MAIN INCLUSION CRITERIA

HNSCC (except oropharynx) that is considered incurable by local therapies.

Progress after platinum-containing systemic therapy

Group 1: PD-1-treatment-naïve HNSCC cohort

Group 2: PD-1-treatment-failure HNSCC cohort must be refractory to an anti-PD-1/PD-L1 mAb and must meet all of the following criteria:

- Have received at least 2 doses of anti-PD-1/PD-L1 mAb at a local regulatory agency-approved dose and schedule.
- Have progressive disease after anti-PD-1/PD-L1 mAb defined according to RECIST 1.1. The initial evidence of PD is to be confirmed by a second assessment, no less than 4 weeks from the date of the first documented PD, in the absence of rapid clinical progression.
- Have documented PD within 24 weeks of the last dose ofanti-PD-1/PD-L1 mAb. Patients who were re-treated withanti-PD-1/PD-L1 mAb and patients who were on maintenance with anti-PD-1/PD-L1 mAb will be allowed to enter the trial as long as there is documented PD within 24 weeks of the last treatment date (with anti-PD-1/PD-L1 mAb).

Inoperable Adenocarcinoma of the stomach and/or gastric-esophageal junction (GEJ) that has progressed on, at least 1 prior chemotherapy regimen or HER2/neu-targeted approved therapy (if HER2/neu-positive). In both cases, subjects must not have been treated with prior anti-PD-1/PD-L1 therapy.

For all cohorts

- Measureable disease by irRECIST 1.1 criteria
- ECOG 0 -1
- evaluable baseline tumor sample for PD-L1 analysis (either a newly obtained or archival tumor sample

MAIN EXCLUSION CRITERIA

- Chemotherapy, radiation, or biological cancer therapy within 4 weeks prior to the first dose of study therapy
- Previous treatment with another agent targeting the LAG-3 receptor.
- Previous treatment with an immunomodulatory therapy (eg,anti-PD-1/PD-L1 or CTLA-4 agent) and was discontinued from that therapy due to a Grade 3 or higher irAE.
- History of a previous, additional malignancy, unless potentially curative treatment has been completed, with no evidence of malignancy for 5 years.
- Known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate
- Symptomatic ascites or pleural effusion (if clinically stable after trt of this condition: eligible)

On d1 every 21d-cycle:

Pembrolizumab (PD-1 AB) administered first and then, following a 30-minute interval, MK-4280 (LAG3 AB) ca. 30 min i.v.

CT-Stagings: at screening, every 9 weeks

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