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A study of selicrelumab (RO7009789) in combination with atezolizumab in participants with locally advanced and/or metastatic solid tumors

Submission date
14/06/2021

Recruitment status
No longer recruiting

Registration date
24/08/2021

Overall study status
Completed

Last Edited
25/08/2021

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This study is designed to assess the safety, response to treatment, and therapeutic activity of the drug selicrelumab in combination with atezolizumab in participants with metastatic solid tumors not amenable to standard treatment. The aim is to increase the number of immune cells in the body that can fight cancer.

Who can participate?
Patients aged over 18 years living with locally advanced and/or metastatic solid tumors that are not treatable by standard therapy. 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.

What does the study involve?
In Part IA participants are treated with an infusion/injection of selicrelumab at a starting dose of 1 mg on Day 1 of Cycle 1 (21-day cycle), which is increased in later groups of participants. Atezolizumab 1200 mg is given into a vein (intravenous) on Day 1 of Cycle 2 and every 3 weeks as long as the participant experiences clinical benefit in the opinion of the investigator or until the side effects are unacceptable.
In Part IB participants are treated with an injection of selicrelumab at a starting dose of 1 mg on Day 2 of Cycle 1 (21-day cycle), which is increased in later groups of participants, and intravenous atezolizumab 1200 mg on Day 1 of Cycle 1 and followed every 3 weeks as long as the participant experiences clinical benefit in the opinion of the investigator or until the side effects are unacceptable.
In Part II participants are treated with intravenous atezolizumab 1200 mg on Day 1 of Cycle 1, followed by every 3 weeks. They are treated with selicrelumab at the dose defined in Part IB on Day 2 (1 day after atezolizumab) of every second cycle from Cycles 1 to 7, and every fourth cycle thereafter as long as the participant experiences clinical benefit in the opinion of the investigator or until the side effects are unacceptable.

What are the possible benefits and risks of participating?
All patients are treated with high-quality technical advanced assessments designed by a group of leading experts in the field of cancer therapy. Their medical condition may improve from taking selicrelumab and atezolizumab, although the researchers cannot guarantee that there are any benefits. Taking part in the study may help future patients by providing important information about selicrelumab and atezolizumab and the treatment of cancer.
Participants may have side effects from the drugs or procedures used in this study. Side effects can vary from mild to very serious and may vary from person to person. Everyone taking part in the study is watched carefully for any side effects from taking selicrelumab and/or atezolizumab including injection or biopsy procedure discomforts, immune-mediated side effects, systemic immune activation, abnormal blood tests, inflammatory disorders, and allergic reactions, some of which are rare. Therefore participants are regularly assessed for signs of liver toxicity as this study progresses.

Where is the study run from?
Genentech, Inc (USA)

When is the study starting and how long is it expected to run for?
December 2014 to March 2020

Who is funding the study?
Genentech, Inc (USA)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2014-002835-32

IRAS number

ClinicalTrials.gov number

NCT02304393

Secondary identifying numbers
BP29392

Study information

Scientific Title
An open-label, multicenter, dose-escalation Phase Ib study to investigate the safety, pharmacokinetics, pharmacodynamics, and therapeutic activity of selicrelumab (CD40 agonist) in combination with atezolizumab (anti PD-L1) in patients with locally advanced and/or metastatic solid tumors

Study objectives
To investigate the safety, processing by the body, mechanism of action, and therapeutic activity of selicrelumab (CD40 agonist) in combination with atezolizumab (anti PD-L1) in patients with locally advanced and/or metastatic solid tumors.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/12/2014, University Health Network Research Ethics Board (700 University Avenue, 8th Floor, Room 8-19, M5G1Z5, Toronto, Ontario, Canada; +45 (0)45 44889123; kf@dkma.dk), ref: not available

Study design
Open-label multicenter interventional non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

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

Interventions
Part IA: selicrelumab (IV) + atezolizumab
Selicrelumab at a dose of 16 mg was administered intravenously (IV) on Day 1 of Cycle 1 (the

first cycle in this group was 42 days, with subsequent 21-day cycles); and atezolizumab 1200 mg was administered IV after 6 weeks on Day 1 of Cycle 2, followed by every 3 weeks during Part IA until disease progression, death, loss of follow-up, or withdrawal of consent.

Part IA: selicrelumab (SC) + atezolizumab
Selicrelumab at a starting dose of 1 mg was administered subcutaneously (SC) on Day 1 of Cycle 1 (21-day cycle) which follows escalation in sequential cohorts; and atezolizumab 1200 mg was administered IV on Day 1 of Cycle 2, and followed by every 3 weeks during Part IA as long as the participant experiences clinical benefit in the opinion of the investigator or until unacceptable toxicity.

Part IB: selicrelumab + atezolizumab
Selicrelumab was administered at a starting dose of 1 mg SC on Day 2 of Cycle 1 (21-day cycle) which follows escalation in sequential cohorts; and atezolizumab 1200 mg was administered IV on Day 1 of Cycle 1, and followed by every 3 weeks during Part IB as long as the participant experienced clinical benefit in the opinion of the investigator or until unacceptable toxicity.

Part II: selicrelumab + atezolizumab
Atezolizumab 1200 mg was administered IV on Day 1 of Cycle 1, followed by every 3 weeks; and selicrelumab was administered at the dose defined in Part IB (not exceeding 80 mg SC [unless IV administration in Part IB demonstrates better benefit/risk ratio]) on Day 2 (1 day after atezolizumab administration) of every second cycle from Cycles 1 to 7, and every fourth cycle thereafter during Part II as long as the participant experienced clinical benefit in the opinion of the investigator or until unacceptable toxicity.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Selicrelumab, atezolizumab

Primary outcome measure
Part IA:
Percentage of participants with adverse events and serious adverse events, classified according to the NCI CTCAE v4.0 toxicity grade, measured from baseline up to 28 days after the last dose (approximately 60 months)

Part IB:
1. Percentage of participants with adverse events and serious adverse events, classified according to the NCI CTCAE v4.0 toxicity grade, measured from baseline up to 28 days after the last dose (approximately 60 months)
2. Percentage of participants with dose-limiting toxicities (DLTs), measured using the National Cancer Institute-Common Terminology Criteria for Adverse Events version 4.03 (NCI-CTCAE v 4.03) from Cycle 1 Day 1 up to Cycle 2 Day 2 (cycle length = 21 days)
3. Maximum tolerated dose (MTD) of selicrelumab, measured using the National Cancer Institute-Common Terminology Criteria for Adverse Events version 4.03 (NCI-CTCAE v 4.03) from Cycle 1

Day 1 up to Cycle 2 Day 2 (cycle length = 21 days)
4. Recommended Part II dose of selicrelumab calculated from the MTD, measured from Cycle 1 Day 1 up to Cycle 2 Day 2 (cycle length = 21 days)

Part II:
1. Percentage of participants with adverse events and serious adverse events, classified according to the NCI CTCAE v4.0 toxicity grade, measured from baseline up to 28 days after the last dose (approximately 60 months)
2. Percentage of participants with best overall response, as determined by the investigator using Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 from baseline up to disease progression (PD) or death due to any cause, whichever occurs first (up to approximately 60 months)
3. Progression-free survival (PFS), as determined by the investigator using RECIST Version 1.1 from baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
4. Duration of objective response, as determined by investigator using RECIST Version 1.1 from the first occurrence of a complete response or partial response, whichever occurs first, until progressive disease or death due to any cause, whichever occurs first (up to approximately 60 months)
5. Percentage of participants with disease control, as determined by the investigator using RECIST Version 1.1 from baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
6. Percentage of participants with disease control, as determined by the investigator using unidimensional immune-related response criteria (irRC) from baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
7. PFS, as determined by the investigator using unidimensional irRC from baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
8. Percentage of participants with best overall response, as determined by the investigator using irRC from baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
9. Duration of objective response, as determined by investigator using unidimensional irRC from the first occurrence of a complete response or partial response, whichever occurs first, until progressive disease or death due to any cause, whichever occurs first (up to approximately 60 months)
10. Overall survival measured from patient records from baseline up to death due to any cause (up to approximately 60 months)

Secondary outcome measures

Part IA:
1. Area under the concentration time curve (AUC) of selicrelumab measured from serum samples taken at pre selicrelumab dose (1 h) on Cycle (Cy) 1 Day 1 (D1); 4, 8, 24, 48, 72 h post D1 dose; D8, 15 of Cy 1; D1 Cy 2&3 (10 minutes pre ATZ dose); at radiographic disease progression (PD) (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
2. Maximum serum concentration (Cmax) of selicrelumab, measured from serum samples taken at pre selicrelumab dose (within 1 h) on Cy 1 D1; 4, 8, 24, 48, 72 h post D1 dose; D8, D15 of Cy1; D1 of Cy2 & 3 (10 minutes [min] pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
3. Time to Cmax (Tmax) of selicrelumab, measured from serum samples taken at pre selicrelumab dose (within 1 h) on Cy 1 D1; 4, 8, 24, 48, 72 h post D1 dose; D8, D15 of Cy 1; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)

4. Minimum serum concentration under steady-state (Cmin) of selicrelumab, measured from serum samples taken at pre selicrelumab dose (within 1 h) on Cy1 D1; 4, 8, 24, 48, 72 h post D1 dose; D8, D15 of Cy1; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
5. Apparent clearance (CL/F) of selicrelumab, measured from serum samples taken at pre selicrelumab dose (within 1 h) on Cy1 D1; 4, 8, 24, 48,72 h post D1dose; D8, D15 of Cy1; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)

All other endpoints measured using serum samples (as applicable):
6. Half-life (t1/2) of selicrelumab, measured pre selicrelumab dose (within 1 h) on Cy1 D1; 4, 8, 24, 48,72 h post D1 dose; D8, D15 of Cy1; D1 of Cy2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
7. Cmax of atezolizumab measured pre ATZ (within 10 min) and at end of 60-min ATZ infusion on Cy2D1; pre ATZ dose (within 10 min) on D1 of Cy 3, 4, 5, 9 & every 8 Cy thereafter (up to 60 months); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
8. Cmin of atezolizumab, measured pre ATZ (within 10 min) and at the end of 60-min ATZ infusion on Cy2 D1; pre ATZ dose (within 10 min) on D1 of Cy 3, 4, 5, 9 and every 8 Cy thereafter (up to 60 months); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
9. Levels of circulating Ki67 T cells assessed by immunophenotyping by flow cytometry at Cy1 D1: predose selicrelumab D4 D8 D15 Cy2 D1: predose Atezo D3 D8 Cy3 D1: predose Atezo D8 PD at IRR/ISR (Cy = 21 days)
10. Levels of cluster of differentiation 8 (CD8+) cells tumor infiltration assessed by immunophenotyping by flow cytometry at Cy1 D1: predose selicrelumab D4 D8 D15; Cy2 D1: predose Atezo D3 D8; Cy3 D1: predose Atezo D8 PD at IRR/ISR (Cy= 21 days)
11. Levels of programmed death ligand 1 (PD-L1) expression on both tumor and immune-infiltrating cells assessed by immunophenotyping by flow cytometry at Cy1 D1: predose selicrelumab D4 D8 D15; Cy2 D1: predose Atezo D3 D8; Cy3 D1: predose Atezo D8 PD at IRR/ISR (cycle = 21 days)
12. V/F of selicrelumab, measured pre selicrelumab dose (within 1 h) on Cy1 D1; 4, 8, 24, 48, 72 h post D1 dose; D8, D15 of Cy1; D1 of Cy2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
13. Percentage of participants with incidence of ADA responses to RO7009789, measured pre-dose Day 1 on Cycles 1, 2, 3, 4, 7 (cycle length = 21 days); safety follow-up visit (up to 52 days post final dose)
14. Percentage of participants with incidence of ADA responses to vanucizumab, measured pre-dose Day 1 on Cycles 1, 2, 4, 6, 8 (cycle length = 21 days); safety follow-up visit (up to 52 days post final dose)

Part IB:
1. AUC of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
2. Cmax of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D 3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
3. Tmax of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ

dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
4. Cmin of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D 3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
5. CL/F of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D 3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
6. Apparent volume of distribution (V/F) of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1 D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy1 D 3, 4, 5, 9, 15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
7. t1/2 of SC selicrelumab, measured pre ATZ dose (within 1 h) on Cy1D1, pre selicrelumab dose (within 1 h) on Cy1 D2; Cy 1 D3, 4, 5, 9,15 post D2 dose; D1 of Cy 2 & 3 (10 min pre ATZ dose); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
8. Cmax of atezolizumab, measured pre ATZ (within 1 h) and at end of 60 min ATZ infusion on Cy1 D1; pre ATZ dose (within 10 min) on D1 of Cy 2, 3, 4, 8 and every 8 Cy thereafter (up to 60 months); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
9. Cmin of atezolizumab, measured pre ATZ (within 1 h) and at end of 60 min ATZ infusion on Cy1 D1; pre ATZ dose (within 10 min) on D1 of Cy 2, 3, 4, 8 and every 8 Cy thereafter (up to 60 months); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
10. Percentage of participants with best overall response, as determined by investigator using unidimensional immune-related response criteria (irRC) at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
11. Percentage of participants with best overall response, as determined by investigator using Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
12. Percentage of participants with disease control, as determined by investigator using RECIST Version 1.1 at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
13. Percentage of participants with disease control, as determined by investigator using unidimensional irRC at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
14. Duration of objective response, as determined by investigator using RECIST Version 1.1 at first occurrence of response up to relapse or death due to any cause, whichever occurs first (up to approximately 60 months)
15. Duration of objective response, as determined by investigator using unidimensional irRC at first occurrence of response up to relapse or death due to any cause, whichever occurs first (up to approximately 60 months)
16. Progression-free survival (PFS), as determined by investigator using RECIST Version 1.1 at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
17. Levels of circulating Ki67 T cells assessed by immunophenotyping by flow cytometry at Cy1: D3 D4 D5 D9 D15; Cy2: D1 D8; Cy4-47: D1 PD at IRR/ISR (Cy = 21 days)
18. Levels of CD8+ cells tumor infiltration assessed by immunophenotyping by flow cytometry at Cy1: D1 predose, D3, D4, D5, D9, D15; Cy2: D1 predose, D8; Cy4-47: D1 predose, PD at IRR/ISR (Cy = 21 days)

19. Levels of PD-L1 expression on both tumor and immune-infiltrating cells assessed by immunophenotyping by flow cytometry at Cy1: D1 predose, D3, D4, D5, D9, D15; Cy2: D1 predose, D8; Cy4-47: D1 predose, PD at IRR/ISR (Cy = 21 days)
20. PFS, as determined by investigator using unidimensional irRC at baseline up to PD or death due to any cause, whichever occurs first (up to approximately 60 months)
21. AUC of IV selicrelumab, measured pre ATZ (1 h) Cy1 D1,2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1 D2; 24, 30-36, 48, 72 h post Cy 1 D2 dose; Cy 1 D9; D1 Cy 2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
22. Cmax of IV selicrelumab, measured pre ATZ (1 h) Cy1 D1,2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1 D2; 24, 30-36, 48, 72 h post Cy1D2 dose; Cy 1 D9; D1 Cy 2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
23. Cmin of IV selicrelumab, measured pre ATZ (1 h) Cy1 D1,2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1 D2; 24, 30-36, 48, 72 h post Cy1 D2 dose; Cy 1D9; D1 Cy 2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
24. Total clearance (CL) of IV selicrelumab, measured pre ATZ (1 h) Cy1 D1,2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1D2; 24, 30-36, 48, 72 h post Cy1D2 dose; Cy 1D9; D1 Cy2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months) (Cy = 21days)
25. Volume of distribution (Vss) of IV selicrelumab, measured pre ATZ (1 h) Cy 1 D1, 2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1 D2; 24, 30-36, 48, 72 h post Cy1 D2 dose; Cy 1D9; D1 Cy 2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 & 150days after last ATZ dose (up to 60 months) (Cy = 21 days)
26. t1/2 of IV selicrelumab, measured pre ATZ (1 h) Cy1 D1, 2; end of 30-min selicrelumab infusion, 0.25, 2, 4, 6, 8, 10 h post infusion start Cy1 D2; 24, 30-36, 48, 72 h post Cy1 D2 dose; Cy 1 D9; D1 Cy 2, 3 (10 min pre ATZ); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
27. Percentage of participants with incidence of ADA responses to RO7009789, measured pre-dose Day 1 on Cycles 1, 2, 3, 4, 7 (cycle length = 21 days); safety follow-up visit (up to 52 days post final dose)
28. Percentage of participants with incidence of ADA responses to vanucizumab, measured pre-dose Day 1 on Cycles 1, 2, 4, 6, 8 (cycle length = 21 days); safety follow-up visit (up to 52 days post final dose)

Part II:
1. AUC of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2 of Cy 3, 5, 11, 15, 19; D 8 of Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21 days)
2. Cmax of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2-Cy3, 5, 11, 15, 19; D8-Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21 days)
3. Tmax of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2 of Cy 3, 5, 11, 15, 19; D8 of Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21days)
4. Cmin of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2-Cy 3, 5, 11, 15, 19; D8-Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21

days)
5. CL/F of Selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2-Cy 3, 5, 11, 15, 19; D8-Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21days)
6. V/F of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D 5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2-Cy 3, 5, 11, 15, 19; D8-Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21days)
7. t1/2 of selicrelumab, measured pre selicrelumab (within 1 h) on Cy1 D2; Cy 1, 5 D5, 8, 15; pre ATZ (10 min) on D1-Cy 2, 4, 6, 8 and thereafter except Cy 11, 15, 19; pre selicrelumab (10 min) on D2-Cy 3, 5, 11, 15, 19; D8-Cy 11, 15, 19; 28 and 150 days after last ATZ (up to 60 months) (Cy = 21 days)
8. Cmax of atezolizumab, measured at Cy1D1: pre ATZ dose (within 1 h), at end of ATZ infusion (60 min infusion); pre-ATZ dose (within 10 min) on D1 Cy2, 3, 4, 5, 6, 8, and thereafter (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
9. Cmin of atezolizumab, measured at Cy1D1: pre ATZ dose (within 1 h), at end of ATZ infusion (60 min infusion); pre-ATZ dose (within 10 min) on D1 Cy2, 3, 4, 5, 6, 8, and thereafter (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)
10. Levels of circulating Ki67 T cells assessed by immunophenotyping by flow cytometry at Cy1: D1 pre-Atezo, D8, D15; Cy2D1: pre-Atezo; Cy3 D1 pre-Atezo, D8; Cy4D1: pre-Atezo; Cy5: D1 pre-Atezo, D8, D15; Cy6D1: Pre-Atezo; Cy11, 15 and 19: D1 pre Atezo and D8; after last Atezo dose SFU at IRR/ISR (Cy= 21 days)
11. Levels of PD-L1 expression on both tumor and immune-infiltrating cells assessed by immunophenotyping by flow cytometry at Cy1: D1 pre-Atezo, D8, D15; Cy2D1: pre-Atezo; Cy3 D1 pre-Atezo, D8; Cy4D1: pre-Atezo; Cy5: D1 pre-Atezo, D8, D15; Cy6D1: Pre-Atezo; Cy11, 15 and 19: D1 pre-Atezo and D8; After last Atezo dose SFU at IRR/ISR (Cy= 21 days)
12. Levels of CD8+ cells tumor-infiltration assessed by immuphenotyping by flow cytometry pre ATZ (within 1 h) Cy 1, 6, 11, 15, 19 D 1; Cy 1 D 8, 15; pre ATZ (within 10 min) Cy 2, 3, 4, 5 D1; Cy 3, 5, 11, 15, 19 D8; Cy 5 D15; 28 days after last ATZ dose (up to 60 months); at radiographic tumor regression/PD (up to 60 months) (Cy = 21 days)
13. Percentage of participants with incidence of ADA responses to RO7009789, measured pre-dose Day 1 on Cycles 1, 2, 3, 4, 7 (cycle length = 21 days); safety follow-up visit (up to 52 days post final dose)

Part IA, IB, and II:
1. Percentage of participants with auto-antibodies measured pre selicrelumab dose (within 1 h) on Cy1 D1;pre ATZ dose (within 10 min) on D1 Cy 2, 3, 4, 5 and every 8 cycles thereafter, up to 60 months); at radiographic PD (up to 60 months); 28 and 150 days after last ATZ dose (up to 60 months overall) (Cy = 21 days)
2. Percentage of participants with anti-therapeutic antibodies (ATA) to selicrelumab, measured pre selicrelumab dose (within 1 h) on Cy1 D1;pre ATZ dose (within 10 min) on D1 Cy2, 3, 4, 5 and every 8 cycles thereafter, up to 60 months); at radiographic PD (up to 60 months); 28 & 150 days after last ATZ dose (up to 60 months overall) (Cy = 21 days)
3. Percentage of participants with ATA to ATZ measured pre ATZ (within 10 min) on D1 Cy 2, 3, 4, 5 (Part IA), 9 (Cy 8 for Part II) and every 8 cycles thereafter (up to 60 months); pre ATZ (within 1 h) on Cy1 D1(for Part IB & II); at radiographic PD (up to 60 months), 28 and 150 days after last ATZ dose (up to 60 months) (Cy = 21 days)

Overall study start date
04/12/2014

Completion date
31/03/2020

Eligibility

Key inclusion criteria
1. Histologically confirmed diagnosis of locally advanced and/or metastatic solid tumors, which are not amenable to standard therapy:
Part I: histologically confirmed diagnosis of advanced/metastatic small and large bowel carcinomas (small bowel and CRC), CPI-experienced non-small cell lung cancer (NSCLC) and head and neck squamous cell carcinoma (HNSCC)
Part II: CPI-experienced NSCLC patients must have experienced documented disease progression on or after PD-L1 or PD-1 inhibitor therapy (investigational or approved): screening tumor assessment should confirm prior progression
2. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
3. Life expectancy greater than or equal to 16 weeks
4. Adequate hematologic and end organ function
5. Measurable disease per RECIST Version 1.1
6. Ability to comply with the protocol requirements
7. Female participants of childbearing potential must have a negative pregnancy test (urine /serum) within seven days prior to the first study drug administration
8. For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of less than (<) 1% per year during the treatment period and for at least 5 months after the last dose of study treatment
9. For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm during the treatment period and for at least 28 days after the last dose of study treatment

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
230

Total final enrolment
140

Key exclusion criteria
1. If one of the following laboratory results obtained within 14 days prior to the first study treatment (Cycle 1 Day 1) are: soluble interleukin 2 receptor (sCD25) greater than (>) 2 × upper limit of normal (ULN); Serum ferritin >1000 ng/ml
2. Any approved anti-cancer therapy that includes chemotherapy, hormonal therapy, or radiotherapy within 2 weeks prior to the first dose of study treatment; the following is, however,

allowed: Palliative radiotherapy for bone metastases less than or equal to (</=) 2 weeks prior to Cycle 1 Day 1
3. Adverse events from prior anti-cancer therapy that have not resolved to Grade </= 1 except for any grade alopecia and </= Grade 2 peripheral neuropathy
4. Bisphosphonate therapy for symptomatic hypercalcemia. Use of bisphosphonate therapy for other reasons (example: bone metastasis or osteoporosis) is allowed
5. Uncontrolled pleural effusion, pericardial effusion, or ascites that require recurrent drainage procedures (one monthly or more frequently). Participants with indwelling catheters are allowed
6. Known clinically significant liver disease which includes active viral, alcoholic, or other hepatitis, cirrhosis, fatty liver, and inherited liver disease
7. History (within the previous year) of congestive heart failure, stroke, arrhythmia, or myocardial infarction
8. History of peripheral venous thrombosis or thromboembolic event (within 12 months prior to Cycle 1 Day 1)
9. Significant cardio- or cerebrovascular disease within 6 months prior to Cycle 1 Day 1
10. Known hereditary or acquired coagulopathies
11. Clinically meaningful proteinuria
12. Requiring dialysis (peritoneal or hemodialysis)
13. Known primary central nervous system (CNS) malignancy or symptomatic or untreated CNS metastases: participants with asymptomatic-treated CNS metastases may be enrolled after consultation with the Medical Monitor, provided they meet the following criteria:
13.1. Radiographic demonstration of improvement upon completion of CNS-directed therapy and no evidence of interim progression between the completion of CNS-directed therapy and the screening radiographic study
13.2. No stereotactic radiation or whole-brain radiation within 28 days prior to Cycle 1 Day 1
14. Pregnancy, lactation, or breastfeeding
15. Allergy or hypersensitivity to components of the RO7009789 formulation or to components of atezolizumab formulation
16. History of autoimmune diseases (participants with a history of autoimmune hypothyroidism on a stable dose of thyroid replacement hormone may be eligible; participants with controlled Type 1 diabetes mellitus on a stable insulin regimen may be eligible for this study)
17. History of idiopathic pulmonary fibrosis, pneumonitis (excluding infectious disease-induced), organizing pneumonia, or evidence of active pneumonitis
18. History of radiation pneumonitis in the radiation field (fibrosis) is permitted
19. Participants with human immunodeficiency virus (HIV) infection, active hepatitis B (chronic or acute), or hepatitis C infection
20. Active tuberculosis
21. Severe infections within 4 weeks prior to Cycle 1 Day 1
22. Signs or symptoms of infection within 2 weeks prior to Cycle 1 Day 1
23. Received oral or IV antibiotics within 2 weeks prior to Cycle 1 Day 1
24. Major surgical procedure within 28 days prior to Cycle 1 Day 1 or anticipation of need for a major surgical procedure during the course of the study
25. Administration of a live, attenuated vaccine within 4 weeks before Cycle 1 Day 1 or anticipation that such a live attenuated vaccine will be required during the study
26. Malignancies other than disease under study within 3 years prior to Cycle 1 Day 1 with the exception of those with a negligible risk of metastasis or death and with expected curative outcome
27. Previous treatment with any other compound that targets cluster of differentiation 40 (CD40) (like Chi Lob 7/4 and ADC1013)
28. Treatment with systemic immunostimulatory agents (including but not limited to interferon (IFN)-alpha, Interleukin-2 (IL-2) within 4 weeks or 5 times the half-life of the drug, whichever is shorter, prior to Cycle 1 Day 1

29. Treatment with investigational agent within 4 weeks prior to Cycle 1 Day 1 (or within 5 times the half-life of the investigational product, whichever is longer)
30. Concomitant treatment with anticoagulants (example: coumadin, heparin) except low dose molecular weight heparin for prophylactic purposes and direct factor Xa inhibitors
31. Treatment with systemic immunosuppressive medications (including but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor (TNF) agent within 2 weeks prior to Cycle 1 Day 1
31.1. Participants who have received acute, low-dose, systemic immunosuppressant medications (example: a one-time dose of dexamethasone for nausea) may be enrolled in the study after discussion with and approval by the Medical Monitor
31.2. The use of corticosteroids as premedication in case of dye allergy previous to computed tomography (CT) scan is allowed
32. History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
33. Participants with prior allogeneic bone marrow transplantation or prior solid organ transplantation
34. Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or that may affect the interpretation of the results or render the participants at high risk from treatment complications

Date of first enrolment
12/12/2014

Date of final enrolment
26/11/2018

Locations

Countries of recruitment
Canada

Denmark

France

Netherlands

Spain

United States of America

Study participating centre
University Health Network; Princess Margaret Hospital; Medical Oncology Dept
Toronto
Canada
M5G 2M9

Study participating centre
Jewish General Hospital
Quebec
Montreal
Canada
H3T 1E2

Study participating centre
Hospital Univ Vall d'Hebron
Servicio de Oncologia
Barcelona
Spain
08035

Study participating centre
Institut Gustave Roussy; Sitep
Villejuif
France
94805

Study participating centre
APHM
CPCET
Marseille
France
13385

Study participating centre
Hopital Saint Louis
Service D'Oncologie Medicale
Paris
France
75475

Study participating centre
Antoni van Leeuwenhoek Ziekenhuis
Amsterdam
Netherlands
1066 CX

Study participating centre
Rigshospitalet
Onkologisk Klinik
København Ø
Denmark
2100

Study participating centre
Erasmus Medisch Centrum Rotterdam
Lokatie Daniel den Hoed
Rotterdam
Netherlands
3015 GD

Study participating centre
University of Pennsylvania
Philadelphia
United States of America
19104

Study participating centre
START Madrid
Centro Integral Oncologico Clara Campal (CIOCC)
Madrid
Spain
28050

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Sponsor details
Grenzacherstr. 124
Basel
Switzerland
4070
+1 (0)888 662 6728
global-roche-genentech-trials@gene.com

Sponsor type
Industry

Website
https://www.roche.com/about_roche/roche_worldwide.htm

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
Genentech, THE GENENTECH FOUNDATION, GF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Publication and dissemination plan
Pre-print EudraCT results available. No protocol/additional study documents will be made available.

Intention to publish date

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement for Phase I studies.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		30/10/2020	05/08/2021	No	No