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Pilot Study of TQ Formula in Combination with Nivolumab and Ipilimumab in Metastatic Gastroenteropancreatic Neuroendocrine Carcinomas (GEP-NECAs)

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BACKGROUND

TQ Formula (TQ, C10H12O2), is an oral formulation, derived from the black seed (Nigella sativa, Ranunculaceae family), and has anti-oxidant, anti-angiogenic effects. TQ Formula has been shown to induce significant immune modulatory effects in a recently published Covid-19 study. Previous studies reported blackseed's apoptotic and anti-proliferative effects of its components on multiple cancer types, including colon, breast and ovarian adenocarcinoma. Our preliminary results in high grades neuroendocrine carcinoma (NEC) cell lines (NEC-T2) indicate that TQ Formula plus Immune checkpoint inhibitors (ICIs) can suppress cell growth and induce apoptosis through suppression of commons driver pathways. Additionally, TQ Formula synergized with ICIs leading to significantly enhanced cell kill in NEC cellular models. Clinically, in a case report of three subjects with NEC of GEP origin administered TQ Formula derived black seed capsules with dual ICIs (nivolumab plus ipilimumab) showed improved response rate of 100%, with two years median progression free survival without additional toxicities. Based on our preliminary data, this pilot study is in progress to evaluate the anti-tumor efficacy of this novel combined regimen (TQ plus nivolumab and ipilimumab) in the second line setting for metastatic GEP-NEC.

METHODS

The study is a single-arm clinical trial to investigate the synergistic anti-angiogenesis and apoptotic effect of combined TQ Formula plus dual ICPIs in a small pilot study of 10 patients with metastatic high grade GEP-NECs refractory to first-line chemotherapy. All patients will receive TQ Formula (oral capsules), three 500mg tabs (1500mg) BID daily, plus triweekly ICPIs (intravenous nivolumab 240 mg and Ipilimumab 1 mg/kg) for 4 cycles then resume TQ Formula with the same daily dose with maintenance biweekly nivolumab to complete a total of 6 months treatment. Primary end point of the study is to determine the antitumor activity of TQ Formula plus nivolumab and ipilimumab in subjects with metastatic GEP-NECs who progressed on first line therapy. Secondary endpoints include time to progression (TTP) and safety profile using this combined regimen.

Predictive biomarkers include MMR status, and TMB level, PDL-1 expression, and angiogenesis profile (VEGFR1, VEGFR2, CD34, PGF and microvascular density) for association with clinical benefit. The final analysis will be performed to assess efficacy after 10 patients become evaluable. *Clinicaltrials.gov*: NCT05262556.

RESULTS

NA

CONCLUSIONS

NA

ABSTRACT ID 21559