Elderly outcomes in clinical trials and priorities of patients starting palliative chemotherapy

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SPAEN Conference, 23rd April 2021

Sarcoma
Patients
EuroNet

Introduction

- Increasing life expectancy has led to greater proportion of elderly in population

- Older age is a risk factor for cancer

- Elderly patients with cancer have historically been under-represented in clinical trials; limited evidence base and extrapolation of data from younger patients.

- Chronological age and (mis)perception of frailty and tolerability, empirical dose reductions, under/over-treatment of patients.

- Around half of STS are diagnosed in patients aged ≥65 years, however data are limited.

Overview of presentation

- Pooled analysis of outcomes of elderly in EORTC-STBSG trials of 1st line palliative chemotherapy for patients with advanced STS

- Subgroup analysis of outcomes and adverse events in older patients in the SARC021 trial

- Priorities of elderly patients starting palliative chemotherapy (HOLISTIC study).

Elderly outcomes in EORTC-STBSG trials

- Retrospective subgroup analysis of elderly patients treated in EORTC-STBSG trials between 1980-2012.

- All trials of 1st line chemotherapy for advanced STS

- Elderly patients defined as age ≥65 years

- Endpoints: OS, PFS and response rate.

Results

- Total of 2,810 patients in 12 trials
- 348 elderly patients (**12%** of participants)

- Median age of elderly: 68 years (IQR 67-71), max. 84 years.
- Patients <65 years: median 49 years; IQR 39-57.

Patient characteristics

	< 65 yrs. (n=2462)	≥65 yrs. (n=348)
Performance status	n (%)	n (%)
0	1122 (45.6)	134 (38.5)
1	1127 (45.8)	177 (50.9)
2+	187 (7.6)	32 (9.2)
Histological Grading		
1	213 (8.7)	33 (9.5)
2	703 (28.6)	71 (20.4)
3	841 (34.2)	89 (25.6)
Missing	705 (28.6)	155 (44.5)
Histological cell type		
MFH/UPS**	239 (9.7)	55 (15.8)
Leiomyosarcoma	741 (30.1)	**130 (37.4)**
Liposarcoma	242 (9.8)	30 (8.6)
Synovial sarcoma	**254 (10.3)**	11 (3.2)

Overall survival

Median OS by age group:

≥65 years: **10.8 months** (95% CI, 9.43-11.83)
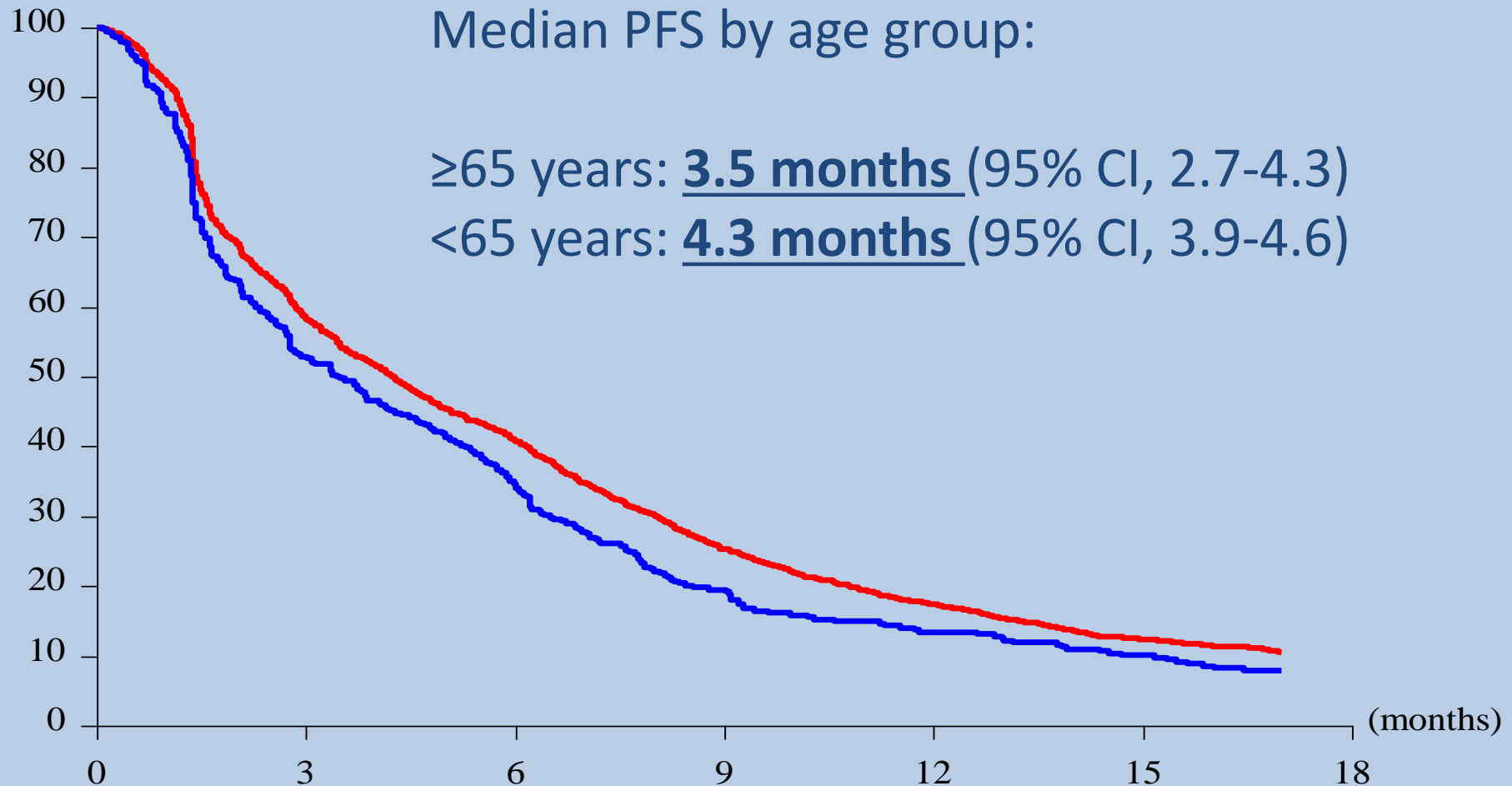<65 years: **12.3 months** (95% CI, 11.9-12.9)
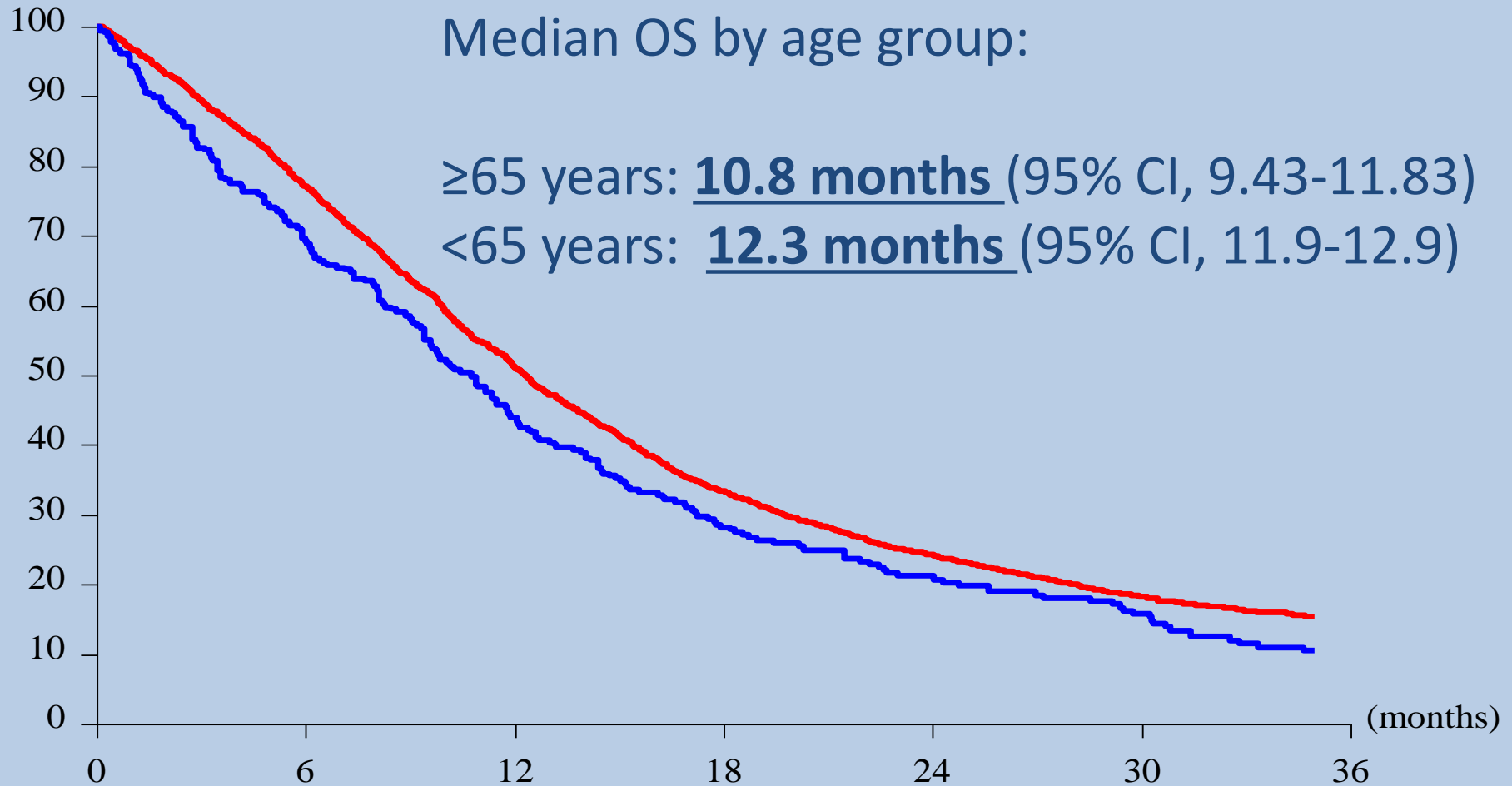
O	N	Number of patients at risk :					
1997	2462	1826	1150	717	490	332	── < 65 yrs
264	348	221	122	72	48	34	── >= 65 yrs

Progression free survival

Median PFS by age group:

≥65 years: **3.5 months** (95% CI, 2.7-4.3)
<65 years: **4.3 months** (95% CI, 3.9-4.6)

O	N	Number of patients at risk :					
2318	2462	1425	990	607	413	290	< 65 yrs
331	348	182	118	64	44	33	>= 65 yrs

Best response by age group
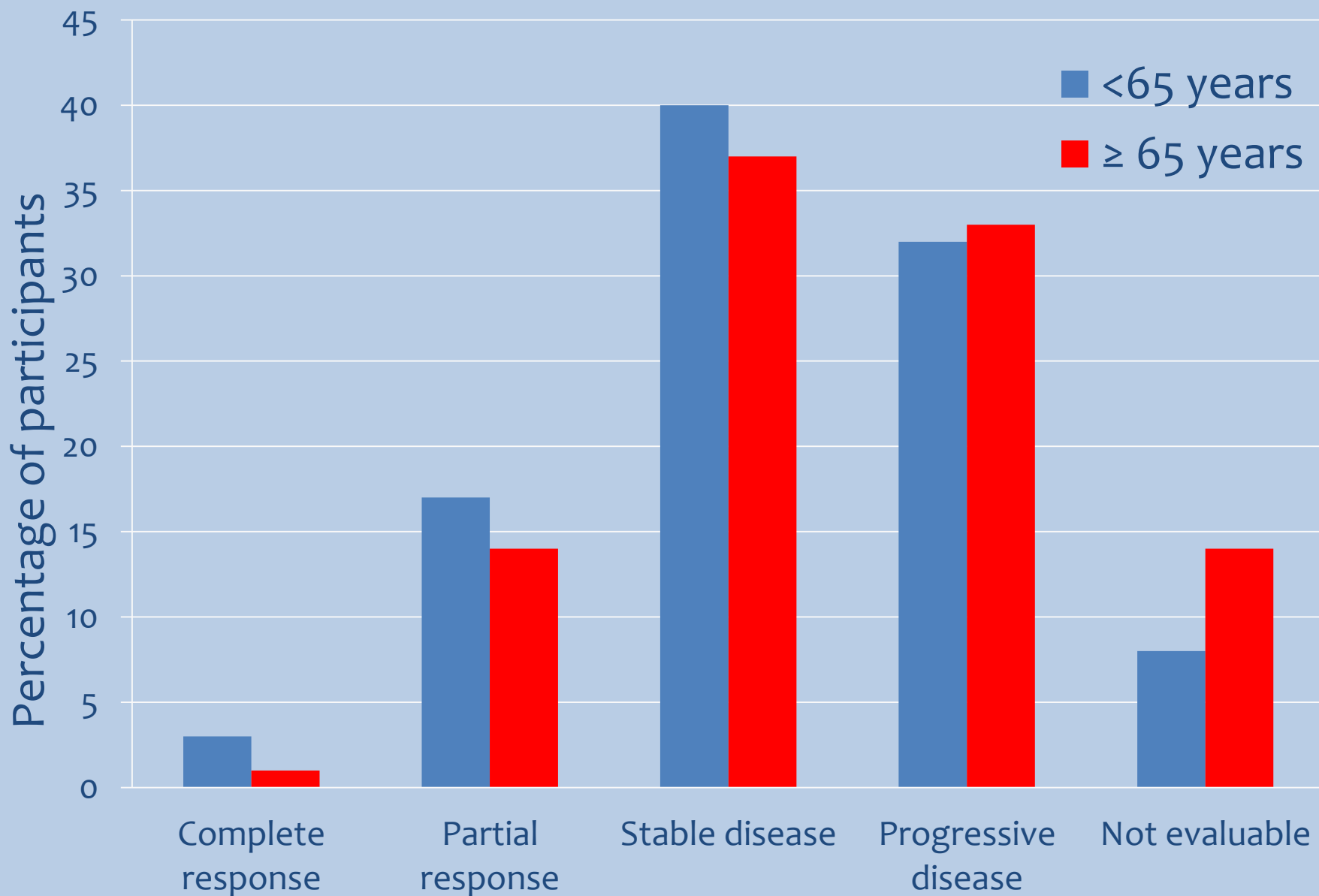
Summary

- Although half of STS diagnoses occur elderly patients, only 12% of participants were aged ≥65 years.

- Vast majority had excellent PS (0 or 1)

- Despite this, elderly had slightly worse outcomes than young patients in EORTC first line chemotherapy trials.

Subgroup analysis of older patients in SARC021

- Randomised phase III study of doxorubicin vs. doxorubicin + evofosfamide
- Aim: to compare outcome and safety of anthracycline-based chemotherapy in older patients with those <65 years.
- Older patients defined as ≥65 years.
- Endpoints: OS, PFS, RR, adverse effects, QoL (EQ-5D-5L and EQ-VAS)

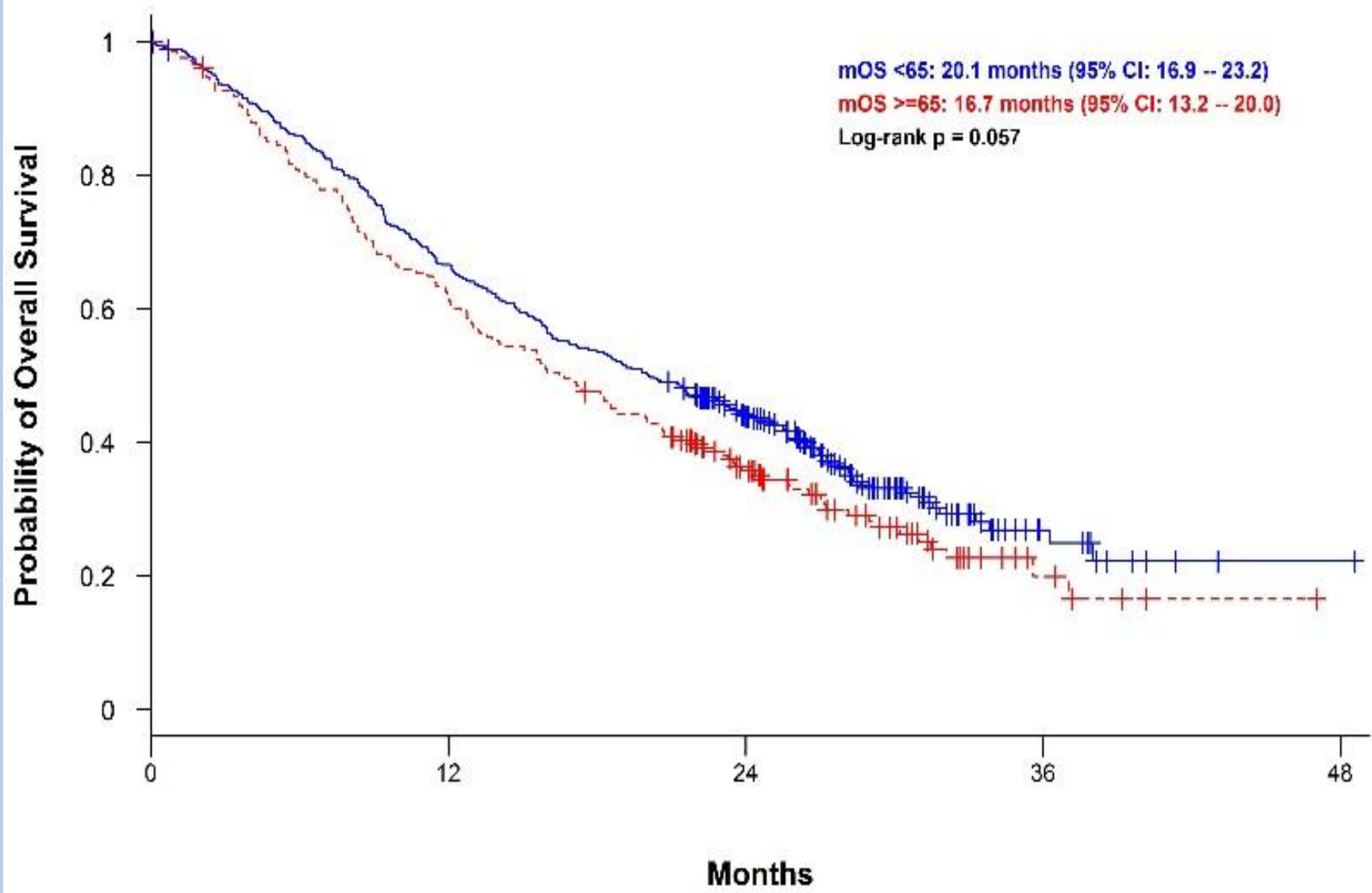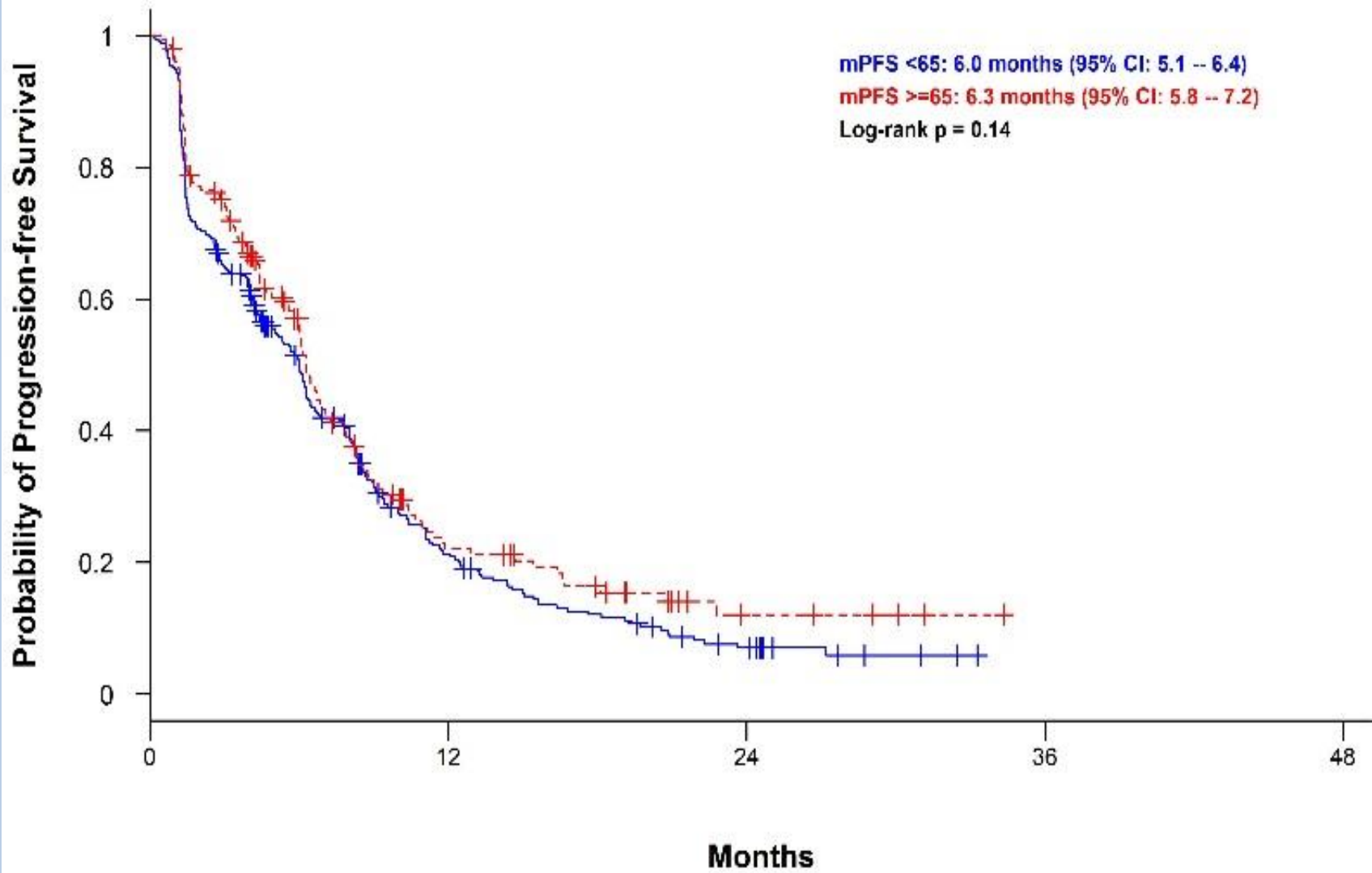# Results

- Of 640 participants, 209 were ≥65 years (**33%**)
- Median age of elderly was 70 (range 65-89) yrs.
- Median age of younger patients was 53 years.

Patient characteristics	Patients < 65 years (n=431)	Patients ≥ 65 years (n=209)	p-value
Gender **Female** **Male**	**246 (57%)** 185 (43%)	99 (47%) **110 (53%)**	**0.021**
PS **0** **1** **2**	**267 (62%)** 160 (37%) 3 (1%)	98 (47%) **110 (53%)** 1 (0%)	**0.0011**
Histology **Leiomyosarcoma** **Liposarcoma** **UPS** **Other**	153 (35%) 75 (17%) 41 (10%) **162 (38%)**	77 (37%) 36 (17%) **38 (18%)** 58 (28%)	**0.0056**

Comparison of outcomes

- Median OS in elderly **16.7 months** (95% CI 13.2-20.0) vs. **20.1 months** (95% CI 16.9-23.2) in patients <65years. *p*=0.057.

- Median PFS in elderly was **6.3 months** (95% CI 5.8-7.2) compared to **6.0 months** (95% CI: 5.1-6.4) in patients <65 years. *p*=0.14.

- Response rates similar between patients <65 years (*n*=103, **24%**) vs. elderly patients (*n*=46, **22%**), *p*=0.60.

mOS <65: 20.1 months (95% CI: 16.9 -- 23.2)
mOS >=65: 16.7 months (95% CI: 13.2 -- 20.0)
Log-rank p = 0.057

mPFS <65: 6.0 months (95% CI: 5.1 -- 6.4)
mPFS >=65: 6.3 months (95% CI: 5.8 -- 7.2)
Log-rank p = 0.14

Adverse events

	Patients < 65 years (n=431)	Patients >= 65 years (n=209)	p-value
Hematological AE			
No	205 (48%)	67 (32%)	**<0.0001**
Yes	208 (48%)	**141 (67%)**	
Non-Hematological AE			
No	198 (46%)	77 (37%)	**0.0097**
Yes	215 (50%)	**131 (63%)**	
Cardiac AE			
No	295 (68%)	144 (69%)	0.60
Yes	35 (8%)	20 (10%)	
>= Grade 3 AE			
No	114 (26%)	30 (14%)	**0.0002**
Yes	299 (69%)	**178 (85%)**	

QoL Data

Baseline QoL data for only for <u>29%</u> of younger and <u>29%</u> of elderly patients.

- Patients aged <65 years had a significantly higher (worse) mean anxiety/depression score (2.04, SD 0.98) at baseline compared with older patients (1.62, SD 0.78), p=0.004.
- Older patients had numerically higher (worse) mean mobility score (1.82, SD 1.14) at termination of the study compared to <65 years (1.5, SD 0.78), p=0.063.

There were no differences in EQ-VAS scores between patients aged <65 years and older patients.

Summary

- Anthracycline based treatment effective in elderly sarcoma patients however high rates of AEs highlight need for more tolerable treatments/optimisation of supportive care.

- Limited completion of QoL assessments limiting interpretation. Are these short tools sensitive enough to detect differences between groups?

Priorities of elderly sarcoma patients

- HOLISTIC study: international observational cohort study evaluating health-related quality of life (HRQoL) in patients with advanced STS treated with palliative chemotherapy

- All patients complete baseline questionnaire to assess priorities and preferences.

- Here we focus on priorities for QoL vs. LoL: based on quality-quantity questionnaire (8 items)

Participants in HOLISTIC study

- 137 patients
- Median age of patients was 62 (27-79) years
- Gender distribution even (male: n= 68, female: n=69).
- 72 patients were recruited in the UK and 65 patients in the NL
- Most patients were Caucasian (n=115, 84%).

Age-specific priorities

Variable	Preference for QoL vs. LoL			p-value
	QoL	LoL	Equal	
Age				
18-39 years	0 (0)	11 (100)	0 (0)	0.001
40-65 years	29 (42)	36 (52)	4 (6)	
>65 years	27 (50)	19 (35)	8 (15)	

Conclusions

- Clinical trials with broader eligibility criteria, specifically for older patients, or innovative trial designs should be considered.

- Assessment of the utility of comprehensive geriatric assessment and individualised, tailored intervention in elderly sarcoma patients is needed.

- HRQoL is an important outcome for elderly patients and should be routinely incorporated into clinical trial endpoints.

Questions?

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