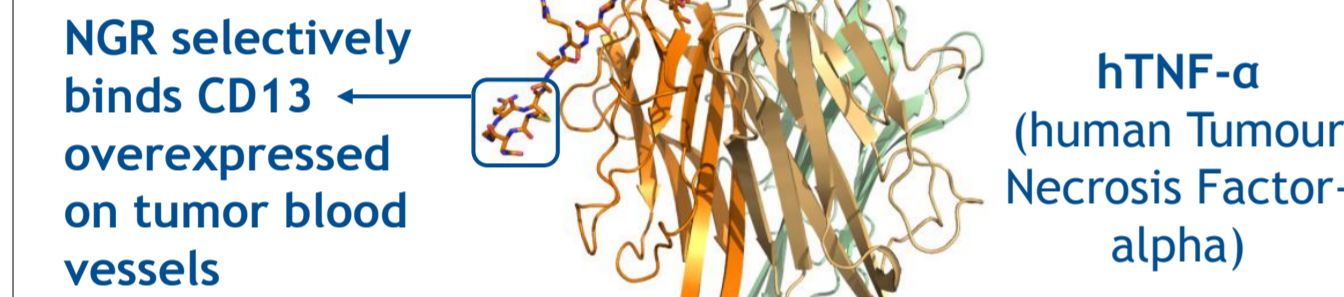


# Randomized phase II trial of NGR-hTNF and chemotherapy in chemo-naïve patients with non-small cell lung cancer (NSCLC): preliminary results

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## Background and methods

- TNF-α has shown potent antitumor and antivascular activity in preclinical models. However, its clinical use has been hampered by severe systemic toxicity, with MTD significantly lower than ED<sup>1</sup>
- NGR-hTNF consists of TNF-α fused with the tumor-homing peptide NGR<sup>2</sup>

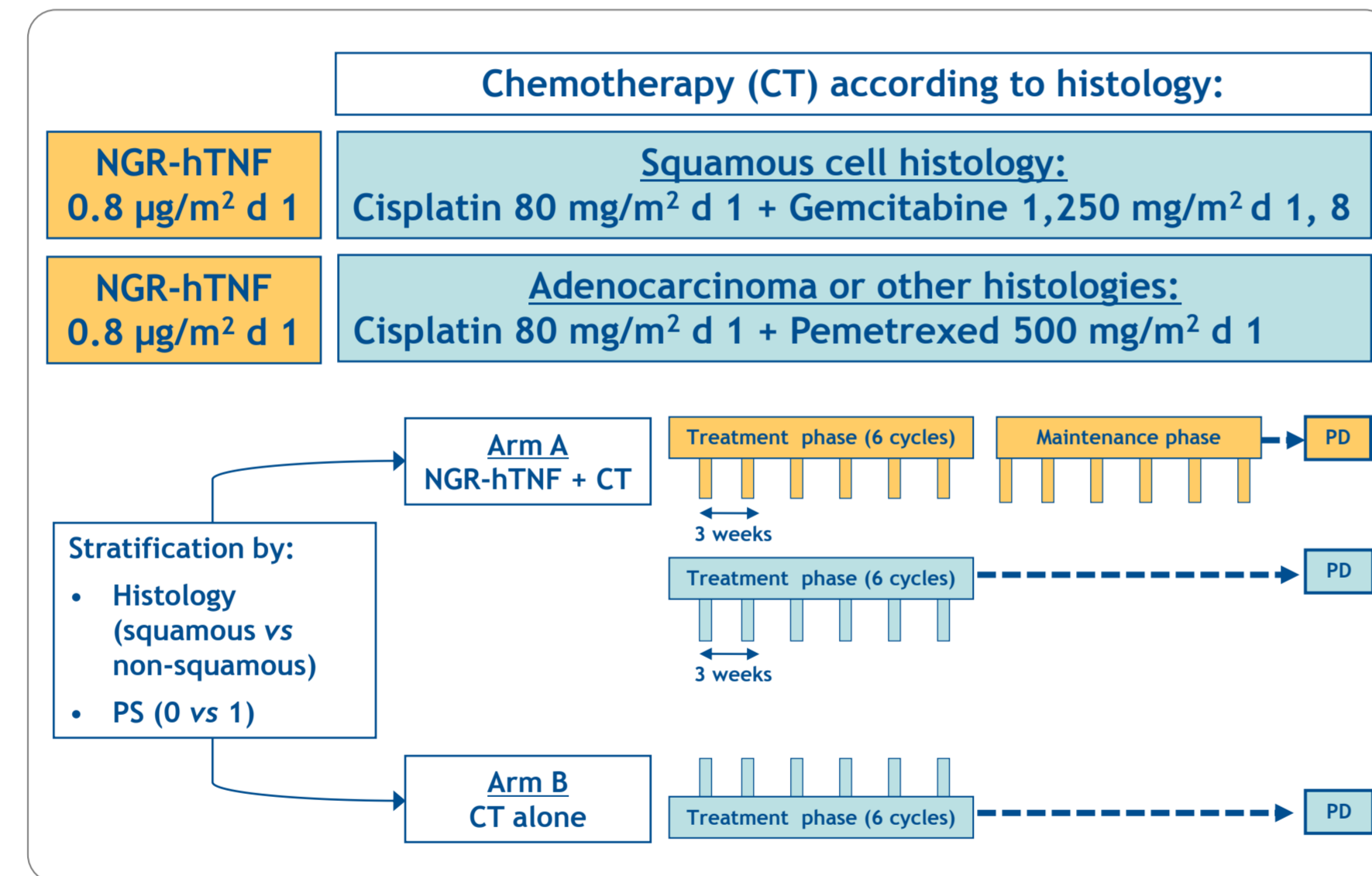


- Overexpression of CD13 in patients with NSCLC has been associated with poor prognosis and angiogenesis<sup>3</sup>
- In phase I trial,<sup>4</sup> the optimal biological low dose of NGR-hTNF was established at 0.8 µg/m<sup>2</sup> in combination with cisplatin 80 mg/m<sup>2</sup>, with a favorable 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 hemorrhage<sup>5</sup>
- For chemotherapy, an improved survival was reported in patients with adenocarcinoma for the cisplatin plus pemetrexed regimen compared with the cisplatin plus gemcitabine combination. By contrast, the reverse was seen for patients with squamous cell carcinoma, with survival favoring cisplatin plus gemcitabine compared with cisplatin plus pemetrexed<sup>6</sup>

## Study design

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



## Study status

- 107 patients enrolled so far
- After median follow-up time of 9.3 months (95% CI 5.1-13.5), 50 events (progressive disease or death) occurred and data are still highly censored and immature for primary analysis
- 80 patients (40 in each arm) presently analyzed for safety and preliminary activity
- Early treatment discontinuations:
  - Arm A, n=5 (1 for toxicity, 2 for local therapy, 2 for symptomatic deterioration)
  - Arm B, n=5 (3 for toxicity, 2 for symptomatic deterioration)

## Baseline characteristics

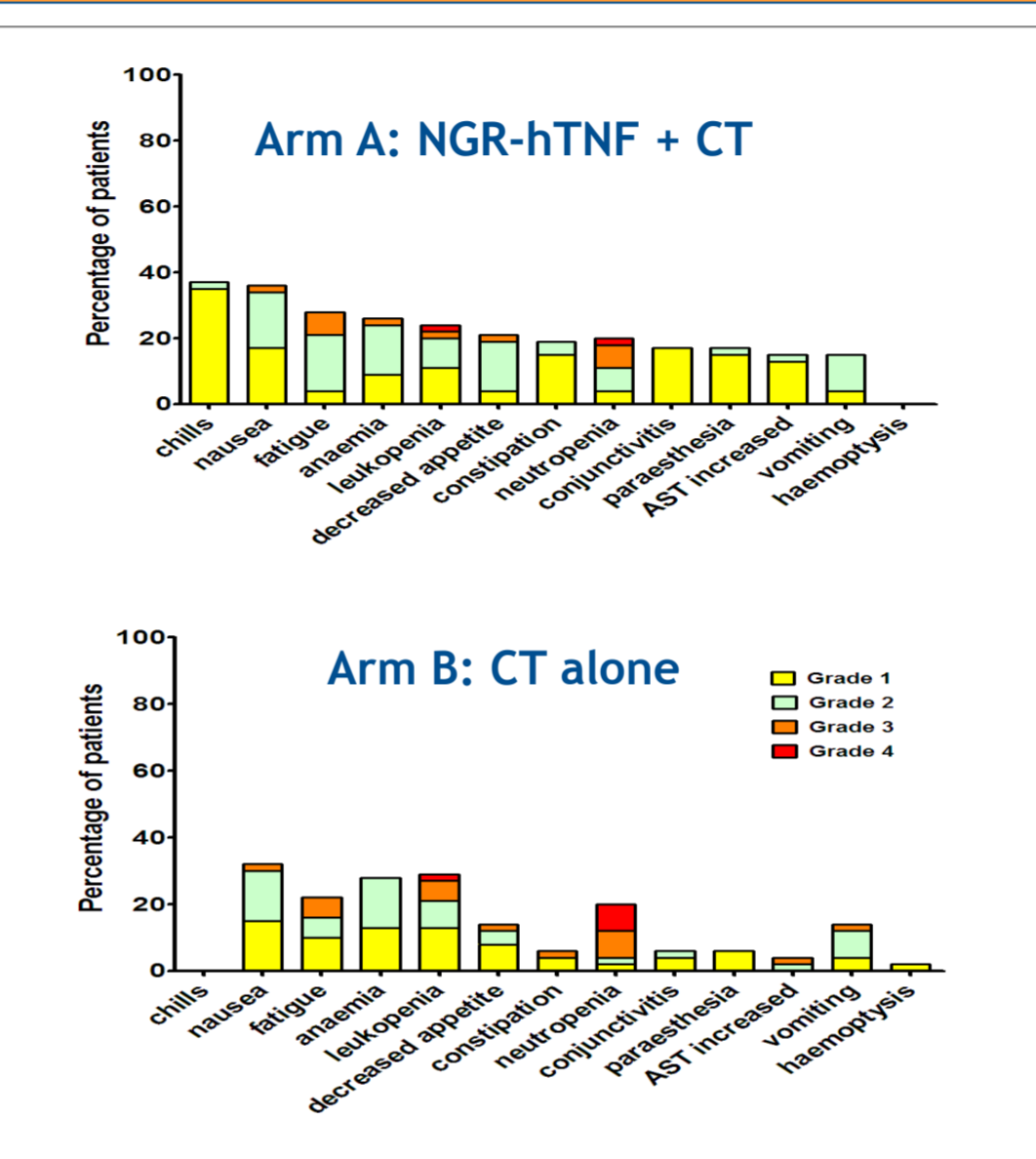
All patients	CT + NGR-hTNF n=40	CT n=40
<b>Age</b>		
median, years (range)	62 (38-74)	62 (38-77)
25th percentile, years	58	58
75th percentile, years	67	67
<b>Gender</b>		
male	23 (57%)	26 (65%)
female	17 (43%)	14 (35%)
<b>ECOG PS</b>		
0	25 (63%)	26 (65%)
1	15 (37%)	14 (35%)
<b>Histologic subtype</b>		
Squamous	10 (25%)	11 (27%)
Adenocarcinoma (+ large cell)	30 (75%)	29 (73%)

## Treatment exposure

All patients	CT + NGR-hTNF n=40	CT n=40
<b>Total # cycles</b>	233	170
median (range)	5 (1-18)	4.5 (1-6)
mean	5.9	4.3
patients with ≥ 6 cycles (%)	18 (45)	17 (42)
<b>Adenocarcinoma</b>	CT + NGR-hTNF n=30	CT n=29
<b>Total # cycles</b>	176	132
median (range)	4.5 (1-18)	5 (1-6)
mean	5.9	4.5
patients with ≥ 6 cycles (%)	12 (40)	13 (45)
<b>Squamous</b>	CT + NGR-hTNF n=10	CT n=11
<b>Total # cycles</b>	57	38
median (range)	5.5 (2-11)	3 (1-6)
mean	5.7	3.4
patients with ≥ 6 cycles (%)	4 (40)	4 (36)

## Results

### Adverse events by treatment arm

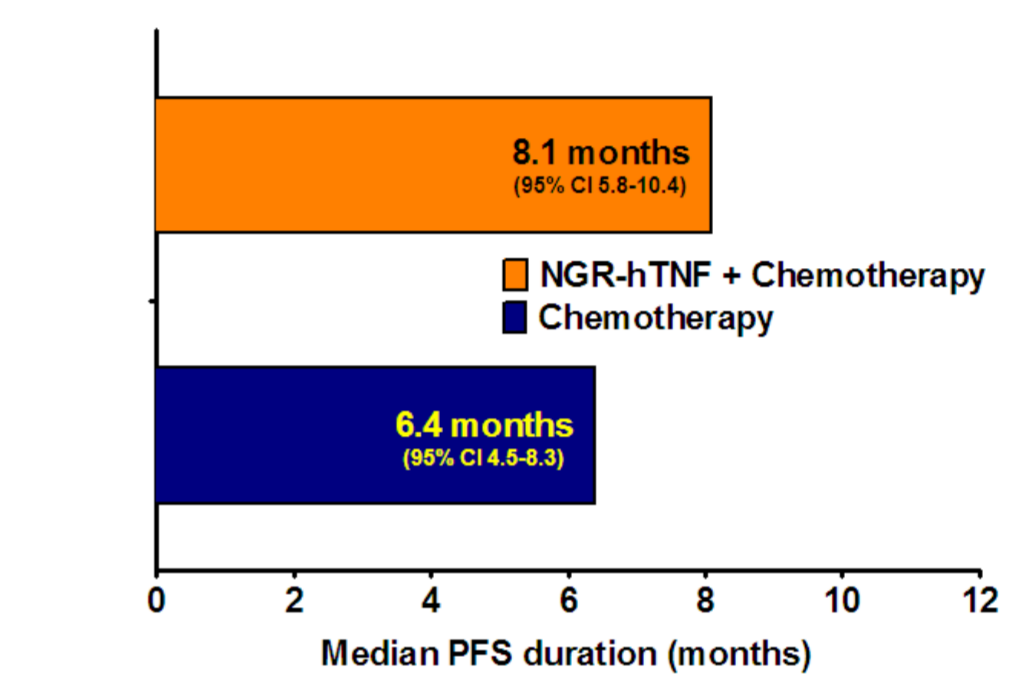


## Conclusions

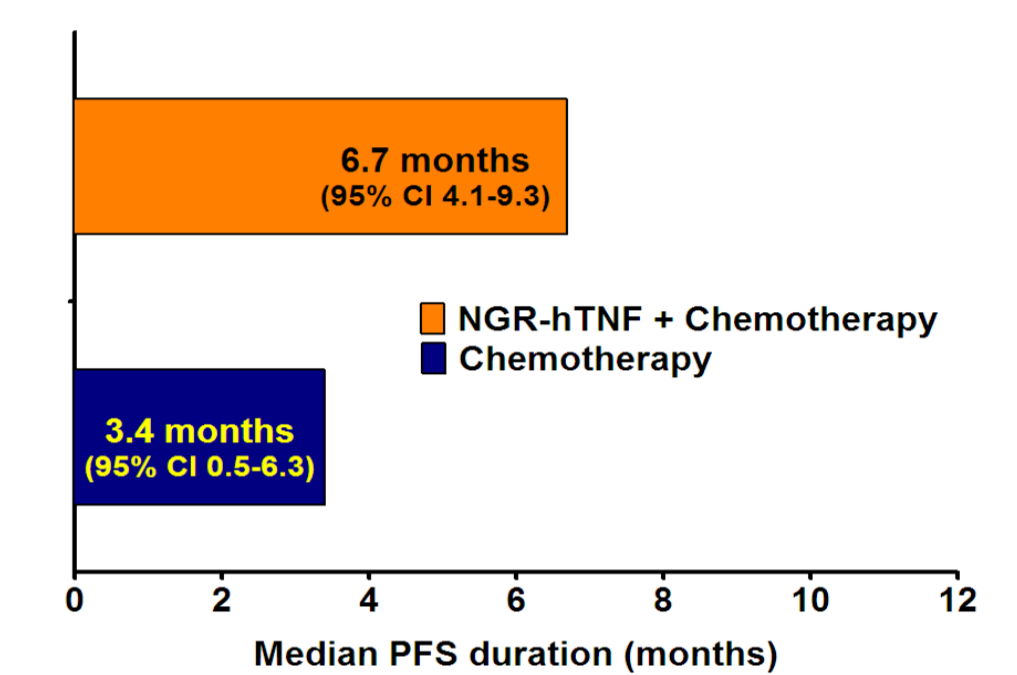
- Regardless of histology, NGR-hTNF was well tolerated in combination with both chemotherapy regimens, cisplatin plus pemetrexed and cisplatin plus gemcitabine
- There were no pulmonary hemorrhage or bleeding events, which have been associated with use of antiangiogenic agents in patients with squamous cell histology
- Preliminary results showed promising antitumor activity of NGR-hTNF plus chemotherapy compared to chemotherapy alone either in patients with squamous cell histology or in patients with adenocarcinoma continuing NGR-hTNF as maintenance after completing 6 cycles of chemotherapy

### Subset analysis in patients with nonsquamous histology

PFS in patients completing 6 cycles and continuing NGR-hTNF as maintenance

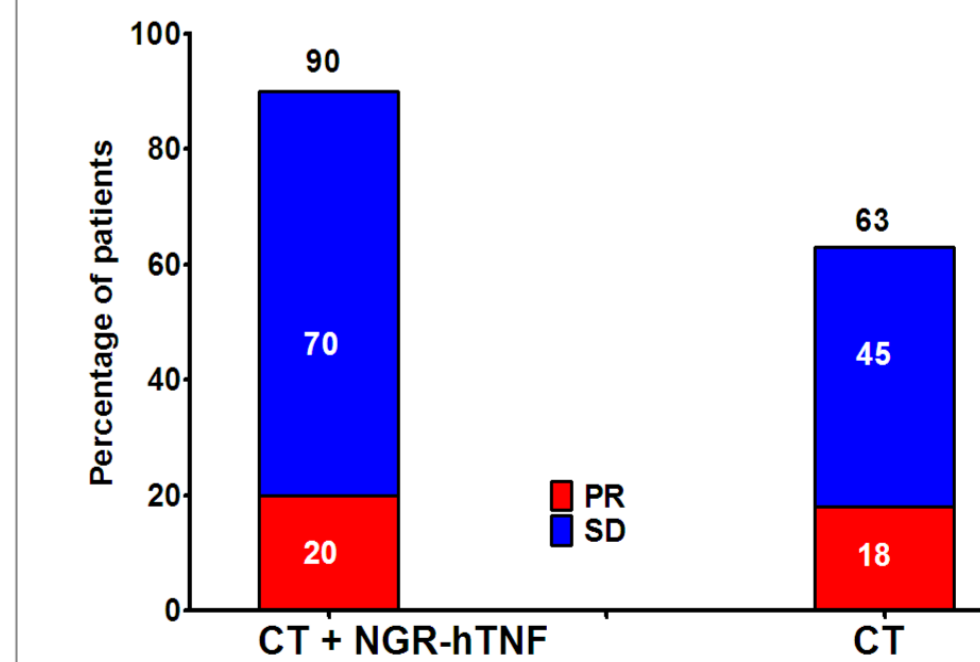


PFS in younger patients (<25th percentile, 58 years)

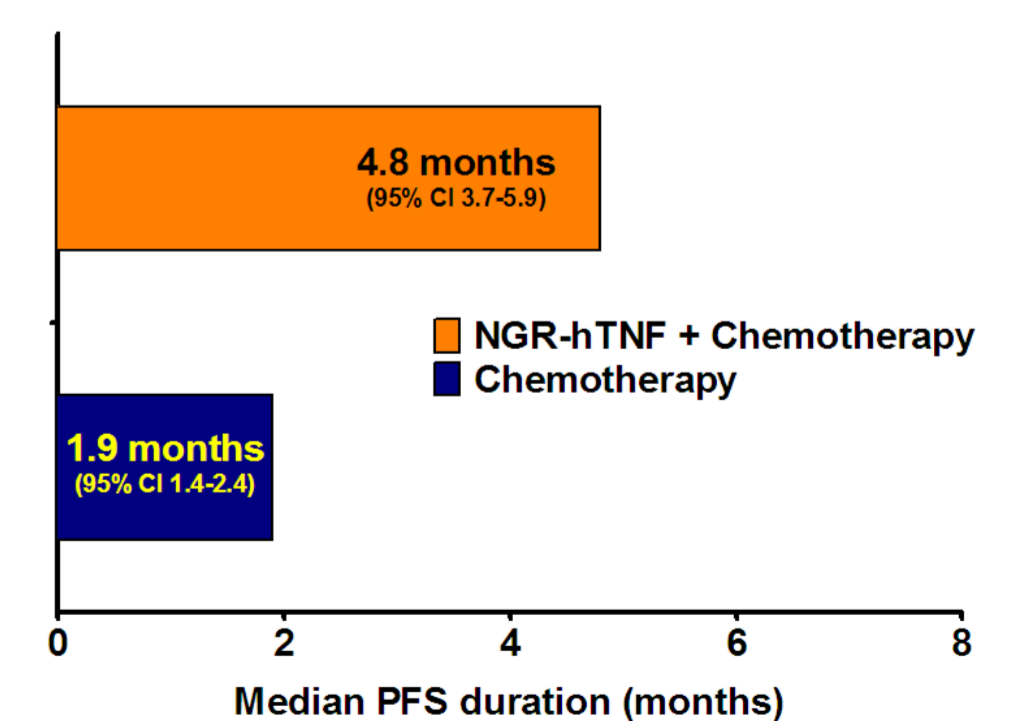


### Subset analysis in patients with squamous cell histology

Disease control rate



Progression-free survival



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### Acknowledgements (MolMed)

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