the UK versus those recruited in the NL.

Responses to items of the quality-quantity questionnaire were summarised using mean and standard deviation (SD). For each patient, the total score for all four items of each domain (LoL or QoL) was calculated and the minimum score (4) was subtracted, the total was then divided by the maximum score; for example a score of 3 (midpoint answer) for all four questions, produces the following calculation: $(12-4)/(20-4) = 0.50$ (midpoint overall score). A higher score indicates greater preference for that domain.

Preferred role and actual role in treatment decisions (control preferences) were summarised using proportions. Patients were then categorised into three groups; active (fully active or active-collaborative), collaborative, or passive (passive-collaborative or fully passive). Differences between control preferences (preferred role) and actual role were calculated and dichotomised into 'concordant' or 'discordant'.

The sum of the four items from the 'SURE' Decisional Conflict Scale, answer options yes (score 1) or no (score 0), was calculated.²⁴ Any score of ≤ 3 indicates some degree of decisional conflict.²⁴

The chi-square test was used to determine associations between participant characteristics, preferences for QoL versus LoL (or equal priority), decisional control preferences, and decisional conflict. Fisher's exact test was used where observed cell count was ≤ 5 and *P* values of ≤ 0.05 were considered statistically significant. Adjusted standardized residuals (± 2.0) were used to identify cells contributing to significant results. Multiple logistic regression analysis was carried out to determine factors associated with preference for QoL versus LoL and beliefs about curability.

Missing data

Participants who completed online questionnaires (*n* = 127) had no missing data. Missing answers for patients completing paper questionnaires (*n* = 10) were reported where applicable, and only available data were analysed.

RESULTS

One hundred and thirty-seven patients completed the baseline questionnaire (Table 1). The median age of patients was 62 (27-79) years and gender distribution was even (male: *n* = 68, female: *n* = 69). Seventy-two patients were recruited in the UK and 65 in the NL. The majority of patients were Caucasian (*n* = 115, 84%). One-third of patients described themselves as religious (*n* = 45, 33%). Patients were commonly married or in a relationship (*n* = 114, 83%), and most were cohabiting (*n* = 119, 87%). A minority of patients had children aged ≤ 18 years (*n* = 30, 22%). Participants were well educated (*n* = 110, 80%: college, diploma, vocational qualification, or higher) and almost half (*n* = 67, 49%) were currently employed (full-time/part-time or on sick-leave).

Most patients had metastatic disease (*n* = 125, 91%) and 12 patients (9%) had locally-advanced disease. More than half of patients had a >6 month interval between diagnosis of advanced STS and study participation (*n* = 78, 57%). The most common histological subtypes were leiomyosarcoma (*n* = 40, 29%), liposarcoma (*n* = 30, 22%), and undifferentiated pleomorphic sarcoma (*n* = 17, 12%). Most patients had an ECOG PS of 0 (*n* = 46, 34%) or 1 (*n* = 75, 55%).

The mean EORTC-QLQ-C30 global QoL score of participants was 68.3 (SD 20.3). One-quarter of patients (*n* = 34, 25%) had low global QoL (score 0-58.3), 49 patients (36%) had medium global QoL (score >58.3 -78.3), and 53 patients (39%) had high global QoL (score >78.3 -100).

Preferences for QoL versus LoL

Scores for items of the quality-quantity questionnaire are demonstrated in Table 2. The statement which evoked the strongest agreement was: 'If I reached a point during treatment at which I felt like giving up, I would probably manage to find the strength to continue' (mean score: 3.80, SD 1.03). Mean scores of >3 (indicating agreement) for most items demonstrated that patients generally felt that both LoL and QoL were important outcomes. Overall, a slightly higher proportion of patients placed greater importance on LoL (*n* = 66, 48%) than those who felt QoL was more important (*n* = 56, 41%). A minority of patients rated LoL and QoL equally (*n* = 12, 9%). Overall preference could not be calculated for three patients (2%) with one or more missing items.

Decisional control preferences

Preferred role in decisions about treatment (control preferences) was most commonly collaborative (*n* = 59, 44%), active-collaborative (*n* = 35, 26%), or passive-collaborative (*n* = 25, 19%) (Figure 1). A minority preferred a fully active role (*n* = 10, 7%), fully passive role (*n* = 6, 4%), or did not respond (*n* = 2). Actual roles in decisions about treatment were similar to preferred roles; most commonly collaborative (*n* = 54, 39%), active-collaborative (*n* = 38, 28%), or passive-collaborative (*n* = 29, 21%). A smaller number reported a fully active role (*n* = 8, 6%) or fully passive role (*n* = 8, 6%).

Table 1. Participant characteristics

Sociodemographic	All	UK	NL	P value
	n (%)	(n = 72)	(n = 65)	
Age (years)				0.966
18-39	11 (8)	6 (8)	5 (8)	
40-65	70 (51)	36 (50)	34 (52)	
65-90	56 (41)	30 (42)	26 (40)	
Gender				0.609
Male	68 (50)	34 (47)	34 (52)	
Female	69 (50)	38 (53)	31 (48)	
Ethnicity				0.161
Caucasian	115 (84)	57 (79)	58 (89)	
BAME	22 (16)	15 (21)	7 (11)	
Religious beliefs				0.028
Yes	45 (33)	30 (42)	15 (23)	
No	92 (67)	42 (58)	50 (77)	
Relationship status				0.820
Partner	114 (83)	59 (82)	55 (85)	
No partner	23 (17)	13 (18)	10 (15)	
Children (aged ≤18 years)				0.537
Yes	30 (22)	14 (19)	16 (25)	
No	107 (78)	58 (81)	49 (75)	
Education level				0.0001
Low (primary/secondary)	27 (20)	18 (25)	9 (14)	
Medium (vocation/college/diploma)	79 (58)	30 (42)	49 (75)	
High (university/postgraduate)	31 (23)	24 (33)	7 (11)	
Employment				0.865
Employed	67 (49)	36 (50)	31 (48)	
Not employed	70 (51)	36 (50)	34 (52)	
Clinical characteristics				
Disease-extent				0.374
Locally advanced	12 (9)	8 (11)	4 (6)	
Metastatic	125 (91)	64 (89)	61 (94)	
Disease timeline ^a				0.041
≤6 months since diagnosis	59 (43)	25 (35)	34 (52)	
>6 months since diagnosis	78 (57)	47 (65)	31 (48)	
Primary site of disease				0.115
Lower extremity	30 (22)	18 (25)	12 (19)	
Upper extremity	4 (3)	2(3)	2 (3)	
Gynaecological	20 (15)	13 (18)	7 (11)	
Abdominal/pelvic	30 (22)	16 (22)	14 (22)	
Retroperitoneum	25 (18)	14 (19)	11 (17)	
Head + neck	9 (7)	3 (4)	6 (9)	
Thoracic	8 (6)	3 (4)	5 (8)	
Other	11 (8)	3 (4)	8 (13)	
Histological subtype				0.236
Leiomyosarcoma	40 (29)	25 (35)	15 (23)	
Liposarcoma	30 (22)	15 (21)	15 (23)	
UPS	17 (12)	11 (15)	6 (9)	
Angiosarcoma	10 (7)	3 (4)	7 (11)	
Other	40 (29)	18 (25)	22 (34)	
ECOG performance status				0.434
0	46 (34)	29 (40)	17 (30)	
1	75 (55)	40 (56)	35 (63)	
2	7 (5)	3 (4)	4 (7)	
Surgical resection of primary tumour				0.864
Yes	100 (73)	53 (74)	47 (72)	
No	37 (27)	19 (26)	18 (28)	
Planned treatment				1.000
Doxorubicin-based chemotherapy	116 (85)	61 (85)	55 (85)	
Other chemotherapy	21 (15)	11 (5)	10 (15)	

Bold P values indicate significant at level of <0.05.
 BAME, Black, Asian, and minority ethnic; ECOG, Eastern Cooperative Oncology Group; UPS, undifferentiated pleomorphic sarcoma.
^a Interval between diagnosis of metastatic soft tissue sarcomas and questionnaire completion.

Table 2. Quality-quantity questionnaire items

	Mean	SD
Questions relating to preference for quantity (length) of life (LOL)		
If a treatment could prolong my life, I would always accept it, whatever the side-effects might be.	3.50	1.15
If I reached a point during treatment at which I felt like giving up, I would probably manage to find the strength to continue.	3.80	1.03
I would always accept a hard-to-tolerate treatment, even if the chance of it prolonging my life was as little as one percent.	2.88	1.18
In order to live a bit longer, I would clutch at any straw.	3.31	1.25
Questions relating to preference for quality of life (QOL)		
If a life-prolonging treatment would prevent me from leading a normal life, then I would rather not have it.	3.33	0.95
A moment might come at which I would say 'I have done my best, this is the limit'.	3.50	1.01
If I had to endure six months of intensive treatment in order to live for an extra half year, then I wouldn't bother.	2.89	1.05
I can imagine some side-effects being so bad that I would refuse the treatment, even if that meant a shorter life.	3.20	0.97

Scores range from 1 to 5, with 1 indicating strong disagreement and 5 indicating strong agreement.
 SD, standard deviation.

Actual role in treatment decisions was generally concordant with preferred role (n = 104, 76%). Discordance was identified for 33 patients (24%), most commonly patients who preferred a collaborative role but had an active-collaborative role in actual treatment decisions (n = 9).

Decisional conflict

One-third of patients experienced decisional conflict (n = 45, 33%); four patients (3%) had extremely high decisional conflict (score 4). Decisional conflict was not associated with participant characteristics (sociodemographic, clinical, global QoL, or country of recruitment).

Association between patient characteristics and preferences

Table 3 demonstrates associations between patient characteristics, preferred role, and actual role in treatment decisions. Females were significantly more likely to prefer a collaborative role compared with males (55% versus 32%), while males were more likely to prefer a passive role compared with females (31% versus 15%; P = 0.016). Patients with a PS of 2 were significantly more likely to prefer an active role in treatment decisions (P = 0.042) than patients with a PS of 0 or 1, but there was no association between global QoL and preferred role. A higher proportion of Dutch participants preferred an active role compared with UK participants (43% versus 24%), whereas UK participants preferred a collaborative role (49% versus 39%; P = 0.066). Examining this association further, using the original five preferred roles, Dutch patients were significantly more likely to prefer a 'fully active' role than UK patients (14% versus 1%; P = 0.043). Similar patterns were observed in actual treatment decisions; Dutch patients and those with PS 2 were significantly more likely to have an

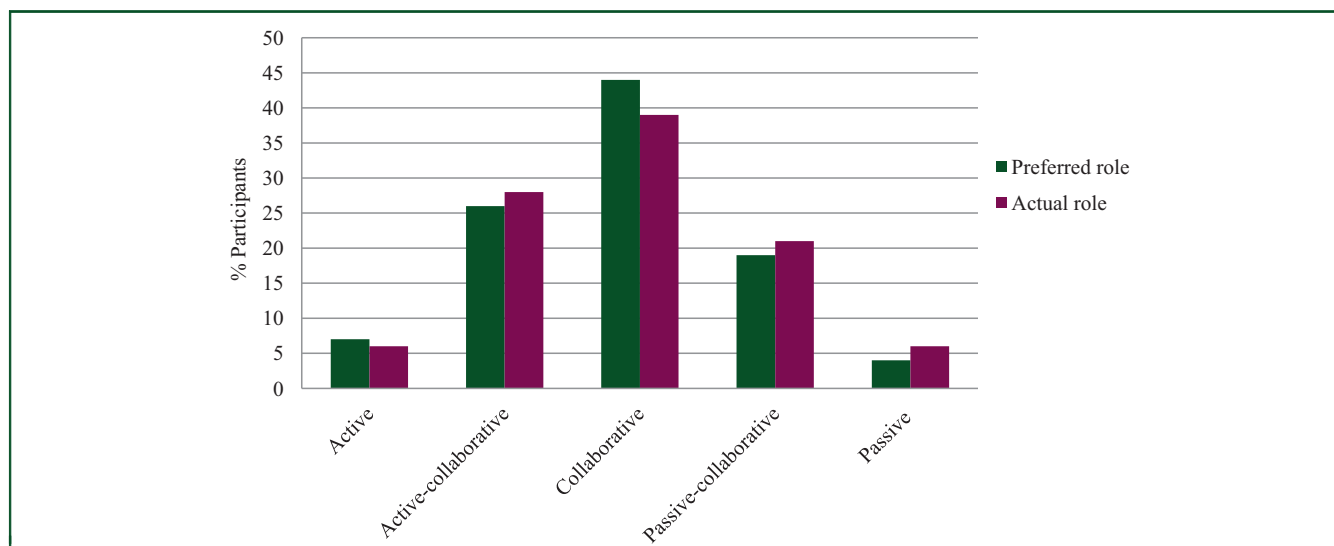


Figure 1. Preferred and actual role in treatment decisions.

active role, while females were more likely to have a collaborative role compared with males (Table 3). Discordance between preferred and actual roles was not related to participant characteristics, or priorities towards QoL versus LoL.

Table 4 demonstrates associations between patient characteristics and preferences for QoL versus LoL. Younger patients aged <40 years were significantly more likely to prioritise extended LoL than older patients ($P = 0.001$). Conversely, almost two-thirds of older patients (aged ≥ 65 years) indicated that QoL was more important ($n = 27$, 50%), or equally as important ($n = 8$, 15%) as LoL. Patients with children aged ≤ 18 years more commonly prioritised LoL than those without (67% versus 44%), however this difference was not statistically significant ($P = 0.093$). Patients who prioritised QoL were significantly more likely to experience decisional conflict than patients prioritising LoL, or with equal preferences ($P = 0.049$). Multiple logistic regression demonstrated that age ($P = 0.020$) and decisional conflict ($P = 0.024$) remained significantly associated with preference for QoL versus LoL.

DISCUSSION

To our knowledge this is the first prospective study evaluating the priorities and preferences for decision making in patients with advanced STS starting palliative first-line chemotherapy. Inclination towards extended LoL was slightly more common than preference for QoL, however, patients generally indicated that both of these outcomes were important. Younger patients prioritised LoL, whereas many older patients felt that QoL was at least equally important. Decisional conflict was highest among patients who prioritised QoL, indicating uncertainty about the potential impact of chemotherapy on QoL. The majority of patients preferred a collaborative role in treatment decisions, and actual roles in treatment decisions were largely concordant with preferred roles. Preferred and actual roles

in treatment decisions were related to gender, country of recruitment, and PS.

Patient preferences are important throughout the disease trajectory; however, they are particularly pertinent in the setting of advanced STS when prognosis is short. Eliciting preferences may be challenging, but this can improve communication and satisfaction with informed decision making.^{15,25} Studies among patients with other advanced cancers have reported variable attitudes towards the trade-off between LoL and QoL, however, younger age has consistently been associated with preference for LoL.^{10,26-29} Our study demonstrated that younger patients with advanced STS were much more likely than older patients to place increased importance on living longer. Intensive treatment is more common among younger patients with cancer, which may be driven by the injustice of death at a young age.^{30,31}

Many participants considered QoL to be more important than LoL, and two-thirds of elderly patients (aged ≥ 65 years) indicated that QoL was at least equally as important as LoL. This finding is particularly important for designing clinical trials in advanced STS, where QoL could be considered as a (co)primary or composite endpoint.³² Our data highlight the importance of considering age-specific priorities and ensuring outcomes are meaningful to patients. Patients who prioritised QoL more commonly experienced decisional conflict. This uncertainty may be due to concern about the adverse effects of chemotherapy, limited available data on the impact of chemotherapy on QoL, and perception that the decision to receive chemotherapy is not aligned with individual priorities. Although our study focused on patients starting first-line chemotherapy, others have shown that QoL may become more important further along the disease trajectory.²⁸

Shared decision making is acknowledged to be an integral component of patient-centred care. Consistent with previous studies of patients with advanced cancers, the majority of patients desired a collaborative role in treatment

Table 3. Associations between participant characteristics and control preferences								
Participant characteristics	Actual role			P value	Preferred role			P value
	Active	Collaborative	Passive		Active	Collaborative	Passive	
	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	
Age, years				0.539				0.497
18-39	3 (27)	4 (36)	4 (36)		3 (27)	6 (55)	2 (18)	
40-65	21 (30)	27 (39)	22 (31)		19 (28)	30 (44)	19 (28)	
>65	22 (39)	23 (41)	11 (20)		23 (41)	23 (41)	10 (18)	
Gender				0.004				0.016
Male	25 (37)	18 (27)	25 (37)		25 (37)	22 (32)	21 (31)	
Female	21 (30)	36 (52)	12 (17)		20 (30)	37 (55)	10 (15)	
Relationship				0.598				0.395
Married/partner	40 (35)	45 (40)	8 (35)		40 (35)	49 (43)	24 (21)	
Single	6 (26)	9 (39)	29 (25)		5 (23)	10 (46)	7 (32)	
Children (≤18 years)				0.073				0.189
Yes	8 (27)	9 (30)	13 (43)		6 (20)	15 (50)	9 (30)	
No	38 (36)	45 (42)	24 (22)		39 (37)	44 (42)	22 (21)	
Religious beliefs				0.609				0.971
Yes	15 (33)	20 (44)	10 (22)		14 (32)	20 (46)	10 (23)	
No	31 (34)	34 (37)	27 (29)		31 (34)	39 (43)	21 (23)	
Education level				0.663				0.769
Low	11 (41)	11 (41)	5 (19)		11 (44)	10 (40)	4 (16)	
Medium	25 (32)	29 (37)	25 (32)		24 (30)	36 (46)	19 (24)	
High	10 (32)	14 (45)	7 (23)		10 (32)	13 (42)	8 (26)	
Country				0.002				0.066
United Kingdom	15 (21)	37 (51)	20 (28)		17 (24)	34 (49)	19 (27)	
The Netherlands	31 (48)	17 (26)	17 (26)		28 (43)	25 (39)	12 (19)	
Ethnicity				0.239				0.272
White Caucasian	39 (34)	48 (42)	28 (24)		37 (33)	53 (47)	24 (21)	
BAME	8 (32)	6 (27)	9 (41)		8 (38)	6 (29)	7 (33)	
Disease timeline				0.283				0.714
≤6 months	21 (36)	19 (32)	19 (18)		17 (29)	28 (47)	14 (24)	
>6 months	25 (32)	35 (45)	18 (23)		28 (36)	32 (42)	17 (22)	
Disease extent				0.928				0.585
Locally-advanced	4 (33)	4 (33)	4 (33)		4 (33)	4 (33)	4 (33)	
Metastatic	42 (34)	50 (40)	33 (26)		41 (33)	55 (45)	27 (22)	
PS				0.003				0.042
ECOG 0	11 (24)	26 (57)	9 (20)		10 (22)	27 (59)	9 (20)	
ECOG 1	22 (29)	27 (36)	26 (35)		25 (34)	27 (38)	20 (27)	
ECOG 2	6 (86)	0 (0)	1 (14)		5 (71)	1 (14)	1 (14)	

Bold P values indicate significant at level of <0.05

BAME, Black, Asian, and minority ethnic; ECOG, Eastern Cooperative Oncology Group; PS, performance status.

decisions.³³⁻³⁶ Preferred role and actual roles in decisions varied according to patient gender, PS, and country of recruitment. The majority of females preferred an active or collaborative role in decisions, whereas more men than women preferred a passive role. Others have reported variable findings concerning the impact of gender on preferred role in treatment decisions.^{17,18,35,37} Patients with poor PS (PS 2) were more likely to prefer an active role than those with a better PS. It is also possible that patients with borderline PS may have been encouraged to take a more active role in treatment decisions. Previous research had indicated that patients with an incurable disease tend to desire greater involvement in decisions further along their disease trajectory.^{38,39} Dutch patients tended to prefer a more active role in treatment decisions compared with UK patients. An international study of 1490 patients with advanced cancers also found country of origin was associated with preferred role in decisions.³⁴

Studies have shown that the majority of patients with incurable metastatic cancer desire realistic communication including accurate disclosure of prognosis.^{40,41}

Demographic, psychological, and disease-related factors have been shown to influence preferred degree of disclosure.⁴⁰ An individualised approach can allow patients control over the extent and delivery of the information provided.⁴¹ Tools to elicit patients' preferences and attitudes towards treatment and decision making are not currently used for patients with advanced STS, however computer-based assessment of patient values, goals, and communication preferences has been shown to have a positive impact on communication and satisfaction with decision making among patients with other metastatic cancers.⁴² Early assessment of preferences could also facilitate appropriate and timely advance care planning that is consistent with individual patient values.⁴³

Limitations

Participants were generally well educated. The HOLISTIC study did not assess the preferences of patients receiving best supportive care. Around one-quarter of patients are not able to start palliative chemotherapy, for example those

Table 4. Factors associated with attitudes towards QoL versus LoL				
Variable	Preference for QoL versus LoL			P value
	QoL (n = 56)	LoL (n = 66)	Equal (n = 12)	
Age, years				0.001
18-39	0 (0)	11 (100)	0 (0)	
40-65	29 (42)	36 (52)	4 (6)	
>65	27 (50)	19 (35)	8 (15)	
Gender				0.933
Male	27 (40)	35 (51)	6 (9)	
Female	29 (44)	31 (47)	6 (9)	
Relationship status				0.208
Married/partner	45 (40)	59 (52)	9 (8)	
Single	11 (52)	7 (33)	3 (14)	
Children (≤18 years)				0.093
Yes	9 (30)	20 (67)	1 (4)	
No	47 (45)	46 (44)	11 (11)	
Religious beliefs				0.516
Yes	16 (36)	25 (57)	3 (7)	
No	40 (44)	41 (46)	9 (10)	
Education level				0.260
Low	11 (44)	10 (40)	4 (16)	
Medium	35 (45)	36 (46)	7 (9)	
High	10 (32)	20 (65)	1 (3)	
Country				0.188
United Kingdom	24 (34)	39 (56)	7 (10)	
The Netherlands	32 (50)	27 (42)	5 (8)	
Ethnicity				0.060
White Caucasian	51 (46)	53 (47)	8 (7)	
BAME	5 (23)	13 (59)	4 (18)	
Time since diagnosis				0.516
≤6 months	27 (47)	26 (46)	4 (7)	
>6 months	29 (38)	40 (52)	8 (10)	
Disease extent				0.391
Locally-advanced	7 (58)	4 (33)	1 (8)	
Metastatic	49 (40)	62 (51)	11 (9)	
Performance status				0.902
ECOG 0	16 (36)	25 (56)	4 (9)	
ECOG 1	29 (40)	37 (51)	7 (10)	
ECOG 2	4 (57)	3 (43)	0 (0)	
Preferred decisional role				0.348
Active	23 (51)	18 (40)	4 (9)	
Collaborative	23 (40)	31 (54)	3 (5)	
Passive	10 (32)	17 (55)	4 (13)	
Decisional conflict				0.049
No conflict	31 (34)	49 (54)	10 (11)	
Conflict	25 (57)	17 (39)	2 (5)	

Bold P values indicate significant at level of <0.05.

BAME, Black, Asian, and minority ethnic; ECOG, Eastern Cooperative Oncology Group; LoL, length of life; QoL, quality of life.

with poor PS, multiple comorbidities, or with chemo-resistant subtypes. Patients who decline chemotherapy may prioritise maintaining QoL and are not willing to accept potential therapy-related toxicity. Treatment preferences were assessed before starting chemotherapy, however, views and priorities may be different after starting chemotherapy. Follow-up HOLISTIC study data, including decisional regret, will provide insight into this question.

Conclusions

This study demonstrates significant heterogeneity in the priorities and preferences of patients with advanced STS, supporting a personalised approach to decisions about palliative treatments. Age-specific differences in attitudes

towards QoL and LoL should be considered when discussing the goals of palliative chemotherapy. Considering personal priorities, values, and cultural and ethnic backgrounds, will optimise communication and enhance patient-centred care. Further studies are needed to determine the optimal approach to assess preferences in clinical practice.

ACKNOWLEDGEMENTS

We would like to thank all the patients who kindly participated in this study.

FUNDING

The work was supported by The Royal Marsden NHS Foundation Trust together with The Institute of Cancer Research, which receives Biomedical Research Centre (BRC) funding through the National Institute for Health Research (NIHR). This work received financial support from Lilly (no grant number).

DISCLOSURE

RLJ is the recipient of grants/research support from Merck Sharp & Dohme, GlaxoSmithKline. RLJ is the recipient of consultation fees from Adaptimmune, Athenex, Blueprint, Clinigen, Eisai, Epizyme, Daichii, Deciphera, Immune Design, Lilly, Merck, Pharmamar, UptoDate. WvdG has received research grants from Novartis, has been on advisory board from Bayer and is consultant for SpringWorks. The other authors have declared no conflicts of interest.

DATA SHARING

The data generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

REFERENCES

- Coindre JM, Terrier P, Guillou L, et al. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas: a study of 1240 patients from the French Federation of Cancer Centers sarcoma group. *Cancer*. 2001;91(10):1914-1926.
- Italiano A, Mathoulin-Pelissier S, Le Cesne A, et al. Trends in survival for patients with metastatic soft-tissue sarcoma. *Cancer*. 2011;117(5):1049-1054.
- Gough NJ, Smith C, Ross JR, et al. Symptom burden, survival and palliative care in advanced soft tissue sarcoma. *Sarcoma*. 2011;2011:1-8.
- Chan A, Lim E, Ng T, et al. Symptom burden and medication use in adult sarcoma patients. *Support Care Cancer*. 2015;23(6):1709-1717.
- World Health Organisation. Measuring Quality of Life. Available at <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/>. Accessed September 16, 2020.
- Judson I, Verweij J, Gelderblom H, et al. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet Oncol*. 2014;15(4):415-423.
- Benjamin RS. Grade 3 nausea, vomiting, and myelosuppression or progressive, metastatic sarcoma? *J Clin Oncol*. 1987;5(6):833-835.
- Gough N, Koffman J, Ross JR, et al. Does palliative chemotherapy really palliate and are we measuring it correctly? A mixed methods longitudinal study of health related quality of life in advanced soft tissue sarcoma. *PLoS One*. 2019;14(9):1-24.

9. Granda-Cameron C, Hanlon AL, Lynch MP, et al. Experience of newly diagnosed patients with sarcoma receiving chemotherapy. *Oncol Nurs Forum*. 2011;38(2):160-169.
10. Stiggelbout AM, de Haes JC, Kiebert GM, et al. Tradeoffs between quality and quantity of life: development of the QQ Questionnaire for cancer patient attitudes. *Med Decis Making*. 1996;16(2):184-192.
11. LeBlanc A, Kenny DA, O'Connor AM, et al. Decisional conflict in patients and their physicians: a dyadic approach to shared decision making. *Med Decis Making*. 2009;29(1):61-68.
12. Koedoot CG, De Haan RJ, Stiggelbout AM, et al. Palliative chemotherapy or best supportive care? A prospective study explaining patients' treatment preference and choice. *Br J Cancer*. 2003;89(12):2219-2226.
13. Fried TR, Bradley EH, Towle VR, et al. Understanding the treatment preferences of seriously ill patients. *N Engl J Med*. 2002;346(14):1061-1066.
14. Barry MJ, Edgman-Levitan S. Shared decision making — pinnacle of patient-centered care. *N Engl J Med*. 2012;366(9):780-781.
15. Meropol NJ, Egleston BL, Buzaglo JS, et al. Cancer patient preferences for quality and length of life. *Cancer*. 2008;113(12):3459-3466.
16. Ziebland S, Evans J, McPherson A. The choice is yours? How women with ovarian cancer make sense of treatment choices. *Patient Educ Couns*. 2006;62(3):361-367.
17. Tricou C, Yennu S, Ruer M, et al. Decisional control preferences of patients with advanced cancer receiving palliative care. *Palliat Support Care*. 2018;16(5):544-551.
18. Levinson W, Kao A, Kuby A, et al. Not all patients want to participate in decision making. A national study of public preferences. *J Gen Intern Med*. 2005;20(6):531-535.
19. Degner LF, Sloan JA, Venkatesh P. The control preferences scale. *Can J Nurs Res*. 1997;29(3):21-43.
20. Ghane A, Huynh HP, Andrews SE, et al. The relative importance of patients' decisional control preferences and experiences. *Psychol Health*. 2014;29(10):1105-1118.
21. Younger E, Jones RL, Desai IME, et al. Health-related quality of life in patients with advanced soft tissue sarcomas treated with chemotherapy (The HOLISTIC study): protocol for an international observational cohort study. *BMJ Open*. 2020;10(6):e035171.
22. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. The patient reported outcomes following initial treatment and long term evaluation of survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer*. 2011;47(14):2188-2194.
23. Fayers PM, Aaronson NK, Bjordal K, et al. *The EORTC QLQ-C30 Scoring Manual*. 3rd ed. Brussels: European Organisation for Research and Treatment of Cancer; 2001.
24. O'Connor AM. Decisional Conflict Scale. Available at http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Decisional_Conflict.pdf. Accessed September 16, 2020.
25. Say RE, Thomson R. The importance of patient preferences in treatment decisions—challenges for doctors. *Br Med J*. 2003;327(7414):542-545.
26. Shrestha A, Martin C, Burton M, et al. Quality of life versus length of life considerations in cancer patients: a systematic literature review. *Psychooncology*. 2019;28(7):1367-1380.
27. Krammer R, Heinzerling L. Therapy preferences in melanoma treatment — willingness to pay and preference of quality versus length of life of patients, physicians and healthy controls. *PLoS One*. 2014;9(11):e111237.
28. Voogt E, van der Heide A, Rietjens JA, et al. Attitudes of patients with incurable cancer toward medical treatment in the last phase of life. *J Clin Oncol*. 2005;23(9):2012-2019.
29. Rietjens JA, van der Heide A, Voogt E, et al. Striving for quality or length at the end-of-life: attitudes of the Dutch general public. *Patient Educ Couns*. 2005;59(2):158-163.
30. Laryionava K, Heußner P, Hiddemann W, et al. Rather one more chemo than one less...: Oncologists and Oncology Nurses' reasons for aggressive treatment of young adults with advanced cancer. *Oncologist*. 2018;23(2):256-262.
31. Knox MK, Hales S, Nissim R, et al. Lost and stranded: the experience of younger adults with advanced cancer. *Support Care Cancer*. 2017;25(2):399-407.
32. Wildiers H, Mauer M, Pallis A, et al. End points and trial design in geriatric oncology research: a joint European organisation for research and treatment of cancer — Alliance for Clinical Trials in Oncology — International Society of Geriatric Oncology position article. *J Clin Oncol*. 2013;31(29):3711-3718.
33. Rothenbacher D, Lutz MP, Porzolt F. Treatment decisions in palliative cancer care: patients' preferences for involvement and doctors' knowledge about it. *Eur J Cancer*. 1997;33(8):1184-1189.
34. Yennurajalingam S, Rodrigues LF, Shamieh OM, et al. Decisional control preferences among patients with advanced cancer: an international multicenter cross-sectional survey. *Palliat Med*. 2018;32(4):870-880.
35. Singh JA, Sloan JA, Atherton PJ, et al. Preferred roles in treatment decision making among patients with cancer: a pooled analysis of studies using the control preferences scale. *Am J Manag Care*. 2010;16(9):688-696.
36. Brom L, De Snoo-Trimp JC, Onwuteaka-Philipsen BD, et al. Challenges in shared decision making in advanced cancer care: a qualitative longitudinal observational and interview study. *Health Expect*. 2017;20(1):69-84.
37. Gaston CM, Mitchell G. Information giving and decision-making in patients with advanced cancer: a systematic review. *Soc Sci Med*. 2005;61(10):2252-2264.
38. Sulmasy DP, Hughes MT, Thompson RE, et al. How would terminally ill patients have others make decisions for them in the event of decisional incapacity? A longitudinal study. *J Am Geriatr Soc*. 2007;55(12):1981-1988.
39. Cohen H, Britten N. Who decides about prostate cancer treatment? A qualitative study. *Fam Pract*. 2003;20(6):724-729.
40. Hagerty RG, Butow PN, Ellis PM, et al. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis. *J Clin Oncol*. 2005;23(6):1278-1288.
41. Hagerty RG, Butow PN, Ellis PA, et al. Cancer patient preferences for communication of prognosis in the metastatic setting. *J Clin Oncol*. 2004;22(9):1721-1730.
42. Meropol NJ, Egleston BL, Buzaglo JS, et al. A Web-based communication aid for patients with cancer: the CONNECT Study. *Cancer*. 2013;119(7):1437-1445.
43. Laryionava K, Winkler EC. Patients' preferences in non-curable cancer disease. *Oncol Res Treat*. 2019;42(1-2):31-34.