

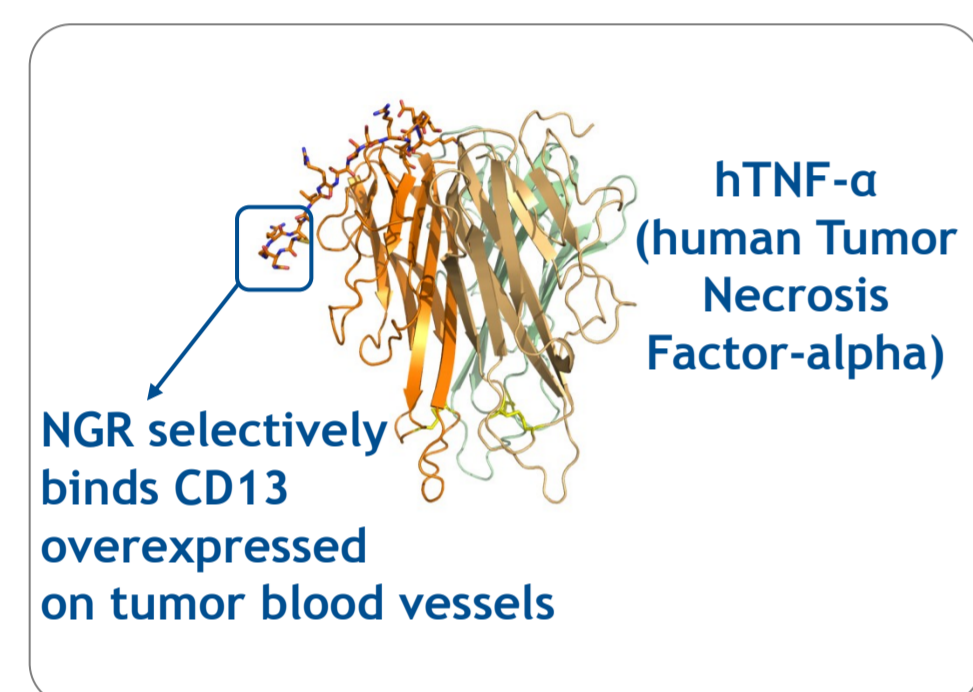
Randomized phase II trial of NGR-hTNF and chemotherapy in chemo-naïve patients with non-small cell lung cancer (NSCLC): preliminary results

V. Gregorc¹, N. Zilembo², F. Grossi³, G. Rossoni¹, F. Pietrantonio², E. Rijavec³, G. Citterio¹, M. Platania², A. Lambiase⁴, C. Bordignon⁴

¹Istituto Scientifico San Raffaele, Milan, Italy; ²IRCCS Fondazione Istituto Nazionale dei Tumori, Milan, Italy; ³Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy; ⁴MolMed, Milan, Italy

Background and methods

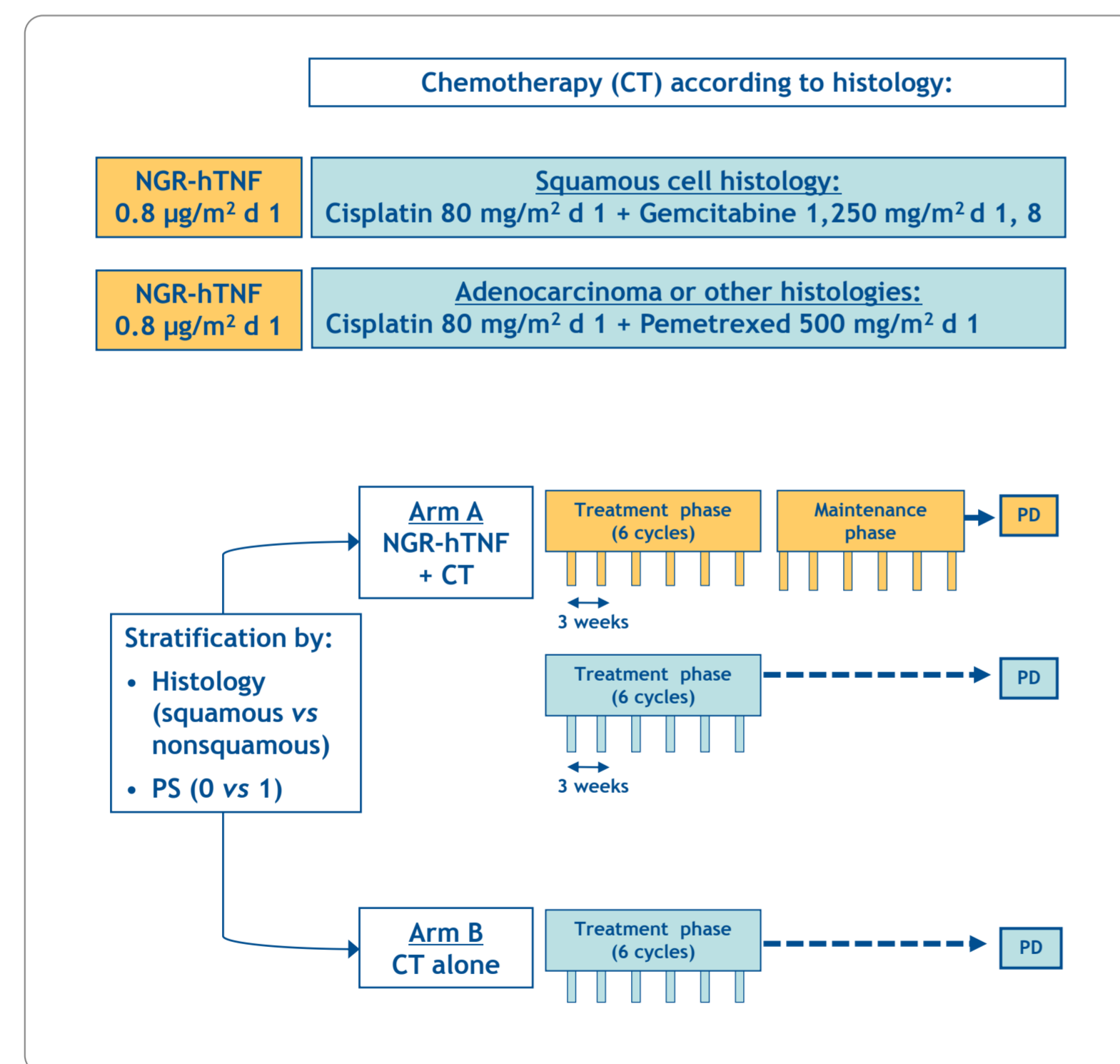
- Preclinically, tumor necrosis factor- α (TNF- α) has shown potent antitumor and antivascular activity. However, its clinical use has been hampered by severe systemic toxicity¹
- NGR-hTNF consists of TNF- α fused with the tumor-homing peptide NGR (asparagine-glycine-arginine)²



- Overexpression of CD13 in patients with NSCLC has been associated with poor prognosis and increased angiogenesis³
- In phase I trial,⁴ the optimal biological dose of NGR-hTNF was established as 0.8 $\mu\text{g}/\text{m}^2$ in combination with cisplatin 80 mg/m^2 , with a favorable safety profile and promising activity
- Recent clinical trials have demonstrated that histology is a key factor for individualizing treatment based on either safety or efficacy outcomes
- For antiangiogenic agents, restriction of the use was due to the association between squamous cell histology and severe pulmonary hemorrhage⁵
- For chemotherapy, an improved survival was reported in patients with nonsquamous histology for the cisplatin plus pemetrexed regimen compared with the cisplatin plus gemcitabine combination. Conversely, the reverse was seen for patients with squamous histology, with survival favoring cisplatin plus gemcitabine compared with cisplatin plus pemetrexed⁶

Study design

- Open-label, randomized phase II trial
- Chemo-naïve, stage IIIB/IV NSCLC
- Brain metastases (if adequately treated)
- Performance status (PS) 0-1
- Primary endpoint: progression-free-survival (PFS)
- Secondary endpoints: response rate (RR), safety and OS
- Hypothesis testing: \uparrow 15% PFS; Sample size/Events: 102/83



Study status

- 112 patients enrolled and 100 (50 for each arm) presently analyzed
- Overall data are still immature for primary analysis of PFS, with 68 events (progressions or deaths) having occurred
- Early treatment discontinuations:
 - Arm A (n=11): 4 for toxicity, 2 for local therapy, 3 for symptomatic deterioration, and 2 for early death
 - Arm B (n=11): 7 for toxicity, 2 for symptomatic deterioration, and 2 for early death

Results

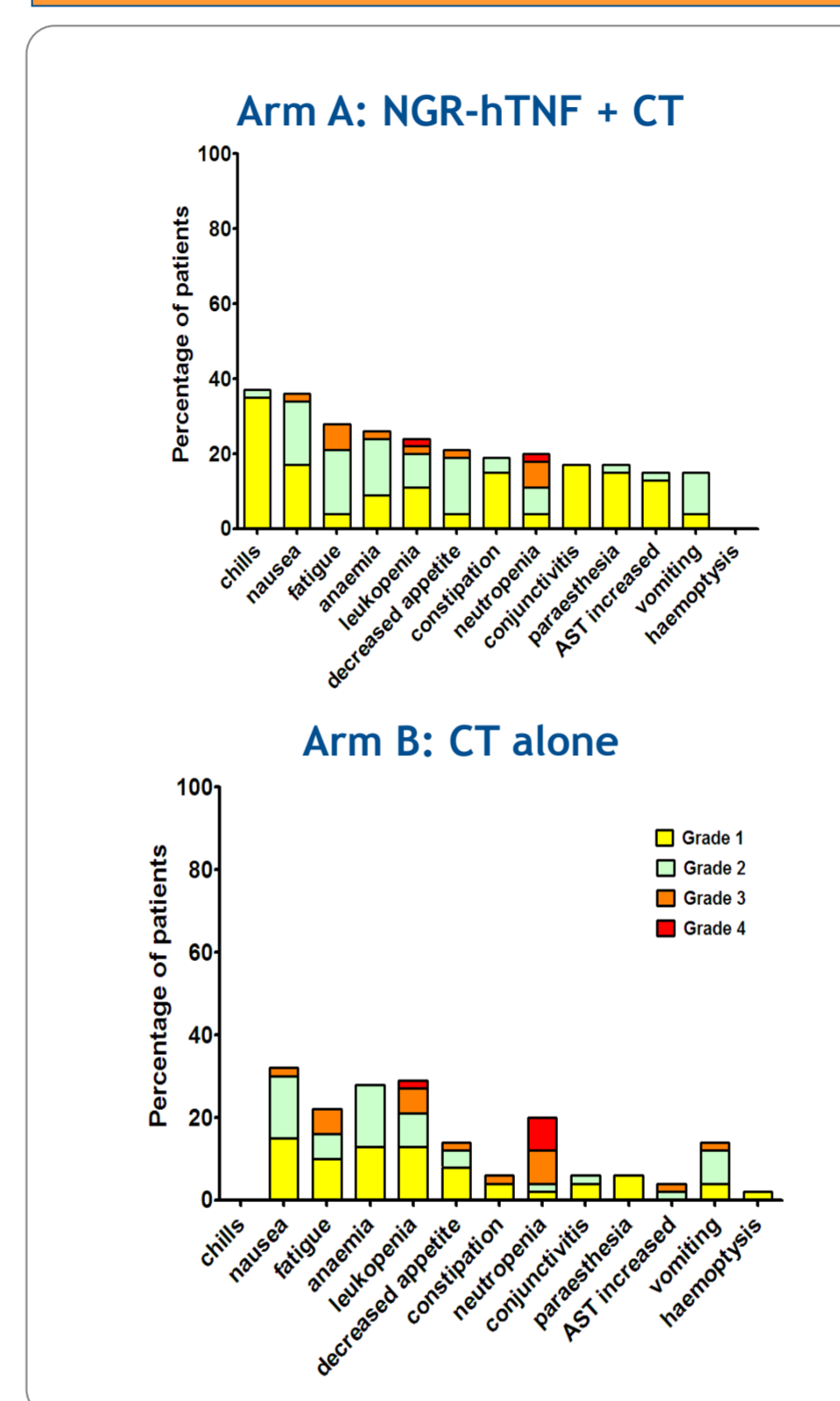
Baseline characteristics

All patients	CT + NGR-hTNF N=50	CT n=50
Age		
median in years (range)	62 (38-74)	62 (38-77)
interquartile range	57 - 68	57 - 66
Gender		
male	30 (60%)	31 (62%)
female	20 (40%)	19 (38%)
ECOG PS		
0	33 (66%)	32 (64%)
1	17 (34%)	18 (36%)
Histologic subtype		
squamous	13 (26%)	13 (26%)
nonsquamous	37 (74%)	37 (74%)
Smoking history		
smoker	36 (72%)	38 (76%)
nonsmoker	14 (28%)	12 (24%)
EGFR mutation status		
Wild type or unknown	47 (94%)	45 (90%)
Mutated	3 (6%)	5 (10%)

Treatment exposure

All patients	CT + NGR-hTNF n=50	CT n=50
Total # cycles	299	221
mean	5.9	4.4
range	1-18	1-6
Adenocarcinoma	CT + NGR-hTNF n=37	CT n=37
Total # cycles	228	173
mean	6.1	4.7
range	1-18	1-6
Squamous	CT + NGR-hTNF n=13	CT n=13
Total # cycles	71	48
mean	5.4	3.7
range	1-12	1-6

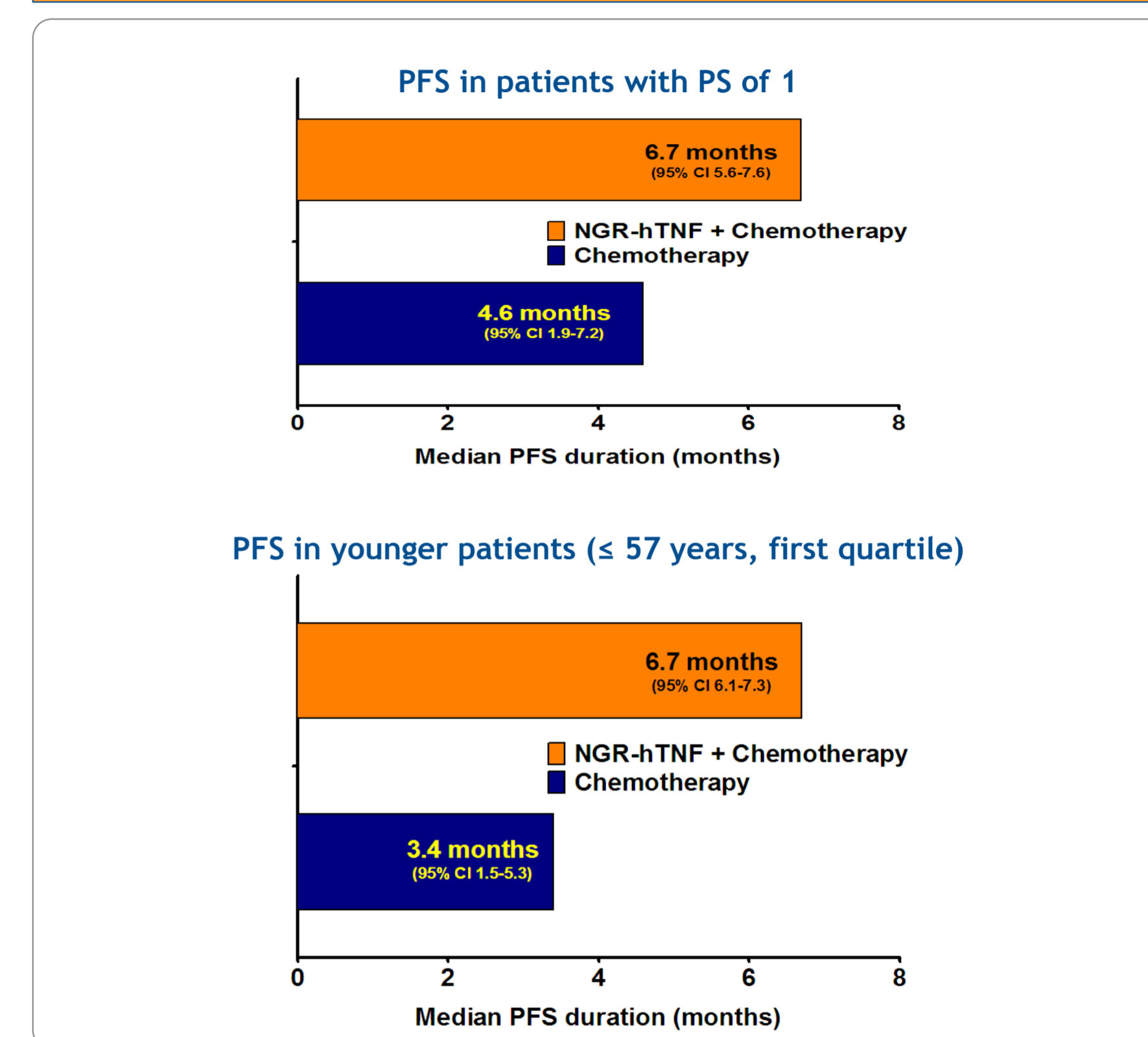
Adverse events by arm



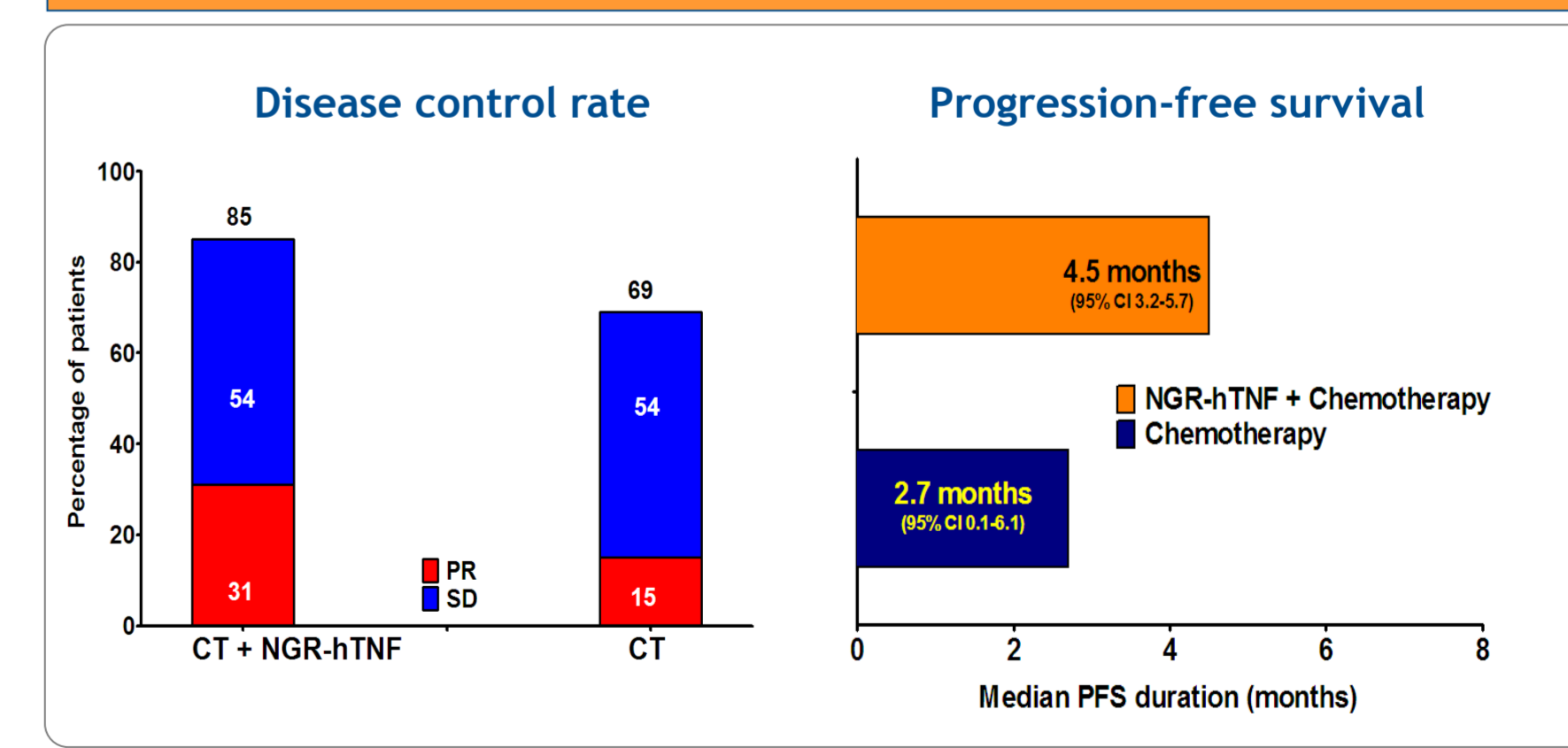
Conclusions

- Regardless of histology, NGR-hTNF was well tolerated in combination with both chemotherapy regimens, cisplatin plus pemetrexed and cisplatin plus gemcitabine
- There were no pulmonary hemorrhage or bleeding events, which have been associated with use of antiangiogenic agents in patients with squamous cell histology
- Preliminary results show promising activity of NGR-hTNF plus chemotherapy compared to chemotherapy alone in patients with squamous cell histology

Subset analyses in patients with nonsquamous histology



Subset analyses in patients with squamous cell histology



References

- Blick M et al. *Cancer Res* 1987;47:2986-9
- Curnis F et al. *Nat Biotechnol* 2000;18 (11): 1185-9
- Tokuhashi T et al. *Clin Can Res* 2006; 12 (13) 3971-3978
- Gregorc V et al. *Clin Can Res* 2011; 17(7); 1964-72
- Langer CJ et al. *JCO* 2010; 20: 5311-5320
- Scagliotti GV et al. *JCO* 2008; 26:3543-3551

Acknowledgements (MolMed)

- Cristina Ammannati
- Shalini Colombi
- Antonella Troysi
- Elena Lungagnani