

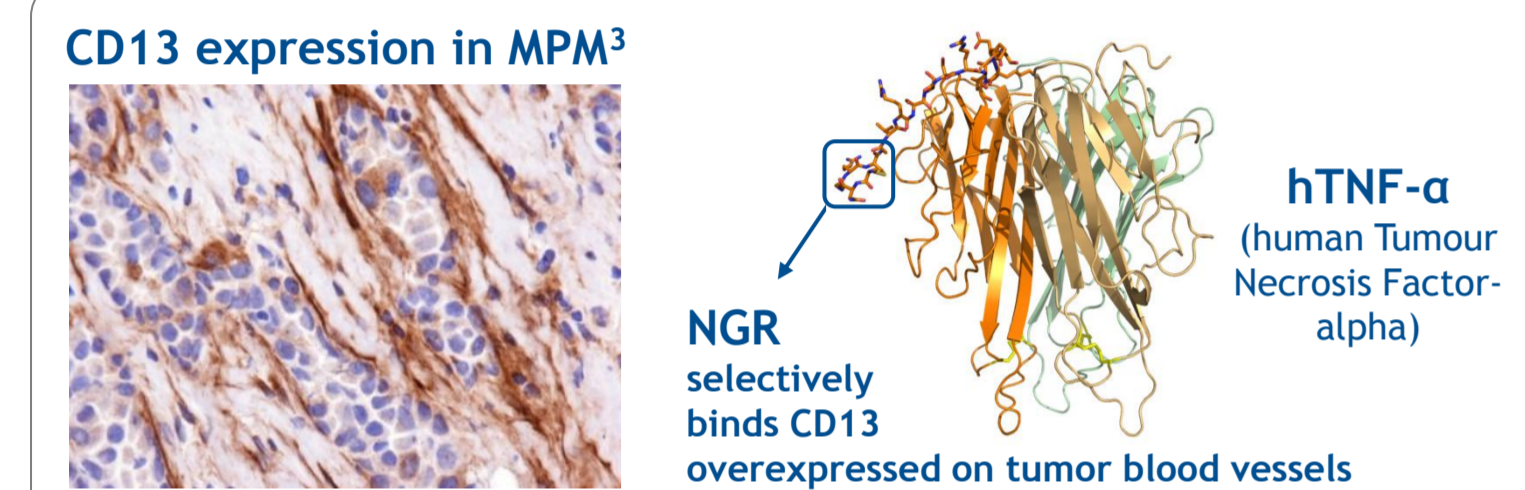
NGR-hTNF in previously treated patients with malignant pleural mesothelioma (MPM)

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Background and methods

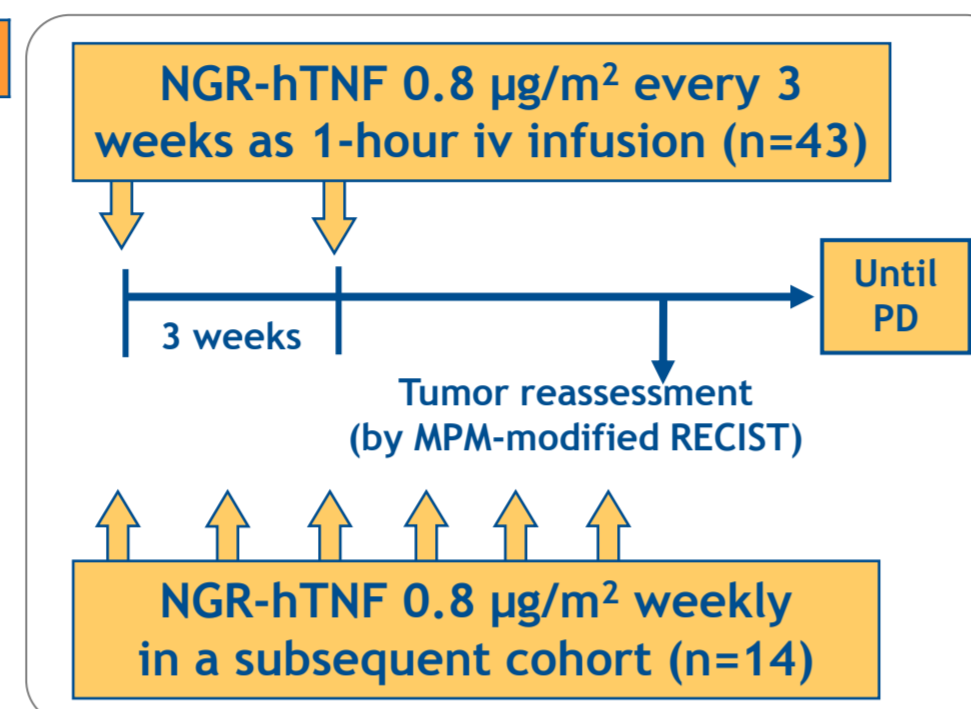
- Preclinically, TNF- α has shown potent antitumor and antivascular activity
- However, its clinical use has been hampered by severe systemic toxicity with MTD significantly lower than ED¹
- NGR-hTNF consists of TNF- α fused with the tumor-homing peptide NGR²



- Malignant pleural mesothelioma (MPM) is a devastating disease with increasing incidence worldwide
- The combination of pemetrexed and cisplatin is standard-of-care as front-line regimen with median survival time of 12.1 months⁴
- However, patients who failed first line have an aggressive disease with median PFS of 1.5 months, disease control of 19%, and median survival of 9.4 months reported in the no-treatment arm of a phase 3 trial⁵
- Neither regulatory-approved nor widely-accepted 2nd line are currently available
- Here we report the long term results of a phase 2 trial testing NGR-hTNF in MPM patients who had failed a pemetrexed-based regimen⁶

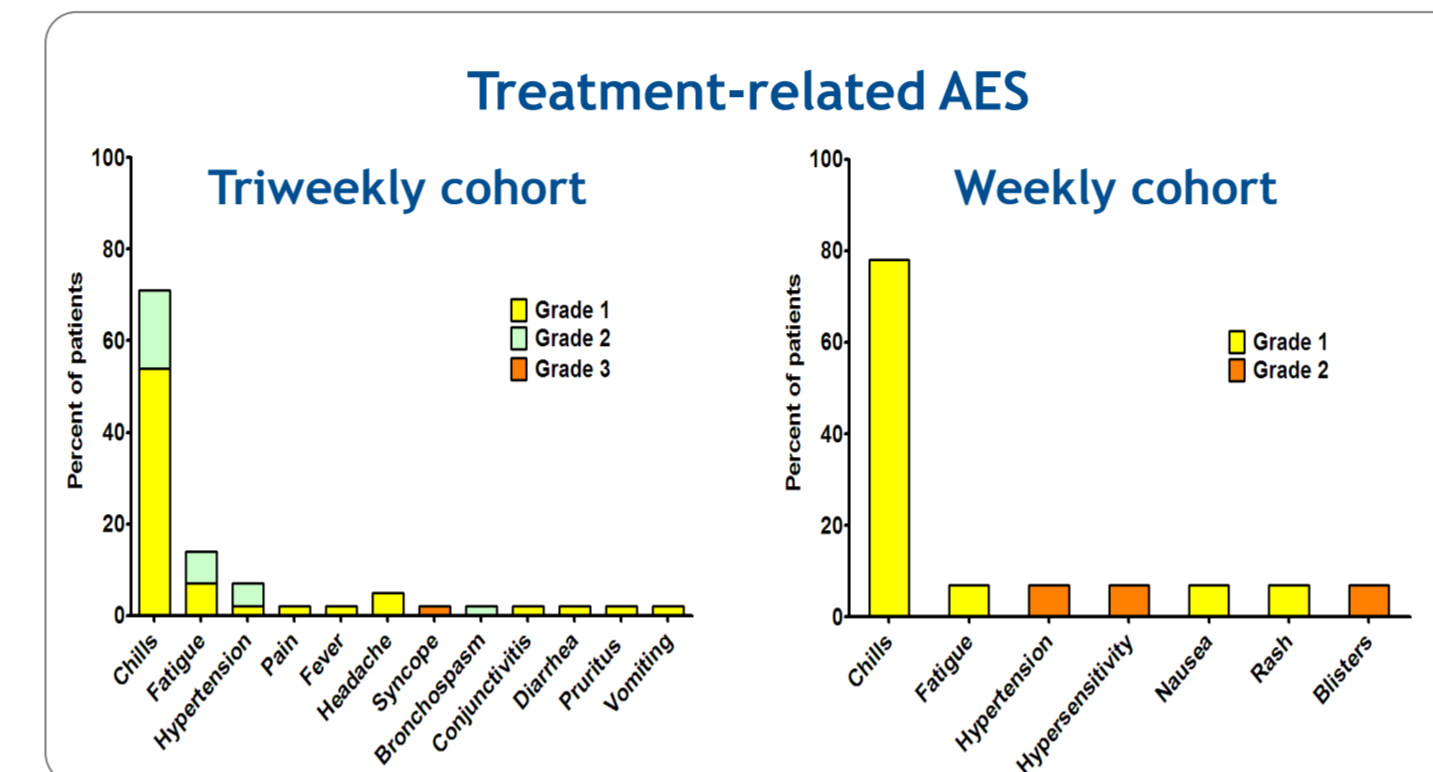
Study design

- Multicenter, single-arm phase II trial
- Two-stage accrual design
 - 16/27 patients after 1st/2nd stage
- Primary endpoint: PFS
- Key inclusion criteria:
 - Age ≥ 18 years
 - ≥ 1 prior systemic regimen
 - Radiologically-documented PD
 - Performance status (PS) 0-2



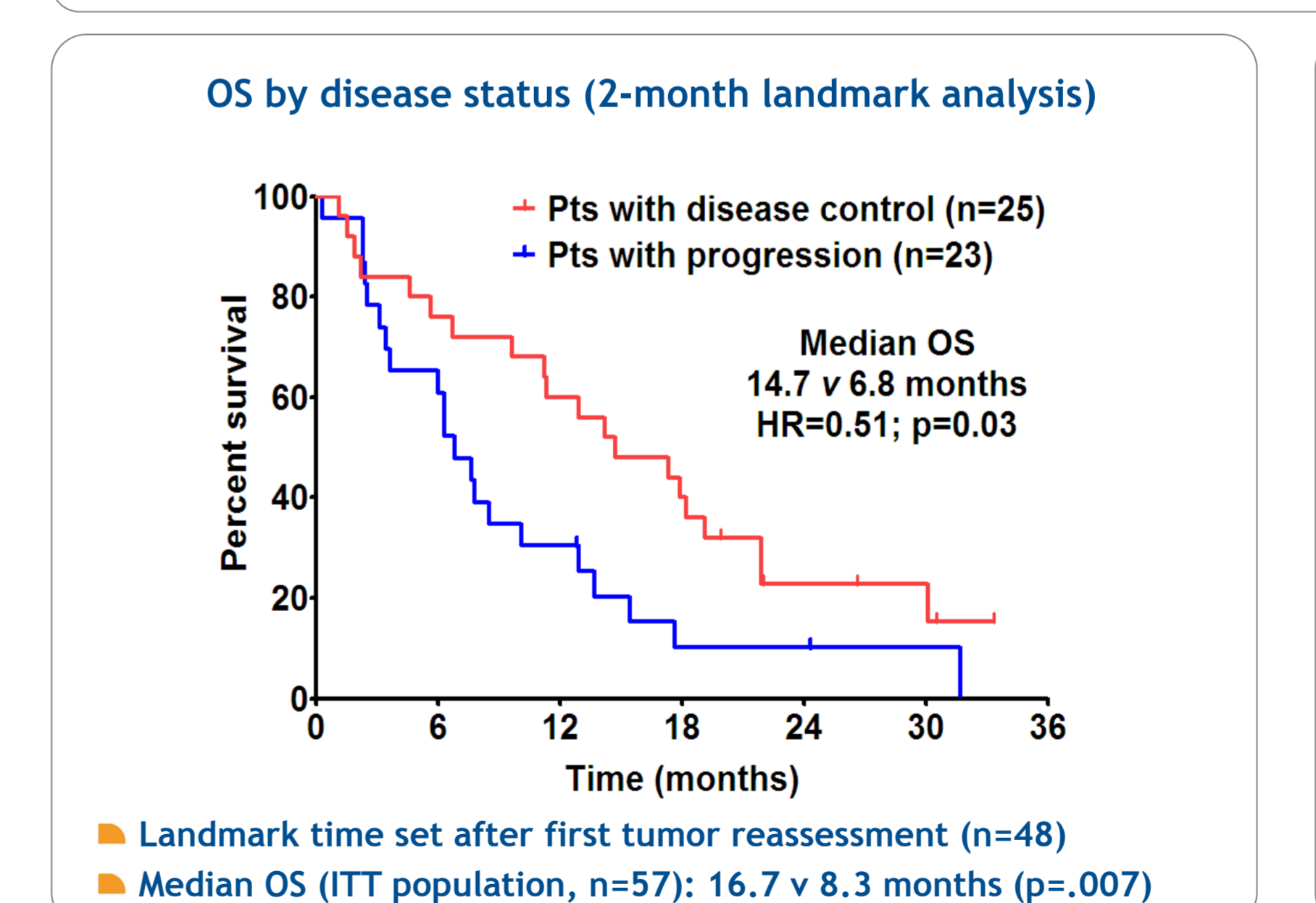
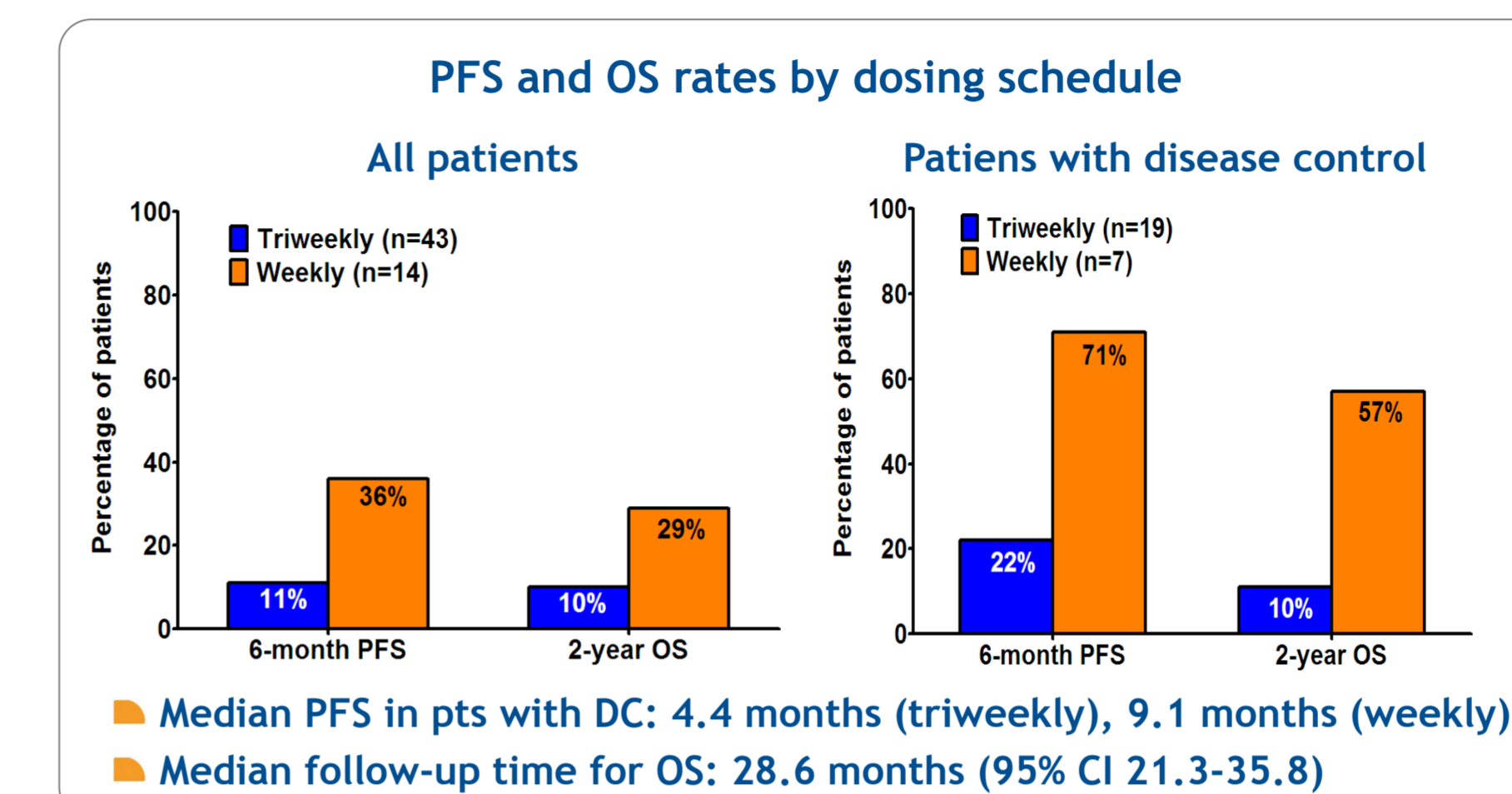
Baseline characteristics by dosing schedule	Triweekly n=43 (%)	Weekly n=14 (%)
Median age in years (range)	64 (54 - 80)	68 (50 - 86)
Gender male / female	27 (63) / 16 (37)	8 (57) / 6 (43)
ECOG PS 0 / 1-2	24 (56) / 19 (44)	7 (50) / 7 (50)
Tumor histology epithelial / nonepithelial	34 (79) / 9 (21)	11 (79) / 3 (21)
EORTC prognostic score good / poor	34 (79) / 9 (21)	11 (79) / 3 (21)
Prior systemic therapy pem-plat / gem-plat	40 (93) / 3 (7)	13 (93) / 1 (7)
PFS on prior therapy ≥ 6 / < 6 months	24 (67) / 19 (33)	9 (64) / 5 (36)

- 171 cycles (range 1 - 18) in the triweekly cohort (n=43)
- 266 infusions (range 4 - 69) in the weekly cohort (n=14)



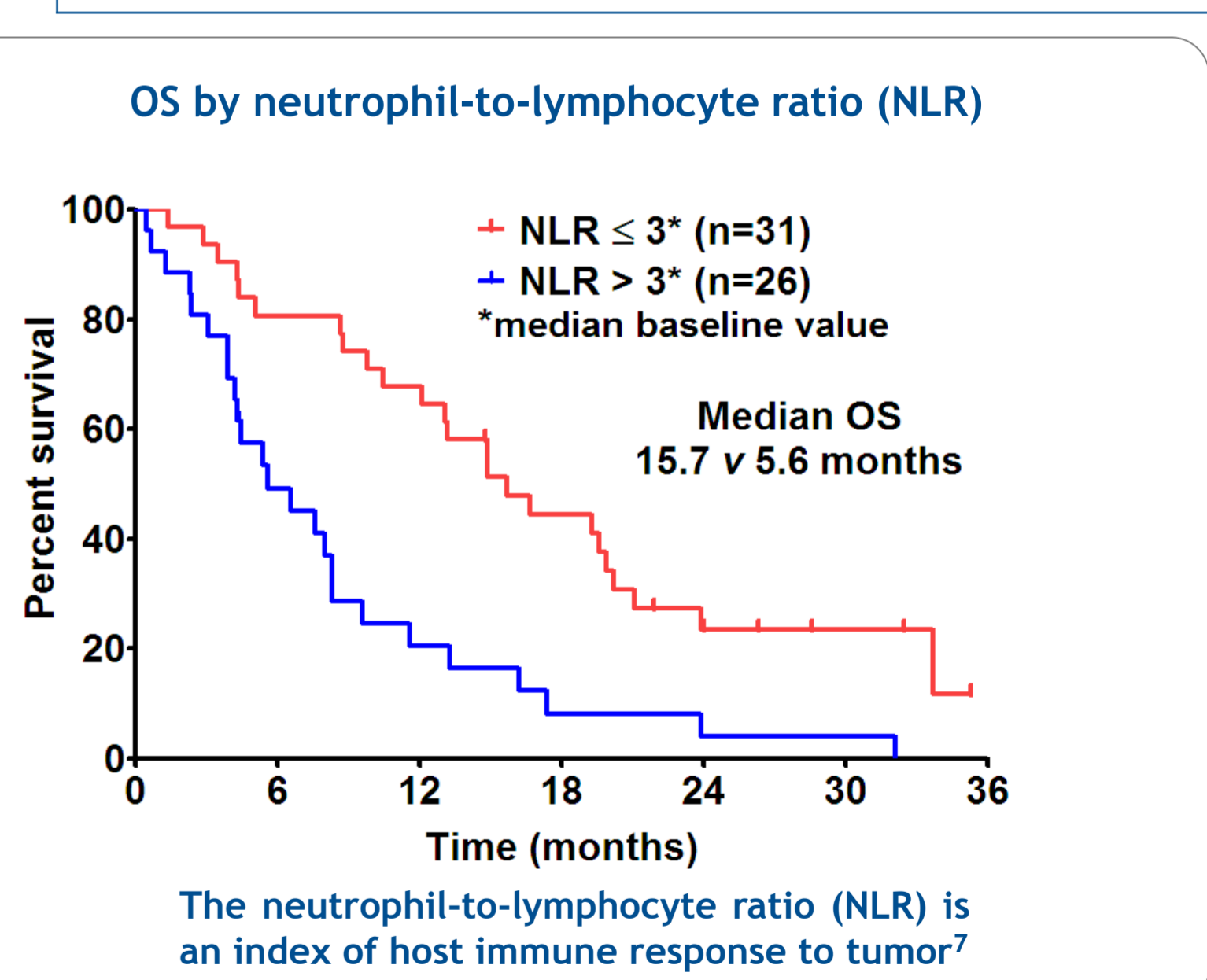
Best tumor response	n=57 (%)
PR	1 (2)
SD	25 (44)
Disease control (DC, PR + SD)	26 (46)
PD	23 (40)
Non assessable	8 (14)
Progression-free survival (PFS)	months
median	2.8
95% CI	2.3 - 3.3
PFS in patients with disease control	months
median	4.7
95% CI	4.0 - 5.4
Overall survival (OS)	months
median	12.1
95% CI	7.2 - 17.0

Results



Multivariate analysis for OS	Exp(B)	p-value
Histologic subtype epithelial v nonepithelial	0.51	0.08
EORTC prognostic score good v poor	0.56	0.21
ECOG performance status (PS) 0 v 1-2	0.38	0.01
Neutrophil-to-lymphocyte ratio (NLR) ≤ 3 v > 3 (median baseline value)	0.40	0.004

At univariate analysis no associations were detected between OS and age, sex, and treatment-free interval on prior therapy



Conclusions

- NGR-hTNF is well tolerated in patients pre-treated with pemetrexed
- Disease control achieved in half of patients and maintained for a median time >4 months with triweekly schedule and >9 months with weekly schedule
- Based on first tumor reassessment, disease control (v progression) associated with longer survival time
- Two double-blind, placebo-controlled randomized trials with NGR-hTNF 0.8 µg/m² weekly are currently open to accrual:
 - A phase 2 trial as maintenance treatment in patients who did not progress after 6 cycles of first-line therapy (NGR019 trial - www.clinicaltrials.gov NCT01358084)
 - A phase 3 study testing best investigator choice with or without NGR-hTNF in relapsed patients (NGR015 trial - www.clinicaltrials.gov NCT01098266)

References

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