



Clinical trial results:

Delivering personalised care in the management of exacerbations of chronic obstructive pulmonary disease: A multi-centre randomised clinical trial

Summary

EudraCT number	2017-001586-24
Trial protocol	GB
Global end of trial date	30 April 2020

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	NA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04458636
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Boundary Brook House, Churchill Drive, Headington, United Kingdom, OX3 7GB
Public contact	Hania Piotrowska, Oxford Respiratory Trials Unit (ORTU), 44 01865225205, hania.piotrowska@ouh.nhs.uk
Scientific contact	Hania Piotrowska, Oxford Respiratory Trials Unit (ORTU), 44 01865225205, hania.piotrowska@ouh.nhs.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2020
Global end of trial reached?	Yes
Global end of trial date	30 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of blood-eosinophil directed corticosteroid therapy using near-patient testing, compared to current standard practice during an exacerbation of COPD.

Protection of trial subjects:

All local ethics and research protocols were followed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 203
Worldwide total number of subjects	203
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	40
From 65 to 84 years	162
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants recruited at time of exacerbation from 14 primary care practices in the Thames Valley in the UK. Recruitment commenced on 6 November 2017. Recruitment closed on 30 April 2020.

Pre-assignment

Screening details:

308 participants were enrolled in the study. Of those 156 participants did not have an exacerbation during the study period

Period 1

Period 1 title	Exacerbation (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

All patients and investigators were blinded to study allocation and IMP receipt.

Arms

Are arms mutually exclusive?	Yes
Arm title	Usual care

Arm description:

All participants received 14 days of blinded prednisolone 30mg for treatment of their COPD exacerbation

Arm type	Blinded usual care
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30mg daily for 14 days

Arm title	Biomarker guided arm
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Arm description:

Patients with a blood eosinophil count of greater than or equal to 2% of total white blood cell count on point of care test received 14 days of blinded prednisolone

Patients with a blood eosinophil count of lower 2% of total white blood cell count on point of care test received 14 days of blinded placebo

Arm type	Experimental
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

30mg daily for 14 days

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
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Dosage and administration details:

14 days of placebo tablets. 1 tablet a day

Number of subjects in period 1	Usual care	Biomarker guided arm
Started	101	102
Completed	101	102

Baseline characteristics

Reporting groups

Reporting group title	Usual care
Reporting group description: All participants received 14 days of blinded prednisolone 30mg for treatment of their COPD exacerbation	
Reporting group title	Biomarker guided arm
Reporting group description: Patients with a blood eosinophil count of greater than or equal to 2% of total white blood cell count on point of care test received 14 days of blinded prednisolone Patients with a blood eosinophil count of lower 2% of total white blood cell count on point of care test received 14 days of blinded placebo	

Reporting group values	Usual care	Biomarker guided arm	Total
Number of subjects	101	102	203
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	70	70	
full range (min-max)	46 to 84	50 to 85	-
Gender categorical Units: Subjects			
Female	39	42	81
Male	62	60	122

Subject analysis sets

Subject analysis set title	Intention to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised in the study	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All participants treated using biomarker guidance included	

Reporting group values	Intention to treat	Per protocol	
Number of subjects	203	143	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	70	70	
full range (min-max)	46 to 83	51 to 85	
Gender categorical Units: Subjects			
Female	81	50	
Male	122	93	

End points

End points reporting groups

Reporting group title	Usual care
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Reporting group description:

All participants received 14 days of blinded prednisolone 30mg for treatment of their COPD exacerbation

Reporting group title	Biomarker guided arm
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Reporting group description:

Patients with a blood eosinophil count of greater than or equal to 2% of total white blood cell count on point of care test received 14 days of blinded prednisolone

Patients with a blood eosinophil count of lower 2% of total white blood cell count on point of care test received 14 days of blinded placebo

Subject analysis set title	Intention to treat
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

All patients randomised in the study

Subject analysis set title	Per protocol
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Subject analysis set type	Per protocol
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Subject analysis set description:

All participants treated using biomarker guidance included

Primary: Treatment failure

End point title	Treatment failure
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End point description:

End point type	Primary
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End point timeframe:

30 days

End point values	Usual care	Biomarker guided arm	Intention to treat	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	101	102	203	
Units: Number of participants who failed rx	34	28	62	

Statistical analyses

Statistical analysis title	Primary outcome
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Statistical analysis description:

Chi squared test

Comparison groups	Usual care v Biomarker guided arm
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Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.23
Variability estimate	Standard error of the mean

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation to end of study

Assessment type	Non-systematic
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Dictionary used

Dictionary name	SNOMED CT
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Dictionary version	CTV3
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Reporting groups

Reporting group title	Usual care
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Reporting group description:

All participants received 14 days of blinded prednisolone 30mg for treatment of their COPD exacerbation

Reporting group title	Biomarker guided arm
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Reporting group description:

Patients with a blood eosinophil count of greater than or equal to 2% of total white blood cell count on point of care test received 14 days of blinded prednisolone

Patients with a blood eosinophil count of lower 2% of total white blood cell count on point of care test received 14 days of blinded placebo

Serious adverse events	Usual care	Biomarker guided arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 101 (0.99%)	2 / 102 (1.96%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Severe COPD Exacerbation			
subjects affected / exposed	1 / 101 (0.99%)	2 / 102 (1.96%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Usual care	Biomarker guided arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 101 (51.49%)	49 / 102 (48.04%)	
Respiratory, thoracic and mediastinal disorders			
COPD Exacerbation			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	50 / 101 (49.50%) 50	46 / 102 (45.10%) 46	
Endocrine disorders Glycosuria subjects affected / exposed occurrences (all)	2 / 101 (1.98%) 2	3 / 102 (2.94%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2017	Section 3.5: 'Pregnant and breastfeeding women' added to exclusion criteria. Section 9.4: Removal of statement on how to treat participants in clinical condition deteriorates.
16 August 2017	Section 7.5: the word 'include' added Section 9.3; description of AE follow-up edited Section 10.1: minimisation changed to stratification
23 January 2018	Wording of primary outcome measure changed from 'frequency' to 'proportion' throughout. Modification to NIMP dosage throughout. Section 7.7: Clarification of the 12 month note review. Section 7.8: Simplification of the withdrawal procedure for this trial. Section 7.9: Modification of end of trial definition.
19 August 2018	Key trial Contacts: Addition of trial manager details Section 1: addition of exacerbation events Section 5: Study duration – added details of re-randomisation. Addition of exacerbation events to sample size Section 7.4: Randomisation eligibility Section 7.6.2: Patients re-randomised for additional exacerbation episodes, detail added. Section 7.6.5: Follow-up visits detail included for re-randomised visits Section 7.9: Added word final Section 14.5: Additional sentence for GDPR

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported