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A study of the safety, pharmacokinetics, and therapeutic activity of cibisatamab in combination with atezolizumab in participants with locally advanced and/or metastatic carcinoembryonic antigen (CEA)-positive solid tumors

Submission date	Recruitment status	[_] Prospectively registered
23/02/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/06/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
30/09/2026	Cancer	

Plain English summary of protocol

Background and study aims

This is a study to evaluate the safety, tolerability (side effects) and effectiveness of cibisatamab in combination with atezolizumab in patients with locally advanced and/or metastatic carcinoembryonic antigen (CEA)-positive solid tumors. Locally advanced cancer is cancer that has spread only to nearby tissues or lymph nodes, while metastatic cancer is cancer that has spread to other parts of the body. CEAs are substances (usually proteins) that are produced by some types of cancer.

Who can participate?

Patients with locally advanced and/or metastatic CEA-positive solid tumors

What does the study involve?

Part I of the study is subdivided into parts IA and IB. In Part IA participants receive increasing doses with a starting dose of 5 mg of cibisatamab given once a week and a fixed, flat dose of 1200 mg of atezolizumab given every 3 weeks, to evaluate the safety and determine the highest tolerated dose of cibisatamab in combination with atezolizumab. Part IB is a dose/schedule finding part that will test different schedules of cibisatamab in combination with atezolizumab.

What are the possible benefits and risks of participating?

Data from previous studies suggest that cibisatamab and atezolizumab could act together in their anti-cancer properties and their combination could provide a meaningful clinical benefit in patients with cancer. Potential side effects for cibisatamab and atezolizumab include gastrointestinal (GI) side effects (diarrhea), breathing side effects (shortness of breath and lack of oxygen), and blood side effects (low white blood cell count and low red blood cell count).

Where is the study run from?
Hospitals in the United States, Canada, Denmark, France, Italy, Netherlands and Spain

When is the study starting and how long is it expected to run for?
May 2015 to January 2020

Who is funding the study?
Genentech (USA)

Who is the main contact?
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Contact information

Type(s)
Public

Contact name
Miss Clinical Trials

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02650713

Clinical Trials Information System (CTIS)
2015-003771-30

Protocol serial number
WP29945

Study information

Scientific Title
An open-label, multicenter, dose-escalation and expansion Phase Ib study to evaluate the safety, pharmacokinetics, and therapeutic activity of cibisatamab in combination with atezolizumab in patients with locally advanced and/or metastatic CEA-positive solid tumors

Study objectives
To evaluate the safety, tolerability and clinical activity of cibisatamab in combination with atezolizumab in patients with locally advanced and/or metastatic CEA-positive solid tumors.

Part I of the study is subdivided into parts IA and IB. Part IA is dose escalation with a starting dose of 5 mg of cibisatamab given QW (once a week) and a fixed, flat dose of 1200 mg given Q3W (every 3 weeks) of atezolizumab, to evaluate the safety and determine the MTD of cibisatamab in combination with atezolizumab. Part IB is a dose/schedule finding part that will explore different administration schedules of cibisatamab in combination with atezolizumab (1200 mg Q3W) to establish the appropriate dose/schedule of cibisatamab in combination with atezolizumab.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/12/2015, Ethics Committee for Clinical Investigation of Navarra (Departamento de Salud, Pabellon de Docencia, C/ Irunlarrea, 3, 31008 Pamplona, Navarra, Spain; +34 (0) 848422495; ceic@cfnavarra.es), ref: 84/15

Primary study design
Interventional

Study design
Open-label multicenter dose-escalation and expansion Phase Ib clinical study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Solid tumors

Interventions
Dose-Escalation (Part IA):
Participants will receive cibisatamab weekly (QW) at escalating doses starting at 5 mg, in combination with a fixed dose (1200 mg) of atezolizumab every 3 weeks (Q3W). Cibisatamab dosage will not exceed the MTD if defined in the BP29541 study.
Atezolizumab will be administered at a fixed dose of 1200 milligrams (mg) by intravenous (IV) infusion.
Cibisatamab is administered by IV infusion weekly (QW) on days 1,8 and 15 of each 21-day cycle.
Step up dose cohorts: cibisatamab starting dose will be 40 mg and increase with each administration up to the MTD or 1200 mg, whichever is lower.
Tocilizumab will be administered as an IV infusion as necessary to treat adverse events.

Dose/Schedule Finding (Part IB):
Part IB will explore different cibisatamab administration schedules in combination with atezolizumab:
Cohort A: will compare the QW vs Q3W dosing schedules at a flat dose of cibisatamab.
Step up dosing schedules: cibisatamab dose will start at 40 mg and increase with each administration up to the MTD or 1200 mg, whichever occurs first.
Atezolizumab will be administered at a fixed dose of 1200 milligrams (mg) by intravenous (IV) infusion.
Cibisatamab is administered by IV infusion weekly (QW) or every 3 weeks (Q3W). Cohort A: cibisatamab starting dose will be 100 mg either QW or Q3W.
Step up dose cohorts: cibisatamab starting dose will be 40 mg and increase with each

administration up to the MTD or 1200 mg whichever is lower.
Tocilizumab will be administered as an IV infusion as necessary to treat adverse events.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Cibisatamab, atezolizumab, tocilizumab

Primary outcome(s)
1. Number of participants with adverse events (AEs) measured using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03 (NCI CTCAE v5 was used for CRS) at baseline up to 60 months
2. Percentage of participants with dose-limiting toxicities (DLTs) measured using NCI CTCAE v4.03 (NCI CTCAE v5 was used for CRS) at Day 1 up to Day 21
3. Maximum-tolerated dose (MTD) of cibisatamab in combination with atezolizumab measured using NCI CTCAE v4.03 (NCI CTCAE v5 was used for CRS) Part IA: Day 1 up to Day 21; Part IB Step-up Cohorts: Day 1 up to Day 7 after each dose escalation
4. Recommended Phase II Dose (RP2D) of cibisatamab in combination with atezolizumab measured using NCI CTCAE v4.03 (NCI CTCAE v5 was used for CRS) at Day 1 up to 60 months

Key secondary outcome(s)
1. Pharmacokinetics (PK): area under the concentration-time curve (AUC) of cibisatamab measured using a validated bi-functional PK assay at baseline up to 60 months
2. PK: volume of distribution at steady state (Vss) of cibisatamab measured using a validated bi-functional PK assay at baseline up to 60 months
3. PK: maximum serum concentration (Cmax) of cibisatamab measured using a validated bi-functional PK assay at baseline up to 60 months
4. PK: clearance (CL) of cibisatamab measured using a validated bi-functional PK assay at baseline up to 60 months
5. Pharmacodynamics: immune cell numbers measured using immunohistochemistry (IHC), gene expression and fluorescence-activated cell sorting (FACS) at pre-infusion (1 hour before infusion start) on Day 1 of Cycles 1, 2, 3, 6; Cycle 1 Days 2 and 8 (cycle length = 21 days)
6. Percentage of participants with objective response (partial response [PR] or complete response [CR] measured using Response Evaluation Criteria in Solid Tumors [RECIST]) at baseline up to 60 months. Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks thereafter until disease progression or treatment discontinuation.
7. Percentage of participants with disease control (PR, CR or stable disease [SD]) measured using RECIST at baseline up to 60 months. Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks thereafter until disease progression or treatment discontinuation.
8. Percentage of participants with stable disease (SD) measured using RECIST at baseline up to 60 months. Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks thereafter until disease progression or treatment discontinuation.
9. Duration of response (DOR) measured using RECIST from initial objective response (PR or CR to the first disease progression or death from any cause (up to 60 months). Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks

thereafter until disease progression or treatment discontinuation.
10. Progression-free survival (PFS) measured using RECIST V1.1 from first study treatment to the first occurrence of objective disease progression or death from any cause (up to 60 months). Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks thereafter until disease progression or treatment discontinuation.
11. Overall survival (OS) measured using the date of death from first study treatment to death from any cause (up to 60 months)
12. Best overall response (BOR) measured using RECIST v1.1 at baseline up to 60 months. Assessed at screening and after the start of treatment every 8 weeks for the first year, then every 12 weeks thereafter until disease progression or treatment discontinuation.

Completion date
13/01/2020

Eligibility

Key inclusion criteria
1. Confirmed locally advanced and/or metastatic solid tumor, with at least one tumor lesion of accessible non-critical location to biopsy, in participants who have progressed on a standard therapy, are intolerant to standard therapy, and/or are non-amenable to standard therapy
2. Radiologically measurable and clinically evaluable disease (as per RECIST v1.1)
3. Life expectancy (in the opinion of the investigator) of at least 12 weeks and lactate dehydrogenase (LDH) levels </= 2.5 ULN (upper limit of normal)
4. Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) 0-1
5. All acute toxic effects of any prior radiotherapy, chemotherapy, or surgical procedure must have resolved to Grade </= 1 or returned to baseline except alopecia (any grade) and Grade 2 peripheral neuropathy
6. Adequate hematological, liver, and renal function
7. Negative serum pregnancy test within 7 days prior to study treatment in premenopausal women and women </= 2 years after start of menopause (menopause is defined as amenorrhea for more than 2 years)
8. Participants must agree to remain abstinent or be willing to use effective methods of contraception as defined in the protocol
9. Participants with non-colorectal cancer should have confirmed CEA expression in tumor tissue. For colorectal cancer (CRC), the CEA assessment should be performed but the result is not required for participant selection

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
228

Key exclusion criteria

1. Active or untreated central nervous system (CNS) metastases as determined by computed tomography (CT) or magnetic resonance imaging (MRI) evaluation during screening and prior radiographic assessments
2. Spinal cord compression not definitively treated with surgery and/or radiation or previously diagnosed and treated spinal cord compression without evidence that disease has been clinically stable for at least 2 weeks prior to enrollment
3. Leptomeningeal disease
4. Participants with paraspinal, paratracheal, and mediastinal pathological lesions larger than 2 cm unless they are previously irradiated
5. Malignancies within 5 years prior to enrollment, with the exception of those with a negligible risk of metastasis or death and treated with expected curative outcome
6. Significant, uncontrolled concomitant diseases which could affect compliance with the protocol or interpretation of results
7. Uncontrolled hypertension, unstable angina, congestive heart failure (CHF), serious cardiac arrhythmia requiring treatment history of myocardial infarction within 6 months of enrollment
8. Administration of a live, attenuated vaccine within 28 days before Cycle 1 Day 1 or anticipation that such a live attenuated vaccine will be required during the study
9. Human Immunodeficiency Virus (HIV), active Hepatitis B or Hepatitis C (HCV)
10. Severe infections within 28 days prior to Cycle 1 Day 1, including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia or active tuberculosis
11. Received oral or intravenous (IV) antibiotics within 14 days prior to Day 1
12. Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
13. Major surgery or significant traumatic injury less than 28 days prior to Cycle 1 Day 1 (excluding biopsies) or anticipation of the need for major surgery during study treatment
14. Known history of autoimmune disease as defined in the protocol
15. History of idiopathic pulmonary fibrosis, pneumonitis (including drug induced), organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia, etc.), or evidence of active pneumonitis (including drug induced) on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted
16. Participants with bilateral lung lesions and dyspnea and/or oxygen saturation level (SaO2) less than 92% (at rest, room air and exertion) or participants with lobectomy or pneumonectomy with lung metastases in the remaining lung and either dyspnea or SaO2 less than 92% (at rest, room air and exertion) at baseline
17. Pregnant or breastfeeding
18. Known hypersensitivity to any of the components of cibisatamab and atezolizumab; hypersensitivity to Chinese hamster ovary cell products or other recombinant human antibodies
19. Investigational therapy (defined as treatment for which there is no regulatory authority approved indication) or last dose of prior immunotherapies within 28 days prior to Cycle 1 Day 1. Participants previously treated with anti-programmed death-ligand 1 (PD-L1), or anti-PD-1 are excluded
20. Last dose of any approved anti-cancer therapy within 28 days prior to the first cibisatamab infusion
21. Prior systemic corticosteroids greater than 10mg prednisone (or equivalent) within 14 days of Cycle 1 Day 1. Inhaled and/or topical steroids are permitted

22. Expected need for regular immunosuppressive therapy
23. Radiotherapy within the last 28 days before Cycle 1 Day 1 with the exception of limited-field palliative radiotherapy

Date of first enrolment
07/01/2016

Date of final enrolment
14/05/2018

Locations

Countries of recruitment
Canada

Denmark

France

Italy

Netherlands

Spain

United States of America

Study participating centre
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Study participating centre
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Sponsor information

Organisation

Genentech, Inc

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, Inc., Genentech USA, Inc., Genentech USA

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		15/05/2024	30/09/2026	Yes	No
Basic results		19/01/2021	23/06/2021	No	No
Study website		11/11/2025	11/11/2025	No	Yes