A plasma proteomic signature predicts outcomes in a Phase 3 study of gemcitabine (G) + cisplatin (C) ± sorafenib in first line stages IIIb or IV non-small cell lung cancer (NSCLC).

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Introduction

- NEUSS trial: Phase 3 study of sorafenib in combination with gemcitabine (G) plus cisplatin (C) versus placebo plus G+GC (GC) in first line non-small cell lung cancer (NSCLC) patients.
- Small statistically significant improvement in progression-free survival (PFS) for sorafenib + GC (HR=0.83, 95% CI 0.71, 0.97, p=0.008).
- No improvement in overall survival (OS).

- VeriStrat® (VS) is a commercial test using Matrix Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry which classifies serum or plasma samples as VeriStrat Good (VS Good) or VeriStrat Poor (VS Poor) based on an 8-peak proteomic mass spectral signature.
- VS identifies advanced NSCLC patients likely to have good or poor outcomes following epidermal growth factor receptor tyrosine kinase inhibitor therapy.
- OBJECTIVE: Retrospective study of plasma samples collected in the NExUS study to determine if VS classification is predictive of sorafenib + GC clinical activity.

Methods

- NEUSS trial design:
  - Stage IIIb or IV NSCLC, predominantly non-squamous histology, ECOG performance status (PS) 0 or 1.
  - Randomized 1:1 to receive G (1250 mg/m2 on days 1 and 8) and C (75 mg/m2 on day 1) for up to six 21-day cycles, in combination with sorafenib 400mg bid or placebo until disease progression or toxicity.
- Retrospective VS Analysis:
  - Only patients with non-squamous histology.
  - All available baseline plasma samples analyzed.
  - Analysis blinded to all clinical outcomes, using the fully-locked standard VS test.
  - PFS and OS were compared by treatment arm and proteomic classification.
- Hazard ratios (HRs) and Kaplan-Meier curves evaluated, multivariate Cox proportional hazards analysis, including evaluation of predictive value of VS; performed by independent statistician.

Results

- Baseline plasma samples available for VS analysis from 419 patients of the 772 non-squamous NSCLC patients enrolled in NEUSS.
  - 276 (66%) samples classified as VS Good, 127 (30%) as VS Poor and 16 (4%) as an equivocal indeterminate status.
  - The 403 patients with samples classified as VS Good or Poor were included in the outcome analyses.
- No significant difference in outcome by treatment arm between patients with or without assigned VS classification (interaction p = 0.11 and 0.45 for PFS and OS respectively).

Univariate Analysis of PFS

- Among patients treated with placebo+GC, the VS Good group had significantly better PFS than the VS Poor group (HR=0.51 [95% CI: 0.37-0.71], p < 0.001), Figure 1A.
- Among patients treated with sorafenib+GC, there was no statistically significant difference in PFS between VS groups (HR=0.82 [95% CI: 0.60-1.13], p = 0.227), Figure 1B.
- Patients with VS Poor status had significantly better PFS in the sorafenib+GC arm compared with the placebo+GC arm (HR=0.63 [95% CI: 0.42-0.93], p = 0.019), Figure 1C.
- Patients with VS Good status had similar PFS for both treatment arms (HR=1.06 [95% CI: 0.83-1.35], p = 0.628), Figure 1D.
- Smoking History Never (N=150) 107 (71%) 56 (36%) 0.048
- Smoking History Ever* (N=332) 220 (66%) 112 (34%) 0.048

Table 1. Patient Characteristics by Proteomic Classification

<table>
<thead>
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<th>Proteomic Classification</th>
<th>VS Good</th>
<th>VS Poor</th>
<th>p value</th>
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<tr>
<td>Gender</td>
<td>Male (N=253)</td>
<td>169 (67%)</td>
<td>84 (33%)</td>
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<tr>
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<td>Female (N=150)</td>
<td>107 (71%)</td>
<td>43 (29%)</td>
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<tr>
<td>Smoking History</td>
<td>Never (N=177)</td>
<td>58 (75%)</td>
<td>51 (25%)</td>
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<tr>
<td></td>
<td>Ever* (N=332)</td>
<td>220 (66%)</td>
<td>112 (34%)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td>0 (N=170)</td>
<td>127 (75%)</td>
<td>43 (25%)</td>
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<tr>
<td></td>
<td>1 (N=233)</td>
<td>149 (64%)</td>
<td>84 (36%)</td>
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<tr>
<td>Stage</td>
<td>IIIb (N=45)</td>
<td>40 (67%)</td>
<td>15 (33%)</td>
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<td></td>
<td>IV (N=358)</td>
<td>246 (69%)</td>
<td>112 (31%)</td>
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<tr>
<td>Ethnicity</td>
<td>Asian</td>
<td>43 (67%)</td>
<td>7 (14%)</td>
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<td></td>
<td>Non-Asian</td>
<td>233 (66%)</td>
<td>120 (34%)</td>
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<tr>
<td>Age</td>
<td>Median Range</td>
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<td>60</td>
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<td>25-78</td>
<td>35-77</td>
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</tbody>
</table>

* Ever smoker = Past, present, or passive smoker.

Conclusions

- VS Good status is associated with better prognosis in first-line NSCLC patients treated with placebo+GC.
- VS Poor patients benefit significantly in terms of PFS from the addition of sorafenib rather than placebo to GC.
- VS test is predictive. VS Poor patients attain significantly more benefit in PFS from the addition of sorafenib rather than placebo to GC than do VS Good patients.

References: