Type 2 low asthma in obese and non-obese patients treated with Tezepelumab

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1) To identify T2 low biomarkers and 2) to unravel the mechanisms and downstream effects of Tezepelumab in T2 low asthma.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON54288

Source
ToetsingOnline

Brief title
POTENT Trail

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Asthma

Research involving
Human

Sponsors and support

Primary sponsor: Longziekten
Source(s) of monetary or material Support: AstraZeneca

Intervention

Keyword: Asthma, Obese, Tezepelumab

Outcome measures

Primary outcome

Outcomes of single cell sequencing

Secondary outcome

NA

Study description

Background summary

Approximately one third of asthma patients have a T2 low biomarker profile. Patients with a T2 low profile, in particular patients with an obese phenotype, benefit poorly from usual care (i.e. Inhaled Corticosteroids, GINA 2020). Development of new drugs and biologicals are necessary to treat patients with severe T2 low asthma. New drugs for this category of patients will hopefully lead to better control of their asthma and thus lowering the number of exacerbations and the burden of disease. However, developments in T2 low asthma have progressed slowly, due to a poor understanding of T2 low pathways. The recent finding of the possible roles of Thymic Stromal Lymphopoietin (TLSP) in T2 low asthma may shed new light on an old theme. Recent trials suggest a central role of TSLP, as anti-TSLP (Tezepelumab), reduced the exacerbation frequency in patients with non-eosinophilic asthma. A clear understanding of the cellular changes during treatment with anti-TSLP in relation to Asthma severity will benefit future treatment regimens with Tezepelumab. Furthermore, studying the differences between obese and non-obese patients is important as these two T2 low phenotypes may have distinct cellular inflammatory patterns.

Study objective

1) To identify T2 low biomarkers and
2) to unravel the mechanisms and downstream effects of Tezepelumab in T2 low asthma.

Study design

Explorative, prospective, open-label, intervention trial

Intervention

Every 4 weeks, for 20 weeks, the patient will receive 210 mg of Tezepelumab by injection under the skin.

Study burden and risks

Tezepelumab decreases the exacerbation rate in patients with severe asthma significantly, regardless of eosinophilia[1-4]. Most common adverse events include bronchitis, nasopharyngitis and headaches. Approximately 9% of patients treated with medium dose Tezepelumab developed at least 1 serious event. No treatment related deaths were reported in earlier trials.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age 18-75 years
- Written informed consent
- BMI >18 with weight >40kg at inclusion
- Documented physician-diagnosed asthma for at least 12 months prior to inclusion (12% reversibility in FEV1 or positive histamine/methacholine provocation test)
- Controller regime with medium- or high dosed ICS
* Medium: >=250µg and <500µg fluticasone daily
* High: >=500µg fluticasone daily
* Or bio-equivalent dose of other type of ICS
- Stable dose of controller medication other than ICS/LABA (leukotriene receptor inhibitors, theophylline, secondary ICS, LAMA, chromones)
- Pre-BD FEV1 value of >= 40%
- ACQ >= 1.5
- T2 low profile:
* Peripheral blood eosinophils < 150 cells/µL
* FeNO < 20 ppb
* No clinically proven allergen driven asthma
* No need for maintenance OCS
- >=2 exacerbation events or >=1 exacerbation with hospitalization in the 12 months prior to inclusion
* Exacerbation: burst of OCS for at least 3 days
- Reproduction:
* Females of childbearing potential who are sexually active with a nonsterilized male partner must use a highly effective method of contraception from screening, and must agree to continue using such precautions for 16 weeks after the final dose of Tezepelumab.

Exclusion criteria

- Current smokers
- Stopped smoking <6 months prior to inclusion but >= 10 pack years
- Use of immune modulatory drugs, Azithromycin, Montelukast and Theophylline
- Concurrent or intercurrent disease that may compromise safety of the patient or may compromise the ability to participate in the trial
- Concomitant respiratory disease that will interfere with the evaluation of the product or the interpretation of the results
- Evidence of active liver disease
- History of cancer
- Acute upper or lower respiratory infections requiring antibiotics or antiviral medications within 15 days prior to first visit
- Pregnant, breastfeeding or lactating females
- Unwillingness or inability to follow the procedures outlined in the protocol

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-08-2022
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tezepelumab
Generic name:	Tezepelumab

Ethics review

Approved WMO Date:	01-03-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2021-004877-29-NL
CCMO	NL78940.100.21
Other	NL9768