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Beat severe asthma

Submission date
27/05/2020

Recruitment status
No longer recruiting

Registration date
29/05/2020

Overall study status
Stopped

Last Edited
25/09/2024

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Asthma affects over 5 million people in the UK and while most respond well to currently available therapy, 3-5 in 100 sufferers have severe asthma. This is when the symptoms persist and have an impact on day-to-day life. This trial is looking at the two sub-types of severe asthma, T2-High and T2-Low which are identified through a simple blood test, and comparing two different drugs (an antibiotic and a biologic) to Placebos (substances containing no active medication) with the aim of understanding more about the condition and reducing the number of exacerbations (sudden worsening of asthmatic symptoms) that individuals experience.

Who can participate?
Patients that are both (i) exacerbation prone (≥ 2 per year, ≥ 3 days use of acute prescription for systemic steroids and/or acute prescription for antibiotics due to a worsening of asthma/airways disease, or admission to hospital/A&E, and have (ii) severe asthma (defined by a hospital specialist or severe asthma Multi-Disciplinary Team [or non-English equivalent]) according to the ATS/ERS consensus criterion. Further details can be found in the eligibility criteria which was provided in the online submission.

What does the study involve?
Stage 1 of the trial involved participants undergoing a screening process to see if they are eligible for the trial via what severe asthma sub-type they have. They will be asked to provide a blood sample, complete 5 short questionnaires, provide details about their medical, asthma and medication history and undergo assessments such as weight, height, BMI, vital signs, pregnancy test (if applicable) and a physical examination.
The Run In period allows the participant to become familiar with an electronic microdiary that they may wish to use during the trial along with confirming that the participant is in a stable disease condition, reviewing their Asthma Action Plan and assessing their maintenance ICS/LABA technique. The participant will also be informed of their severe asthma sub-type.
In Stage 2, participants will be randomised into either the T2-High or T2-Low treatment cohort where they will randomly be assigned to receive either an IMP or a placebo. This trial is doubled blinded so neither the participant nor the clinicians will know which treatment they will receive until the end of the trial. Participants will then be seen on a regular basis for 13.5 months to assess safety and efficacy of the trial treatments. Participants will also be asked to undergo the same assessments as during Stage 1 along with different questionnaires, spirometrys, sputum inductions, ECGs, biochemistry assessments, breathing tests and pregnancy tests (if applicable).

The participant is also asked to provide blood (serum and plasma), DNA, sputum and urine samples throughout the trial to be stored for future ethically approved research.

What are the possible benefits and risks of participating?
Risks: Some appointments may take up to 5 hours but participants will be given a break and provided with refreshments. Also, the full safety information and side effects for both IMPs is still unknown. However, based on results from previous clinical trials, both IMPs are well tolerated and the side effects are mild in intensity.
Benefits: There are no guaranteed benefits to taking part in this trial as there is very limited information about the effectiveness of the trial drugs.
However, recent evidence suggests that receiving a drug or even a placebo may halve the number of exacerbations participants experience. This means there should be a clinically important and measurable effect on the number and severity of exacerbations participants experience by participating in this trial, but this is not certain.
Participants will also be able to take the tablets home with them rather than receiving injections from their care team.

Where is the study run from?
Leicester Clinical Trials Unit, University of Leicester (UK)

When is the study starting and how long is it expected to run for?
January 2020 to December 2022 (updated 04/08/2020, previously: September 2022)

Who is funding the study?
1. National Institute for Health Research (NIHR) (UK)
2. Knopp Biosciences LLC (USA)

Who is the main contact?
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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2019-003013-34

Integrated Research Application System (IRAS)
247350

Central Portfolio Management System (CPMS)
44510

Study information

Scientific Title
Beyond Allergic Th2 Severe Asthma

Acronym
BEAT-SA

Study objectives
1. The development of a severe asthma Multi-Disciplinary Team (MDT) (or non-English equivalent) centred clinical trial platform will facilitate the delivery of severe asthma trials in the UK
2. Stratified approaches utilising blood eosinophils to target exacerbation prone T2-High/T2-Low sub-types of severe asthma will provide a step change in asthma care by reducing asthma exacerbations and improving asthma control and quality of life

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/03/2020, NRES Committee East Midlands – Leicester South (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8285; Leicestersouth.rec@hra.nhs.uk), ref: 20/EM/0015.

Primary study design
Interventional

Study design
Multi-centre platform trial with two (parallel group) randomised interventional double-blind placebo-controlled treatment cohorts

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Severe asthma

Interventions
Participants will initially be screened and stratified into a severe asthma sub-group (either T2-High or T2-Low) using blood eosinophils levels. Participants will then be randomised into either the T2-High treatment cohort to receive either 150mg twice daily of dexpramipexole or a matched placebo or the T2-Low treatment cohort to receive either 100mg once daily doxycycline or a matched placebo. All drugs must be taken orally. Randomisation will be performed electronically and both the participant and the clinical team will be blinded to the intervention but will know which severe asthma sub-type they have. Participants will receive their trial treatment for a maximum of 12 months and will be asked to attend regular trial visits to undertake numerous assessments to monitor safety and trial progression. A wash out safety visit will take place 6 weeks after the participant has ceased taking their trial medication to monitor and assess safety and any after effects.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Dexpramipexole Doxycycline

Primary outcome(s)
Annual rate of severe exacerbations defined as one or more of the following (using patient records):
1. Use of systemic steroids (tablets, suspension or injection) or an increase in systemic steroids (if stable maintenance) for equal to or greater than 3 days
2. A new prescription of antibiotics for worsening asthma/airways disease for equal to or greater than 3 days
3. Both 1 and 2
4. An admission to hospital because of asthma, or an emergency department requiring systemic steroids or antibiotics.

Key secondary outcome(s)
1. Assessing improvements in asthma symptoms is measured using the Juniper six-point Asthma Control Score (ACQ-6) measured at 3, 6, 9 and 12 months
2. Measuring health-related quality of life in trial participants is measured using the Juniper Asthma quality of life questionnaire AQLQ (S) measured at 3, 6, 9 and 12 months
3. Post bronchodilator FEV1 and FEV1/FVC measured at 3, 6, 9 and 12 months using spirometry
4. Absolute blood eosinophil and neutrophil levels (x109/L) measured at 3, 6, 9 and 12 months by taking blood samples from participants and performing full blood and differential cell counts
5. Percentage sputum eosinophils measured at 3, 6, 9 and 12 months through participant sputum samples obtained by sputum induction
6. Fractional exhaled nitric oxide levels (FeNO) in exhaled breath is measured at 3, 6, 9 and 12 months
7. Percentage and total sputum neutrophils measured at 3, 6, 9 and 12 months through participant sputum samples obtained by sputum induction
8. Testing the impact of chronic rhinosinusitis on the participant's quality of life using Sino-nasal Outcome Test (SNOT-22) measured at 3, 6, 9 and 12 months
9. Measuring the participant's subjective experience of severe asthma and the associated symptoms measured using VAS scale measured at 3, 6, 9 and 12 months
10. Assessing the health status of the participants using EuroQol Five Dimension EQ-5D-5L quality of life (Baseline and penultimate visit only i.e. Day 0 and Day 365)
11. Measuring the impairment that severe asthma in both paid and unpaid activities for the participants and is measured using the Work Productivity and Activity Impairment (WPAI) (Baseline and penultimate visit only i.e. Day 0 and Day 365)
12. Time to first severe exacerbation
13. Annual rate of severe exacerbation events defined by the use of systemic steroids, antibiotics or both
14. Adverse events measured by asking the participant to report all adverse events and any changes in adverse events at every scheduled trial visit
15. Patient treatment adherence and compliance measured using participant drug diaries and tablet/capsule counts at each scheduled trial visit

Completion date
31/12/2022

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
For Stage 1 Screening, the trial population will consist of participants that are both:
1. Exacerbation prone (≥2 record confirmed severe exacerbations)
AND
2. Severe asthma (defined by a hospital specialist or severe asthma Multi-Disciplinary Team (MDT, or non-English equivalent), according to the ATS/ERS consensus criterion
3. Aged ≥ 18 years and < 80 years
4. Capable of giving written informed consent
5. Willing and able to comply with study protocol requirements

T2-High and T2-Low Inclusion Criteria:
1. Aged ≥ 18 years and < 80 years

2. Capable of giving written informed consent
3. Diagnosis of severe asthma as per the ATS/ERS severe asthma guidelines. [Participants may be included with a lower dose of current ICS than endorsed by the ATS/ERS criteria at the discretion of the investigator if previous high ICS dose had led to side effects
4. Stable asthma therapy for at least 1 month before screening
5. Willing and able to comply with study protocol requirements
6. History of 'exacerbation prone asthma' defined as ≥ two record confirmed severe exacerbations within 12 months of MDT initial pre-screening review. Defined as worsening asthma symptoms necessitating one or more of the following:
6.1. Use of systemic steroids (tablets, suspension or injection) or an increase in systemic steroids (for those on stable maintenance steroids) for ≥ 3 days
6.2. New prescription of antibiotics because of worsening asthma/airways disease for ≥ 3 days
6.3. Both 6.1. and 6.2.
6.4. Admission to hospital because of asthma, or an emergency department requiring systemic steroids (tablets, suspension or injection) or antibiotics
[If any of the above are identified ≥7days apart, these would be defined as separate/new exacerbation events]

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Current or within the last 6 months (or maximum relevant wash out period, whichever is longer), participation in an investigational drug or device trial at the time of screening
2. Patients who are planning to take more than a 21 day consecutive holiday during the trial period
3. Have received treatment with biologics such as omalizumab, mepolizumab, reslizumab, benralizumab or dupilumab within four months or five half-lives (whichever is longer) prior to screening
4. Recent treatment with bronchial thermoplasty, defined as completion of all thermoplasty treatment sessions within 6 months of screening
5. Patients who have been hospitalised or required a new prescription of high-dose (≥10mg prednisolone/day) oral corticosteroid (OCS) therapy within 4 weeks of the screening visit
6. Recent (within 4 weeks of screening) or current lower respiratory tract infection requiring antibiotics (this excludes antibiotics taken for other purposes other than asthma exacerbations)
7. Acute illness other than asthma which, in the investigator's opinion, may compromise the well-being of the patient or study endpoint assessments at the start of the study
8. History of unstable or severe cardiac, hepatic, or renal disease, or other medically significant illness which the investigator believes would be a contraindication to study participation

9. Current smoking within the past year or a prior smoking history of ≥15 pack-years (including e-cigarettes)
10. Patients with a body mass index (BMI) ≤ 17 or ≥ 45 kg/m²
11. History of human immunodeficiency virus (HIV) or hepatitis B or C
12. History of malignancy of any organ system (other than localised basal cell carcinoma of the skin), treated or untreated, currently or within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
13. History (or suspected history) of alcohol or substance abuse as defined by the Diagnostic and Statistical manual of mental Disorders (5th edition) substance use disorders guidelines within two years of screening
14. If female, is pregnant or lactating or intends to become pregnant during the study period where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
15. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of trial treatment and for a minimum of 1 month after their last treatment
16. Males unwilling to use effective methods of contraception during dosing of trial treatment and for at least 3 months after their last dose
17. Patients with clinically significant laboratory abnormalities (not associated with the study indication) at screening including (but not limited to):
17.1. AST or ALT>2.0x upper limit of normal (ULN) or total bilirubin >1.3 X ULN at screening (with the exception of patients with Gilberts syndrome where suitability for inclusion will be left to the discretion of the local investigator)
17.2. Estimated Glomerular Filtration Rate (eGFR) by the MDRD equation <60 mL/minute/1.73 m² at screening

T2-High Specific Exclusion Criteria:
1. Treatment with pramipexole (Mirapex®) within 4 weeks of baseline
2. Patients where untreated infection with helminthic parasites is suspected by the clinician
3. Concomitant use of drugs known to be associated with significant neutropenia (see Appendix 7, for the list of drugs that should be assessed)
4. Absolute neutrophil count < 2.0 x 109/L at screening, or any documented history of absolute neutrophil count < 2.0 x 109/L on an NHS electronic pathology system available to the local investigator within two years of screening
5. Prior history of a neutropenic illness, such as neutropenic sepsis

T2-Low Specific Exclusion Criteria:
1. Patients who are unwilling to stay out of the sun or wear sun block
2. History of myasthenia gravis or systemic lupus erythematosus
3. Prior history of 'severe' (as defined by the patient), gastrointestinal intolerance to tetracyclines
4. Documented drug allergy to/ or concurrent use of tetracyclines such as doxycycline and Methoxyflurane or prior anaphylaxis due to tetracyclines
5. Current treatment with anticoagulants such as warfarin
6. Current treatment with long term (defined as ≥ 3 months) macrolides for asthma
7. Current use of any prophylactic (defined as ≥ 3 months) antibiotic for asthma or any other condition
8. Recent use of any prophylactic antibiotic (defined as ≥ 3 months), within 3 months of study entry
9. Current or active exfoliative dermatitis

10. Concurrent use of retinoids due to the increased risk of benign intra-cranial hypertension
11. Participant is unwilling to take the trial medication as it contains beef and pork gelatine is not Halal or Kosher certified or vegetarian/vegan

Date of first enrolment
20/08/2021

Date of final enrolment
30/06/2022

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Glenfield Hospital
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Groby Road
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Study participating centre
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Study participating centre
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Study participating centre
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OX3 7LE

Study participating centre
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Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Knopp Biosciences LLC

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other unpublished results	BEAT-SA End of Study Report version 1.0	29/07/2024	25/09/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes