**Abstract #3079 - In silico approaches to patient selection: Credentialing elraglusib as a novel treatment in metastatic melanoma resistant to checkpoint inhibitors**

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**Background**

- Elraglusib (9-ING-41), a novel inhibitor of GSK-3β, has been evaluated in >230 patients (pts) with advanced malignancies, including metastatic melanoma (1801 phase 1/2 trial; NCT03678883).
- Emerging pre-clinical and early clinical data suggest activation and expansion of CTL and NK cells, modulation of cytokine dynamics, and increased neoantigen presentation as novel aspects of elraglusib mechanism of action.
- Metastatic melanoma pts (n=12) were heavily pretreated (mean of 3 prior lines of treatment) including one or more checkpoint inhibitors.
- These pts received single agent elraglusib at doses ranging from 5-15 mg/kg IV 2X/week.
- 5 pts demonstrated durable clinical benefit with 1 CR (ongoing, >1400 days) and prolonged OS of 107, 256, 357, and 556 days.

**Methods**

**Development of a Machine Learning Model to Predict Patient Elraglusib Response with Genomics Input**

1. **Tumor GSK3B Expression is Associated with Poor Survival in Melanoma Pts given αPD-1 Therapy**
   - Expression of GSK3B was used to stratify elraglusib melanoma pts who received αPD-1 therapy (n=77).
   - FNR was obtained from two separate studies of patients with advanced melanoma were taken from pre-treatment tumor samples and standardized before combining for stratification analysis.
   - Strats were separated if having above-average GSK3B expression.

2. **Machine Learning Modeling of Elraglusib Response**
   - Feature SHAP contributions in the best model to predict outcome. The contribution of features to individual predictions was estimated by calculating SHAP values. The x-axis represents the probability of response, with values over 0.5 being predicted responders.

**Results**

- Single agent elraglusib demonstrated signs of clinical activity in heavily pre-treated pts with metastatic melanoma including one CR and prolonged OS in 5 pts.
- AI modeling predicts that checkpoint resistant metastatic melanoma patients may benefit from elraglusib therapy.

**Future Directions**

- Future clinical studies of elraglusib and αPD-1 combination in histologies selected based on clinical data from 1801 and ML modeling.
- Further evaluation of ML models to select patient populations for elraglusib as well as more broadly for other cancer drugs.
- Develop clinical applications of the ML model to inform clinical decision making.

**References**