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Study of HRO761 Alone or in Combination in Cancer Patients With Specific DNA Alterations Called Microsatellite Instability or Mismatch Repair Deficiency.

Last Update: Apr 08, 2025
An Open-label, Multi-center Phase I/Ib Dose Finding and Expansion Study of HRO761 as Single Agent and in Combinations in Patients With Microsatellite Instability-High or Mismatch Repair Deficient Advanced Solid Tumors.
ClinicalTrials.gov Identifier:
NCT05838768
Novartis Reference Number:CHRO761A12101
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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 main purpose of the study is to evaluate the safety and tolerability of HRO761 and identify the recommended dose(s), i.e., the optimal safe and active dose of HRO761 alone or in combination with pembrolizumab or irinotecan that can be given to patients who have cancers with specific molecular alterations called MSIhi (Microsatellite Instability-high) or dMMR (Mismatch Repair Deficient) that might work best to treat these specific cancer types and to understand how well HRO761 is able to treat those cancers. The new drug being tested in the study, HRO761, is an oral drug that acts on a protein called Werner (WRN), which may contribute to cancer growth. By acting on WRN, HRO761 may be able to stop the growth of the cancer.

This is the first time HRO761 is given to patients and the first time HRO761 is used in combination with pembrolizumab or irinotecan.

Pembrolizumab and irinotecan are drugs approved in several countries and used as standard treatment for certain types of cancer (e.g., colon cancer and small cell lung cancer).

This research study will consist of various treatment arms to investigate HRO761 as single agent and in the combinations.

For HRO761 single agent, the research will be done in two parts. The first part is called "dose escalation" and the second part is called "dose optimization". In the dose escalation part, different groups of people will be given different doses of HRO761 to understand how the body reacts to different doses of the drug and how well the drug acts against the cancer. During the dose optimization part, the selected doses will be tested in more patients until a recommended dose(s) is found.

The combinations of HRO761 with pembrolizumab or irinotecan also will be tested in a dose escalation part to

find the recommended doses of HRO761 in these combinations.

Once the recommended doses are determined, more people may be treated with HRO761 alone or together with pembrolizumab or irinotecan to further assess the study treatment effects against various types of MSIhi or dMMR cancers. This part is called dose expansion.

For this research, a number of blood and tissue samples will be collected during the study. Patients may be asked to come approximately 8 times to the clinic during the first 8 weeks and approximately every 2 or 4 weeks thereafter.

Patients will be in the study as long as their study doctor believes that they may be benefiting from the study treatment, unless the patient decides to stop study treatment.

Condition
MSIhi or dMMR Advanced Unresectable or Metastatic Solid Tumors, Including Colorectal Cancers
Phase
Phase1
Overall Status
Recruiting
Number of Participants
327
Start Date
Jun 27, 2023
Completion Date
May 30, 2029
Gender
All
Age(s)
18 Years - 100 Years (Adult, Older Adult)

Interventions

Drug

HRO761

Tablet
Drug

irinotecan

Concentrate for solution for infusion
Biological

pembrolizumab

Concentrate for solution for infusion

Eligibility Criteria

Key Inclusion criteria:

* Patients with advanced unresectable or metastatic MSIhi or MMR deficient (dMMR) solid tumors who have progressed after or are intolerant to prior standard therapy.

* Arm A and C: Patients must have progressed on the most recent therapy for advanced disease including one prior line of immune checkpoint inhibitor therapy.
* Arm B: Patients should have received prior chemotherapy or targeted therapy, and patients should have received prior immune checkpoint inhibitor or should be expected to benefit from immune checkpoint inhibitor therapy.
* Eastern Cooperative Oncology Group (ECOG) Performance Status ≤ 1
* Measurable disease as determined by RECIST version 1.1
* HRO761 s.a. (Arm A) dose finding only: Patients must have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to the treating institution's guidelines. Patients must be willing to undergo a new tumor biopsy at screening, and during therapy on the study. A biopsy from the same lesion is preferred if safe and medically feasible. Exceptions may be considered after documented discussion with Novartis.
* All patients (Arm A, B and C) will have available archival tumor tissue obtained prior to study treatment initiation (in addition to newly obtained tumor biopsy at screening for Arm A), to allow retrospective MSIhi/dMMR status confirmation.

Key Exclusion criteria:

* Impaired cardiac function or clinically significant cardiac disease
* Clinically significant eye impairment
* Patients with a primary Central Nervous System (CNS) tumor or tumor metastatic to the CNS
* Human Immunodeficiency Virus (HIV) infection
* Active Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) or Tuberculosis infection. Patients whose disease is controlled under antiviral therapy should not be excluded.
* History of severe hypersensitivity reactions to any ingredient of study drug(s)
* Impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of study drugs (e.g., severe ulcerative disease, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection), except for prior gastrectomy.

Other protocol-defined inclusion/exclusion criteria may apply

Belgium

Novartis Investigative Site

Recruiting

Bruxelles,1200,Belgium

China

Novartis Investigative Site

Recruiting

Beijing,100036,China

Novartis Investigative Site

Recruiting

Guangzhou,510655,China

France

Novartis Investigative Site

Recruiting

Bordeaux,33076,France

Novartis Investigative Site

Recruiting

Marseille,13273,France

Germany

Novartis Investigative Site

Recruiting

Essen,45147,Germany

Novartis Investigative Site

Recruiting

Ulm,89081,Germany

Israel

Novartis Investigative Site

Recruiting

Tel Aviv,6423906,Israel

Italy

Novartis Investigative Site

Recruiting

Milano,MI,20162,Italy

Novartis Investigative Site

Recruiting

Rozzano,MI,20089,Italy

Japan

Novartis Investigative Site

Recruiting

Kashiwa,Chiba,277 8577,Japan

Korea, Republic of

Novartis Investigative Site

Recruiting

Seoul,03722,Korea, Republic of

Norway

Novartis Investigative Site

Recruiting

Oslo,0310,Norway

Singapore

Novartis Investigative Site

Recruiting

Singapore,119228,Singapore

Spain

Novartis Investigative Site

Recruiting

Barcelona,Catalunya,08035,Spain

Novartis Investigative Site

Recruiting

Valencia,Comunidad Valenciana,46010,Spain

Novartis Investigative Site

Recruiting

Madrid,28009,Spain

Novartis Investigative Site

Recruiting

Madrid,28040,Spain

Sweden

Novartis Investigative Site

Recruiting

Stockholm,17176,Sweden

Taiwan

Novartis Investigative Site

Recruiting

Taipei,10002,Taiwan

United Kingdom

Novartis Investigative Site

Recruiting

Oxford,Ox3 7le,United Kingdom

Novartis Investigative Site

Recruiting

London,Sw3 6jj,United Kingdom

United States

Univ of TX MD Anderson Cancer Cntr

Recruiting

Houston,Texas,77030,United States

Hannah Clemente

Email: hrcantu@mdanderson.org

Timothy Yap

Dana Farber Cancer Institute

Recruiting

Boston,Massachusetts,02215,United States

Asaf Maoz

Karly Griffin

Phone: 617-632-4272
Email: Karly_Griffin@DFCI.HARVARD.EDU

Memorial Sloan Kettering

Recruiting

New York,New York,10017,United States

Michael Bonner Foote

Mina Ito

Phone: +1 646 227 2157
Email: Itom2@mskcc.org

Columbia University Medical Ctr

Recruiting

New York,New York,10032,United States

Edmond Chan

Joy Kim

Phone: 646-317-4850
Email: jk4704@cumc.columbia.edu

University of California LA

Recruiting

Los Angeles,California,90095,United States

Kirllos Boctor

Phone: 310-582-4069
Email: Kboctor@mednet.ucla.edu

Zev A Wainberg

UCSF

Recruiting

San Francisco,California,94115,United States

Pamela Munster

Sherry Chen

Phone: 415-353-7284
Email: Sherry.Chen2@ucsf.edu

Worldwide Contacts

If the location of your choosing does not feature any contact detail, please reach out using the information below.

Novartis Pharmaceuticals

Phone: +41613241111
Email:

Novartis Pharmaceuticals

Phone: 1-888-669-6682
Email: novartis.email@novartis.com

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6. tel:+1 646 227 2157
7. mailto:ltom2@mskcc.org
8. tel:646-317-4850
9. mailto:jk4704@cumc.columbia.edu
10. tel:310-582-4069
11. mailto:Kboctor@mednet.ucla.edu
12. tel:415-353-7284
13. mailto:Sherry.Chen2@ucsf.edu
14. tel:+41613241111
15. mailto:
16. tel:1-888-669-6682
17. mailto:novartis.email@novartis.com