Treatment with recombinant human Interleukin 1 receptor antagonist (Anakinra) in patients with anaplastic thyroid cancer: a proof of concept study

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22269

Source
Nationaal Trial Register

Brief title
ATC-Anakinra

Health condition

anaplastic thyroid carcinoma

Sponsors and support

Primary sponsor: Radboud UMC Nijmegen, The Netherlands
Source(s) of monetary or material Support: Swedish Orphan Biovitrum BVBA (SOBI) provides the study medication.

Intervention

Outcome measures

Primary outcome

Primairy endpoints well be:

- Effect of anakinra on health related quality of life (HRQoL), HR QoL defined according to a newly developed HRQoL questionaire specifically for ATC patients.

- Effects on tumor progression/tumor extent, such as TNM classification and tumor size. This will be assessed using radiological examinations using the Response Evaluation Criteria in Solid Tumors (RECIST) criteria .

- Overall Survival (OS): defined as time interval from date of official inclusion to death due to any cause.

Secondary outcome

To investigate the effect of treatment with IL1Ra (Anakinra) in patients with anaplastic TC on:

- performance status, measured with the Eastern Cooperative Oncology Group (ECOG) performance scale.

- progression free survival (PFS): which is defined as the time interval from date of official inclusioin to date of first progression or death due to any cause, if death occurs before a progression is documented. Progression will be defined according to RECIST criteria.

- safety in terms of occurrence and severity of adverse events according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (NCI CTCAE) (35), - Measurements of (systemic) inflammation, e.g. CRP, IL6 serum levels, etc.

Study description

Background summary

Rationale: Non-medullary thyroid carcinoma (TC) is the most common endocrine malignancy and worldwide one of the most rapidly increasing cancer types. Anaplastic thyroid carcinoma (ATC), is the most aggressive form of TC, with an extremely poor prognosis with a median survival of less than 6 months and a 5 year relative survival of less than 14%.

The locally extensive nature of ATC usually precludes patients from any surgical options. Furthermore, lack of sodium iodine symporter (NIS) expression in ATC renders radioactive iodine treatment ineffective. Patients with unresectable ATC can be offered External Beam Radiation Therapy (EBRT). However, due to rapid progression, even this local treatment is often not feasible and patients still die early.

To improve the prognosis and morbidity of ATC patients, there is an imperative need to explore new treatment options that on the one hand can effectively stop the tumor growth and help reduce tumor burden in order to make room for other local treatments such as surgery and EBRT.

One of the most promising and increasingly used therapy options in many cancers is targeting the antitumoral immune response. Previous studies have shown that ATCs are highly infiltrated with inflammatory cells, and this correlates with aggressiveness of the tumor and a poor prognosis. This local inflammatory response, and especially Interleukin 1 (IL-1) plays an important role in carcinogenesis and tumor progression.

Results from trials using IL- 1 blockade to treat other malignancies, show that IL-1 blockade reduces metastasis and tumor load, and improves Quality of Life (QoL) and is well tolerated in humans with little to no toxicity. We therefore propose a proof-of-concept study to explore the therapeutic potential of targeting this sterile inflammatory response with recombinant human interleukin-1 receptor antagonist (rh IL-1Ra, anakinra) in patients with ATC.

Objective: To investigate the efficacy of treatment with human recombinant IL1Ra (rhIL1Ra, Anakinra) in patients with ATC in terms of improved health related quality of life (HRQoL), tumor progression and Overall Survival (OS).Secondary objectives: To investigate the effect of treatment with IL1Ra (Anakinra) in patients with ATC in terms of safety (occurrence and severity of adverse events), progression free survival, performance status, and (systemic) inflammation.

Study design: Single centre, prospective interventional proof of concept study. Study population: Patients with ATC, for whom no conventional therapy is available. Intervention: IL1Ra (anakinra, Kineret ©) 600 mg/d i.v. for 1 week, followed by 100 mg/d s.c. for a total of 6 months. Main study parameters/endpoints: Health related quality of life (HRQoL) defined based on a newly designed HRQoL score specific for ATC patients. Tumor progression defined as radiological response according to RECIST criteria. Overall Survival (OS) defined as time from official inclusion until death due to any cause.

Study objective

The rationale of the study is based on three arguments:

1. Aggressive thyroid carcinomas are characterized by an abundant local inflammatory tumor microenvironment and associated with systemic inflammation

2. Inflammation, and especially Interleukin 1 (IL-1) plays an important role in carcinogenesis and tumor progression

3. IL-1 blockade has been shown to reduce metastasis and tumor load in malignant tumors, improves symptoms and is well tolerated in humans with little to no toxicity.

Taken together, the three aforementioned arguments show compelling evidence that treatment with rhIL1Ra could be of great benefit in patients with ATC, particularly those with increased tumor immune infiltrates and evidence of systemic inflammation. IL1Ra treatment could reduce tumor burden and tumor-related morbidity, in order to increase efficacy of other local therapies or other chemotherapeutic agents, without inducing additional toxicity.

Study design

On day 3 and day 7 during the first week: peripheral blood tests to monitor the effects of treatment and to investigate markers of systemic inflammation

Once every 2 weeks the QoL and performance status of the patients will be evaluated using a newly developed, disease specific HRQoL questionaire, and the ECOG performance status

After 4, 8, 12 and 24 weeks of therapy repeat imaging (CT/MRI/PET) to establish tumor response.

Intervention

Patients will be treated with 600 mg anakinra i.v. daily for the 7 days. Patients will be admitted on our clinical ward as part of standard care to make arrangements for palliative care etc. and to receive anakinra treatment i.v..

To reach the therapeutic level of anakinra quick we will administer higher dosages. The reason it will be given intravenously is to avoid local side effects at the injection site at this high dosage.

After this stage, patients will be treated with 100 mg s.c. daily, through self administration from home.

The treatment will be continued in the context of the study for a total of 6 months.

Contacts

Public

Scientific

Eligibility criteria

Inclusion criteria

- newly diagnosed patients with a proven diagnosis (cytology or histology) of ATC, for whom surgery is not feasible (as documented after consultation in multidisciplinary tumor board).

- Patients with proven ATC (cytology or histology), presenting with metastasis not amendable for surgery.

- age ≥ 18 years

Exclusion criteria

- unable to give informed consent

- pregnancy or breast feeding

- neutropenia (absolute neutrophil count (ANC)< 1.5 x109/l)

- patients with a known history of allergic reactions to compounds of similar chemical or biological composition to Anakinra.

-concomitant treatment with etanacept

- Any severe condition which could interfere with participation in this trial, including, but not limited to: severe renal dysfunction (creatinin clearance < 30 ml/min), severe cardiac failure, severe respiratory conditions etc.

- Active infection; However, after adequate treatment of infections, patients will be eligible for inclusion again.

- Concomitant use of CYP450 substrates (e.g. warfarin and phenytoin) is not contraindicated. However upon start or end of anakinra treatment in patients on these types of medicinal products, it is relevant to perform therapeutic monitoring of the effect or concentration of these products and the individual dose of the medicinal product may need to be adjusted.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	24-09-2018
Enrollment:	10
Type:	Anticipated

Ethics review

Positive opinion

Date:	21-09-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 46644
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL7272

Register	ID
NTR-old	NTR7487
CCMO	NL62684.091.17
OMON	NL-OMON46644

Study results