Research Area:

Solid Tumors

AMG 193

Amgen Study ID Number: 20210023

NCT Number: 05094336

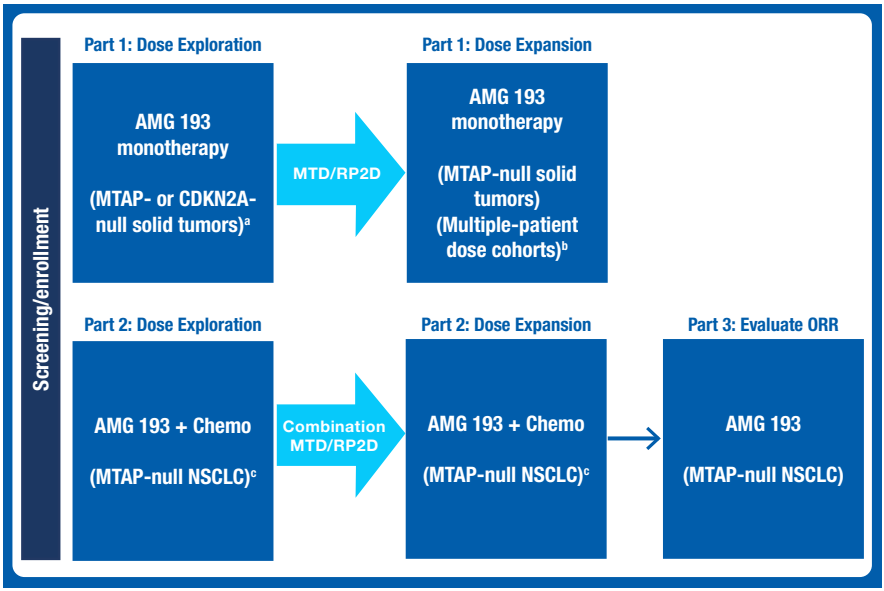
A Phase 1/1b/2 Study Evaluating the Safety, Tolerability, PK, PD, and Efficacy of AMG 193 Alone and in Combination With Docetaxel in Subjects With Advanced MTAP-Null Solid Tumors

Primary Endpoints:

- Parts 1 and 2: Safety and Tolerability
- Part 3: ORR

Key Secondary Endpoints:

- Parts 1 and 2: PK
- Parts 1, 2, and 3: DCR, DoR, TTR, duration of SD, PFS, and OS
- Part 3 only: Safety



[a]Parts 1a and 1b: MTAP- or CDKN2A-null solid tumors; [b]Part 1c: MTAP-null squamous NSCLC; Part 1d: MTAP-null adenocarcinoma NSCLC; Part 1e: MTAP-null BTC; Part 1f: MTAP-null HNSCC; Part 1g: MTAP-null pancreatic adenocarcinoma; Part 1h: MTAP-null solid tumors other than squamous or adenocarcinoma NSCLC, BTC, HNSCC, pancreatic adenocarcinoma, primary brain tumor, and lymphoma; [c]Parts 2a and 2b: MTAP null NSCLC.

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Key Summary Point:

This is an open-label, phase 1/1b/2 study evaluating the safety, tolerability, PK, PD, and efficacy of AMG 193 alone and in combination with chemotherapy in adult subjects with advanced MTAP-null solid tumors

Key Inclusion Criteria:

- Adults (≥ 18 years old) with histologically confirmed metastatic or locally advanced solid tumors not amenable to curative treatment with surgery and/or radiation
- Evidence of homozygous loss of CDKN2A (null) [Parts 1a/b only] and/or MTAP (null) in the tumor tissue or blood [Parts 1a–1h, Parts 2a/b] or lost MTAP expression in the tumor tissue [Parts 1a–1h, Parts 2a/b]
- Measurable disease per RECIST v1.1 criteria
- ECOG PS of ≤ 1
- Adequate hematopoietic, renal, cardiac, and liver function
- Life expectancy ≥ 3 months in the opinion of the investigator
- A total of 25 slides of archived tumor tissue FFPE (sample collected within 5 years) or an archival block must be available
- For Part 1f (MTAP-null or lost MTAP expression HNSCC): Must be willing to undergo tumor biopsy
- For Parts 1a and 1b backfill: Must be willing to undergo tumor biopsy, before start of and while on treatment

Key Exclusion Criteria:

- Spinal cord compression or untreated brain metastases or leptomeningeal disease
- Evidence of current interstitial lung disease or active SARS-COV2 infection
- History of other malignancy within the past 2 years
- Active infection
- History of solid organ transplant
- Prior treatment with an MAT2A inhibitor or a PRMT5 inhibitor or docetaxel [Part 2 only]
- Unresolved toxicity from prior anticancer therapy
- Diagnosis of congenital short QT syndrome
- Known positive test for HIV
- Major surgery
- Prior irradiation to 25% of the bone marrow
- Live vaccine therapy within 4 weeks before study drug administration
- Positive hepatitis B surface antigen or positive HCV RNA by PCR

Additional Information:

- www.clinicaltrials.gov Identifier—NCT05094336

BTC, biliary tract cancer; CDKN2A, cyclin-dependent kinase inhibitor 2A; Chemo, chemotherapy; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FFPE, formalin-fixed, paraffin embedded; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HNSCC, head and neck squamous cell carcinoma; MAT2A, methionine adenosyltransferase 2α; MTAP, methylthioadenosine phosphorylase; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PCR, polymerase chain reaction; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; PRMT5, protein arginine methyltransferase 5; RECIST, Response Evaluation Criteria in Solid Tumors; RNA, ribonucleic acid; RP2D, recommended phase 2 dose; SARS-COV2, severe acute respiratory syndrome coronavirus 2; SD, stable disease; TTR, time to response

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