2024 Areas of Interest for Sac-TMT

Cross-cutting AOI

- Studies of monotherapy to define single agent activity in tumor types known to express TROP2 (1L and 2L or >)
- Studies of combinations with other agents in tumors expressing TROP2, with priority for SOC combinations (1L and 2L or >)
- Studies of combinations with pembrolizumab (1L and 2L or >)
- Studies to include IO refractory/IO responsive (prefer monotherapy) (2L or >)

MISP Clinical Areas of Interest by Tumor Type

- Prostate
    - Studies of monotherapy or combinations with other agents in mCRPC
    - Studies of monotherapy or combinations with other agents in neuroendocrine prostate cancer

- GYN
    - Replacement of single agent chemo in later lines of therapy where monotherapy is used
    - Combination with pembro in early settings where there is a rationale for IO + chemo
    - Rare tumors in need of more effective chemotherapy
    - Combination with radiation +/- pembrolizumab
- Early & Late Bladder
    - Studies of monotherapy in bladder cancer
    - Studies of sac-TMT in combination with pembrolizumab in bladder cancer
- Breast
    - Sac-TMT monotherapy in post-ADC metastatic breast cancers that are more likely to respond to subsequent ADC therapies (segments of patients or biomarker enriched populations in all breast cancer subtypes)
    - Sac-TMT combinations with novel agents for the treatment of metastatic disease breast cancer (in all breast cancer subtypes)
    - Studies investigating the sequencing of ADCs which belong to a different class (for e.g., HER2 ADC or other) with sac-TMT in patients with metastatic disease (in all breast cancer subtypes)
- Innovative Strategies
    - Rare tumors with evidence/rationale/supportive data to show topoisomerase inhibitor efficacy in selected tumor types exhibiting TROP2 expression
- Lung

- Sequential ADC treatment in EGFRm, other oncogene addicted NSCLC, or WT-NSCLC (different or same payload)
- Sac-TMT in combination with novel agents for the treatment of NSCLC
  - Including IO refractory 2nd line wild type NSCLC (after 1st line SoC)
  - 1st line EGFR L858R/rare mutation NSCLC
- Sac-TMT in combination with novel agents in extensive stage SCLC

- <u>Heme</u>
  - Studies of monotherapy or combination therapy in relapsed/refractory setting for Heme malignancies where there is expression of TROP2

Preclinical:

- Investigate the impact on patient tumor samples treated by sac-TMT including alterations in TROP2 expression
- Assess the potential of sac-TMT to effectively target advanced stage cancers, such as metastatic tumors or those resistant to prior treatments through preclinical models
- Use of established preclinical models/patient-derived xenograft (PDX) models, to gain insights into possible mechanisms of resistance to sac-TMT
- Understand the resistance mechanisms to sac-TMT by analyzing evidence obtained from preclinical assessments and patient tumor samples treated ex vivo
- Identify new combination partners, either used concurrently or sequentially, to overcome the anticipated resistance to sac-TMT (i.e., ICB or others)