Study Overview

Brief Summary

The goal of this clinical trial is to evaluate CHM-2101, an autologous CDH17 CAR T-cell therapy for the treatment of advanced gastrointestinal (GI) cancers that are relapsed or refractory to at least 1 standard treatment regimen in the metastatic or locally advanced setting.

Detailed Description

This is a Phase 1/2 open-label study to evaluate CHM-2101, an autologous CDH17 CAR T-cell therapy for the treatment of advanced gastrointestinal (GI) cancers that are relapsed or refractory to at least 1 standard treatment regimen in the metastatic or locally advanced setting.

The study has 2 parts: Phase 1, Dose Escalation and Expansion, and Phase 2. Potential participants will provide written consent and be screened for study eligibility prior to undergoing any screening procedures, including leukapheresis. Protocol-specified criteria must be met prior to the start of leukapheresis for collection of peripheral blood mononuclear cells (PBMCs). Eligible participants will undergo leukapheresis to collect PBMCs for product manufacturing, which comprises enrichment of T cells, lentiviral transduction, ex vivo expansion, and cryopreservation of the CHM-2101 cell product. Participants who have a leukapheresis or manufacturing failure may be permitted a second attempt at leukapheresis.

Bridging chemotherapy (treatment between the time of leukapheresis and first dose of lymphodepleting chemotherapy [LDC]) is permitted at the discretion of the investigator, if needed to maintain disease stability during CHM-2101 manufacturing time. Bridging chemotherapy is prohibited within the 2 weeks prior to leukapheresis and 2 weeks prior to planned CHM-2101 infusion. Specific criteria to proceed should be reviewed prior to leukapheresis, LDC, and CHM-2101 infusion. Participants will be followed in this study for 18 months or until disease progression.

Official Title

A Phase 1/2 Study to Evaluate CHM-2101, an Autologous Cadherin 17 (CDH17) Chimeric Antigen Receptor (CAR) T Cell Therapy for the Treatment of Relapsed or Refractory Gastrointestinal Cancers

Conditions

Neuroendocrine TumorsColorectal CancerGastric Cancer

Intervention / Treatment

- Biological: CHM-2101 CAR-T cells

Other Study ID Numbers

- CHM-2101-001

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies.

Eligibility Criteria

Description

Inclusion Criteria:

1. Documented informed consent of the participant and/or legally authorized representative.
2. Confirmed histologic diagnosis of one of the following solid tumors of GI origin:
    1. Gastric adenocarcinoma Note: for gastric adenocarcinoma patients only, central laboratory confirmation of CDH17+ tumor expression is required.
    2. Colon and/or rectal adenocarcinoma
    3. G1, G2, and well-differentiated G3 neuroendocrine tumors of the midgut and hindgut (ileal, jejunal, cecal, distal colonic, or rectal; with ≤ 55% Ki67 expression)
3. Availability of unstained tumor tissue slides from archived tumor tissue or a new tumor biopsy, if medically feasible. Note: for gastric adenocarcinoma patients only, confirmation of CDH17+ is required prior to study inclusion.
4. Have received at least 1 prior line of systemic anti-cancer treatment in the locally advanced or metastatic setting, as defined by National Comprehensive Cancer Network (NCCN) guidelines. Participants must have received or declined FDA-approved and available treatment options, including targeted therapies for disease mutation or antigen expression status.
5. Age ≥ 18 years and ≤ 85 years.
6. For Phase 1 Dose Expansion and Phase 2 only: Measurable disease as per RECIST v1.1 criteria (Note: Measurable disease is NOT required for Phase 1 Dose Escalation).
7. Eastern Cooperative Oncology Group (ECOG) ≤ 1.
8. Life expectancy ≥ 12 weeks.
9. No known contraindications to leukapheresis, cyclophosphamide, fludarabine, or steroids.
10. Baseline laboratory values as shown in the following table:

    Minimum Laboratory Values for Study Entry Laboratory Assessment Criteria White blood cell count > 4,000/mm3 Absolute neutrophil count (ANC) ≥ 1,500/mm3 Platelets ≥ 100,000/mm3 Hemoglobin ≥ 10 g/dL Total bilirubin ≤ 1.5 x upper limit of normal (ULN) Aspartate amino transferase (AST) ≤ 3 x ULN

Alanine transaminase (ALT) ≤ 3 x ULN Creatinine clearance by Cockroft-Gault equation 60 mL/min Oxygen saturation ≥ 92% on room air Albumin ≥ 3 g/dL

11. Left ventricular ejection fraction ≥ 50%.
12. Seronegative for human immunodeficiency virus (HIV) by antigen/antibody (Ag/Ab) testing.
13. Seronegative for hepatitis B and/or hepatitis C virus.
14. Women of childbearing potential (WOCBP) must have a negative urine or serum pregnancy test. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test is required.
15. Agreement by women and men of childbearing potential to use an effective method of birth control or abstain from heterosexual activity through at least 3 months after the last dose of CHM-2101.

Exclusion Criteria:

1. Previous treatment with CDH17-targeted therapies.
2. Unresolved toxicities from prior therapy except for chronic toxicity no greater than Grade 1 and stable > 30 days (Note: alopecia of any grade is not exclusionary).
3. Uncontrolled seizure activity and/or known central nervous system (CNS) metastases.
4. History of allergic reactions attributed to compounds of similar chemical or biologic composition to study agent.
5. Uncontrolled Crohn's disease, ulcerative colitis, or other autoimmune or inflammatory disorders of the GI tract. "Uncontrolled" is defined as requiring hospitalization, corticosteroids, or chronic medication increase (dosage or frequency) within the previous 6 months.
6. Liver involvement ≥ 50%.
7. Active infection requiring oral or IV antibiotics.
8. Current diagnosis of pleural effusions, interstitial lung disease, or heart failure of New York Heart Association Classification of Heart Failure Class III or IV.
9. Ongoing treatment with systemic corticosteroid therapy at doses of prednisone ≥ 20 mg/day or equivalent (lower doses of corticosteroid therapy are allowed until 7 days prior to leukapheresis).
10. No prior malignancy within 5 years except for non-melanomatous skin cancer or cervical cancer treated with curative intent
11. Currently breastfeeding or planning to become pregnant within 9 months of study enrollment.
12. Any other clinically significant uncontrolled illness or other comorbid condition that would, in the investigator's judgment, contraindicate the participant's participation in the clinical study.

Ages Eligible for Study
18 Years to 85 Years (Adult, Older Adult)
Sexes Eligible for Study
All
Accepts Healthy Volunteers
No

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Autologous CDH17CAR T-cell Therapy After receiving three daily doses of IV fludarabine and cyclophosphamide, participants will receive a single dose of IV CHM-2101. The dose of CHM-2101 during Phase 1 will be based on "3+3" rules of dose escalation. The recommended Phase 2 dose will be based on results from the Phase 1.	Biological: CHM-2101 CAR-T cells • Cadherin 17 (CDH17) Chimeric Antigen Receptor (CAR)-positive T cells

What is the study measuring?
Primary Outcome Measures

Outcome Measure	Measure Description
Dose-Limiting Toxicity (DLT)	Assessed according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 5.0.
Rates and Grades of Cytokine Release Syndrome (CRS)	Assessed per American Society for Transplant and Cellular Therapy (ASTCT) consensus grading guideline
All other adverse events and toxicities	Assessed per NCI CTCAE v5.0

Outcome Measure	Measure Description
Objective Response Rate (ORR)	Assessed by RECIST v 1.1

Secondary Outcome Measures

Outcome Measure	Measure Description
Disease control rate (DCR)	Assessed as the percentage of patients with advanced or metastatic cancer who have achieved complete response, partial response, and stable disease to a therapeutic intervention in clinical trials of anticancer agents.
Time to response (TTR)	Measured as the amount of time elapsed until drug response is achieved for the first time.
Duration of response (DOR)	Measured as the amount of time a patient responds to a treatment before disease progresses or the patient dies.
Progression-free survival (PFS)	Measured from the date of first infusion of CAR-T cells until the first date when progressive disease (PD) is objectively documented or death from any cause, whichever is earlier.
Overall survival (OS)	Measured from the date of first infusion of CAR-T cells until death.