Response to capmatinib in patients (pts) with advanced non-small cell lung cancer (NSCLC) and MET exon 14 skipping (METex14) mutation: Whole transcriptome analysis from Phase 2 GEMETRY Mono-1 study

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This study is funded by Novartis

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Figure 1. MET and PD-L1 gene expression and response to capmatinib

Figure 2. Baseline MET and PD-L1 gene expression

Figure 3. PFS and OS in MET low/high subgroups

Figure 4. PFS and OS in PD-L1 high/low subgroups

Table 1. GES analysis

<table>
<thead>
<tr>
<th>Gene</th>
<th>Odds ratio†</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET</td>
<td>1.74</td>
<td>1.08–2.72</td>
<td>0.19</td>
</tr>
<tr>
<td>CD74</td>
<td>0.03</td>
<td>0.00–0.60</td>
<td>0.01</td>
</tr>
</tbody>
</table>

†Odds ratio derived from logistic regression model including MET expression

METHODS

• Patients enrolled in the GEMETRY mono-1 study received oral capmatinib 400 mg twice daily.

• Baseline tumour samples were collected and analysed from both treatment-naïve (recruiting patients in the first line, [1L]) and previously treated (recruiting patients in second or third line [2/3L]) patients with METex14 NSCLC.

• The RNAseq libraries were prepared using the TruSeq RNA v2 Library Preparation kit (Illumina).

• RNAseq data were normalised using trimmed mean of 2500 and counts per million reads (CPM).

RESULTS

• Baseline tumour biopsies from 100 of the 160 enrolled METex14 NSCLC patients were successfully profiled by RNAseq.

• 41/60 libraries from patients who received capmatinib in 1L, and 59/103 libraries from patients who received capmatinib in 2/3L.

• In both 1L (Figure 1A) and 2/3L (Figure 1B), there was a trend towards higher MET expression in patients with response.

• PD-L1 expression levels were not found to be significantly different between responders and non-responders in 1L (Figure 1C) and 2/3L (Figure 1D).

• Among patients receiving capmatinib in 1L, those with high MET expression had significantly longer PFS (Figure 2A).

• There was no significant difference in PFS among patients receiving capmatinib in 2/3L based on MET expression (Figure 2B).

• Among patients receiving capmatinib in 1L, those with high PD-L1 expression had significantly longer OS (Figure 2C).

• There was no significant difference in OS among patients receiving capmatinib in 2/3L based on PD-L1 expression levels (Figure 2D).

• There was no difference in PFS based on PD-L1 expression levels in patients receiving capmatinib in 1L (Figure 3A, 3B), and 2/3L (Figure 3C).

• A non-significant trend towards longer OS was observed in patients with high PD-L1 expression in both 1L (Figure 4C) and 2/3L (Figure 4D).

Study Limitations

• Differences in characteristics or response for patients with vs without valid NGS data were not formally compared in this analysis.

• With a relatively small sample size, these results should be validated in a larger study.

ACKNOWLEDGEMENTS

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DISCLOSURES

• Prof. Wolf reports personal fees from Amgen, AstaVera, Bayer, Blueprint, Boehringer-Ingelheim, Chugai, Daiichi-Sankyo, Ignyte, Lilly, Merck, MSD, Roche, Seattle-Genetics, and Teclis; grants and personal/familial fees from BDMA, Genentech, ResMed, and Pfizer.

REFERENCES


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BACKGROUND AND RATIONALE

• METex14 is an oncogenic driver mutation that occurs in approximately 3–4% of patients with NSCLC, typically in the absence of other driving mutations, and is associated with poor prognosis.1

• A recent large-scale analysis showed that expression levels of MET, programmed death-ligand 1 (PD-L1), and gene expression signatures (GES) associated with IFN-γ and T-cell infiltration were significantly higher in the METex14 versus MET wildtype (WT) tumour gene expression trends.2

• Capmatinib is a highly selective and potent MET signalling inhibitor.1

• The GEMETRY mono-1 (NCT02414139) investigated the efficacy of capmatinib in patients with advanced NSCLC and MET exon 14 skipping (METex14) both previously treated and treatment-naïve patients.2

• Capmatinib demonstrated efficacy and safety in patients with NSCLC with METex14, including those with brain metastases.3

• Here, we report a whole transcriptomes analysis of METex14 NSCLC tumour samples collected at baseline from patients who were treated with capmatinib in the GEMETRY mono-1 study.

KEY FINDINGS AND CONCLUSIONS

• GEMETRY mono-1: A phase 1 study demonstrated efficacy and safety of capmatinib in patients with METex14 NSCLC, resulting in global approval.

• This was an exploratory whole transcriptomic analysis of baseline tumour gene expression and an unbiased GES analysis, including T-cell infiltration (GES IFN-γ).3

• High MET expression was associated with better response to treatment and was significantly associated with longer PFS and OS in patients receiving capmatinib in 1L, but was not significantly associated with response to capmatinib in 2/3L.

• PD-L1 gene expression showed no association with response to capmatinib in either 1L or 2/3L patient samples.

• MET gene expression was the only independent RNA pattern that was significantly associated with tumour response in unbiased GES and subsequent multivariate analyses.