Advances in Immuno-Oncology: Evaluating a Bispecific, Bifunctional Fusion Protein
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Dr. Gulley has nothing to disclose.
PD-L1 binds to PD-1 and inhibits T cell killing of tumor cell

Blocking PD-L1 or PD-1 allows T cell killing of tumor cell
• 19 heavily pre-treated patients with ECOG 0-1

• Safety
  – Grade ≥3 treatment-related AE in 4 patients
    • Skin infection secondary to localized bullous pemphigoid
    • Asymptomatic lipase increase
    • Colitis
    • Gastroparesis

19 heavily pre-treated patients with ECOG 0-1

- Efficacy
  - 1 ongoing confirmed complete response (cervical cancer)
  - 2 durable confirmed partial responses (pancreatic and anal cancer)
  - 1 near partial response (cervical cancer)
  - 2 prolonged stable disease (pancreatic cancer; carcinoid)
  - Sequestered all activated TGF-beta in plasma throughout dosing period

• Lung cancer
  – 40 pts at the 1200mg dose
    • 28% ORR
    • All responders were PDL1 with ~80% response in the hi PDL1+ subgroup
KEY FINDINGS IN HPV-RELATED CANCERS

• HPV-associated cancers
  – 17 pts
    • ORR 35%
    • 42% of patients with HPV+ tumors responded
Combination therapy is key
- This agent alone works like combination therapy by targeting two different pathways
- Still room to target additional pathways

Several ongoing studies combining this agent with other therapeutic options/anti-cancer vaccines
- The goal is to generate a good immune response in those T-cell-poor tumors and then allow those immune cells to work by blocking TGF-beta and by blocking PD-L1 in the tumor microenvironment
LOOKING FORWARD: IMMUNE CHECKPOINT INHIBITION (CON’T)

- M7824 will potentially work as a single agent in multiple different indications, not only in the refractory setting where there is resistance, and may lead to improved response rate
- Impacts of M7824 are already seen in lung and HPV-positive cancers