Background and methods

Treatment-free interval (TFI) after first-line therapy as a prognostic and predictive factor in malignant pleural mesothelioma (MPM): Findings from the NGR015 phase 3 trial with NGR-hTNF versus placebo plus BIC

Results of the phase 3 trial NGR015

<table>
<thead>
<tr>
<th>TFI</th>
<th>Median OS (months)</th>
<th>PFS on prior therapy (median, 5.8 months)</th>
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<tbody>
<tr>
<td>Short TFI</td>
<td>6.3</td>
<td>15.7</td>
<td>10.2</td>
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<tr>
<td>Long TFI</td>
<td>11.7</td>
<td>1.81</td>
<td>10.2</td>
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Results and conclusions

- **Poor prognostic effects of short TFI**
  - Median OS (months): Short TFI (6.3) vs Long TFI (11.7), p<0.0001
  - PFS on prior therapy (months): Short TFI (15.7) vs Long TFI (1.81), p<0.0001

- **Continuous TFI data were independently related to OS (p=0.0001)**. In comparison with patients with a long TFI, those with a short TFI have been found to experience a significantly worse OS. Poor prognostic effects of short TFI in agreement with LDH and NLR levels, reported to indicate an elevated tumor hypoxia/angiogenesis and poor prognosis.

- **High levels of serum LDH have been reported to indicate an augmented tumor hypoxia/angiogenesis** (as evaluated by high baseline serum LDH levels).

- **Patients with a short TFI subset achieved statically increased median OS levels**: HR for OS was 0.56 (p=0.001) with TFI levels: HR for PFS was 0.56 (p=0.001) with TFI levels.

- **Consistently, similar differences in outcome were noted in the TFI population with high LDH and lymphocytes)**, with a median OS of 10.9 months for NGR-hTNF vs 6.6 months, p=0.12 (4.1 vs 2.6 months, p=0.03; median OS, 10.9 months for NGR-hTNF vs 6.6 months, p=0.12).

- **Multivariate HR**
  - Short TFI (1.30 - 2.52) vs Long TFI (1.81 - 2.89), p<0.0001
  - Adjusted for age, sex, performance status, histology, EORTC score, best response to prior therapy and NLR

- **High baseline blood lymphocyte counts** have been found to predict improved outcomes after NGR-hTNF combined with chemotherapy.

- **In the short TFI subset, the magnitude of NGR-hTNF effects was further increased in patients exhibiting LDH and lymphocytes > first quartile, with a median OS for NGR-hTNF plus BIC more than double that for placebo plus BIC (p=0.001)**.

- **Consistently, similar differences in outcome were noted in the TFI population with high LDH and lymphocytes (n=198; median PFS, 4.1 vs 2.6 months, p=0.03; median OS, 19.3 vs 6.6 months, p=0.12)**.

References

5. ASCO 2015 Abs 7501 oral
6. ASCO 2013 Abs 3038 poster
7. ASCO 2015 Abs 3004 poster

Results from the NGR015 phase 3 trial with NGR-hTNF plus best investigator choice (BIC) versus placebo plus BIC

<table>
<thead>
<tr>
<th>TFI</th>
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