Background and Rationale

- Increasing incidence of neuroendocrine neoplasms including HG-NENs
- No current standard of care after failure of first line platinum/etoposide doublet
- Various chemotherapy agents used with poor response to therapy despite increased risk of toxicity
- Promising activity of checkpoint inhibitors in small cell lung cancer and Merkel cell carcinoma
- Previously published literature suggesting a higher rate of mutations in HG-NENs compared to low grade NENs
- Provided rationale for conducting a phase II study of Pembrolizumab in HG-NENs with the primary objective to assess response (NCT02939651)

Study design and statistical methods

- **Eligibility:**
  - Metastatic HG-NEN (within 28 days)
  - Screening period
  - Exclude any high grade
  - Informed consent
  - PS: ECOG 0-1
  - Histologically confirmed increased risk of toxicity

Background and Rationale

- Pembrolizumab, though generally well tolerated, showed limited activity as a single agent in HG-NENs in this study
- Study highlights that high grade GI NENs differ from small cell lung cancer, also reflected by their varying molecular profile
- Correlative testing suggestive of high PD-L1 staining and presence of TILs
- Future studies using combination immunotherapies and/or combination with cytotoxic drugs may be of interest in this aggressive tumor type as many patients progressed before the 12 week mark.

Conclusions

References

5. Acknowledgement: Shafat Quadri, PhD (Merck MSL), Siddhartha Rawat (protocol developer)