



# Introduction

## **AIR-NET: Testing anti-inflammatories for the treatment of bronchiectasis**

A randomised, open-label, multifactorial, multicentre, platform trial using a range of repurposed anti-inflammatory treatments to improve outcomes in patients with bronchiectasis within the EMBARC clinical research network.

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Trial Management: Tayside Clinical Trials Unit, University of Dundee

Sponsor: University of Dundee & NHS Tayside

## BACKGROUND

- Bronchiectasis is a debilitating chronic respiratory disease characterised by cough, sputum production and associated with a vicious cycle of lung inflammation and infection
- The dominant mechanism of disease in bronchiectasis is chronic neutrophilic inflammation
- The purpose of this platform trial is to repurposing anti-inflammatory therapies in bronchiectasis to investigate therapeutic targets

## PRIMARY OBJECTIVE

- To evaluate the effect of a range of interventions compared to usual care on the activity of neutrophil elastase in sputum

### **Outcome Measure:**

Activity of sputum NE

### **Timepoint(s)**

Day 0 and 28

Secondary Objectives	
Objectives	Outcome Measures
To evaluate the effect of a range of interventions compared to usual care on the activity of NE in sputum	Activity of sputum NE
To evaluate the effect of a range of interventions compared to usual care on time to onset of first bronchiectasis exacerbation	Time to first pulmonary exacerbation (EMBARC definition)
To evaluate the effect of a range of interventions compared to usual care on quality of life	Quality of life-bronchiectasis (QOL-B) respiratory symptom scale, Bronchiectasis Impact Measure (BIM) questionnaire
To evaluate the effect of a range of interventions compared to usual care on walking distance	Distance covered during 6-minute walk
To evaluate the safety of a range of interventions compared with usual care	Frequency of adverse events (AEs) and serious adverse events (SAEs)
To evaluate the effect of a range of interventions on peripheral blood neutrophil function	Phagocytosis of bacteria Reactive oxygen species generation Degranulation Ex-vivo formation of neutrophil extracellular traps Mass cytometry (endpoints may vary depending on the experimental arm)

## Sub-Study Objectives

Objectives	Outcome Measures
To evaluate the effect of a range of interventions compared to usual care on endothelial dysfunction	Change in skin perfusion with iontophoresis of acetylcholine and sodium nitroprusside using laser doppler perfusion imaging
To evaluate the effect of a range of interventions compared to usual care on the cardiovascular system	Change in arterial stiffness index Change in pulse wave velocity



## Treatment allocation

Participants will be randomised to one of four treatment arms:

		Dosage, form and strength	
<b>Arm 1</b>	Usual care	N/A	
<b>Arm 2</b>	Disulfiram	Two 200 mg oral tablets, once daily	
<b>Arm 3</b>	Dipyridamole	One 200 mg oral prolonged/modified release capsule, twice daily	
<b>Arm 4</b>	Doxycycline	One 100 mg oral capsule, once daily	

Treatment cycle will be 28 days.

## IMPs

- **Disulfiram**

Blocks the body's usual routes to break down alcohol and is currently licensed to treat alcohol dependence. Disulfiram has anti-inflammatory properties.

- **Dipyridamole**

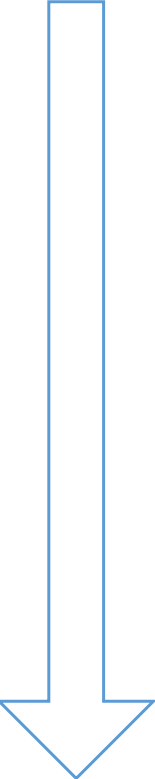
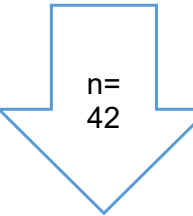
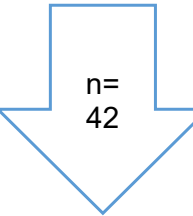
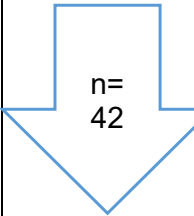
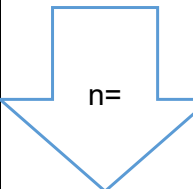
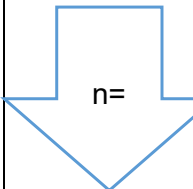
Is a blood thinner that is currently licensed to prevent blood clots and strokes. Dipyridamole has anti-inflammatory properties.

- **Doxycycline**

Is an antibiotic with anti-inflammatory properties that is used to treat a range of bacterial infections, including bronchiectasis exacerbations.



## Adding new treatment arms

Open/close to recruitment					New arms to be added in future	
<div style="border: 1px solid black; padding: 5px; width: fit-content;">           Dates arms closed/new arms opened will be added         </div>	Arm 1: Usual Care  <b>OPEN</b>	Arm 2: Disulfiram  <b>OPEN</b>	Arm 3: Dipyridamole  <b>OPEN</b>	Arm 4: Doxycycline  <b>OPEN</b>		
					Arm: 5 XXX  <b>N/A</b>	
						Arm: 6 XXX  <b>N/A</b>

