ForPatients
by Roche

Solid TumorsBladder CancerCancerNeoplasms

My Pathway: A Study Evaluating Herceptin/Perjeta, Tarceva, Zelboraf/Cotellic, Erivedge, Alecensa, and Tecentriq Treatment Targeted Against Certain Molecular Alterations in Participants With Advanced Solid Tumors

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	NCT02091141 PRO 02 ML28897

The clinical trial information herein is sourced from public registries such as ClinicalTrials.gov, EuClinicalTrials.eu, and ISRCTN.com. Additional patient-friendly (lay) content has been prepared by Roche to support understanding.

Official Title:

My Pathway: An Open-Label Phase IIa Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib/Cobimetinib, Vismodegib, Alectinib, and Atezolizumab in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents

Trial Summary:

This multicenter, non-randomized, open-label study will evaluate the efficacy and safety of six treatment regimens in participants with advanced solid tumors for whom therapies that will convey clinical benefit are not available and/or are not suitable options per the treating physician's judgment.

Genentech, Inc.
Sponsor

Phase 2
Phase

NCT02091141 PRO 02 ML28897
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

Inclusion Criteria:

General Inclusion Criteria:

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- Life expectancy greater than or equal to (#) 12 weeks
- Histologically documented metastatic cancer (solid tumors, not including hematologic malignancies)
- Participants who have received standard first-line therapy for metastatic cancer (except for the tumors for which no first-line therapy exists) and in whom a trial of targeted therapy is considered the best available treatment option. Eligible participants should not have available therapies that will convey clinical benefit and/or are not suitable options per the treating physician's judgment
- No previous treatment with the specific assigned study drug or any other drug sharing the same target
- Measurable disease by RECIST v1.1
- Eastern Cooperative Oncology Group Performance Status (ECOG PS) score of 0 or 1 (For patients enrolling in the atezolizumab arm, ECOG score must be documented within 7 days prior to first treatment and confirmation of ECOG PS must be entered into the interactive web response system [IWRS] prior to initiation of treatment)
- Adequate hematologic, renal, and liver function as defined by the protocol
- If applicable, use of contraception methods or abstinence as defined by the protocol

Study-Drug Specific Inclusion Criteria:

Trastuzumab plus Pertuzumab

- Molecular testing results from clinical laboratory improvement amendments (CLIA)-certified laboratories (using tissue and/or blood) demonstrating HER2 overexpression or amplification. Participants must have one of the following tumor types: biliary cancer, salivary cancer, or bladder cancer

a) For participants screened using a blood assay: obtain tissue-based testing result confirming study eligibility (within first 4 weeks after enrollment)

- Left ventricular ejection fraction (LVEF) greater than (>) 50 percent (%) or above the lower limit of the institutional normal range, whichever is lower
- Availability of an archival or new pre-treatment tissue sample is required if molecular testing was not performed by Foundation Medicine. Any available tumor tissue sample can be submitted. The tissue sample must be submitted within 4 weeks after enrollment

Erlotinib

- Molecular testing results from CLIA-certified laboratories (using tissue and/or blood) demonstrating EGFR-activating mutations

Vemurafenib plus Cobimetinib

- Molecular testing results from CLIA-certified laboratories (using tissue and/or blood) demonstrating BRAF V600 mutations a) For participants screened using a blood assay: obtain tissue-based testing result confirming study eligibility (within first 4 weeks after enrollment)

Vismodegib

- Molecular testing results from CLIA-certified laboratories (using tissue and/or blood) demonstrating hedgehog pathway relevant mutation (activating mutation of smoothened [SMO] or loss-of-function mutation of protein patched homolog-1 [PTCH-1])

a) For participants screened using a blood assay: obtain tissue-based testing result confirming study eligibility (within first 4 weeks after enrollment)

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- All non-hematological adverse events related to any prior chemotherapy, surgery, or radiotherapy must have resolved to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Grade less than or equal to (#) 2 prior to starting therapy

Alectinib

- Molecular testing results from CLIA-certified laboratories (using tissue and/or blood) demonstrating anaplastic lymphoma kinase (ALK) gene rearrangements, ALK mutations, ALK copy number gain or (for melanoma only) increased ALK expression or presence of ALK-alternative transcription initiation transcript (ALKATI) a) For participants screened using a blood assay: obtain tissue-based testing result confirming study eligibility (within first 4 weeks after enrollment)

Atezolizumab

- Molecular testing results from CLIA-certified laboratories (using tissue) demonstrating elevated tissue tumor mutational burden (tTMB #10 mutations/ Megabase [Mb])
- For patients where molecular testing was not performed using Foundation Medicine, submission of an archival or new pretreatment tissue sample is mandatory. For patients where molecular testing was performed using Foundation Medicine, submission of an archival or new pretreatment tissue sample is required, if available. The tissue sample must be submitted within 4 weeks after enrollment

General Exclusion Criteria:

- Participants with hematologic malignancies
- Concurrent administration of any other anti-cancer therapy (except male participants with prostate cancer receiving androgen blockade): Bisphosphonates and denosumab are allowed; Most recent anti-cancer therapy #28 days and have not recovered from the side effects, excluding alopecia; Radiation therapy within #14 days
- Active or untreated brain metastases
- History of carcinomatous meningitis
- Uncontrolled concurrent malignancy (early stage is allowed if not requiring active therapy or intervention)
- Pregnant or breastfeeding women, or intending to become pregnant during the study
- Any significant cardiovascular events within 6 months prior to study entry
- Pulmonary embolism within 30 days prior to study entry
- History or presence of clinically significant ventricular or atrial dysrhythmia >Grade 2 per NCI CTCAE v4.0
- Any other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or may interfere with the interpretation of study results
- Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol

Study-Drug Specific Exclusion Criteria:

Trastuzumab plus Pertuzumab

- Previous treatment with any HER2-targeted therapy

Erlotinib

- Non-small cell lung cancer (NSCLC) or pancreatic cancer identified by exon 19 deletions or exon 21 L858R substitution mutations

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- EGFR amplifications in the absence of EGFR-activating mutations
- Cancers with exon 20 mutations
- Previous treatment with erlotinib or any other EGFR inhibitor
- Inability to swallow pills
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude absorption of erlotinib

Vemurafenib plus Cobimetinib

- Malignant melanoma, papillary thyroid cancer, colorectal cancer, or hematologic malignancy including multiple myeloma
- LVEF below institutional lower level of normal (LLN) or below 50%, whichever is lower
- History of or evidence of retinal pathology on ophthalmologic examination that is considered a risk factor for neurosensory retinal detachment, retinal vein occlusion (RVO), or neovascular macular degeneration
- Presence of any of the following conditions, which are risk factors for RVO: Uncontrolled glaucoma with intraocular pressure >21 millimetres of mercury (mm Hg); Serum cholesterol #Grade 2; Hypertriglyceridemia #Grade 2; Hyperglycemia (fasting) #Grade 2; Grade #2 uncontrolled hypertension (participants with a history of hypertension controlled with anti-hypertensive medication to Grade </=1 are eligible)
- Prior or concurrent malignancy with known RAS mutation
- Previous treatment with vemurafenib or any other BRAF inhibitor (prior sorafenib is allowed)
- Previous treatment with cobimetinib or any other mitogen-activated protein/extracellular signal-regulated kinase (MEK) inhibitor
- Prior treatment with a RAF inhibitor
- Inability to swallow pills
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude absorption of vemurafenib
- History of congenital long QT syndrome or mean (average of triplicate measurements) corrected QT (QTc) measured using Fridericia's method #450 millisecond (ms) at baseline or uncorrectable abnormalities in serum electrolytes (sodium, potassium, calcium, magnesium, phosphorus)

Vismodegib

- Basal cell carcinoma of the skin, medulloblastoma, small-cell lung cancer, or hematologic malignancies
- Previous treatment with vismodegib or any other hedgehog pathway inhibitor
- Inability to swallow pills
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude absorption of vismodegib

Alectinib

- ALK-positive NSCLC, neuroblastoma, and childhood tumors
- Previous treatment with alectinib or any other ALK inhibitor
- Participants with symptomatic bradycardia
- Administration of strong/potent cytochrome P3A4 (CYP3A4) inhibitors or inducers within 14 days prior to the first dose of study treatment and while on treatment with alectinib
- Inability to swallow pills
- Refractory nausea and vomiting, malabsorption, external biliary shunt, or significant bowel resection that would preclude absorption of alectinib

Atezolizumab

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- History of leptomeningeal disease
- Uncontrolled tumor pain
- Asymptomatic metastatic lesions that would likely cause functional deficits or intractable pain with further growth (e.g., epidural metastasis that is not currently associated with spinal cord compression) should be considered for loco-regional therapy if appropriate prior to enrollment
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring recurrent drainage procedures (once monthly or more frequently). Patients with indwelling catheters are allowed
- Uncontrolled or symptomatic hypercalcemia
- Previous treatment with atezolizumab or another programmed death-1 (PD-1)/PD-L1 inhibitor
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Known hypersensitivity to biopharmaceutical agents produced in Chinese hamster ovary cells
- Known allergy or hypersensitivity to any component of the atezolizumab formulation
- Active or history of autoimmune disease or immune deficiency
- Prior allogeneic stem cell or solid organ transplantation
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Positive human immunodeficiency virus (HIV) test, active hepatitis B virus (HBV) infection, active hepatitis C virus (HCV) infection or active tuberculosis
- Severe infection within 4 weeks prior to initiation of study treatment
- Treatment with therapeutic oral or IV antibiotics within 2 weeks prior to initiation of study treatment
- Significant cardiovascular disease, such as New York Heart Association cardiac disease (Class II or greater), myocardial infarction, or cerebrovascular accident within 3 months prior to initiation of study treatment, unstable arrhythmia, or unstable angina
- Major surgical procedure other than for diagnosis within 4 weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the course of the study
- Treatment with a live, attenuated vaccine within 4 weeks prior to initiation of study treatment, or anticipation of need for such a vaccine during the course of the study or within 5 months after the final dose of atezolizumab
- History of other malignancy within 5 years prior to screening, with the exception of those with a negligible risk of metastasis or death, such as adequately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, localized prostate cancer, ductal carcinoma in situ, or Stage I uterine cancer
- Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the participant at high risk from treatment complications
- Prior treatment with cluster of differentiation 137 (CD137) agonists or immune checkpoint blockade therapies
- Treatment with systemic immunostimulatory agents within 4 weeks or five half-lives of the drug (whichever is longer) prior to randomization
- Treatment with systemic immunosuppressive medication within 2 weeks prior to initiation of study treatment, or anticipation of need for systemic immunosuppressive medication during the course of the study

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