A phase II study of oral ENMD-2076 administered to patients with advanced soft tissue sarcomas

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Background

- The use of anti-angiogenic therapy has been proven to be useful in preclinical studies on soft tissue sarcoma (STSs)
- Clinical evidence from the phase III PALETTE study showed significant PFS improvement with pazopanib versus placebo
- ENMD-2076 (C25H31O6N7.(2.5 H2O)) is an oral, Aurora A/angiogenic kinase inhibitor evaluated pre-clinically and in phase I dose escalation studies in pts with solid tumours, multiple myeloma (MM) and leukaemia (L)

Methods

Single arm, open-labeled phase II study of Once Daily Dosing of oral ENMD-2076 in 28-Day cycles

Pertinent Eligibility Criteria:
- ECOG 0 or 1
- Histological diagnosis of STS with exception of GIST
- Measurable disease within 4 weeks of study entry
- No more than 1 line of treatment in advanced/metastatic setting
- Use of prior anti-angiogenics and neoadjuvant/adjuvant treatment allowed
- Adequate cardiac function with MUGA scan with EF > 50%
- Consent to access archival material for correlative studies or for fresh biopsy if no archival tissue available

Pertinent Exclusion Criteria:
- Known CNS metastases
- Uncontrolled hypertension, active angina pectoris, stroke or myocardial infarction within last 6 months
- Requiring therapeutic anticoagulation. Pts with prior history of DVT or pulmonary embolism were ineligible

Conclusions

- ENMD-2076 has shown clinical activity in pts with advanced STS, with clinical benefits and side effects profile typical of this class of agent.
- Drug toxicities were of low grade and tolerable. High grade toxicities include hypertension (30%) and diarrhoea (15%). Other high grade toxicities were rare.
- All pts who derived clinical benefit (2 PR and 1 SD > 6months) received ENMD-2076 in the first-line setting.
- Whilst majority of pts in the trial had leiomyosarcomas, significant responders to treatment were not of leiomyosarcoma but of an array of disease subtypes. Molecular characterization of these responders are on-going.


*Data Cutoff: April 1st, 2014