A Phase I Study of IAG933 in Patients With Advanced Mesothelioma and Other Solid Tumors

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An Open-label, Multi-center, Phase I Study of Oral IAG933 in Adult Patients With Advanced Mesothelioma and Other Solid Tumors
ClinicalTrials.gov Identifier:
NCT04857372
Novartis Reference Number:CIAG933A12101
See if you Pre-qualify
All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The purpose of this study is to characterize the safety and tolerability of IAG933 in patients with mesothelioma, NF2/LATS1/LATS2 mutated tumors and tumors with functional YAP/TAZ fusions and to identify the maximum tolerated dose and/or recommended dose. This is a phase I, open-label, multi-center study of IAG933 as a single agent consisting of a dose escalation part, followed by a dose expansion part. The escalation part will characterize the safety and tolerability. After the determination of the recommended dose/maximum tolerated dose, dose expansion will assess the preliminary anti-tumor activity in defined patient populations and further assess the safety and tolerability at RD/MTD.

Condition
Mesothelioma
Phase
Phase1
Overall Status
Recruiting
Number of Participants
156
Start Date
Oct 21, 2021
Completion Date
Sep 04, 2026
Gender
All
Age(s)
18 Years - 120 Years (Adult, Older Adult)

Interventions

Drug

IAG933

Capsule

Eligibility Criteria

Inclusion Criteria:

1. Signed informed consent must be obtained prior to participation in the study.
2. Male or female patients must be ≥ 18 years of age.
3. Dose escalation part: patients with histologically or cytologically confirmed diagnosis of advanced (unresectable or metastatic) mesothelioma or other solid tumors. Patients with solid tumors other than mesothelioma must have local available data for loss-of-function NF2/LATS1/LATS2 genetic alterations (truncating mutation or gene deletion; LATS1/LATS2 mutations will only be included in the dose escalation part), or functional YAP/TAZ fusions. Patients with malignant EHE can be enrolled with only histological confirmation of the disease. Patients must have failed available standard therapies, be intolerant of or ineligible for standard therapy, or for whom no standard therapy exists.
4. Dose expansion part: the following patients will be enrolled into 3 different treatment groups:

Group 1: Advanced (unresectable or metastatic) MPM patients who have failed available standard therapies for advanced/metastatic disease, be intolerant or ineligible to receive such therapy, or for whom no standard therapy exists.

Group 2: Advanced (unresectable or metastatic) solid tumor patients with available local data for NF2 truncating mutation or deletions. Patient must have failed available standard therapies, be intolerant or ineligible to receive such therapy, or for whom no standard therapy exists.

Group 3: Advanced (unresectable or metastatic) solid tumor patients with available local data for functional YAP/TAZ fusions. EHE patients can be included with only histological confirmation of the disease. Patient must have failed available standard therapies, be intolerant or ineligible to receive such therapy, or for whom no standard therapy exists.

Group 4: Advanced (unresectable or metastatic) non-pleural mesothelioma patients who have failed available standard therapies for advanced/metastatic disease, are intolerant or ineligible to receive such therapy, or for whom no standard therapy exists.
5. Presence of at least one measurable lesion according to mRECIST v1.1 for mesothelioma patients, RECIST v1.1 for patients with other solid tumors, or RANO for patients with primary brain tumors.
6. Patient must have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to the treating institution's guidelines. Patient must be willing to undergo a new tumor biopsy at screening/baseline, and again during therapy on this study. An archival tumor sample may be used at screening. During the dose expansion part of the study, a decision may be made to stop the collection of on-treatment biopsies.

Exclusion Criteria:

1. Treatment with any of the following anti-cancer therapies prior to the first dose of study treatment within the stated timeframes:

1. ≤ 4 weeks for thoracic radiotherapy to lung fields or limited field radiation for palliation within ≤ 2 weeks prior

to the first dose of study treatment. An exception to this exists for patients who have received palliative radiotherapy to bone, who must have recovered from radiotherapy-related toxicities but for whom a 2-week washout period is not required.
2. ≤ 4 weeks or ≤ 5 half-lives (whichever is shorter) for biological therapy (including monoclonal antibodies) or continuous or intermittent small molecule therapeutics or any other investigational agent.
3. ≤3 weeks for treatment with cytotoxic agents or ≤ 6 weeks for cytotoxic agents with risk of major delayed toxicities, such as nitrosoureas and mitomycin C.
4. ≤ 4 weeks for immuno-oncologic therapy, such as CTLA4, PD-1, or PD-L1 antagonists
5. Prior treatment with TEAD inhibitor at any time
2. For mesothelioma patients: use of non-invasive antineoplastic therapy (e.g., tumor treating fields, brand name Optune LuaTM) within 2 weeks of the tumor assessment at screening.
3. Malignant disease, other than that being treated in this study.
4. Insufficient renal function at Screening.
5. Clinically significant cardiac disease or risk factors at screening
6. Insufficient bone marrow function at screening.
7. Insufficient hepatic function at screening.
8. Patients who have the following laboratory values \> Common Terminology Criteria for Adverse Events (CTCAE) grade 1:

1. Potassium
2. Magnesium
3. Total calcium (corrected for low serum albumin)
9. Known active COVID-19 infection.
10. Pregnant or nursing (lactating) women,
11. Japan only: patients with a history of drug- and/or non-drug-induced interstitial lung disease (ILD) ≥ Grade 2.

Other protocol-defined inclusion/exclusion criteria may apply.

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