Avelumab in neuroendocrine tumours of gastroenteropancreatic or lung origin
David L Chan, Parneet Cheema, Eugene Hsieh, Simron Singh
Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, Canada

Background:
• High-grade neuroendocrine tumours (NET) are aggressive malignancies. Recent advances in systemic treatment focus on Grade 1-2 NET, and there remain few options for advanced G3 NETs.
• Poorly-differentiated histology confers a particularly poor prognosis in pancreatic NETs. (Tang 2015).
• Immunotherapy, particularly monoclonal agents targeting the PD-1/PD-L1/PD-L2 axis, has transformed the treatment of solid organ tumours such as melanoma, non-small-cell lung cancer and bladder cancer.
• There has been little published data thus far regarding immunotherapy in NETs. The KEYNOTE-028 study (ESMO 2017) demonstrated modest response rates for pembrolizumab in NET (12% in carcinoid tumours, 6% in pancreatic NET), but this mainly investigated G1-2 NETs.
• Two recent trials of immunotherapy (avelumab, pembrolizumab) in Merkel cell carcinoma, or neuroendocrine carcinoma of the skin, (Kaufman 2016, Nghiem 2016) have shown response rates of 32% and 56%. (Fig.1)

Methods:
• We plan to conduct two parallel single-arm, open-label trials at Sunnybrook Health Sciences Centre for patients with G2-3 NETs. Avelumab will be given every 2 weeks, with CT imaging every 12 weeks. Treatment post progression is allowed until a confirmatory CT scan 4 weeks after the initial CT scan.

Key inclusion criteria:
• Histology: Grade 3 poorly-differentiated NET of GI or lung origin (NET-001); Grade 2-3 well-differentiated Net of GI or lung origin (NET-002)
• Both functional and non-functional tumours are eligible
• Progression on imaging in last 12 months
• 0-2 prior lines of systemic therapy (excluding SSA)
• The presence of sufficient archival tissue for analysis (a core biopsy should be sufficient in most cases)

Key Exclusion criteria:
• Histology other than NET (e.g. MANEC)
• Prior use of PD-1, PD-L1, CTLA-4 inhibitors
• Current use of systemic immunosuppressants (equivalent of oral prednisone >10mg/day)
• Brain metastases which have not received local therapy, are clinically unstable, or result in neurological symptoms
• Leptomeningeal disease

Endpoints:
• Primary outcome: Response rate by RECIST v1.1
• Secondary outcomes: Safety, duration of response, OS, PFS, efficacy outcomes by irRECIST
• Correlative analyses of PD-L1 status and mutational load are planned.

Trial status and registration
• NET-001 (G3 PDNEC) – 10 patients; NET-002 (G2-3 WDNET) – 36 patients. Planned to open end-Oct 2017
• Both trials have been approved by the Sunnybrook Research Ethics Board and Health Canada (NCT03278405, NCT03278379). The sponsor is the Sunnybrook Research Institute.
• NET-001 is supported by a grant from the Kavelmann Fonn Foundation and in-kind drug support from Merck KGaA. NET-002 is supported by a grant from Merck KGaA. Correlative components will be supported by a grant from CNETs.

References

For further details contact: Simron Singh, Simron.singh@sunnybrook.ca

For up to 52 weeks

Trial Schema

Follow-up

Avelumab 10mg/kg D1 Q2wk

Enrolment

Fig.1: Waterfall plot for avelumab in Merkel cell carcinoma –from Kaufman 2016

Fig:1 Waterfall plot for avelumab in Merkel cell carcinoma –from Kaufman 2016