A Phase I Study of TRC105 (Anti-CD105 [Endoglin] Antibody) in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

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**Biology of CD105**

- CD105 (endoglin) is a 180 kDa transmembrane protein abundantly expressed on the surface of proliferating vascular endothelial cells
- CD105 expression is required for the formation of new blood vessels
- CD105 expression is increased during hypoxia and protects hypoxic endothelial cells from apoptosis
- CD105 expression releases endothelial cells from the inhibitory effects of TGF-β signaling

**CD105 is essential for angiogenesis**

- CD105 is expressed in developing blood vessels in mice
- Blood vessels develop normally in mice with CD105 knockout

**Tumor MVD assessed with anti-CD105 antibodies correlates with Gleason score, stage, metastasis, proliferative index and survival in prostate cancer**

**TRC105**

- TRC105 is a human/murine chimeric IgG1 kappa monoclonal antibody that binds with high avidity to human CD105 (endoglin) on proliferating endothelial cells
- TRC105 inhibits angiogenesis and tumor growth through inhibition of endothelial cell proliferation, antibody-dependent cellular cytotoxicity and induction of apoptosis

**Objectives**

- Primary objective is to define the maximum tolerated dose of TRC105
- Secondary objectives include assessment of TRC105 pharmacokinetics, PSA response rate, and overall response rate

**Methods**

- Eligibility requires ECOG PS ≤ 2 and progressive mCRPC
- Three cohorts of 3-6 patients receive increasing doses of TRC105 over 1-4 hours, based on the dosing schedule below
- Premedications include dexamethasone, acetaminophen, famotidine and diphenhydramine
- PSA is evaluated prior to each treatment and response is assessed every two cycles with imaging studies

**Preferred CTCAE Term**

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<td>2</td>
<td>Fever</td>
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<tr>
<td>3</td>
<td>Chills</td>
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<tr>
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<td>Pain</td>
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<td>Sinus Tachycardia</td>
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**Summary of Results**

- 8 out of 30 total patients have enrolled (3 pts in cohort 1, 3 in cohort 2 and 2 in cohort 3)
- Median time on study is 14 weeks (range 7-16)
- No DLTs in any of the dosing cohorts to date
- No related grade 3 or 4 toxicities
- PSA declines of 26% and 51% from baseline were seen in two patients in cohort three (both had progressed on docetaxel and at least one 2nd line agent)
- 5 out of 6 patients with measurable soft tissue disease achieved stable disease (two in cohort 1, two in cohort 2 and one in cohort 3); the latter 3 patients in cohorts 2 and 3 remain on study

**Conclusion**

- TRC105 is tolerated at doses up to 10 mg/kg every two weeks with early evidence of clinical activity in mCRPC
- Accrual is ongoing to evaluate higher doses and more frequent dosing, ORR, PFS and OS