OPEN LABEL PHASE 2 BASKET TRIAL WITH ATEZOLIZUMAB AND TIRAGOLUMAB IN SOLID TUMORS: TIRACAN

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This study has been transitioned to CTIS with ID 2024-512616-21-00 check the CTIS register for the current data. The main objective of the trial is to determine the pathological response rate in cohort 1 and the radiological response rates in cohort...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON53466

Source
ToetsingOnline

Brief title
TIRACAN

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, Solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Medische Oncologie
Source(s) of monetary or material Support: Farmaceutische industrie,Hoffman - La

Roche

Intervention

Keyword: Atezolizumab, Cancer, tiragolumab

Outcome measures

Primary outcome

Pathologic response of the primary tumor in patients with HNSCC and objective response rate according to RECIST 1.1 and iRECIST in patients with advanced or metastatic MSI-H cancer, metastatic melanoma, and patients with a locally advanced or metastatic solid tumor whom, in the opinion of the investigator, based on available clinical data, may benefit from treatment with anti-PD-L1 immunotherapy.

Secondary outcome

The secondary endpoints are toxicity scored according to the common criteria for adverse events version 5.0, disease free survival in patients with HNSCC, overall response rate, progression free survival and duration of response in the patients in cohort 2, 3 and 4 as well as The correlation between the expression of the proteins TIGIT, PD-1, PD-L1 and CD8 on tumor tissue and pathologic and radiographic response rate.

Study description

Background summary

Tumor immunotherapy has demonstrated that therapies focused on enhancing T cell responses against cancer can result in a significant survival benefit in subjects with advanced stages of cancer. The most frequently used immunotherapy drugs bind to the Programmed death-ligand 1 (PD-L1) or programmed death protein

1 (PD-1). This binding interrupts the PD-L1/PD-1 pathway which inhibits an anti-tumor response of the immune system. Not all patients respond to anti-PD-1 or anti-PD-L1 treatment and therefore, combinations of immunotherapy drugs have been investigated and proven more effective than single-agent immunotherapy. These combinations, however, also increase the chance of immune toxicity. Possible strategies to overcome this problem are to develop less toxic combinations of immunotherapy drugs.
The T-cell immunoreceptor with immunoglobulin and ITIM domain (TIGIT) protein is also a target for immunotherapy. TIGIT is overexpressed in several malignancies including, melanoma, head and neck squamous cell carcinoma (HNSCC), and microsatellite instability high (MSI-H) colorectal cancer. The combination of the anti-TIGIT drug tiragolumab with the anti-PD-L1 drug atezolizumab increased the overall response rate by 15.1% compared to atezolizumab alone in a phase 2 study with 135 non-small cell lung cancer patients (NSCLC), without increasing toxicity.
In this trial, we will assess anti-tumor activity, safety, and tolerability of atezolizumab in combination with tiragolumab in subjects with cancer. We will also investigate proteins in the tumor to determine if we can predict which patients will respond to the atezolizumab and tiragolumab treatment. Patients will be included in one of four cohorts, namely: cohort 1, patients with localized HNSCC who will be treated with atezolizumab and tiragolumab followed by tumor resection, cohort 2, patients with metastatic MSI-H tumors, cohort 3, patients with irresectable or metastatic melanoma who progressed after PD-1 treatment, or cohort 4, with patients with a locally advanced or metastatic solid tumor for whom, based on available clinical data, treatment with anti-PD-L1 immunotherapy may be beneficial. Acquired data could lead to improved, more patient-tailored immune checkpoint inhibition.

Study objective

This study has been transitioned to CTIS with ID 2024-512616-21-00 check the CTIS register for the current data.

The main objective of the trial is to determine the pathological response rate in cohort 1 and the radiological response rates in cohort 2, 3 and 4. The secondary objectives of the trial are the safety of atezolizumab and tiragolumab, the response rates measured by overall response rate, disease free survival rate, duration of response and the last secondary objective is to determine the correlation between the protein expression of different proteins involved in the immune response of cancer to immunotherapy and the different response rates as mentioned before.

Study design

Open label phase 2 basket trial with atezolizumab and tiragolumab in patients with localized HNSCC who will undergo surgery, and advanced or metastatic MSI-H

cancer, PD-1 resistant metastatic melanoma, and patients with a locally advanced or metastatic solid tumor who, in the opinion of the investigator, based on available clinical data, may benefit from treatment with anti-PD-L1 and anti-TIGIT immunotherapy.

Intervention

Subjects will receive atezolizumab and tiragolumab every 3-weeks until 1) resection as scheduled for HNSCC after 2 courses, 2) resectable disease for the MSI-H tumors, 3) progressive disease or side effects requiring treatment termination or 4) a maximum of 2 years. At baseline archival tissue or a tumor biopsy will be obtained and tissue will be collected once during the trial and when lesions are surgically resected. Blood samples will be collected during the trial to measure circulating tumor DNA. During the trial regular CT or MRI scans will be made to monitor the response to the treatment.

Study burden and risks

Encouraging clinical data emerging in the field of tumor immunotherapy have demonstrated that therapies focused on enhancing T cell responses against cancer can result in a significant survival benefit in patients with cancer. Targeting the PD-L1 pathway with atezolizumab has demonstrated activity in patients with advanced malignancies, who have failed standard of care therapies.
Patient are required to provide tumor material during screening and on treatment. For cohort 1 this will be the archival diagnostic biopsy and the surgical specimen. For cohort 2, 3 and 4, the pre-treatment biopsy can be replaced by archival tissue provided that this tissue was obtained at the time of metastatic or irresectable disease, which holds no risk for patients. Based on a literature review, the risk of tumor biopsies is considered low with a small risk on significant/major complications (0 to 1.6%) or death (0 to 0.48%). For patients with HNSCC there is a risk of delay of surgery due to toxicity of the atezolizumab and tiragolumab treatment as well as progressive disease and subsequent loss of resectability. These risks are however deemed limited because of the short duration of the neo-adjuvant treatment in the study. In order to account for the possibility of pseudoprogression/tumor immune infiltration (i.e., radiographic increase in tumor volume due to the influx of immune cells) and the potential for delayed anti-tumor activity, this trial. Subjects will be allowed to receive atezolizumab and tiragolumab beyond apparent radiographic progression in cohort 2, 3 and 4. Because it is not yet possible to reliably differentiate pseudoprogression/tumor immune infiltration from true tumor progression, the risk exists that some subjects not responding to treatment yet continuing to receive atezolizumab and tiragolumab may experience a decline in performance status related to progression and may not be fit to receive subsequent therapies for which they would otherwise have been eligible. Investigators will make every effort to fully inform subjects of this

risk. In contrast to the cytotoxic therapies approved for treatment, atezolizumab and tiragolumab have been generally well tolerated and have not been associated with bone marrow suppression or other systemic toxicities (i.e., neuropathy, nephrotoxicity, or febrile neutropenia) that may limit the ability to administer subsequent treatments.
In summary, treatment with atezolizumab and tiragolumab offers the potential for clinical benefit in subjects. Because most atezolizumab and tiragolumab -related toxicities observed to date have been mild and transient in nature and do not overlap with the adverse effects of chemotherapy, subjects who do not respond to study treatment are considered likely to be able to subsequently receive standard therapies for which they would otherwise have been eligible. Subjects will be fully informed of the risk of continuing study treatment in spite of apparent radiographic progression, and investigators should make a careful assessment of the potential benefit of doing so, considering radiographic data, biopsy results, and the clinical status of the subject.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Tumor lesion(s) of which a histological biopsy can be safely obtained according to standard clinical care procedures.
• Measurable disease, as defined by RECIST v1.1. Previously irradiated lesions should be discarded as target lesions.
• Participate in the GE-269-001 CD8 investigational imaging trial provided that there are slots is that trial.
• Signed informed consent.
• Age >=18 at the time of signing informed consent.
• Life expectancy >=12 weeks.
• Eastern Cooperative Oncology Group (ECOG) performance status 0-1 (Appendix 5)
• Adequate organ and bone marrow function as defined below:
o Hemoglobin >=9.0 g/dL
o Platelet count >=100 x 109 /L
o Serum creatinine <=1.5 x upper limit of normal (ULN) or estimated glomerular filtration rate > 30 mL/min/1.73 m2 . A 24-hour urine creatinine collection may substitute for the calculated creatinine clearance to meet eligibility criteria.
o Adequate hepatic function:
* Total bilirubin <=1.5 x ULN (<=3 x ULN if liver tumor involvement); Patients with Gilbert*s syndrome do not need to meet total bilirubin requirements, provided their total bilirubin is unchanged from their baseline. Gilbert*s syndrome must be documented appropriately as past medical history.
* Aspartate aminotransferase (AST) <=2.5 x ULN (<=5 x ULN if liver tumor involvement)
* Alanine aminotransferase (ALT) <=2.5 x ULN (<=5 x ULN if liver tumor involvement)
* Alkaline phosphatase (ALP) <=2.5 x ULN (<=5 x ULN if liver or bone tumor involvement)
• Ability to comply with the protocol.
• For female patients of childbearing potential and male patients with partners of childbearing potential, agreement (by the patient and/or partner) to use a highly effective form(s) of contraception (i.e., one that results in a low failure rate (< 1% per year) when used consistently and correctly).
For the head and neck squamous cell carcinoma cohort specific eligibility criteria apply
• clinical T2-4a, or node positive resectable HPV-unrelated HNSCC (oral cavity, larynx, hypopharynx, p16-negative oropharynx or p16 negative unknown primary)
• no evidence of distant metastases
• no previous radiotherapy to the head and neck region

Exclusion criteria

• Signs or symptoms of infection within 2 weeks prior to atezolizumab and tiragolumab administration.
• Prior immune checkpoint inhibitor treatment, including but not limited to anti-PD1 and anti-PD-L1 antibodies (only for cohort 1, 2 and 4).
• History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.
• Any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use atezolizumab and tiragolumab, or that may affect the interpretation of the results or render the patient at high risk from complications.
• Pregnant or lactating women.
• Positive test for HIV, active hepatitis B (chronic or acute defined by positive hepatitis B surface antigen (HBsAg) during screening) or hepatitis C. Patients with a medical history of hepatitis B infection (defined as a positive hepatitis B core antibody (HBcAb) and absence of an HBsAg) are eligible for this study. Patients who test positive for hepatitis C antibodies are only eligible with a negative hepatitis C RNA PCR.
• Acute or chronic active EBV infection at screening EBV status should be assessed by EBV serology (e.g., anti-VCA IgM and IgG, anti-EA IgG, anti-EBNA IgG) and EBV PCR (plasma or serum). If EBV serology results indicate prior EBV infection, patients must have a negative EBV PCR (plasma or serum) to be eligible for the study.
• Active tuberculosis.
• Treatment with systemic immunostimulatory agents (including but not limited to interferons (IFNs) or, IL-2). The agents may not have been used within 6 weeks or five half-lives of the drug, whichever is shorter, prior to the first full dose of atezolizumab and tiragolumab.
• Treatment with systemic immunosuppressive medications (including but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor (TNF) agents) within 2 weeks prior to cycle 1, day 1, with the exception of inhaled corticosteroids for chronic obstructive pulmonary disease, mineralocorticoids (e.g., fludrocortisone) for subjects with orthostatic hypotension, low-dose supplemental corticosteroids for adrenocortical insufficiency and topical steroids are allowed.
• medications (e.g., a one-time dose of dexamethasone for nausea) may be allowed in the study after discussion with and approval by the principal investigator (PI).
• Brain metastases, leptomengeal metastases.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-10-2023
Enrollment:	97
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	tiragolumab
Generic name:	tiragolumab

Ethics review

Approved WMO

Date:	05-07-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	12-07-2023
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-06-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-07-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-512616-21-00
EudraCT	EUCTR2021-006894-48-NL
ClinicalTrials.gov	NCT05483400
CCMO	NL82143.042.22