A Phase II Multi-Center Study of SM-88 in Patients with Pancreatic Cancer Whose Disease Has Progressed or Recurred after/on First Line Chemotherapy

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**BACKGROUND**
- Pancreatic cancer is a debilitating disease still treated with indolentistant harish cytotoxics that do not produce meaningful benefit for the majority of patients.
- SM-88's primary component dysfunctional tyrosine derivative, used in conjunction with low "physiologic" doses of an mTOR inhibitor, CYP3a4 inducer and an oxidative stress catalyst.
- Labeled amino acid based imaging suggests rapid and selective tumor uptake of tyrosine like molecules.
- SM-88 appears highly specific with few observed off-target effects.

**STUDY DESIGN**

- **Study Design**
  - Open label Phase 2 with 117 subjects across approximately 30 sites in the USA (Figure 3)
  - Stage 1 randomized (n=36) among 2 dose levels of tyrosine derivative to determine optimum RP2
  - Stage 2 expanded cohort of RP2 (n=81 total)

- **Enrollment Criteria**
  - All patients improved or maintained ECOG PS after initiating SM-88 DO
  - 084
  - 096
  - 031
  - JP

- **Mechanism of Action**
  - TRMT1 and resulting oxidative stress within cancer cells
- **Recent data reported activity in solid tumors without significant toxicity (Hoffman et al ASCO 2017 J Clin Oncol 36, 2018)**
- **Effectiveness in metastatic pancreatic cancer (Figure 2, Table 1)**
- **Previous SM-88 Pancreatic Cancer Experience**
  - 12 patients (10 evaluable) with actively progressing pancreatic cancer treated with single agent SM-88 (J Clin Oncol 36, 2018 (suppl 45; abstr 457))
  - Median PFS of 4.6 months (median one prior line of systemic therapy (range 0-8)
  - One CR (10%), 3 PRs (25%), 4 PRs (40%): Stable disease duration 2-4 months (Table 1)
  - 4/10 (40%) subjects showed survival of greater than 12 months
  - All patients improved or maintained ECOG PS after initiating SM-88

**RESULTS**

- **SUMMARY OF PREVIOUSLY REPORTED EFFECTIVITY**
  - Table 2**
  - **TMY Trial (report date)**
  - **Endpoints**
  - **Evaluable Subject Response**
  - **CR+PR Response Rate**

- **DISCUSSION**
- SM-88 has potential antiangiogenic activity and appears well tolerated based on 3 previous cohorts (J Clin Oncol 31, 2013 (suppl e22095), J Clin Oncol 36, 2018 (suppl 65; abstr 175); J Clin Oncol 36, 2018 (suppl abstr e14353))
- As a relatively non-toxic treatment, SM-88 could provide clinicians with an option that is more applicable to poor performance patients
- This trial is currently enrolling with interim results expected in 2019
- SM-88 being evaluated for potential additional trials in other metastatic settings (retrospective data on use in metastatic cancer being reported elsewhere with this J Clin Oncol 2018 (suppl e4900) and J Clin Oncol 36, 2018 (suppl abstr e16940))

**REFERENCES**

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