

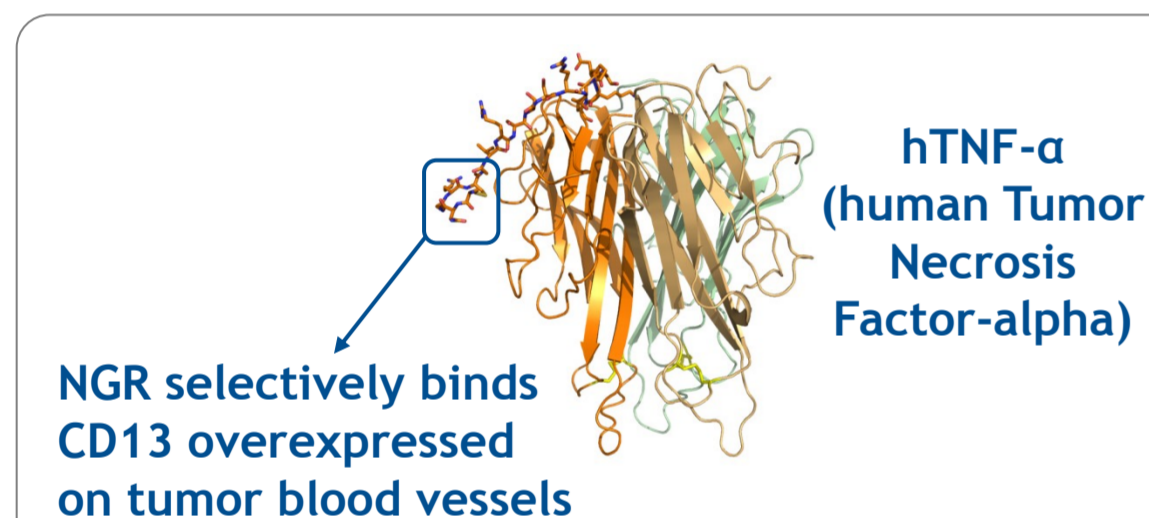
Phase II trial of NGR-hTNF and doxorubicin in relapsed small-cell lung cancer (SCLC)

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Background and methods

- Tumor necrosis factor-alpha (TNF-α) showed powerful preclinical antitumor activity, but its clinical use was hampered by severe toxicity¹
- NGR-hTNF consists of TNF-α fused with the tumor homing peptide NGR (asparagine-glycine-arginine)²⁻⁴
- Maximal synergism achieved with 2-hour delay between low-dose NGR-TNF and doxorubicin dosing²⁻³
- Low-dose NGR-TNF increased both number of tumor cells reached by doxorubicin and intracellular amount of doxorubicin³
- In phase I trial, NGR-hTNF 0.8 μg/m² plus doxorubicin 75 mg/m² was selected for phase 2 trial and showed favorable tolerability and promising activity⁴



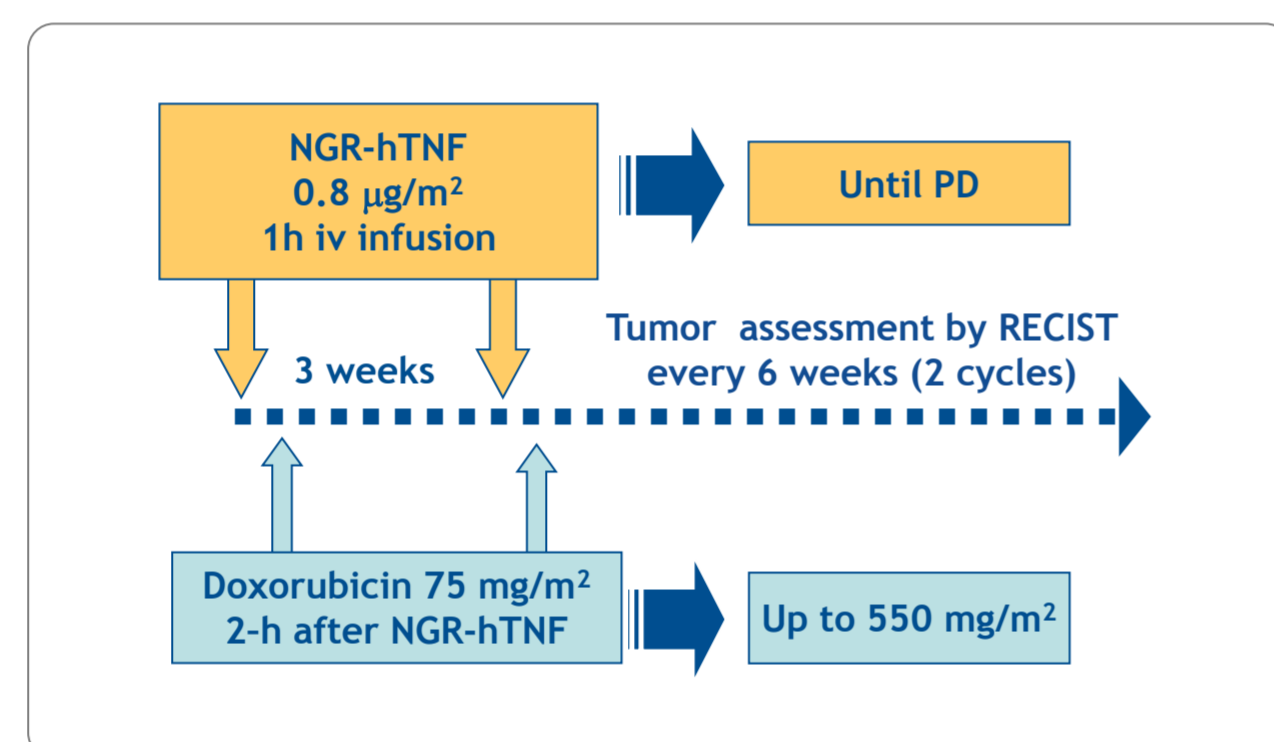
- Despite initial responsiveness to chemotherapy, SCLC is characterized by a rapid progression and short survival
- Patients who progress while receiving first-line therapy or within 3 months of its completion have refractory/resistant disease
- Patients who progress after more than 3 months from completion of first-line therapy have sensitive-relapsed disease

Conclusions

- The combination of NGR-hTNF and doxorubicin can be safely given in relapsed SCLC patients
- NGR-hTNF plus doxorubicin showed evidence of activity, which was weakly correlated with prior platinum sensitivity
- Low baseline NLR strongly associated with improved survival in both platinum-resistant and platinum-sensitive patients
- Further development of this combination is of interest

Study design

- Multicenter, single-arm phase II trial
- Two-stage accrual design
 - 16/27 patients after first/second stage
- Primary endpoint: PFS
- Key inclusion criteria
 - age ≥ 18 years
 - ≥ 1 prior systemic regimen
 - PS 0-2 and LVEF ≥ 55%



Baseline characteristics (n=28)

Median age in years (range)	63 (41-76)
Gender	
male	19 (68%)
female	9 (32%)
ECOG performance status	
0	13 (46%)
1-2	15 (54%)
Prior number of regimens	
1	20 (71%)
2-3	8 (29%)
Best response to prior therapy	
complete + partial responses	13 (46%)
stable + progressive diseases	15 (54%)
Sensitivity to platinum therapy	
refractory/resistant	16 (57%)
sensitive-relapsed	12 (43%)

References

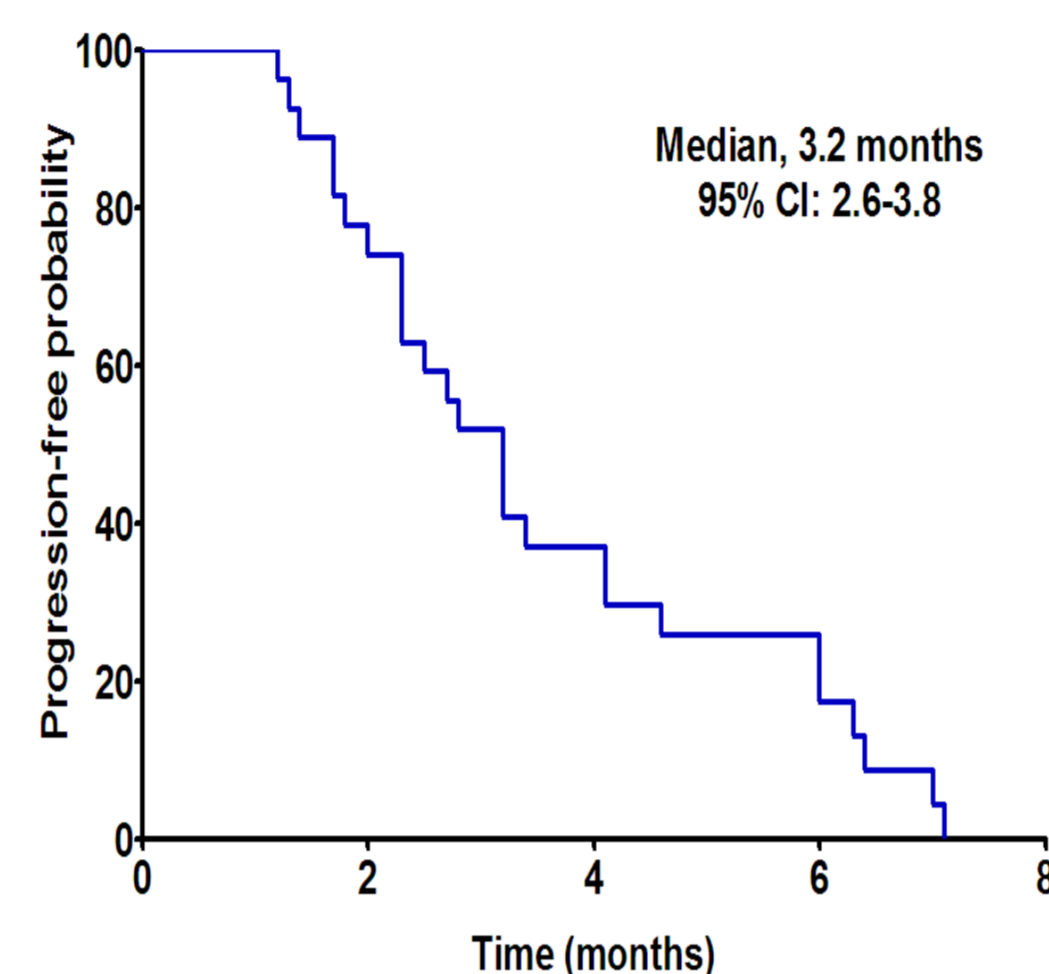
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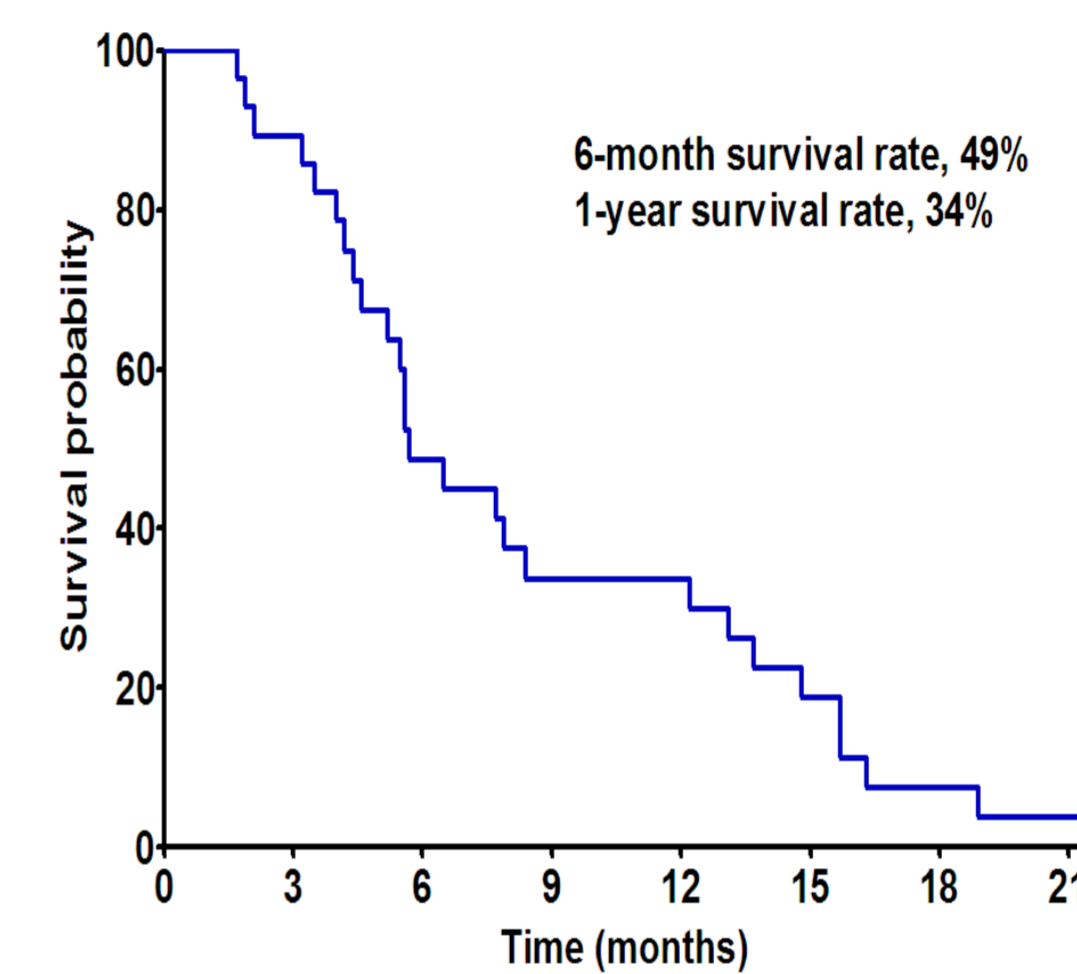
Results

Progression-free survival



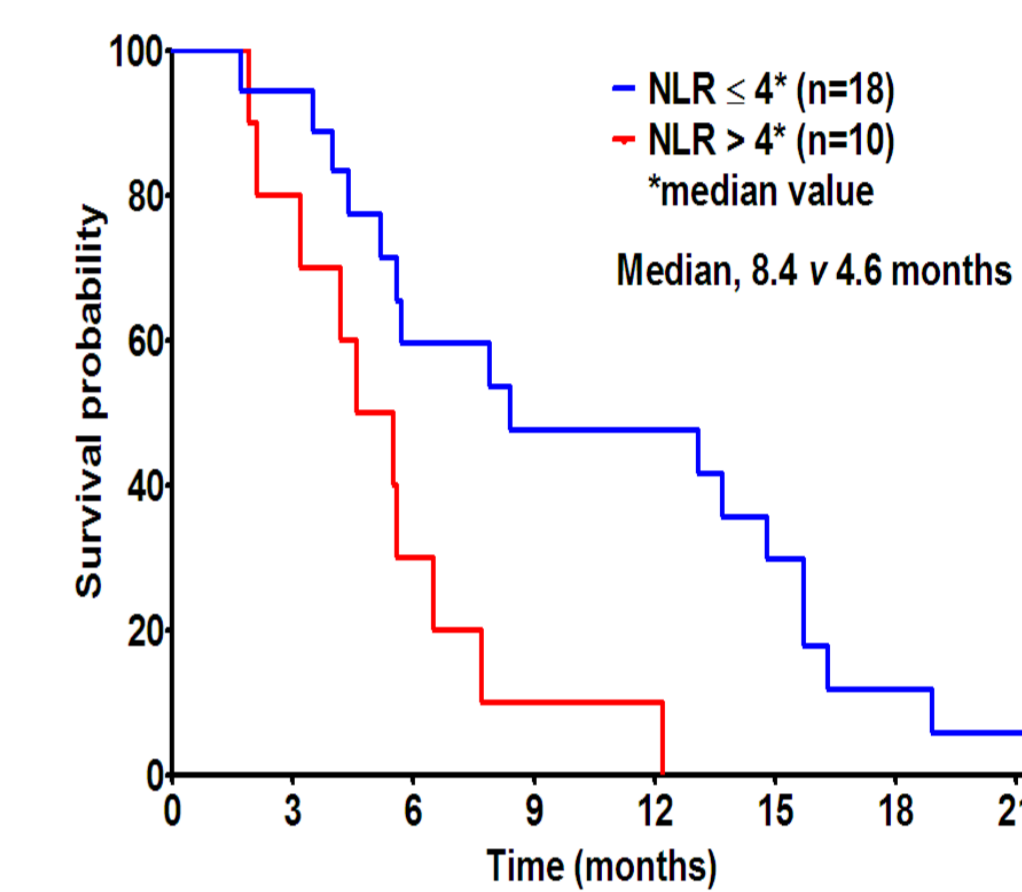
- Median PFS in patients with:
 - partial response (n=6): 6.3 months
 - stable disease (n=9): 4.1 months
 - disease control (n=15): 4.6 months

Overall survival



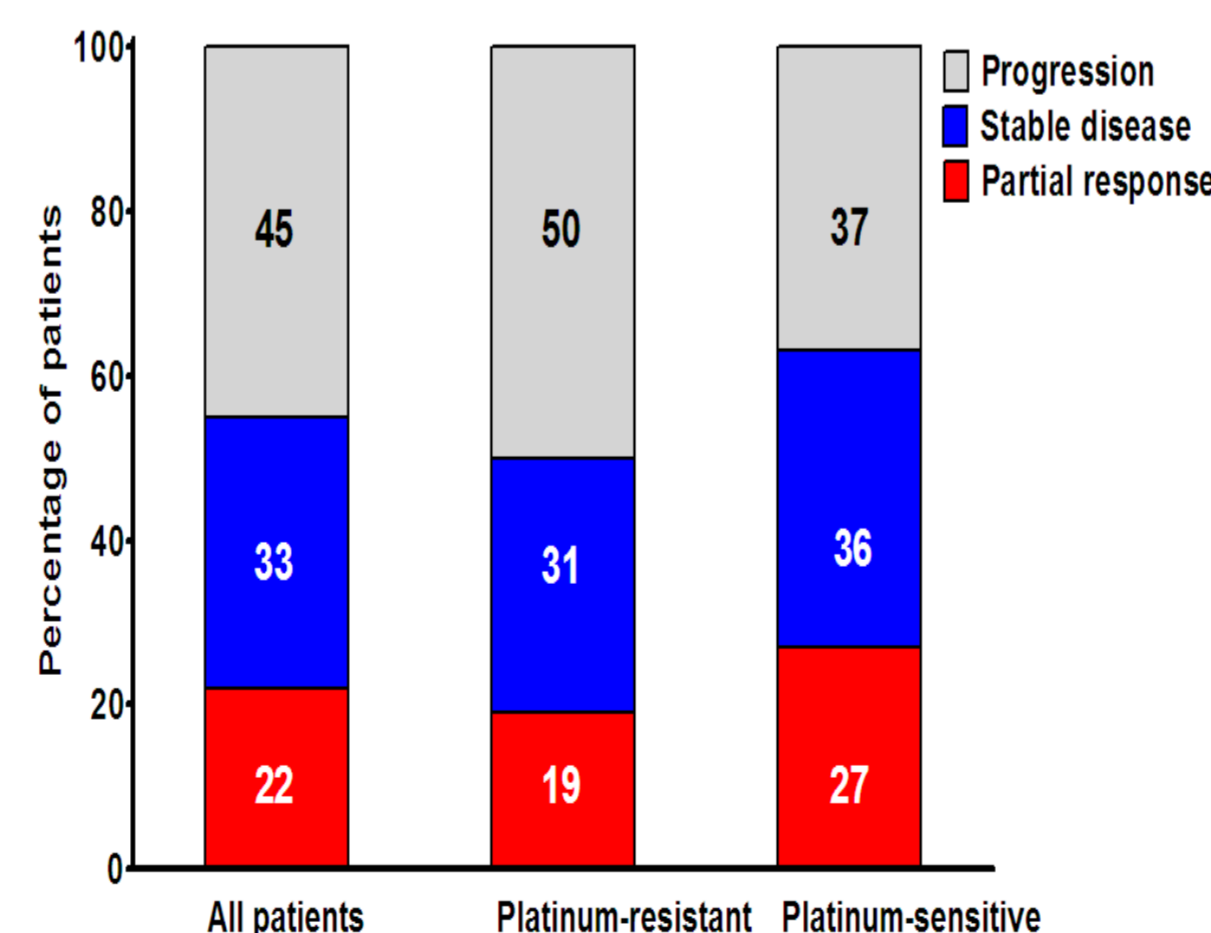
- By univariate Cox analyses, only baseline neutrophil-to-lymphocyte ratio (NLR)⁵ associated with OS (HR=0.30; p=0.01)

Overall survival by baseline neutrophil-to-lymphocyte ratio (NLR)

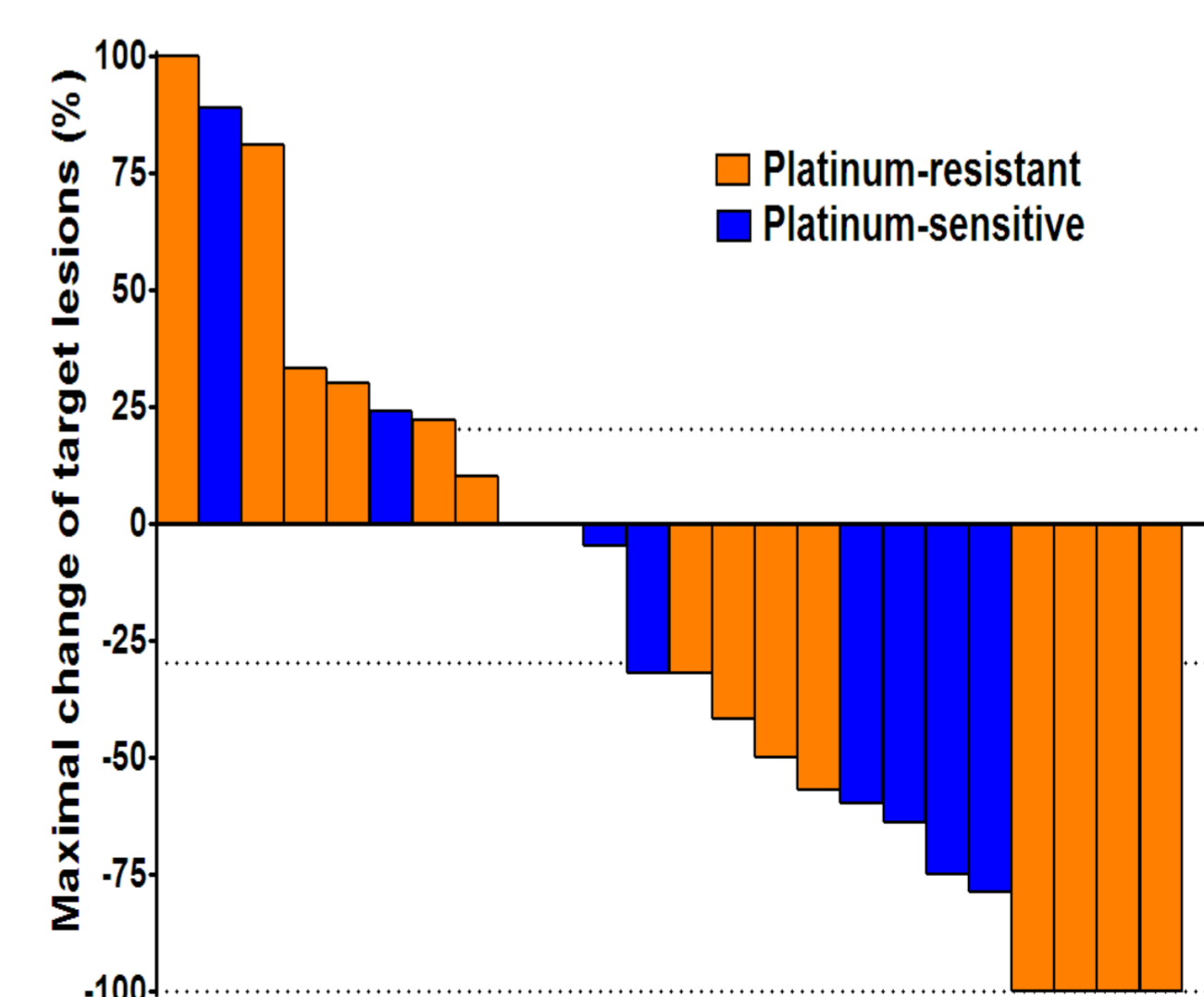


- Median OS in patients with NLR ≤ 4 and:
 - refractory/resistant (n=10): 8.4 months
 - sensitive-relapsed (n=8): 7.9 months

Best response by platinum-sensitivity



Waterfall plot by platinum-sensitivity



PFS and OS by platinum-sensitivity

