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

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25171

Source
NTR

Brief title
POTENT Trail

Health condition

Type 2 low asthma

Sponsors and support

Primary sponsor: Unknown
Source(s) of monetary or material Support: Grant

Intervention

Outcome measures

Primary outcome

1) To unravel the mechanisms and downstream effects of Tezepelumab in T2 low asthma, 20 weeks after therapys
2) To identify T2 low biomarkers

Secondary outcome

1) To identify predictive biomarkers for the effect of Tezepelumab in T2 low asthma

Study description

Background summary

Rationale: 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[1]. 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.
Objectives: 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
Study population: We will include a total of 8 patients (4 obese, BMI ≥ 30 kg/m2 and 4 non-obese, BMI 18.5 - 25 kg/m2), aged 18-65 years with proven asthma for at least 12 months before screening (asthma reversibility of at least 12% and at least 200 mL documented during the 12 months before screening or during run-in, or positive histamine/methacholine provocation test), FEV1 less than 80% of the predicted normal value during the run-in period, T2-low phenotype (peripheral blood eosinophils < 150 cells/µL, FeNO < 20 ppb, no clinically allergy driven asthma and no need for maintenance OCS) with ≥2 exacerbations without hospitalization or ≥1 exacerbations with hospitalization in the past 12 months and an ACQ > 1.5).
Intervention: Patients will be treated (per protocol) with 210mg of Tezepelumab every 4 weeks for a duration of 20 weeks. Blood samples will be collected at baseline and at 20 weeks and analysed with single cell sequencing. ACQ, lung function and FeNO will be measured at every visit. Censored patients will be replaced.
Main study parameters/endpoints: Chromium Single Cell Multiome ATAC + Gene Expression
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: 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.

Study objective

Unravel the mechanisms and downstream effect in patients with Type 2 low asthma who are recieve Anti-TSLP (Tezepelumab) treatment, and to find biomarkers to identify patients who will benefit future treatment regimens with Tezepelumab.

Study design

• T0: Start of treatment: blood withdrawl for single cell analysis, Tezepelumab 210mg sc, longfunctie, questionaire (ACQ)
• T1: 4 weeks after T0: lung function, Tezepelumab 210mg sc, questionaire (ACQ)
• T2: 4 weeks after T1: lung function, Tezepelumab 210mg sc, questionaire (ACQ)
• T3: 4 weeks after T2: lung function, Tezepelumab 210mg sc, questionaire (ACQ)
• T4: 4 weeks after T3: lung function, Tezepelumab 210mg sc, questionaire (ACQ)
• T5: 4 weeks after T4: lung function, Tezepelumab 210mg sc, questionaire (ACQ)
• T6: 4 weeks after T5, final visit / end of study: blood withdrawl for single cell analysis, lung function, questionaire (ACQ)

Intervention

210 mg of Tezepelumab s.c. every 4 weeks for 20 weeks.

Contacts

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Eligibility criteria

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2022
Enrollment:	8
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL9768
Other	EudraCT / EMA : 2021-004877-29

Study results