

Prognosis scores to assess impact of fatigue and anemia on overall survival

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Disclosure

- I have no disclosure
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Background

- Fatigue is a symptom related both to disease and treatment in cancer patients
- Fatigue and anemia have negative impact on Quality of Life but impact on Overall Survival is still unknown
- Anemia correlates with poor ECOG-PS and many patients remain untreated (ECAS*).
- Given incidence of fatigue and anemia in cancer patients, early detection could be helpful to prevent recurrence

* European Cancer Anaemia Survey (2004), Ludwig et al., Eur. J. cancer, 40, 2293

Study Objectives

- Is there a link between patient's reported fatigue and overall survival?
- Is there a relationship between patient's reported fatigue and concomitant Hb profiles?
- Could anemia be a surrogate of fatigue when considering overall survival?
- Could prognosis scores be helpful to classify patients in risk groups for overall survival?

Study Design

- Prospective interventional study.
- Patients with solid tumors treated in daily hospital (single institution).
- Patients with ongoing chemotherapy (CT) at EOS were excluded.
- Patients contacted by phone (nurse) at D-2 prior to CT to assess clinical safety (questionnaire). Biological safety performed at least once before each cycle (D-3 \pm D-7): “PROCHE” program¹.
- Anemia corrected according to ESMO recommendations²
- Outcome=overall survival (from CT initiation to death/last-contact).
- Multivariate analysis adjusted on age at study entry, baseline performance status, type of cancer, setting and current line.

¹ Scotte, et al., Eur. J. Cancer, Oncologist, (2012, submitted)

² Scrijvers, De Samblanx, Roila (2010), Annals of Oncology, 21, v244

² Scrijvers, De Samblanx, Roila (2009), Annals of Oncology, 20, iv159

Methods: score calculation

- Patient reported fatigue (asthenia):

0: none	2: moderate	4= disabling
1: mild	3: severe	5= unknown

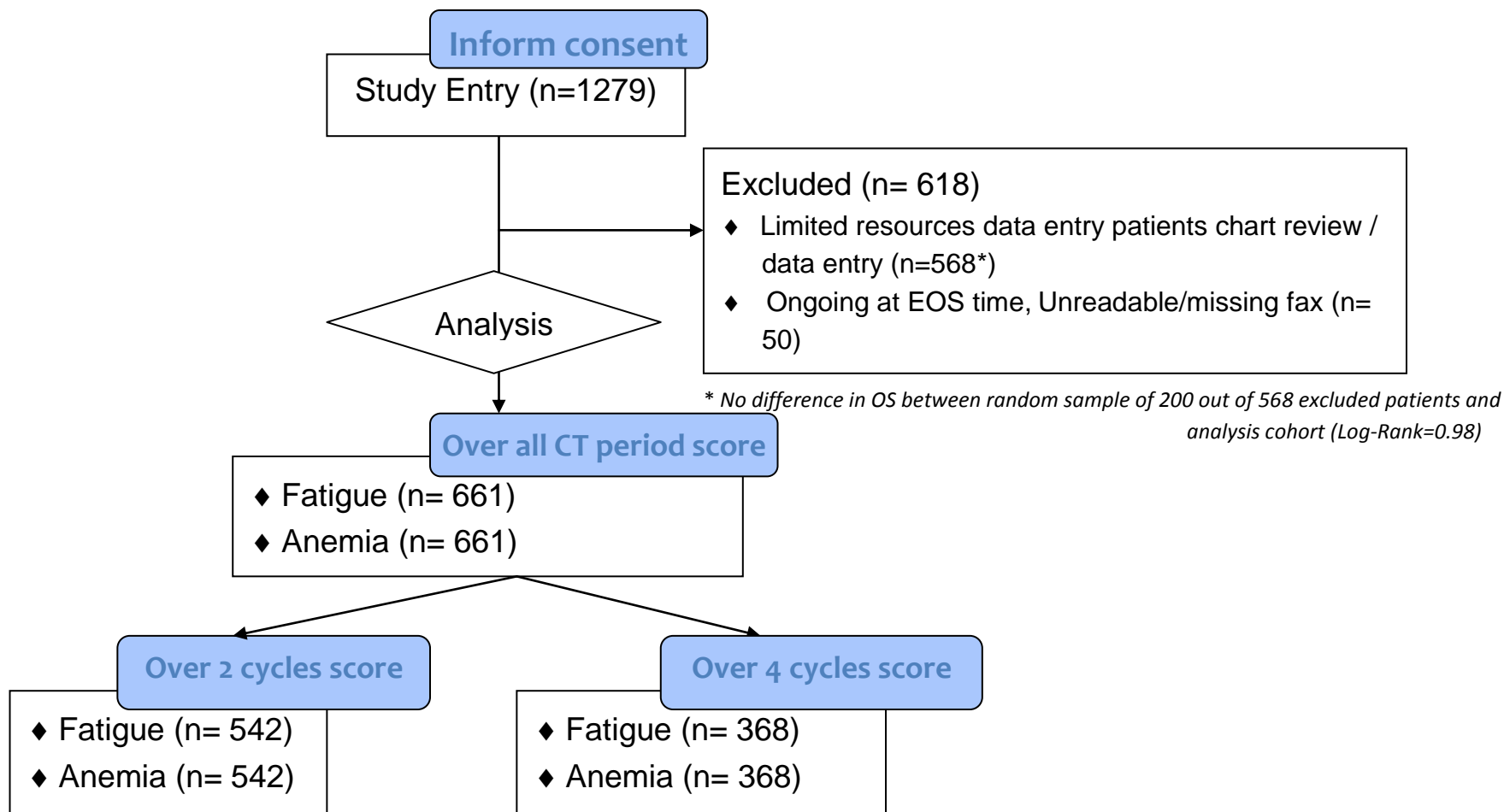
- Anemia (g/dl):

0: ≥ 12	1:]12-10]	2:]10-9]	3:]9-8]	4: < 8
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⇒ **Score = weighted mean (grades)**

- *One calculated over complete CT period, one on 4 first cycles, one on 2 first cycles*

Analysis population



FPFC=1 Oct 2008, LPLC=31 Oct 2011; Cut-off date for analysis: 31 Mar 2012.

Results: Baseline characteristics

Ntotal=661 patients	N	%
Age (years)	Median: 63.0	Range: 16-91
Sex-ratio (H/F)	333/328	
Cancer		
- <i>H&N</i>	81	12.3
- <i>Digestive</i>	17	2.6
- <i>Gynaecological</i>	89	13.5
- <i>Lung</i>	165	24.9
- <i>Breast</i>	143	21.6
- <i>Urological</i>	139	21.0
- <i>Other</i>	27	4.1
Setting		
- (Neo)-Adjuvant	241	36.4
- Metastatic	404	61.1
- Missing	16	2.5
Cycle completed / patient (N=3077 cycles)	Median: 4	IQR: 4

Fatigue score distribution

Ntotal=661 patients / 3078 Fatigue assessments

Baseline ECOG-PS (N=652)	<i>N</i>	<i>%</i>
0-1	489	75
2-3	163	25
# of Fatigue questionnaires	<i>Mean</i>	<i>SD</i>
Per patient	4.65	3.7
Per cycle	1	
Fatigue		<i>%</i>
0		24.7
1		45.2
2		24.2
3		5.6
4		0.3
Fatigue score	<i>Min - Median - Max</i>	<i>IQR</i>
- whole period	0.00 - 1.00 - 3.00	0.75
- 4 first cycles	0.00 - 1.00 - 3.00	0.75
- 2 first cycles	0.00 - 1.00 - 3.00	1.00

Anemia score distribution

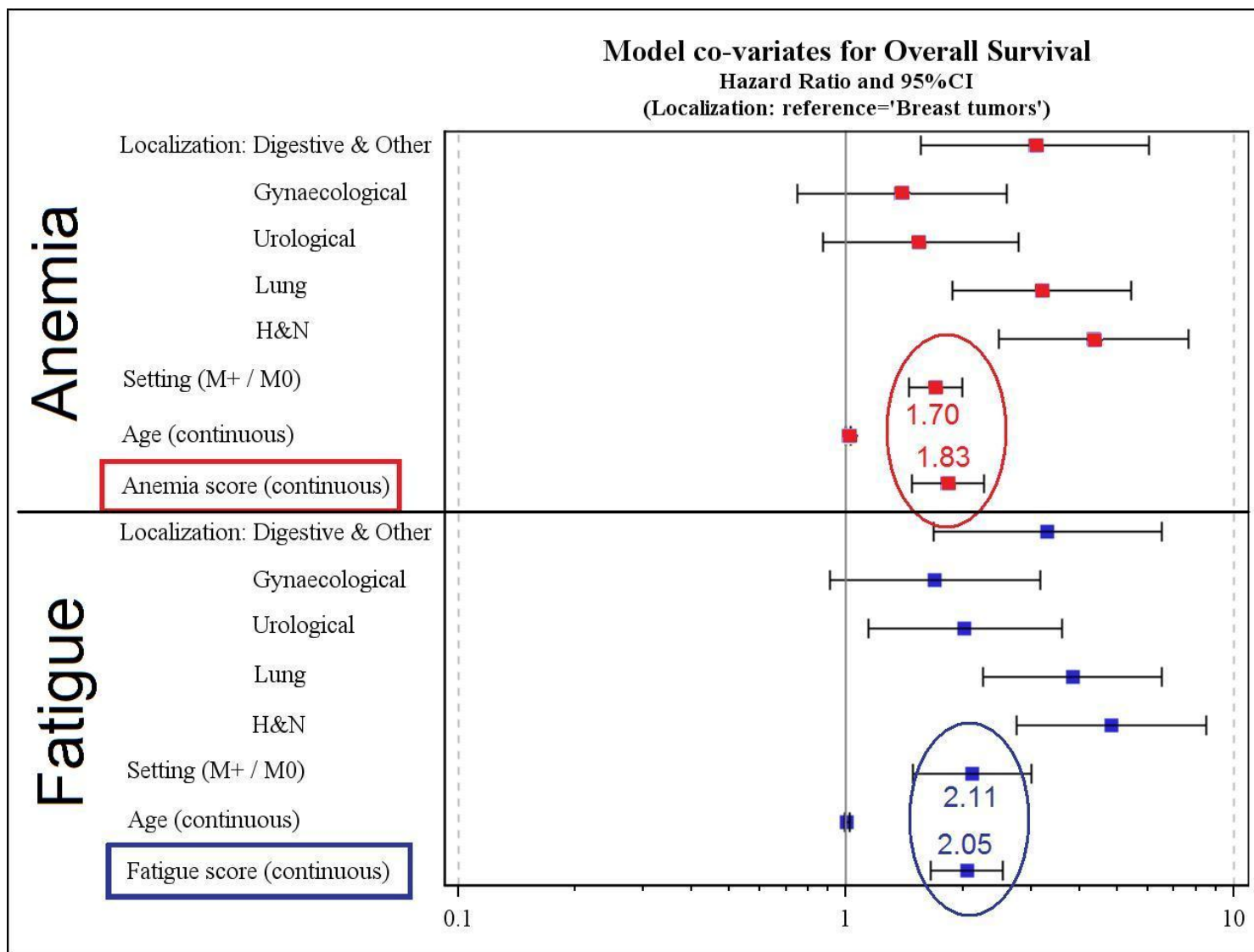
Ntotal=661 patients / 5585 Haemoglobin results

Haemoglobin results per patient	Median: 6 (≈ 1.5 / cycle)	IQR: 8
Haemoglobin (g/dl)	Mean: 11.5	Range: 6.5-18.9 (IQR: 2.0)
Haemoglobin level (g/dl)		%
≥ 12		31.5
]12.0; 10.0]		53.7
]10.0; 9.0]		10.6
]9.0; 8.0]		4.1
< 8		0.2
Anemia score	Min - Median - Max	IQR
- whole period	0.00 - 0.90 - 3.00	0.80
- 4 first cycles	0.00 - 0.75 - 3.00	0.74
- 2 first cycles	0.00 - 0.67 - 3.33	1.00

Overall Survival – Follow-up

Ntotal=661 patients	Median	Range
Median follow-up (FU) time (months)	18.6 (censored=14.6)	95%CI: 16.7-19.9 (censored: 13.5-16.2)
Completeness FU index	52.3%	
Overall survival (months)	24.3 (249 events)	95%CI: 21.2-34.7

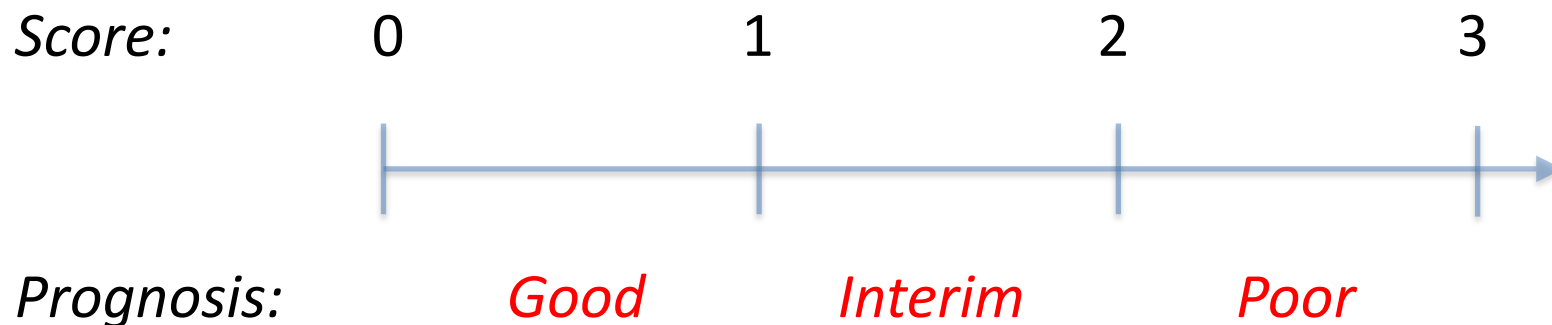
Results: continuous score



Results: categorical score

In order to investigate prognosis groups, continuous scores were categorized:

1. “Natural” score (cut-off: 1 score unit):



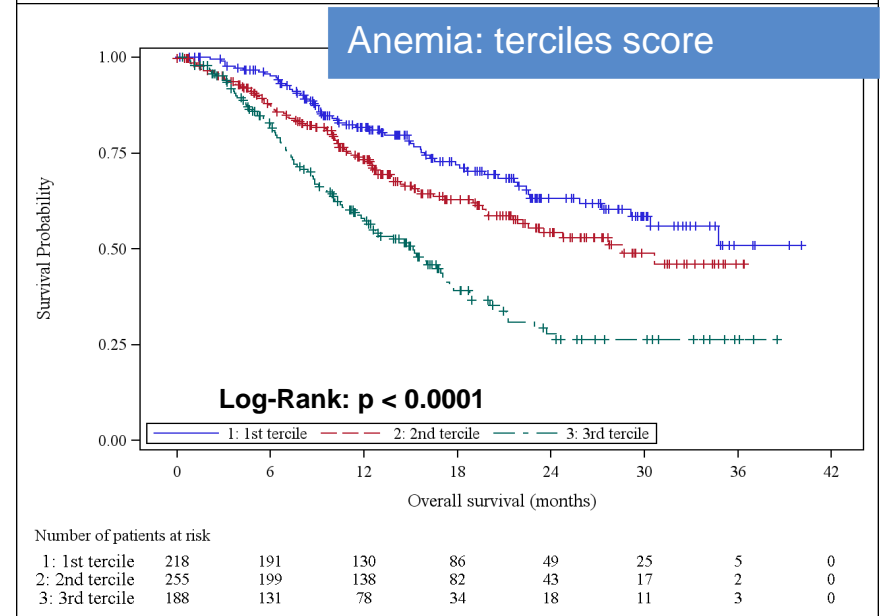
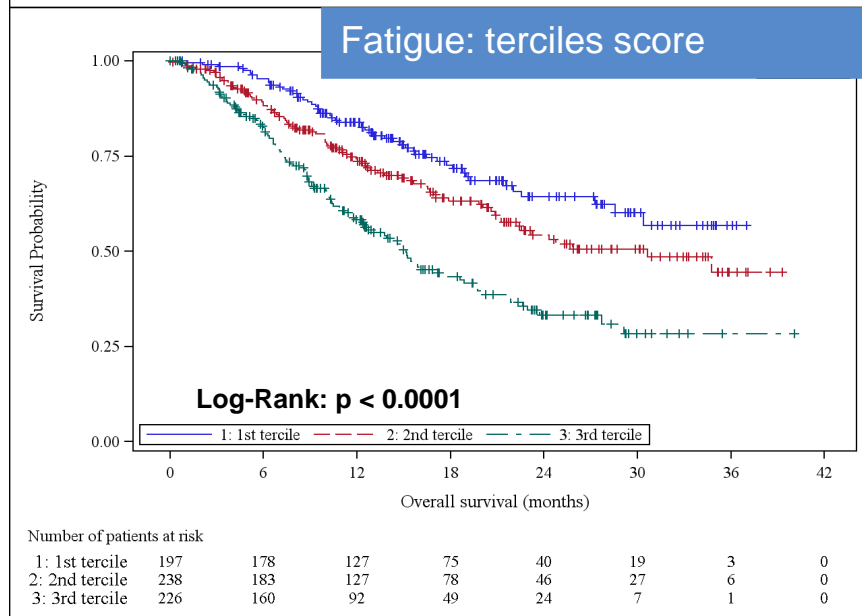
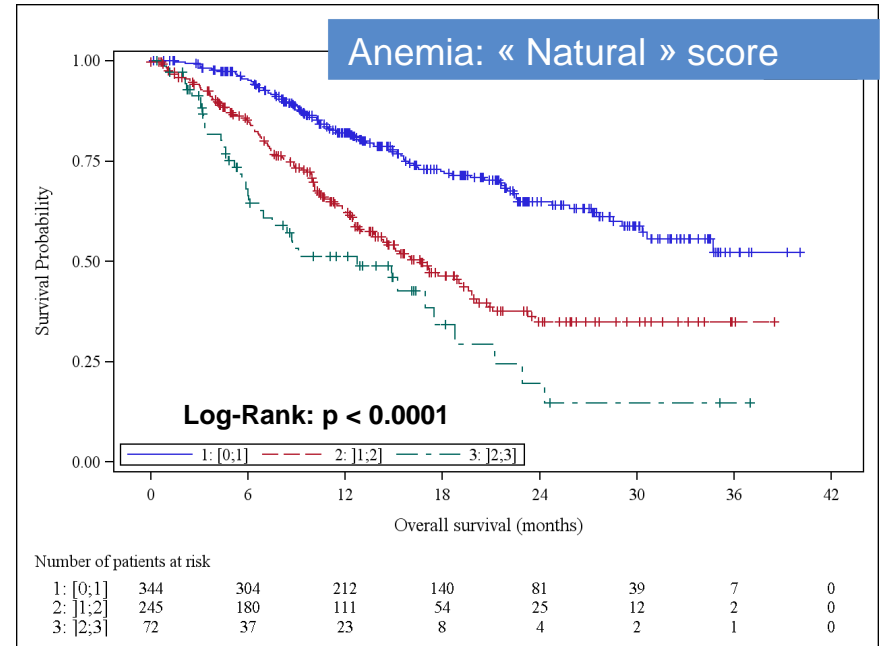
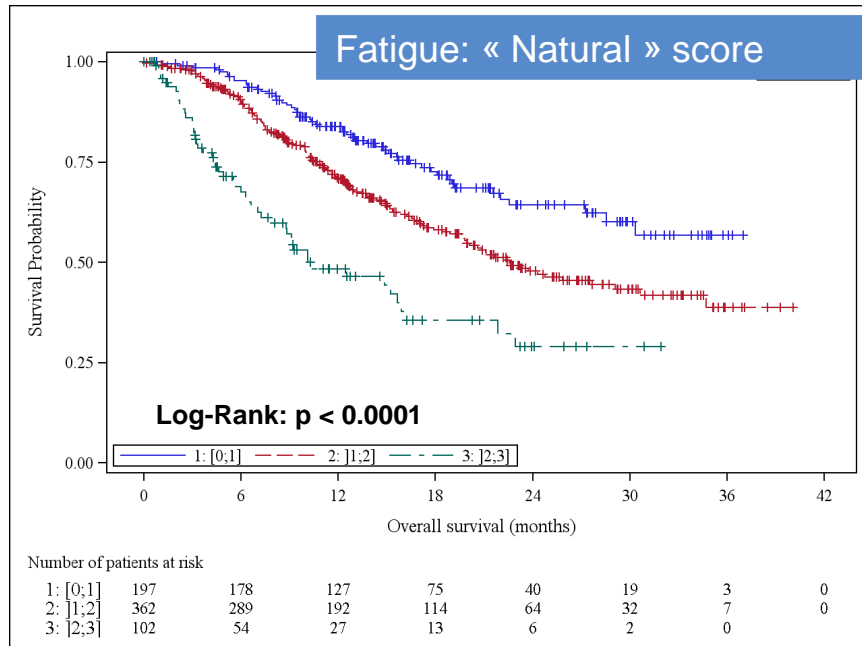
2. Terciles (model cut-off sensitivity ?)

OS : multivariate analysis of scores

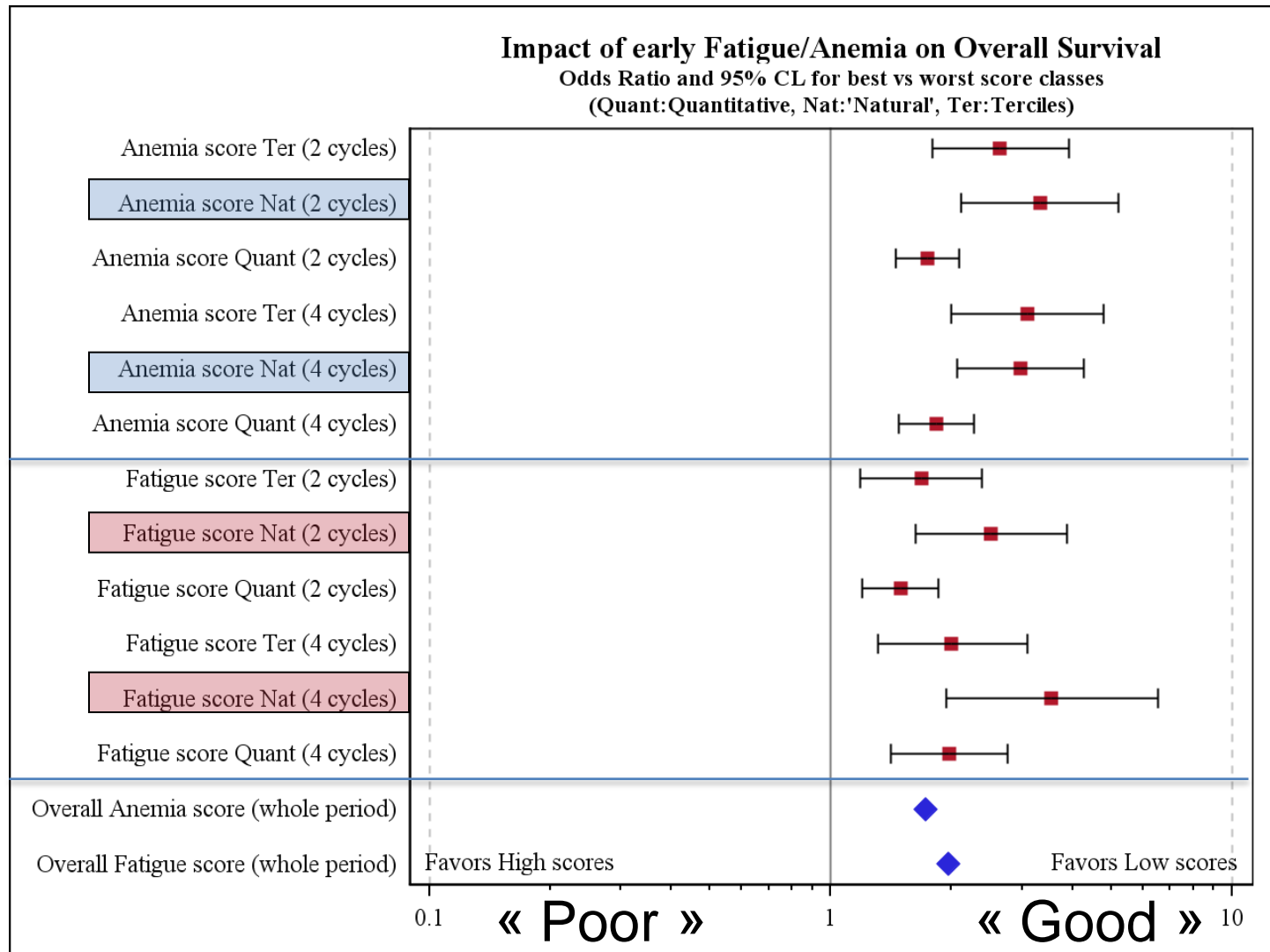
Score categories	N	HR	95%CI	p
Fatigue (whole period)				
• Continuous score	661	2.05	[1.65-2.54]	< 0.0001
• Prognosis group score				
« Natural » Strata: Good*	197	-		
Interm	362	1.62	[1.18-2.23]	0.0028
Poor	102	3.89	[2.59-5.85]	< 0.0001
Terciles: 1st*	197			
2nd	238	1.47	[1.04-2.08]	0.029
3rd	226	2.40	[1.72-3.35]	< 0.0001
Anemia (whole period)				
• Mean Hb	661	0.71	[0.65-0.78]	< 0.0001
• Continuous score	661	1.83	[1.48-2.27]	< 0.0001
• Prognosis group score				
« Natural » Strata: Good*	344	-		
Interm	245	2.67	[2.01-3.54]	< 0.0001
Poor	72	3.53	[2.38-5.24]	< 0.0001
Terciles: 1st*	218			
2nd	255	1.72	[1.24-2.40]	0.0013
3rd	188	2.57	[1.85-3.58]	< 0.0001

* reference category

Overall survival (whole period score)



Fatigue & Anemia early score*



Discussion

- “Natural” score is easy to monitor and more universal than terciles (data driven cut-offs).
- Score allow patients stratification according to “Good”, “Intermediate” and “Poor” prognosis for OS.
- “Poor” prognosis patients can be identified as earlier as 2 first cycles.
- Anemia correlates strongly with patient’s reported fatigue, whatever the period, and can be considered as a surrogate for OS.
- Study limitations: limited follow-up, more events needed, external validation ongoing.

Conclusion

- Fatigue is an independent prognosis factor for OS in patients treated with CT.
- Early assessment/management of both fatigue and anemia should be implemented to maintain patients in “Good” risk stratum.
- Fatigue should be managed as soon as possible, especially through anemia correction (ESMO recommendations).

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Fatigue¹ & Anemia¹ Correlations

Correlation (χ^2)	Over whole period (N=661)	Over 4 cycles (N=368)	Over 2 cycles (N=542)
Fatigue score x Mean Hb (Kruskal-Wallis)	16.1*	-	-
Fatigue score x Anemia score	82.9*	15.7 ($p=0.003$)	33.5*
Fatigue score x baseline ECOG-PS²	188.1*	81.2*	156.3*
* $p < 0.0001$	¹ « Natural » score	² PSS strongly related to ECOG-PS among whole cohort (N=1279pts, $\chi^2=7330$)	

Correlation (χ^2): score at Cycles₁₋₂ x Cycles₃₋₄

Fatigue	45.7*
Anemia	516.8*
* $p < 0.0001$	¹ « Natural » score

Backup: Improvement / Worsening

- Patients with no fatigue/anemia during the first 2 cycles who worsened (score: $Q/T_1 \Rightarrow Q/T_{>1}$ or $Q/T_{>2}$)
- Patients with fatigue/anemia during the first 2 cycles who improved (score: $Q_4/T_3 \Rightarrow Q_{<4}/T_{<3}$ or $Q_{<3}/T_{<2}$)
- Patients with : $\delta_{C34-C12} = (S_{C34} - S_{C12}) + \max(S_{C34}; S_{C12})$
 < 0 vs ≥ 0 (quantitative & categorical)

None statistically related to OS