**BACKGROUND**

Cancer Immunotherapy

- Cancer immunotherapy (CIT) is an emerging therapeutic modality that aims to reactivate essential T-cell activity in the cancer-immune cycle.
- The use of immune-modulating checkpoints that target the programmed death-1 (PD-1) pathway represents a novel approach to immunity and benefit across a range of advanced malignancies, including non-small cell lung cancer, head and neck squamous cell carcinoma, melanoma, and gastric cancer.

However, only subsets of patients experience durable responses with CIT monotherapy.

**CIT Combinations**

- PD-1/L1 inhibitors and targeted agents are being evaluated in enteropancreatic tumors (mFOLFOX-6, high-dose CDDP, T-cell density or presence of a strong interferon gamma cytokine, T-cell signature).
- Anti-PD-1 treatments are being explored in combination with other treatments, such as chemotherapy (CDK4/6 inhibitors and cytotoxic chemotherapy).

**Key Inclusion and Exclusion Criteria for MORPHEUS-GC**

- Only 15% to 20% of patients have resectable disease, while the trials have the flexibility to open new treatment arms with novel CIT combinations and biomarkers.
- Anti-stromal, extracellular matrix modulation.
- The number of CIT combination studies initiated per year has increased exponentially.

**The MORPHEUS Platform**

- The MORPHEUS platform consists of multiple global, open-label, randomized, Phase Ib/II trials designed to investigate multiple combinations of CIT in patients with different tumor types.
- The platform assesses the impact of simultaneously targeting multiple mechanisms of immune escape through immune cell priming and activation, tumor infiltration by immune cells and antitumor immunity.

**Key Study Objectives/Endpoints for MORPHEUS-GC**

- Investigator-assessed disease control rate (DCR) per RECIST v1.1.
- Investigator-assessed progression-free survival (PFS) per RECIST v1.1 during Stage 1.
- OS (Table 4).

**The MORPHEUS Platform**

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**Table 4. Key Inclusion and Exclusion Criteria for MORPHEUS-GC**

- Age ≥ 18 years (exclusion criteria).
- Symptomatic or untreated CNS metastases.
- Treatment with investigational agents or participation in a clinical trial within the past 15 days or 5 half-lives of the drug, whichever is longer.
- Prior treatment within 3 months of protocol-specified study treatments, with the exception of chemotherapy.

**MORPHEUS-GC (NCT03281369)**

- Standard of Care and Unmet Medical Need in Patients With GC
  - GC is the 4th leading cause of cancer-related deaths globally, accounting for 1,085,000 deaths worldwide in 2015.
  - Patients with advanced GC (locally advanced or metastatic) have a poor prognosis, with a 5-year survival rate of 20%.

**Key Inclusion and Exclusion Criteria for MORPHEUS-GC**

- All patients with measurable disease per RECIST v1.1
- ECOG 0-2 (Stage 2)
- Prior treatment with chemotherapeutic regimens (CDK4/6 inhibitors and cytotoxic chemotherapy)
- Clinical response to previous treatment.

**Key Study Objectives/Endpoints for MORPHEUS-GC**

- Investigator-assessed DCR per RECIST v1.1
- Prior treatment with any of the protocol-specified study treatments, with the exception of chemotherapy.
- Investigator-assessed duration of response (DOR) per RECIST v1.1 during Stage 1.

**MORPHEUS-PDAC (NCT03193190)**

- Standard of Care and Unmet Medical Need in Patients With PDAC
  - PDAC is the leading cause of cancer-related deaths globally, accounting for 420,000 deaths worldwide in 2015.
  - Surgical resection is currently the only therapeutic means of cure.

**Key Inclusion and Exclusion Criteria for MORPHEUS-PDAC**

- Age ≥ 18 years (exclusion criteria).
- Symptomatic or untreated CNS metastases.
- Treatment with investigational agents or participation in a clinical trial within the past 15 days or 5 half-lives of the drug, whichever is longer.
- Prior treatment within 3 months of protocol-specified study treatments, with the exception of chemotherapy.

**Key Study Objectives/Endpoints for MORPHEUS-PDAC**

- Primary endpoint: investigator-assessed PFS per RECIST v1.1
- Secondary endpoints:
  - Investigator-assessed OS per RECIST v1.1 during Stage 1.
  - Landmark OS (eg, 6 and 12 months).
  - Investigator-assessed DOR per RECIST v1.1 during Stage 1.

**MORPHEUS-GC**

- Atezolizumab + PEGPH20
- DPP-4
- mFOLFOX-6 or gemcitabine + gemcitabine-based chemotherapy in the metastatic setting

**MORPHEUS-PDAC**

- Atezolizumab + mFOLFOX-6, modified folinic acid, fluorouracil, and oxaliplatin.
- mFOLFOX-6 and ECF (gemcitabine and cisplatin).
- OS (Table 5).

**TREATMENTS EVALUATED IN MORPHEUS-GC**

- A variety of single agents, including docetaxel, paclitaxel, irinotecan, and ramucirumab.
- New efficacious treatments are needed in all disease settings.

**TREATMENTS EVALUATED IN MORPHEUS-PDAC**

- Key Inclusion and Exclusion Criteria: Patients who experience disease progression, loss of clinical benefit, or unacceptable toxicity with the initial treatment regimen (Stage 1) may be eligible to continue treatment with a different CIT combination (Stage 2).

**Further Information**

- MORPHEUS-GC: http://clinicaltrials.gov/ct2/show/study/NCT03281369
- MORPHEUS-PDAC: http://clinicaltrials.gov/ct2/show/study/NCT03193190

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**References**