Detection of Endoglin-Expressing CTCs in Patients Enrolled in an Adaptive Enrichment Phase 3 Trial of TRC105 And Pazopanib versus Pazopanib alone in Patients with Advanced AngioSarcoma (TAPPAS)

INTRODUCTION

• TRC105 is a chimeric IgG1 endoglin monoclonal antibody with high avidity (Kd = 5 pM) that inhibits angiogenesis (Seon 2011, Nolan 2011, Kollar A, CTOS 2016, 1999)
• Endoglin is densely expressed on angiosarcoma (Fritchie K, EORTC 2012), and endoglin expression is associated with poor prognosis (Parallel 2011)
• TRC105 combined with pazopanib demonstrated encouraging activity in angiosarcoma patients, including durable CRs by RECIST 1.1, improved PFS compared to prior studies of single agent VEGF pathway inhibitors (Kollar 2016), and superior disease control compared to prior treatment
• The randomized phase 3 TAPPAS study of TRC105 in combination with pazopanib compared to single agent pazopanib in patients with angiosarcoma is designed to detect a hazard ratio of 0.55 for the primacy endpoint of progression free survival, using a two stage method and a two sided alpha of 0.05, with >80% power as the baseline statistical assumption. However, the trial includes an adaptive design that allows for sample size re-estimation or enrichment of cutaneous disease based on an interim analysis
• Circulating tumor cells (CTC) are collected in patients enrolled in TAPPAS at baseline and following six weeks of protocol treatment

METHODS

• CTCs were enriched by ApoStream® from 8 mL whole blood samples drawn prior to treatment, with either pazopanib at 800 mg p.o. daily or pazopanib 800 mg p.o. daily + TRC105 at 10 mg/kg weekly
• Prior cancer therapies 0 vs 1

RESULTS

• Paired samples were available for 51 patients (63% of those enrolled with sufficient time to process paired samples)
• Changes were also tabulated for cases of a CTC increase or decrease by at least two fold and by at least 1 cell/mL from baseline
• Changes were considered significant for a CTC increase or decrease by at least ten fold and by at least 1 cell/mL from baseline
• Significant changes in endoglin+ CTC were observed following treatment with TRC105 + pazopanib and/or single agent pazopanib. Endoglin+DAPI+ CTCs were further characterized as atypical cells using DAPI staining
• Changes were also tabulated for cases of a CTC increase or decrease by at least two fold and by at least 1 cell/mL from baseline
• Significant changes in endoglin+ CTC were observed following treatment with TRC105 + pazopanib and/or single agent pazopanib

CONCLUSIONS

• Significant changes in endoglin+ CTC were observed following treatment with TRC105 and pazopanib and/or single-agent pazopanib
• Baseline endoglin+ CTC and response to treatment will be correlated with efficacy endpoints at the time of final analysis
• The interim analysis to determine the final sample size and study population of the Phase 3 TAPPAS trial is expected in 1Q 2019

Table 1: Summary statistics (Endoglin+ DAPI+ cells/mL)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD105</td>
<td>66.5</td>
<td>1.38</td>
<td>0 - 1172</td>
</tr>
<tr>
<td>CD107</td>
<td>1.30</td>
<td>1.38</td>
<td>0 - 185</td>
</tr>
</tbody>
</table>

Table 2: Summary statistics (Changes in Endoglin+ DAPI+ cells/mL from Baseline)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD105</td>
<td>19/51 (37%)</td>
<td>13/51 (25%)</td>
<td></td>
</tr>
<tr>
<td>CD107</td>
<td>18/51 (35%)</td>
<td>13/51 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Patients With Increases in Total CD105+, DAPI+ Count per mL Blood

Figure 2: Patients With Decreases in Total CD105+, DAPI+ Count per mL Blood

Summary statistics (Changes in Endoglin+ DAPI+ cells/mL from Baseline)

Figure 3: Representative Patient with Increase in Total CTCs

Figure 4: Representative Patient with Decrease in Total CTCs

REFERENCES

Looking for more information on this topic? Visit the author's website or contact them directly for further details. This poster is intended for educational purposes only. Reproduction in any form is not allowed without permission from the author.