ISRCTN35774409 https://doi.org/10.1186/ISRCTN35774409

A study to evaluate the safety, pharmacokinetics, pharmacodynamics and therapeutic activity of RO7009789 (selicrelumab) in combination with vanucizumab or bevacizumab in patients with metastatic solid tumors

Submission date 12/11/2020	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/03/2021	**Overall study status** Stopped	
Last Edited 05/12/2023	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

This study is designed to assess the safety, biological responses to treatment, and therapeutic activity of the drug selicrelumab in combination with vanucizumab or bevacizumab in participants with metastatic solid tumors not amenable to standard treatment. These drugs are all laboratory-produced molecules designed to mimic molecules produces by the body's immune system to target cancer cells. Part I of the study is designed to establish the highest dose of selicrelumab in this combination that does not cause unacceptable side effects. Part II of the study is intended to characterize the safety and tolerability of selicrelumab in combination with bevacizumab among a cancer patient cohort, and to confirm the recommended dose.

Who can participate?

Participants with advanced/metastatic solid tumor and advanced/metastatic platinum-resistant ovarian carcinoma.

What does the study involve?

This study consists of two parts.

Part I aims to define the highest dose of selicrelumab in this combination that does not cause unacceptable side effects and/or dose of selicrelumab in this combination that is reliably effective. Participants will receive treatment over 24 months, as long as they experience a clinical benefit, or until there are unacceptable side effects or toxicity, or if the participant withdraws their consent. Participants will receive a fixed dose of vanucizumab, via a small plastic tube in a vein on days 1 and 15 of every 28-day cycle of treatment over the 24 month period. This will be followed by selicrelumab in an increasing dose, via an injection under the skin, on day 2 of cycles 1-4, and then day 2 of every third cycle after. There will be 4 groups of participants each

receiving the same dose of vanucizumab but starting on different doses of selicrelumab. Due to the discontinuation of vanucizumab development, participants ongoing in Part I switched from vanucizumab to bevacizumab.

In part II of the study participants will receive treatment over 18 months until there is no clinical benefit, there are unacceptable side effects or toxicity, or the participant withdraws their consent. Participants diagnosed with head and neck squamous cell carcinoma (HNSCC), checkpoint-inhibitor (CPI)-experienced non-squamous non-small cell lung cancer (NSCLC), or advanced platinum-resistant ovarian cancer (aPROC) will receive bevacizumab 10 mg/kg , via a small plastic tube in a vein, on days 1 and 15 of every 28-day cycle, followed by selicrelumab 16 mg, via an injection under the skin, on day 2 of cycles 1-4, and then day 2 of every third cycle after.

What are the possible benefits and risks of participating?
Safety data from previous studies of vanucizumab, bevacizumab, and RO7009789 have shown an increased risk of blood clots developing which may obstruct a blood vessel. There may also potentially be an increased risk of immune-mediated adverse events with the combination treatment.

Where is the study run from?
The study will be run from Genentech, Inc (USA) and conducted in hospitals across 6 countries (Belgium, USA, Spain, Netherlands, Denmark, and Canada).

When is the study starting and how long is it expected to run for?
From March 2015 to October 2019

Who is funding the study?
F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact?
global-roche-genentech-trials@gene.com

Contact information

Type(s)
Public

Contact name
Dr Clinical Trials

Contact details
1 DNA Way
South San Francisco
United States of America
94080
+1 888-662-6728
global-roche-genentech-trials@gene.com

Additional identifiers

ClinicalTrials.gov (NCT)

NCT02665416

Clinical Trials Information System (CTIS)
2015-003480-11

Protocol serial number
BP29889

Study information

Scientific Title
An open-label, multicenter, dose escalation phase Ib study with expansion cohorts to evaluate the safety, pharmacokinetics, pharmacodynamics and therapeutic activity of RO7009789 (CD40 agonistic monoclonal antibody) in combination with vanucizumab (Anti-Ang2 and Anti-VEGF bi-specific monoclonal antibody, part I) or bevacizumab (Anti-VEGF monoclonal antibody, part II) in patients with metastatic solid tumors

Study objectives
To assess the safety, tolerability and therapeutic activity of selicrelumab in combination with vanucizumab or bevacizumab in participants with metastatic solid tumors not amenable to standard treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 15/12/2015, De Videnskabsetiske Komitéer for Region Hovedstade (Kongens Vænge 2, 3400, Hillerød Telefon, Denmark; no telephone contact provided; no email contact provided), ref: 288621
2. Approved 10/11/2015, CEIC Parc de Salut Mar; IMIM- Hospital del Mar (C/ Dr. Aiguader, 88, Planta 1, 08003, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 288642
Approved 10/11/2015, CEIC Hospital Vall D'Hebron (Passeig Vall D'hebrón, 119-129 - Edificio Materno-Infantil Planta 13, 08035, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 288643
3. Approved 10/11/2015, CEIC Parc de Salut Mar; IMIM- Hospital del Mar (C/ Dr. Aiguader, 88, Planta 1, 08003, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 288643
4. Approved 10/11/2015, CEIC Hospital Madrid Norte Sanchinarro (Av Montepríncipe Nº 25, Edificio Docente. CEIC, 28660, Boadilla Del Monte, Madrid, Spain; no telephone contact provided; no email contact provided), ref: 288644
5. Approved 10/11/2015, CEIC Parc de Salut Mar (IMIM- Hospital del Mar, C/ Dr. Aiguader, 88, Planta 1, 08003, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 288644
6. Approved 01/12/2015, University Health Network Research Ethics Board (700 University Avenue, 8th Floor, Room 8-19, M5G1Z5, Toronto, Ontario, Canada; no telephone contact provided; no email contact provided), ref: 288797
7. Approved 25/02/2016, Instiutional Review Board of the Dutch Cancer Institute/Antonie von Leeuwenhoek Hospital (PTC NKI/AvL) (Plesmanlaan 121, 1066 CX, Amsterdam, Netherlands; no telephone contact provided; no email contact provided), ref: 289627
8. Approved 31/03/2016, Instiutional Review Board of the Dutch Cancer Institute/Antonie von

Leeuwenhoek Hospital (PTC NKI/AvL) (Plesmanlaan 121, 1066 CX, Amsterdam, Netherlands; no telephone contact provided; no email contact provided), ref: 289629
9. Approved 08/11/2018, Lehigh Valley Health Network IRB (1019 39th Avenue SE, Suite 120, Puyallup, WA, 98374-2115, USA; no telephone contact provided; no email contact provided), ref: 313237
10. Approved 02/07/2018, Lehigh Valley Health Network IRB (1019 39th Avenue SE, Suite 120, Puyallup, WA, 98374-2115, USA; no telephone contact provided; no email contact provided), ref: 313549
11. Approved 12/06/2018, CEIC Parc de Salut Mar; IMIM- Hospital del Mar (C/ Dr. Aiguader, 88, Planta 1, 08003, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 316083
12. Approved 08/08/2018, CEIC Parc de Salut Mar; IMIM- Hospital del Mar (C/ Dr. Aiguader, 88, Planta 1, 08003, Barcelona, Spain; no telephone contact provided; no email contact provided), ref: 316084
13. Approved 15/11/2018, Cliniques Universitaires St-Luc, Comité d'Ethique (Avenue Hippocrate 10, 1200 Bruxelles, Belgium; no telephone contact provided; no email contact provided), ref: 316821

Primary study design
Interventional

Study design
Open-label, multicenter, dose-escalation phase Ib two-part non-randomized parallel assignment study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Metastatic solid tumor

Interventions
This open-label, two-part study is designed to assess the safety, PK, PD, and therapeutic activity of selicrelumab in combination with vanucizumab or bevacizumab in participants with metastatic solid tumors not amenable to standard treatment. Part I (dose escalation) is designed to establish the maximum tolerated dose (MTD) of selicrelumab in this combination. Part II (expansion) is intended to characterize the safety and tolerability of selicrelumab in combination with bevacizumab among indication-specific cohorts and to confirm the recommended dose.

Part I (dose escalation):
1. Cohorts 1-4: Selicrelumab 1-8 mg + vanucizumab. Participants will receive a fixed dose of vanucizumab, 2 g via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 1-8 mg, subcutaneous (SC) injection on day 2 of cycles 1 to 4, and every third cycle thereafter.
2. Cohorts 5-7: Selicrelumab 12-18 mg + vanucizumab. Participants will receive a fixed dose of vanucizumab, 2 g via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 12-18 mg, subcutaneous (SC) injection on day 2 of cycles 1 to 4, and every third cycle thereafter.
3. Cohorts 8-9: Selicrelumab 24-32 mg + vanucizumab. Participants will receive a fixed dose of vanucizumab, 2 g via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 24-32 mg, subcutaneous (SC) injection on day 2 of cycles 1 to 4, and every third cycle thereafter.

4. Cohorts 10-12: Selicrelumab 40-72 mg + vanucizumab. Participants will receive a fixed dose of vanucizumab, 2 g via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 40-72 mg, subcutaneous (SC) injection on day 2 of cycles 1 to 4, and every third cycle thereafter.

For each cohort, treatment will be continued as long as the participant experiences clinical benefit or until unacceptable toxicity, withdrawal of consent, or the end of Part I of the study (approximately 24 months). Due to the discontinuation of vanucizumab development, participants ongoing in Part I will be switched from vanucizumab to bevacizumab. All the dose escalations were performed using vanucizumab.

Part II (expansion):
1. Selicrelumab + Bevacizumab (HNSCC). Participants diagnosed with head and neck squamous cell carcinoma (HNSCC) will receive bevacizumab 10 mg/kg via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 16 mg via SC injection on day 2 of cycles 1 to 4, and every third cycle thereafter.
2. Selicrelumab + Bevacizumab (NSCLC). Participants diagnosed with checkpoint-inhibitor (CPI)-experienced non-squamous non-small cell lung cancer (NSCLC) will receive bevacizumab 10 mg /kg via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 16 mg via SC injection on day 2 of cycles 1 to 4, and every third cycle thereafter.
3. Selicrelumab + Bevacizumab (aPROC). Participants diagnosed with advanced platinum-resistant ovarian cancer (aPROC) will receive bevacizumab 10 mg/kg via IV infusion on days 1 and 15 of every 28-day cycle followed by selicrelumab 16 mg via SC injection on day 2 of cycles 1 to 4, and every third cycle thereafter.

For each cohort, treatment will be continued until loss of clinical benefit, unacceptable toxicity, withdrawal of consent, or end of Part II of the study (approximately 18 months).

The safety follow-up visit will take 45 days post-last dose, which will occur at a maximum of approximately 42 months after the first dose (day 1, cycle 1).

The safety analysis population will include all participants who enrol in the study and receive at least one dose of study medication. The efficacy analysis population will include all evaluable participants who enrol in the study and receive at least one dose of study medication. The pharmacokinetic (PK) analysis population will include participants who receive at least one dose of selicrelumab during the study and have at least 3 quantifiable plasma concentrations post selicrelumab administration.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Selicrelumab (RO7009789), vanucizumab, bevacizumab

Primary outcome(s)
Part I (dose escalation):
1. 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) between 1 and 28 days. DLTs will be defined as an adverse event or abnormal laboratory

value, (judged clinically significant by the investigator) considered related to selicrelumab and /or vanucizumab that occurrs during the first 28 days of treatment.
2. Maximum Tolerated Dose (MTD) of selicrelumab in combination with vanucizumab measured using the National Cancer Institute-Common Terminology Criteria for Adverse Events version 4.03 (NCI-CTCAE v 4.03) between 1 and 28 days. MTD will be defined as the dose level for which the probability of DLT (as defined above) was equal to a protocol-specified target probability.
3. Recommended Phase II Dose (RP2D) of selicrelumab in combination with vanucizumab calculated from the MTD (as defined above) which was measured between 1 and 28 days
4. Percentage of participants with Anti-Drug Antibodies (ADAs) to vanucizumab measured from serum samples taken predose (within 10 min before infusion) on day 1 of cycles 1, 2, 4, and every 2 cycles until disease progression and/or 45 days after the last dose (up to approximately 42 months).

Parts I (dose escalation) and II (expansion):
1. Percentage of Participants With Adverse Events (AEs) measured between day 1 and treatment discontinuation and/or safety follow up visit (45 days post-last dose, up to approximately 42 months). An AE will be defined as any untoward medical occurrence in a participant who received a pharmaceutical product, and which did not necessarily have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Any new disease or preexisting conditions which worsen during a study are also considered adverse events.
2. Percentage of Participants With Anti-Drug Antibodies (ADAs) to selicrelumab measured from serum samples taken predose (-1 h) on day 2 of cycles 1, 2, 3, 4, 7, and every 3 cycles until disease progression and/or 45 days after the last dose (up to approximately 42 months).

Part II (expansion):
1. Overall Response Rate (ORR) measured using local protocol for oncological imaging and evaluated using the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Criteria from baseline until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). The ORR will be defined as the percentage of participants with confirmed complete response (disappearance of all target lesions) and partial response (at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters) on two consecutive occasions ≥4 weeks apart, as determined by the investigator.
2. Duration of Objective Response (DOR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria from baseline until participant's discontinuation or death, whichever occurs first (up to approximately 42 months). DOR will be defined as the time from the first occurrence of a documented objective response to the time of relapse or death from any cause, and will be analysed in participants who have a best overall response of either a complete or partial response.
3. Disease control rate (DCR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria from baseline until participant's discontinuation or death, whichever occurs first (up to approximately 42 months). DCR will be defined as the percentage of participants who achieved a best overall response of confirmed complete response, confirmed partial response, or stable disease lasting at least 8 weeks. Where complete and partial response are defined above and stable disease is defined as neither sufficient shrinkage to qualify for partial response, nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum of the diameters while on study. Progressive disease is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including baseline.

4. Clinical Benefit Rate (CBR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria from baseline until participant's discontinuation or death, whichever occurs first (up to approximately 42 months). CBR will be defined as the percentage of participants who achieved a best overall response of confirmed complete response, confirmed partial response, or stable disease.
5. Progression-free Survival (PFS) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria from baseline until participant's discontinuation or death, whichever occurs first (up to approximately 42 months). PFS will be defined as the time from the start of treatment to radiographical disease progression (as defined above) or death, whichever occurred first. If no disease progression was recorded and no death occurred within 100 days from the last tumor assessment, participants were censored at the last tumor assessment. If no post-baseline tumor assessment was performed, participants were not evaluable.

Key secondary outcome(s)

Part I (dose escalation):
1. Overall Response Rate (ORR) measured using local protocol for oncological imaging and evaluated using the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) Criteria during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). The ORR will be defined as the percentage of participants with confirmed complete response (disappearance of all target lesions) and partial response (at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters) on two consecutive occasions ≥4 weeks apart, as determined by the investigator.
2. Duration of Objective Response (DOR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). DOR will be defined as the time from the first occurrence of a documented objective response to the time of relapse or death from any cause, and will be analysed in participants who have a best overall response of either a complete or partial response.
3. Disease control rate (DCR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). DCR will be defined as the percentage of participants who achieved a best overall response of confirmed complete response, confirmed partial response, or stable disease lasting at least 8 weeks. Where complete and partial response are defined above and stable disease is defined as neither sufficient shrinkage to qualify for partial response, nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum of the diameters while on study. Progressive disease is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study including baseline.
4. Clinical Benefit Rate (CBR) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). CBR will be defined as the percentage

of participants who achieved a best overall response of confirmed complete response, confirmed partial response, or stable disease.
5. Progression-free Survival (PFS) measured using local protocol for oncological imaging and evaluated using the RECIST v1.1 Criteria during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months). PFS will be defined as the time from the start of treatment to radiographical disease progression (as defined above) or death, whichever occurred first. If no disease progression was recorded and no death occurred within 100 days from the last tumor assessment, participants were censored at the last tumor assessment. If no post-baseline tumor assessment was performed, participants were not evaluable.
6. Area Under the concentration-time Curve from time 0 to last measurable concentration of vanucizumab (AUClast) following subcutaneous (SC) administration measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and/or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8
7. Area Under the concentration-time Curve from time 0 to infinity (until participant's discontinuation or death, whichever occurs first, up to approximately 42 months) of vanucizumab (AUCinf) following subcutaneous (SC) administration measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and/or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8
8. Concentration at the end of infusion (Cend) of vanucizumab measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and/or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8
9. Apparent Clearance (CL/F) of vanucizumab measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and/or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8
10. Apparent volume of distribution at steady state (Vss) of vanucizumab measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and/or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8.
11. Apparent Terminal Half-Life (t1/2) of vanucizumab measured from serum samples taken at predose on day 1 of cycle 1, 2, 4, 6, 8, and every 2 cycles thereafter until disease progression and /or 45 days after last dose, predose and at end of infusion on day 15 of each cycle until disease progression and/or 45 days after last dose, and 6 and 24 h postdose on day 15 of cycle 1 and 8.

Parts I (dose escalation) and II (expansion):
1. AUClast of selicrelumab following subcutaneous (SC) administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
2. AUCinf of selicrelumab following subcutaneous (SC) administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)

3. Maximum Concentration (Cmax) of selicrelumab following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
4. Time to Maximum Concentration (Tmax) of selicrelumab Following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
5. Apparent Clearance (CL/F) of selicrelumab following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
6. Apparent Volume of distribution (Vd/F) of selicrelumab following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
7. Apparent terminal half-life (t1/2) of selicrelumab following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h of cycle 1 and taken at -1 and 8 h of cycle 3, 4, 5, 7 and every 3 cycles thereafter until disease progression and/or 45 days after the last dose (up to approximately 42 months)
6. Trough Concentration (Ctrough) of selicrelumab following SC administration for cycle 1 measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h on day 2 of cycle 1 during Part 1; or taken at -1, 24, 48, and 72 h on day 1 and day 8, and -10 min on day 15, of cycle 1 during Part II
7. Trough Concentration (Ctrough) of selicrelumab following SC administration for cycle 3 measured from serum samples taken at -1 and 8 h on day 2 of cycle 3 during Part I; or taken at -1 h on day 1 of cycle 3 during Part II
8. Time taken to achieve the first quantifiable plasma concentration of selicrelumab following SC administration measured from serum samples taken at -1, 4, 8, 24, 48, and 72 h on day 2 of cycle 1, and -1 and 8 h on day 2 of cycle 3, during Part I; or taken at -1, 24, 48, and 72 h on day 1 and day 8, and -10 min on day 15, of cycle 1, and -1 h on day 1 of cycle 3, during Part II
9. Blood and tumor tissue immune cell subpopulations measured from serum samples taken pre-dose of vanicizumab on day 1, 4, and 9 of cycle 1 (as well as pre-dose and 6 h post-dose on day 15 for cohort 8), day 1 and 9 of cycle 2, 4, 7, and 10, during Part I; or pre-dose on day 1, 3, 8 and 15 of cycle 1 and day 1 and 8 of cycles 2, 4, 7, and 10, during Part II
10. Peripheral blood level of cytokines measured from serum samples taken pre-dose of vanicizumab on day 1 of cycles 1 and 2, or pre-dose and 3 h post-dose of selicrelumab on day 2 of cycle 1, 2, and 4
11. Blood soluble proteins measured from serum samples taken on day 1, 2, 3, 9, and 15 of cycle 1, day 1, 3, 9, and 15 of cycle 2, day 1 of cycle 4 and 5, day 1 and 15 of cycle 7, and day 1 of cycle 10
12. Best overall response assessed by unidimensional Immune-Related Response Criteria (irRC) during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months)
13. Duration of objective response assessed by irRC during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months)
14. Disease control assessed by irRC during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death,

whichever occurs first (up to approximately 42 months)
15. PFS assessed by irRC during tumor assessments at baseline and on day 1 of cycle 3, 5, and 7, and every 12 weeks thereafter, until disease progression until the first documentation of a complete or partial response, or participant's discontinuation or death, whichever occurs first (up to approximately 42 months)
16. Clinical activity of SC selicrelumab in combination with bevacizumab as assessed by unidimensional Immune-Related Response Criteria (irRC) from day 1 of cycle 1 to safety follow up visit (45 days post final dose)
17. Overall Survival (OS) measured from patient records from baseline until participant's discontinuation or death, whichever occurs first (up to approximately 42 months)
18. Concentration at the end of Infusion (Cend) of Bevacizumab measured from serum samples taken at day 1 of every cycle until cycle 7 and at day 15 of cycle 1, at radiographical disease progression/tumor regression, and at safety follow up visit (45 days post final dose)
19. Minimum Concentration (Cmin) of bevacizumab after infusion measured from serum samples taken at day 1 of every cycle until cycle 7 and at day 15 of cycle 1, at radiographical disease progression/tumor regression, and at safety follow up visit (45 days post final dose)

Completion date
30/10/2019

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
Part I (dose escalation):
1. Histologically confirmed advanced/metastatic solid tumor (except prostate cancer and squamous non-small cell lung cancer [NSCLC])

Part II (expansion):
1. Histologically confirmed advanced/metastatic platinum-resistant ovarian carcinoma (aPROC), head and neck squamous cell carcinoma (HNSCC), or non-squamous NSCLC previously treated with anti-PD-L1/PD-1 inhibitor alone or in combination (e.g. atezolizumab, nivolumab, pembrolizumab, durvalumab, avelumab)
2. Checkpoint inhibitor (CPI)- experienced patients must have experienced documented disease progression on or after PD-L1/PD-1 inhibitor therapy
3. In CPI-experienced patients, the PD-L1/PD-1 inhibitor must have been part of the most recent systemic anticancer therapy administered prior to study enrollment
4. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2
5. Life expectancy ≥16 weeks
6. Adequate hematologic, renal, hepatic, and cardiovascular function
7. Measurable disease per Response Evaluation Criteria in Solid Tumors, v 1.1 (RECIST v1.1)
8. Tumors must be acceptable for biopsy. Participants in part II may be enrolled without a biopsy if the collection is not clinically feasible.
9. Agreement to use adequate contraceptive measures among men or among women of childbearing potential

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
94

Key exclusion criteria
Part I (dose escalation):
1. Prostate cancer or squamous NSCLC
2. Recent systemic anti-cancer treatment
3. Prior treatment with anti-programmed death (PD) 1 or anti-programmed death ligand (PD-L) 1 therapeutic antibody, vanucizumab, or compounds targeting cluster of differentiation (CD) 40 less than 4 weeks or 5xt1/2 (whichever is shorter) prior to enrollment

Part II (expansion):
1. Treatment targeting vascular endothelial growth factor (VEGF) or receptor within 12 months prior to enrollment
2. Systemic immunosuppressive medication within 2 weeks prior to day 1 of cycle 1
3. Chronic daily treatment with non-steroidal anti-inflammatory drugs
4. Unacceptable/unresolved toxicity from prior anti-cancer therapy
5. Patients who have had a surgical procedure or significant traumatic injury within 28 days prior to initiation of study treatment, or a core biopsy or other minor surgical procedure within 7 days prior to initiation of study treatment
6. Bisphosphonate therapy for symptomatic hypercalcemia
7. Significant vascular disease
8. History of hypertensive crisis or hypertensive encephalopathy
9. Current or recent use of aspirin (>325 mg/day) or clopidogrel (>75 mg/day)
10. History of vein thrombosis/thromboembolism, or use of anticoagulants within 7 days prior to study drug
11. Primary tumor in place in participants with colorectal cancer, or evidence of bowel involvement (metastasis, direct tumor invasion) in participants with other non-gastrointestinal cancer
12. Significant cardiovascular or cerebrovascular disease within 6 months prior to D1 of C1
13. History of fistula, bowel obstruction, perforation, or abscess
14. Prior radiotherapy to pelvis or abdomen, recto-sigmoid involvement, or bowel involvement among participants with aPROC
15. Severe non-healing wound, active ulcer, or untreated bone fracture
16. Pregnant or lactating women
17. History of autoimmune disease
18. Human immunodeficiency virus (HIV) or hepatitis B or C
19. Severe infection or receipt of a live/attenuated vaccine within 4 weeks prior to D1 of C1
20. Other significant malignancies within 3 years prior to D1 of C1
21. Allergy/hypersensitivity to study drug
22. Prior allogeneic bone marrow or solid organ transplant
23. Other conditions/findings that may contraindicate the use of study drug

24. Major surgery within 4 weeks prior to study drug
25. Known clinically significant liver disease
26. History of hemoptysis or bleeding diathesis, or known coagulopathies
27. Known symptomatic or untreated central nervous system (CNS) malignancy

Date of first enrolment
25/01/2016

Date of final enrolment
15/05/2019

Locations

Countries of recruitment
Belgium

Canada

Denmark

Italy

Netherlands

Spain

United States of America

Study participating centre
Cliniques Universitaires St-Luc
Avenue Hippocrate 10
Brussels
Belgium
1200

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

Study participating centre
Rigshospitalet Onkologisk Klinik
Blegdamsvej 9

Copenhagen
Denmark
2100

Study participating centre
Antoni van Leeuwenhoek Ziekenhuis
Plesmanlaan 121
Amsterdam
Netherlands
1066 CX

Study participating centre
Erasmus Medisch Centrum Rotterdam
Lokatie Daniel den Hoed Clinic
Internal Oncology
Molewaterplein 40
Rotterdam
Netherlands
3015 GD

Study participating centre
START Madrid, Centro Integral Oncologico Clara Campal (CIOCC)
Calle de Oña, 10
Madrid
Spain
28050

Study participating centre
University of Colorado Health Sciences Center
4200 E 9th Ave
Denver
United States of America
80262

Study participating centre
University of North Carolina at Chapel Hill
Chapel Hill
United States of America
27514

Study participating centre
Hospital del Mar, Servicio de Oncologia
Passeig Marítim de la Barceloneta, 25, 29
Barcelona
Spain
08003

Study participating centre
Hospital Univ Vall d'Hebron, Servicio de Oncologia
Passeig de la Vall d'Hebron, 119
Barcelona
Spain
08035

Study participating centre
Hospital Clinico Universitario de Valencia, Servicio de Onco-hematologia
Av. de Blasco Ibáñez, 17
Valencia
Spain
46010

Study participating centre
ICO L'Hospitalet, Servicio de Oncologia Medica
Hospital Duran i Reynals
Avinguda de la Gran Via de l'Hospitalet, 199-203
L'Hospitalet de Llobregat
Barcelone
Spain
08908

Study participating centre
IRCCS Ospedale San Raffaele, Oncologia Medica
Via Olgettina, 60
Milan
Italy
20132

Sponsor information

Organisation
Genentech, Inc

ROR
https://ror.org/017w8ej57

Funder(s)

Funder type
Industry

Funder Name
Genentech

Alternative Name(s)
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

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository.

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results	version v1.0	23/10/2020	09/03/2021	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes