Phase II Trial of SM-88 in Non-Metastatic Biochemical Recurrent Prostate Cancer

Mack Roach III MD, Avi S. Retter2, Zachary Gostout1, Patricia Zawisny1, Gerald H. Sokol3, Steve Hoffmann2, Giuseppe Del Priore MD, MPH1,5
1University of California at San Francisco, 2-Albert Einstein School of Medicine, 3-QliO Inc (NY, NY), 4-Tyme Inc (NASDAG: TYME, New York, New), 5-Morehouse School of Medicine (Atlanta, GA)

ABSTRACT
Background: Prior studies have shown SM-88, a novel recombinant prostate cancer protein (PRC) that is typically treated with castration therapy, to have potent anti-androgen activity. The current study was designed to evaluate the safety and efficacy of SM-88 in patients with non-metastatic biochemical recurrent prostate cancer (nmPC). The trial was a single-arm, open-label, Phase II trial at 13 centers in US to evaluate the safety, tolerability, antitumor activity, and pharmacokinetics of SM-88 in these patients. The patients were treated with SM-88 at an initial dose of 551 mg/day, increased by 220 mg/day in 7-day increments to a maximum dose of 551 mg/day. The primary outcome was the percentage of patients with PSA reductions of 50% or greater 12 weeks after the first dose of SM-88.

INTRODUCTION
Introduction: PRCs are a family of proteins that are expressed on prostate cancer cells and are shed into the bloodstream. SM-88 is a recombinant PRC that has shown promising anti-tumor activity in preclinical and clinical studies. This study aimed to evaluate the safety, tolerability, and antitumor activity of SM-88 in patients with nmPC.

OBJECTIVES
To assess SM-88 use for treatment of nmPC. Efficacy specifically with adenovirus correlated with:
• To quantify any reduction in circulating tumor cells (CTCs)
• To determine radiographic progression from scored (PRI)
• To report effects on testosterone and PSA

RESULTS

Table 1. Demographics

Table 2. Areas of Typical ADT Toxicity

Table 3. Reported Adverse Event by Causality

Table 4. EORTC Patient Reported Outcomes

Figure 1. CTC RESIDENCE: Overall 57% had >50% reduction, 92% had ≤50% reduction, and 86% had ≤10% reduction in CTSC.

Figure 2. PSA RESPONSE: 92% (129/133) subjects had a last cycle with improvement in velocity ≥1 or increase in PSA.

Figure 3. ADV: Advance events were evaluated in all patients. Therapy was well tolerated with no treatment-related adverse events. No adverse events resulted within 30 days of enrollment, at discharge, or on follow-up.

CONCLUSIONS
SM-88 had a significant impact on tumors typically seen with ADT. Weight loss, hyperglycemia, BMI, mean arterial pressure, glucose and hematocrit were not significantly affected while on SM-88. SM-88 also had no drug-related AE. Chronic toxicity already present and typical in this population (obesity, HTN) continued to progress among those already affected but there were no new cases. Assessment of metabolic牵制 and immunity was encouraging with 100% reporting an improved or stable "intermediate term". Overall outcomes reported "excellent” "overall health” and "QOL". SM-88 may provide clinicians an option between an observation strategy and more toxic treatments such as chemotherapy with ADT.

We believe this data supports the growing body of evidence that CTCs may be a better prognostic biomarker than PSA levels, especially in earlier stage prostate cancer where PSA levels may be affected by multiple non-cancerous conditions. This non-toxic treatment may be useful in patients with h/sMC and questions the necessity of chemical castration to control mPC.

FUTURE DIRECTIONS
The current Phase III trial is expected to be completed in the latter half of 2018. Its results will be used to design a potential pivotal Phase III trial. Current expectations for the Phase III trial would be a randomized controlled trial comparing SM-88 against placebo in biochemically recurrent non-metastatic prostate cancer, with primary endpoints of metastatic free survival, time to initiation of subsequent hormone therapy and CT.

REFERENCES

READINGS

PREDICTED

AVIAN

SUMMARY

OBSTETRICS

Figure 4. QoL-PR35: QoL-PR35 questionnaire showed no clinical or statistical worsening of mental function domain (QoL-PR35), with average score (1.5: 4: 6: 4) based on the individual patient’s responses measured at each cycle.

Figure 5. Table 2. Areas of Typical ADT Toxicity

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