A Study of Multiple Immunotherapy-Based Treatment Combinations in Participants With Metastatic Pancreatic Ductal Adenocarcinoma (Morpheus-Pancreatic Cancer)

ClinicalTrials.gov Identifier: NCT03193190

Recruitment Status: Recruiting
First Posted: June 20, 2017
Last Update Posted: June 15, 2018

See Contacts and Locations

Sponsor:
Hoffmann-La Roche

Information provided by (Responsible Party):
Hoffmann-La Roche

Study Description

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Brief Summary:
A Phase Ib/II, open-label, multicenter, randomized study designed to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumor activity of immunotherapy-based treatment combinations in participants with metastatic Pancreatic Ductal Adenocarcinoma (PDAC).

Condition or disease	Intervention/treatment	Phase
Pancreatic Adenocarcinoma	Drug: Nab-Paclitaxel Drug: Gemcitabine Drug: Oxaliplatin Drug: Leucovorin Drug: Fluorouracil Drug: Atezolizumab Drug: Cobimetinib Drug: PEGPH20 Drug: BL-8040	Phase 1 Phase 2

Study Design

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Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	185 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Immunotherapy-Based Treatment Combinations in Patients With Metastatic Pancreatic Ductal Adenocarcinoma (Morpheus-Pancreatic Cancer)
Actual Study Start Date:	July 5, 2017
Estimated Primary Completion Date:	November 16, 2019
Estimated Study Completion Date:	April 4, 2020

Arms and Interventions

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Arm	Intervention/treatment
Active Comparator: Chemotherapy (Gemcitabine + Nab-Paclitaxel or mFOLFOX6) Participants who progressed on a prior fluoropyrimidine-based regimen will receive gemcitabine + nab-paclitaxel. Participants who progressed on a prior gemcitabine-based regimen will receive 5-fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6). Participants who progressed on treatment, may have the option of receiving Atezolizumab + Cobimetinib treatment, provided they meet the eligibility criteria.	Drug: Nab-Paclitaxel Nab-Paclitaxel 125 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Days 1, 8, and 15 of each 28-day cycle. Drug: Gemcitabine Gemcitabine 1000 mg/m^2 IV infusion on Days 1, 8, and 15 of each 28-day cycle. Drug: Oxaliplatin Oxaliplatin 85 mg/m^2 IV infusion on Days 1 and 15 of each 28-day cycle. Drug: Leucovorin Leucovorin 400 mg/m^2 IV infusion on Days 1 and 15 of each 28-day cycle. Drug: Fluorouracil Fluorouracil 400 mg/m^2 IV push on Days 1 and 15; and fluorouracil 2400 mg/m^2 IV continuous infusion over 46 hours on Days 1 and 2 and on Days 15 and 16 of each 28-day cycle.
Experimental: Atezolizumab + Cobimetinib Participants will receive cobimetinib 60 milligrams (mg) once daily orally on Days 1-21 of each 28-day cycle; and atezolizumab 840	Drug: Atezolizumab Atezolizumab will be administered as per the schedule specified in the

mg IV infusion on Days 1 and 15 of each 28-day cycle.	respective arm. Drug: Cobimetinib Cobimetinib will be administered as per the schedule specified in the respective arm.
Experimental: Atezolizumab + PEGPH20 Participants will receive PEGPH20 3 micrograms per kilogram (mcg/kg) IV infusion on Days 1, 8 and 15 of each 21-day cycle; and atezolizumab 1200 mg IV infusion on Day 1 of each 21-day cycle. Participants who progressed on treatment, may have the option of receiving Atezolizumab + Cobimetinib treatment, provided they meet the eligibility criteria.	Drug: Atezolizumab Atezolizumab will be administered as per the schedule specified in the respective arm. Drug: PEGPH20 PEGPH20 will be administered as per the schedule specified in the respective arm.
Experimental: Atezolizumab + BL-8040 Participants will receive BL-8040 1.25 milligrams per kilogram (mg/kg) subcutaneously (SC) on Days 1-5 of the first week, followed by combination treatment consisting of BL-8040 1.25 mg/kg SC three times a week on non-consecutive days and atezolizumab 1200 mg IV infusion on Day 1 of each 21-day cycle. Participants who progressed on treatment, may have the option of receiving Atezolizumab + Cobimetinib treatment, provided they meet the eligibility criteria.	Drug: Atezolizumab Atezolizumab will be administered as per the schedule specified in the respective arm. Drug: BL-8040 BL-8040 will be administered as per the schedule specified in the respective arm.

Outcome Measures

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Primary Outcome Measures:

1. Percentage of Participants With Objective Response, as Determined by Investigator According to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 (v1.1) [Time Frame: From randomization until disease progression or loss of clinical benefit (up to approximately 3-5 years)]
2. Percentage of Participants With Adverse Events (AEs) [Time Frame: From first study treatment administration until 30 days after the last dose or until initiation of new systemic anti-cancer therapy, whichever occurs first (up to approximately 3-5 years)]

Secondary Outcome Measures:

1. Progression-Free Survival (PFS), as Determined by Investigator According to RECIST v1.1 [Time Frame: From randomization up to the first occurrence of disease (up to approximately 3-5 years)]
2. Overall Survival [Time Frame: From randomization up to death from any cause (up to approximately 3-5 years)]
3. Percentage of Participants who are Alive at Month 6 [Time Frame: Month 6]
4. Duration of Response, as Determined by Investigator According to RECIST v1.1 [Time Frame: From the date of first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first (up to approximately 3-5 years)]

5. Percentage of Participants With Disease Control, as Determined by Investigator According to RECIST v1.1 [Time Frame: From randomization until disease progression or loss of clinical benefit (up to approximately 3-5 years)]
6. Serum Concentration of Atezolizumab [Time Frame: Pre-infusion (0 hour [hr]), 30 minutes (min) post-infusion (infusion duration=60 min) on Day 1 of Cycle 1; pre-infusion (0 hr) on Day 1 of Cycles 2, 3, 4, 8, 12, 16 (each cycle=28 days); 30 days and 120 days after last dose(up to approximately 3-5 years)]
7. Plasma Concentration of Cobimetinib [Time Frame: Pre-dose (0 hr) and 2-4 hrs post-dose on Day 15 of Cycle 1 (cycle length=28 days)]
8. Plasma Concentration of PEGPH20 [Time Frame: Pre-infusion (0 hr) on Day 1 of Cycle 1 up to 30 days and 120 days after last dose (up to approximately 3-5 years) (Detailed timeframe is provided in outcome measure description)]

   Pre-infusion (0 hr), 5 min and 1-3 hrs post infusion (infusion duration=10-12 min) on Day 1 of Cycle 1; pre-infusion (0 hr) on Days 8 and 15 of Cycle 1, Day 1 of Cycles 3, 4, 8, 12, 16; pre-infusion (0 hr) and 5 min post-infusion on Day 1 of Cycle 2 (each cycle=21 days); 30 days and 120 days after last dose (up to approximately 3-5 years)

9. Plasma Concentration of BL-8040 [Time Frame: Pre-dose (0 hr) on Day 1 of priming period (1 week prior to Day 1 of Cycle 1) up to 30 days after last dose (up to approximately 3-5 years) (Detailed timeframe is provided in outcome measure description)]

   Pre-dose (0 hr) on Day 1 of priming period (1 week prior to Day 1 of Cycle 1); 1 hr post-dose on Days 1, 5 of priming period; pre-dose (0 hr), 1 hour post-dose on Day 15 of Cycle 1 and Day 1 of Cycles 2, 3, 4, 8, 12, 16; pre-dose (0 hr) on Day 1 of Cycle 20 and every 4 cycles thereafter (each cycle=21 days) (up to approximately 3-5 years); 30 days after last dose (up to approximately 3-5 years)

10. Percentage of Participants With Anti-Drug Antibody (ADA) to Atezolizumab [Time Frame: Pre-infusion (0 hr) on Day 1 of Cycles 1, 2, 3, 4, 8, 12, 16 (each cycle=28 days); 30 days and 120 days after last dose (up to approximately 3-5 years)]
11. Percentage of Participants With ADA to PEGPH20 [Time Frame: Pre-infusion (0 hr) on Day 1 of Cycles 1, 2, 3, 4, 8, 12, 16 (each cycle=21 days); 30 days and 120 days after last dose (up to approximately 3-5 years)]
12. Percentage of Participants With ADA to BL-8040 [Time Frame: Pre-dose (0 hr) on Day 1 of priming period (1 week prior to Day 1 of Cycle 1) up to 30 days after last dose (up to approximately 3-5 years) (Detailed timeframe is provided in outcome measure description)]

    Pre-dose (0 hr) on Day 1 of priming period (1 week prior to Cycle 1 Day 1), Day 15 of Cycle 1 and Day 1 of Cycles 2, 3, 4, 8, 12, 16, 20 and every 4 cycles thereafter (each cycle=21 days) (up to approximately 3-5 years); 30 days after last dose (up to approximately 3-5 years)

Eligibility Criteria

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Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Histologically or cytologically confirmed metastatic pancreatic ductal adenocarcinoma
- Disease progression during or within 6 months after treatment with one line of 5-Fluorouracil (5-FU)- or gemcitabine-based chemotherapy in the metastatic setting
- Life expectancy greater than or equal to (>/=3) months
- Availability of a representative tumor specimen that is suitable for determination of programmed death-ligand 1 (PD-L1) and/or additional biomarker status via central testing
- Measurable disease (at least one target lesion) according to RECIST v1.1
- Adequate hematologic and end-organ function test results
- Tumor accessible for biopsy
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures as outlined for each specific treatment arm
- For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm, as outlined for each specific treatment arm

Exclusion Criteria:

- Symptomatic, untreated, or actively progressing central nervous system (CNS) metastases
- History of leptomeningeal disease
- Active or history of autoimmune disease or immune deficiency
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Positive human immunodeficiency (HIV) test at screening or at any time prior to screening
- Active hepatitis B or C virus infection or active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Prior allogeneic stem cell or solid organ transplantation
- History of malignancy other than pancreatic carcinoma within 2 years prior to screening, with the exception of those with a negligible risk of metastasis or death

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03193190***

Contacts

Locations

United States, California

Helen Diller Fam Comp Can Ctr — **Recruiting**
San Francisco, California, United States, 94158

United States, Connecticut

Smilow Cancer Hospital at Yale New Haven — **Recruiting**
New Haven, Connecticut, United States, 06510

United States, Massachusetts

Massachusetts General Hospital — **Recruiting**
Boston, Massachusetts, United States, 02114

Beth Israel Deaconess Medical Center — **Recruiting**
Boston, Massachusetts, United States, 02215

Dana-Farber Cancer Institute — **Recruiting**
Boston, Massachusetts, United States, 02215

United States, New York

Columbia University — **Suspended**
New York, New York, United States, 10032

Memorial Sloan Kettering Cancer Center — **Recruiting**
New York, New York, United States, 10065

United States, Oregon

Oregon Health and Science University — **Recruiting**
Portland, Oregon, United States, 97239

United States, Pennsylvania

Hillman Cancer Center;Medical Oncology — **Recruiting**
Pittsburgh, Pennsylvania, United States, 15232

United States, Tennessee

Sarah Cannon Cancer Center — **Recruiting**
Germantown, Tennessee, United States, 38138

Germany

Charite - Campus Virchow-Klinikum — **Recruiting**
Berlin, Germany, 13353

Universitätsklinikum Essen; Innere Klinik und Poliklinik für Tumorforschung — **Recruiting**
Essen, Germany, 45122

Korea, Republic of

Seoul National University Hospital — **Recruiting**
Seoul, Korea, Republic of, 03080

Asan Medical Center — **Recruiting**
Seoul, Korea, Republic of, 05505

Samsung Medical Center — **Recruiting**
Seoul, Korea, Republic of, 6351

Spain

Clínica Universidad de Navarra — **Recruiting**
Pamplona, Navarra, Spain, 31620

Hospital Universitario Vall d'Hebron — **Recruiting**
Barcelona, Spain, 08035

Sponsors and Collaborators

Hoffmann-La Roche

Investigators

Study Director: Clinical Trials Hoffmann-La Roche

More Information

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Responsible Party:	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT03193190 History of Changes
Other Study ID Numbers:	WO39608
	2016-004126-42 (EudraCT Number)
First Posted:	June 20, 2017 Key Record Dates
Last Update Posted:	June 15, 2018
Last Verified:	June 2018

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

Adenocarcinoma	Atezolizumab
Pancreatic Neoplasms	Albumin-Bound Paclitaxel
Carcinoma	Fluorouracil
Neoplasms, Glandular and Epithelial	Antibodies, Monoclonal
Neoplasms by Histologic Type	Antineoplastic Agents, Phytogenic
Neoplasms	Antineoplastic Agents
Digestive System Neoplasms	Tubulin Modulators
Neoplasms by Site	Antimitotic Agents
Endocrine Gland Neoplasms	Mitosis Modulators
Digestive System Diseases	Molecular Mechanisms of Pharmacological Action
Pancreatic Diseases	Antimetabolites, Antineoplastic
Endocrine System Diseases	Antimetabolites
Paclitaxel	Antiviral Agents
Gemcitabine	Anti-Infective Agents
Oxaliplatin	Enzyme Inhibitors