Estra with Full Dose Enz is Similar to 120 mg - Masofaniten 600 mg BID Dosing Mitigates Drop in Exposure

Patient Baseline Characteristics

Summary

- To assess possible DIBs and establish PK parameters at 34 days. A 7-day run in phase with masofaniten alone was initiated at the beginning of Cycle 1 for each dose level. Enz was then introduced at 120 mg. Estra, masofaniten, and Enz are not a "perpetrator" of Enz exposure.

In vitro, masofaniten is a strong inhibitor of CYP3A4, the main enzyme involved in the metabolism of Enz, suggesting that masofaniten may enhance the plasma level of the other. Enz is a potent inducer of CYP3A4, which is involved in the metabolism of masofaniten.

Masofaniten plasma levels might increase due to decreased metabolism. Estra is a potent inducer of CYP3A4. The Phase 1 study focused on the PK and safety of masofaniten and Enz when administered in combination to mCRPC patients naïve to second-generation anandrogens. Estra increases masofaniten exposure (likely through induction of CYP3A4)

BID dosing of masofaniten is not a "perpetrator" of Enz exposure. In the combination group, masofaniten exposure was significantly reduced (likely through induction of CYP3A4), but BID dosing of masofaniten was independent from the baseline levels (patients have not yet reached steady state).

Across All Cohorts, Patients Showed Rapid, Deep and Durably Positive PSA Drop

Conclusions

Based on the total safety and the PK data from the Phase 1 part of the study, the recommended Phase 2 combination doses are 600 mg in BID dosing - 160 mg Enz + 600 mg Enz.

- Combination of masofaniten and Enz at all doses tested is safe and well tolerated.
- The combination has no effect on Enz exposure thus allowing the use of full dose of Enz in combination with masofaniten.
- Estra dose rapidly induces masofaniten exposure (likely through induction of CYP3A4), but BID dosing of masofaniten can mitigate the drop and maintain clinically relevant CYP3A4 activity.
- Rapid, deep, and durable PSA reductions were observed in patients, regardless of previous chemotherapy status. 9/16 evaluable patients reached prior described in mHSPC setting and 5/6 of total dose (i.e., 120 mg/day).

- Grade 3 rash in 1 patient, no DLT
- No association seen between response rate and previous chemotherapy status. The combination regimen is safe and effective, demonstrating rapid, deep, and durable PSA reductions in mCRPC patients.

- At the B22DCs, data is still immature; patients have not yet reached steady state.
- 5/6 of the patients show PSA declines in patients from the bicalutamide Arm.

The Phase 2 study is currently enrolling.