



Can geriatric screening tools predict toxicity in older patients with metastatic colorectal cancer treated with chemotherapy?

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Kræftens Bekæmpelse

Region of
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Toxicity?

At least half of older cancer patients experience grade 3 toxicity during treatment with chemotherapy¹

- Performance status can not identify older patients at risk for chemotherapy-induced toxicity^{2,3}
- Larger models to predict toxicity (CARG, CRASH)

Predictive value of geriatric screening tools?

¹Versteeg et al, Ann Oncol, 2014

²Jolly et al, Oncologist, 2015

³Hurria et al, J Clin Oncol., 2011

NORDIC9 – study design

Randomization stratified according to:

- Institution
- Planned therapy with bevacizumab

EudraCT no. 2014-000394-39

160 patients:

- Non-resectable mCRC
- ≥ 70 years
- Not candidate for full-dose combination therapy
- PS 0-2

Geriatric screening tools

- G-8
- VES-13
- Timed-Up-and-Go
- Handgrip strength
- Charlson Comorbidity Index

R
A
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Optional bevacizumab

PFS

TTFS

S1

30 mg/m² x 2
d 1-14

PD

Iri

180 mg/m² q 2 w or
250 mg/m² q 3w

mSOx

20 mg/m² x 2 d 1-14
100 mg/m² x d1

PD

mIriS

20 mg/m² x 2 d 1-14
180 mg/m² x d1

Primary Endpoint:

- Progression-Free Survival

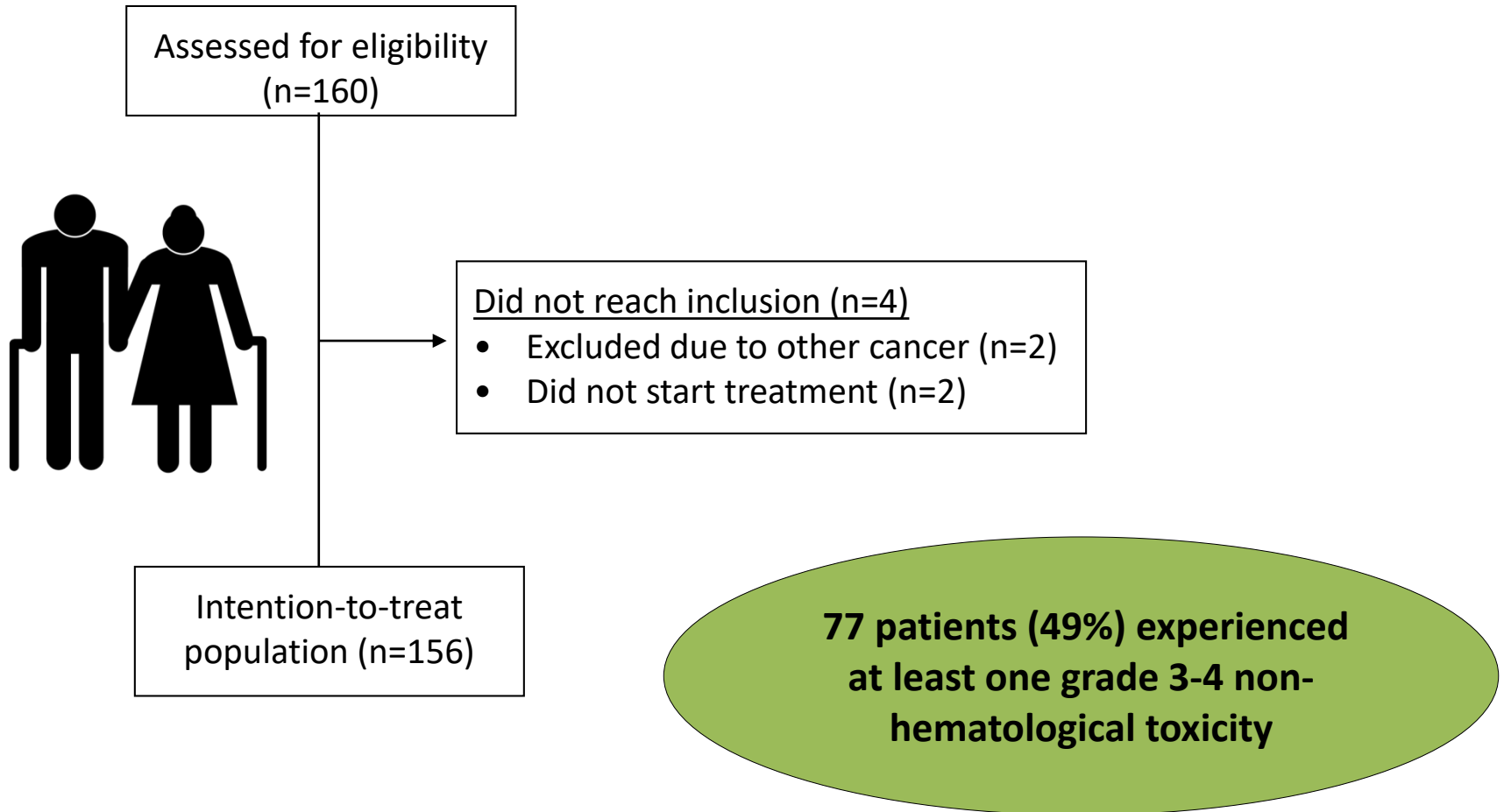
Secondary Endpoints:

- TTFS, OS, RR, toxicity, QoL, correlation: tumormarkers and outcome, predictive value of pre-treatment characteristics

Enrollment: March 2015 - October 2017

¹Winther et al, BMC Cancer, 2017; 17:548

NORDIC9



Who are at risk for at least one grade 3-4 toxicity?

Clinical relevant variables

- Treatment arm
- Addition of bevacizumab
- Performance status
- Resection of primary tumor
- No. of involved organs
- Weight loss > 5% within 2 months
- Comorbidity (CCI)

Interactions

- Treatment arm and bevacizumab (0.731)

Univariable analyses ($p < 0.1$)

- No resection of primary tumor (0.017)
- ≥ 3 involved organs (0.010)
- Weight loss (0.002)

Multivariable model – logistic regression

- Performance status
- Treatment arm # addition of bevacizumab
- Resection of primary tumor
- Weightloss (except for with G8)



Geriatric screening tools

- G8¹
- VES-13²
- Timed-up-and-Go³
- Hand grip strenght³

¹Bellera et al., 2012, ²Saliba et al., 2012, ³Median value of TUG and HGS is used as cut-off point

Can geriatric screening tools help us select?

Results of the multivariable analyses

- at least one grade 3-4 non-hematological toxicity

TUG ≥ 9

OR: 0.52
95% CI: 0.24-1.12
p = 0.097

Grip strenght- male

Weak: OR: 0.69, 95% CI: 0.25-1.96, p=0.491

Grip strenght- female

Weak: OR: 0.47, 95% CI: 0.16-1.41, p=0.180

G8 ≤ 14

OR: 1.10
95% CI: 0.51-2.39
p = 0.809



VES13 ≥ 3

OR: 1.31
95% CI: 0.55-3.09
p = 0.542

No resection of primary tumor

OR: 2.16, 95% CI: 1.11-4.20, p=0.024

Weightloss > 5% within 2 months

OR: 3.49, 95% CI: 1.35-9.00, p=0.010

Who receive less than 3 cycles?

≥ 3 organs involved
(p=0.039)

Treatment arm A
(p=0.040)

G8 ≤ 14
(p=0.042)

22 patients received
< 3 cycles of treatment
- surrogate for toxicity?

Alkaline
phosphatase > 105U/l
(p=0.017)

CRP ≥ 10 mg/L
(p=0.004)

Not significant difference: PS, age, sex, sidedness, add. of bevacizumab, TUG, GS, VES-13, CCI

Can geriatric screening tools help us select?

Results of the multivariable analyses

– receiving less than 3 cycles of chemotherapy

G8 \leq 14

OR: 3.12
95% CI: 0.63-15.5
p = 0.164

Grip strenght- male

Weak: OR: 0.41, 95% CI: 0.07-2.49, p=0.333

Grip strenght- female

Weak: OR: 0.53, 95% CI: 0.11-2.53, p=0.423

VES13 \geq 3

OR: 1.28
95% CI: 0.39-4.19
p = 0.683



TUG \geq 9

OR: 0.91
95% CI: 0.29-2.87
p = 0.866

No resection of primary tumor

OR: 2.51, 95% CI: 0.92-6.85, p=0.073

Weightloss > 5% within 2 months

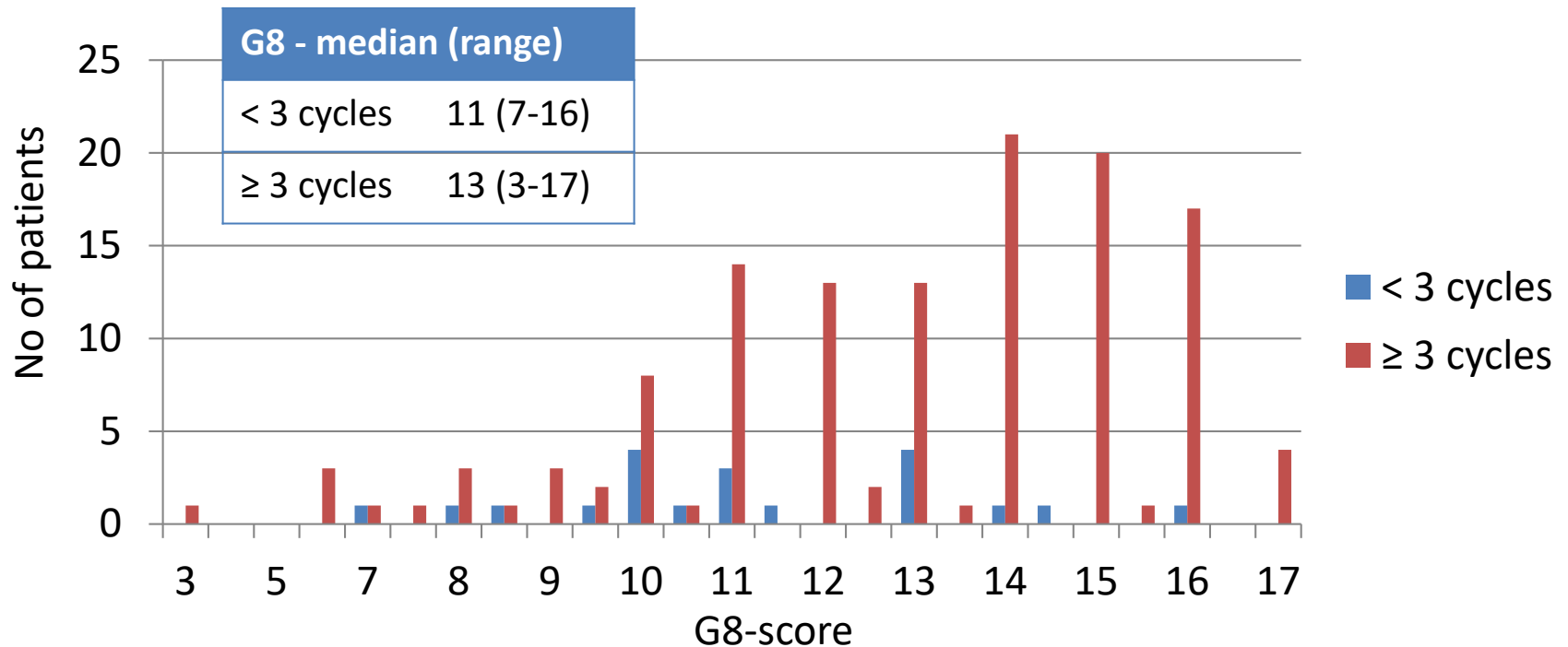
OR: 1.56, 95% CI: 0.51-4.79, p=0.433

Conclusion

➔ No significant association between geriatric screening tools

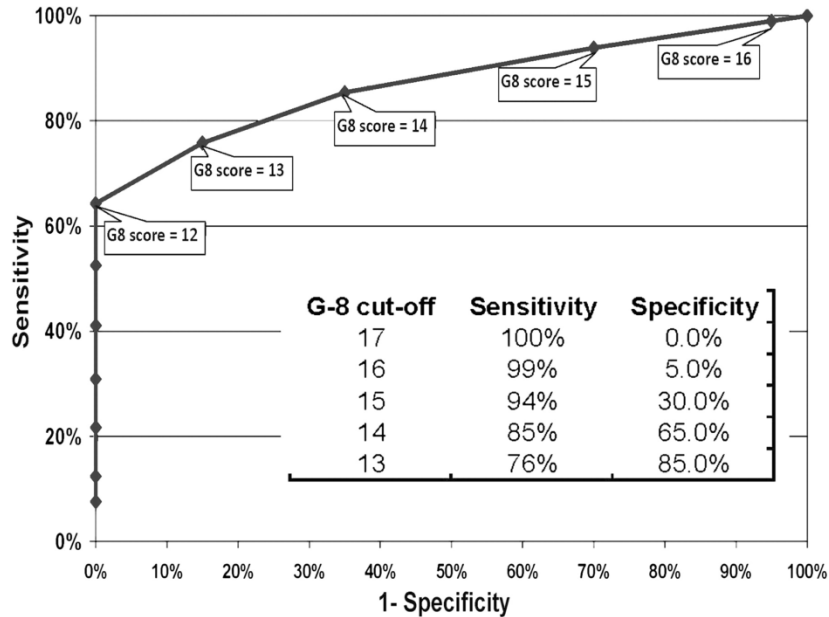
- At least 1 grade 3-4 toxicity
- Receiving < 3 cycles of chemotherapy

Significant difference in $G8 \leq 14$ between < 3 vs. ≥ 3 cycles ($p=0.042$)



Conclusion

G8 cut-off: ≤ 14 – is it optimal?



G8 ≤ 11 ?

At least 1 grade 3-4 toxicity

- G8 ≤ 11 : OR 2.41, 95% CI: 1.05-5.51 , p=0.037
- Primary tumor resected: OR 0.53, 95% CI: 0.27-1.05 , p=0.069

Receiving < 3 cycles of chemotherapy

- G8 ≤ 11 : OR 3.34, 95% CI: 1.02-11.0 , p=0.046
- Primary tumor resected: OR 0.34, 95% CI: 0.11-0.997 , p=0.049

Thoughts for discussion!

No significant association between the geriatric screening tools and toxicity in the NORDIC9-trial.

Figure from: Bellera et al. Ann Oncol. 2012;23(8):2166-2172.

Thank you for your attention!

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And the NORDIC9-investigators and sites!

