Treatment with Recombinant human Interleukin 1 receptor antagonist (Anakinra) in patients with Anaplastic Thyroid Cancer: a proof of concept study

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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...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Thyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON46644

Source
ToetsingOnline

Brief title
ATC-Anakinra1

Condition

- Thyroid gland disorders
- Endocrine neoplasms malignant and unspecified

Synonym
Anaplastic Thyroid Carcinoma; Anaplastic Thyroid Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Anaplastic Thyroid Cancer, IL-1Ra (anakinra)

Outcome measures

Primary outcome

Health related quality of life (HRQoL) defined based on a newly designed HRQoL score specific for ATC patients.

Tumor dimensions/ progression defined as tumor volume etc. according to RECIST criteria.

Overall Survival (OS) defined as time from official inclusion until 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

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.

Study 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.

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

Study burden and risks

Anakinra has been used in other diseases for a longer time now and is well tolerated and associated with only few side effects, which can be monitored easily.
In this study, only a few additional study procedures will be conducted compared to standard care. As part of standard care, patients will be admitted to the hospital. During this stay, they will receive anakinra treatment and some additional blood will be drawn. For the remainder of the study, some additional blood will be drawn (max 40 ml extra per visit), questionnaires will need to be filled out bi-weekly, and some additional imaging (total of 4 time points) will take place. This is will not be a significant burden for patients.
The risks of this study are minimal and thus acceptable for patients participating in this study because it will provide them with a treatment option which could possibly improve their symptoms and prognosis. Patients with ATC are faced with a very poor prognosis and current treatment options such as surgery and EBRT are not always applicable for all ATC patients because of advanced disease, leaving them with no other treatment options and an even worse prognosis. Treatment with anakinra could offer these patients a second chance, possibly leading to improved QoL, reduced tumor growth and less morbidity, and making room for surgery or EBRT again.

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

- newly diagnosed patients with a proven diagnosis (cytology or histology) of ATC, for whom surgery is not feasible.;- 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 x10^9/l);- patients with a known history of allergic reactions to compounds of similar chemical or biological composition to Anakinra. ;- Any severe condition which could interfere with participation in this trial, including, but not limited to: severe renal dysfunction (creatinin clearance < 15 ml/min), severe cardiac failure, severe respiratory conditions etc.;- Active infection; However, after adequate treatment of infections, patients will be eligible for inclusion again.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-10-2018
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kineret
Generic name:	Anakinra
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-03-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-06-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 22269
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-003028-59-NL
CCMO	NL62684.091.17
OMON	NL-OMON22269