Impact of treatment free interval (TFI) and disease control rate (DCR) on survival outcome in relapsed malignant pleural mesothelioma (MPM)

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Background and methods
• TFI (time elapsing from end of first-line to start of second-line therapy) has been expected to predict subsequent outcomes in some tumor types, including MPM.
• We tested whether TFI and DCR (the non-progression rate at first tumor evaluation) predict overall survival (OS) by a pooled analysis of 447 MPM patients who had failed a platinum-based first-line regimen and were treated with NGR-HIVTP alone (n = 345); parallel or gemcitabine, vincristine, or doxorubicin with or without cisplatin (pooled n = 102).
• Tumor response was assessed every 4 weeks by RECIST and was categorized as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD).
• Outcomes for TFI in relation to OS was set at the median (4.7 months; 95% CI 3.8-5.3).
• Hazard ratio (HR) for OS was derived from regression models adjusted for baseline risk factors (age, sex, PS, histology, EORTC score, best response to prior therapy, neutrophil-to-lymphocyte ratio (NLR)).

Methodology
- NLR was calculated as the ratio of the absolute neutrophil count to the absolute lymphocyte count.
- TFI was defined as the interval between the end of first-line chemotherapy and the start of second-line therapy.
- DCR was defined as the non-progression rate at first tumor evaluation.
- OS was defined as the interval from the start of first-line chemotherapy to the date of death or last follow-up.

Results
- Median TFI was 4.7 months (95% CI 3.8-5.2).
- Median OS was 15.8 months (95% CI 12.8-17.5).
- Median OS was longer for patients with TFI of >4.7 months compared to those with TFI of ≤4.7 months (p = 0.0001).
- Median OS for patients with DCR was 21.9 months (95% CI 18.7-25.0) compared to 15.8 months (95% CI 12.8-17.5) for patients without DCR (p = 0.0001).
- Median OS for patients with TFI >4.7 months and DCR was 27.6 months (95% CI 21.8-33.3) compared to 15.8 months (95% CI 12.8-17.5) for patients with TFI ≤4.7 months and DCR (p = 0.0001).

Conclusions
- A short TFI independently predicted worse survival outcome, and identified a patient population with increased disease aggressiveness and chemoresistance.
- Recently, in the NGR105 phase III trial, NGR-HIVTP provided clinically meaningful benefit to these resistant patients, significantly improving OS, PFS and DCR.

References