A PHASE II STUDY OF THE ANTI-PROGRAMMED CELL DEATH-1 (PD-1) ANTIBODY PENPULIMAB IN PATIENTS WITH METASTATIC NASOPHARYNGEAL CARCINOMA (NPC) WHO HAD PROGRESSION AFTER TWO OR MORE LINES OF CHEMOTHERAPY

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Background NPC is rare but has a distinct geographic distribution, with a predominance in Southeast Asia. Favorable results with PD-1 inhibitors in NPC provide a strong rationale to investigate penpulimab in this disease. Penpulimab was engineered to eliminate FcγR binding and ADCC/ADCP completely, where ADCC/ADCP effects can induce T-cell apoptosis and clearance and then compromise anti-tumor activity. Penpulimab demonstrated a slower PD-1 antigen binding off-rate than marketed PD-1 antibodies, which result in better cellular activity and higher receptor occupancy. Penpulimab also showed numerous contacts with N58 glycosylation on the BC loop of PD-1 which could be an advantage to facilitate interaction of PD-1 antibody and may contribute to slower binding off-rate. These structural differentiations offer more robust biological effect and enhance anti-tumor activity of penpulimab.

Methods AK105-202 (NCT038666967) is a multicenter, single-arm, open-label study of penpulimab in metastatic NPC patients (pts) with disease progression after ≥2 prior lines of therapy including platinum-containing chemotherapy. All patients received penpulimab 200 mg q2w until progression or unacceptable toxicity. The primary endpoint was ORR based on RECIST v1.1 as assessed by an independent review committee (IRC). Key secondary endpoints included DCR, PFS, duration of response (DoR), Archival tissues were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive. Plasma Epstein-Barr virus DNA were retrieved for the analysis of PD-L1 (Shuwen SAB-028). PD-L1 expression of tumor proportion score (TPS)≥50% was regarded as positive.

Results As of 18 September 2020, the median follow-up was 7.9 months (range 0.9 to 16.9). The anti-tumor activity of penpulimab in the 111 pts with disease progression after ≥2 prior lines of therapy evaluable for efficacy (defined as pts who had an opportunity to be followed for at least 16 weeks and had measurable disease at baseline per RECIST v1.1) is shown in the table 1.

<table>
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a. Including 1 complete response and 29 partial response. At data cutoff, 90% of respondents remained ongoing.
b. 3 pts with PD-L1 positive (TPS≥50%) and 66 pts were PD-L1 negative (TPS<50%).
c. Including 1 ongoing response awaiting confirmation classified under SD.

Conclusions Penpulimab demonstrated encouraging anti-tumor activity and favorable safety profile in pts with disease progression after ≥2 prior lines of therapy. A higher proportion of objective responses was observed in NPC pts with PD-L1-positive tumors receiving penpulimab than those with PD-L1-negative tumors.

SAFETY AND EMERGING EVIDENCE OF IMMUNE MODULATION OF THE LIVE BIO THERAPEUTIC MRX0518 IN THE NEOADJUVANT SETTING FOR PATIENTS AWAITING SURGICAL REMOVAL OF SOLID TUMOURS

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Background The gut microbiome has emerged as a promising innovative therapeutic target for immune-stimulation treatment of solid tumours. MRX0518 is a novel, gut microbiome-derived oral live biotherapeutic. It has potent anti-tumorigenic efficacy in the preclinical setting including murine models of lung (LLC1), kidney (Renca) and breast (EMT6) cancer. In these models, a significant reduction in tumour growth has been demonstrated, including induction of immunostimulatory responses with tumour infiltration of NK cells, CD8+ and CD4+ T-cells. MRX0518 is under investigation in various oncological settings, including in combination with immune checkpoint inhibitors (NCT03637803) and radiotherapy (NCT04193904).

Methods Treatment naive patients were recruited from April 2019 to February 2020. Patients were eligible if they received a histologically confirmed diagnosis of cancer (solid tumours) scheduled for surgical resection. Patients received 1 capsule of MRX0518 (1x1010 to 1x1011 CFU) twice daily from planned to undergo surgical removal of solid tumours. MRX0518 is a novel, gut microbiome-derived oral live biotherapeutic. It has potent anti-tumorigenic efficacy in the preclinical setting including murine models of lung (LLC1), kidney (Renca) and breast (EMT6) cancer. In these models, a significant reduction in tumour growth has been demonstrated, including induction of immunostimulatory responses with tumour infiltration of NK cells, CD8+ and CD4+ T-cells. MRX0518 is under investigation in various oncological settings, including in combination with immune checkpoint inhibitors (NCT03637803) and radiotherapy (NCT04193904).

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http://dx.doi.org/10.1136/jitc-2020-SITC2020.0804