**Background**

- Prior treatment with KIT/PDGFR
- Pts with advanced refractory cancers (KIT/PDGFRA mutated) with a focus on GIST.
- Tumor biopsy analysis: Tumor DNA extracted from formalin-fixed paraffin-embedded
- Tumor assessment: CT scans every 2 month cycles per local assessment.

**Methods**

- Phase 1 dose-escalation study of oral DCC-2618 in 28-day cycles (daily doses of 20
- Identifying KIT/PDGFR

**Results**

- 100 pts at 150 mg QD was recently presented (Janku et al, AACR 2018).

**Conclusions**

- In addition to KIT/PDGRA, other mutations such as IDH2, RB1, TP53, were detected in

**Table 1: Baseline Demographics of GIST Patients Receiving >100 mg/d (n=54)**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Median (Min, Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-60</td>
<td>59 (50, 60)</td>
</tr>
<tr>
<td>61-70</td>
<td>65 (61, 70)</td>
</tr>
</tbody>
</table>

**Table 2: Mutation Detection by ctDNA (n=136) and Tumor Biopsy (n=97)**

<table>
<thead>
<tr>
<th>Exon 13 (%)</th>
<th>Exon 14 (%)</th>
<th>Exon 17 (%)</th>
<th>Exon 18 (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35(33%)</td>
<td>55(57%)</td>
<td>40(40%)</td>
<td>45(45%)</td>
<td>136(90%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exon 13 (n)</th>
<th>Exon 14 (n)</th>
<th>Exon 17 (n)</th>
<th>Exon 18 (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>29(29)</td>
<td>54(54)</td>
<td>29(29)</td>
<td>36(36)</td>
<td>136(90%)</td>
</tr>
</tbody>
</table>

**Table 3: KIT Mutations in Baseline Biopsy (n=81) and ctDNA (n=95)**

- KIT mutations in Exons 13, 14, 17, 18 were detected by tumor biopsy or ctDNA at baseline and counted by each exon. Some patients had multiple mutations within one exon.
- No correlation was observed between the sum of the longest diameter of the target lesions and ctDNA shedding.
- Long-term KIT ctDNA negativity on treatment was observed in pts with prolonged stable disease.
- 57 pts (78%) achieved a reduction in KIT MAF of more than 50%.
- In 10 pts, KIT mutations were not detected at any time point. 1 pt has an exon unsuitable and one MAF at less than 0.5%.

**Table 4: Objective Response of 2nd and 3rd Line Pts at >100 mg/d (n=54)**

<table>
<thead>
<tr>
<th>Line Of Therapy</th>
<th>Pts</th>
<th>DCR</th>
<th>ORR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd Line</td>
<td>25</td>
<td>92%</td>
<td>79%</td>
</tr>
<tr>
<td>3rd Line</td>
<td>24</td>
<td>64%</td>
<td>21%</td>
</tr>
</tbody>
</table>

**Figure 1: KIT Mutations in Baseline Tissue DNA (n=95) in 100 GIST pts**

- Each column represents an individual pt.
- In pts where a KIT mutation was detected in baseline ctDNA, secondary KIT mutations in exons 13, 14 and 17 were found to be 24% and 18% of total ctDNA.

**Figure 2: Spaghetti Plot of 2nd and 3rd Line Pts at >100 mg/d (n=54)**

- In pts with detectable KIT mutations by ctDNA at baseline, 35 pts became KIT ctDNA negative (MaF is below detection limit). I.e. MaF <0.05% at treatment at least one time point. 8 pts are Pts and 24 pts have no ctDNA detected.
- In 10 pts at baseline and 8 pts became non-detectable after treatment; 1 pt has an exon unsuitable and one MAF at less than 0.5%.
- In 1 pt (Exon 11 and 13) does not have any post treatment sample.
- In 1 pt (C6D1 only) followed until C7D1.
- In 10 pts, KIT mutations were not detected at any time point.
- Long-term KIT-cDNA negativity on treatment was observed in pts with prolonged stable disease (shown in Figure 3). Clear ctDNA patterns at disease progression were not observed.

**Figure 3: Spaghetti Plot of 2nd and 3rd Line Pts at >100 mg/d (n=54)**

- The GIST pts in this study are one of the largest prospective cohorts of ctDNA from liquid biopsies to be analyzed by NGS and compared with tumor tissue data.
- The mutational profile of KIT in tumors and plasma at baseline in GIST pts supports the need for a broad spectrum KIT inhibitor in all post-imatinib lines of therapy.
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