Platform trial of two embedded (parallel group), randomised, double blind, placebo controlled, treatment approaches in patients stratified into T2-High/T2-Low severe asthma phenotypes (using blood eosinophil levels): BEyond Allergic Th2 Severe Asthma

T2-HIGH Treatment Cohort

End of Study Report

Trial registration: ISRCTN57935812

Report details:

Report Version: Final 1.0

Date: 29th July 2024

Author: Ana Suazo Di Paola

Reviewers: Cassey Brookes, Shaun Barber and Professor Salman Siddiqui

Data lock date: 29th February 2024

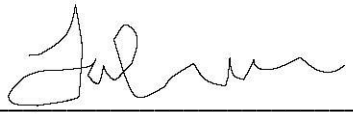
Based on Protocol v4.0 18th January 2021

Based on SAP v2.1 22nd February 2024

Software: Stata v18

FUNDED BY NIHR | National Institute for Health Research

End of Study Report approval for finalised version:

Trial Statistician	Ana Suazo Di Paola	
		29/07/2024
	Signature	**Date**
Chief Investigator	Professor Salman Siddiqui	
		30.08.2024
	Signature	**Date**
Senior Statistician	Dr Shaun Barber	
		**01/08/2024**
	Signature	**Date**

FUNDED BY NIHR | National Institute for Health Research

UNIVERSITY OF LEICESTER

List of Contents

FUNDED BY NIHR | National Institute for Health Research

FUNDED BY NIHR | National Institute for Health Research

UNIVERSITY OF LEICESTER

List of Tables

FUNDED BY NIHR | National Institute for Health Research

FUNDED BY NIHR | National Institute for Health Research

FUNDED BY NIHR | National Institute for Health Research

1. Introduction

The statistical analysis was carried out in accordance with the BEAT-SA T2-HIGH Statistical Analysis Plan v2.1. Data reported in this report was extracted from the MACRO database after the 29th February 2024, which is the database lock date.

BEyond Allergic Th2 Severe Asthma (BEAT-SA) is a platform study made-up of 5 participants, with 3 participants allocated to the Dexpramipexole group and another 2 being allocated to the Placebo group. The trial was closed to recruitment following the withdrawal of the support of the pharmaceutical industry partner for trial purposes. No participants attended the last dispensing visit at 365 days follow-up, however, 4 (80%) participants attended the Safety Follow-up visit.

Due to the premature closure and the small numbers randomised the SAP was amended to reflect the fact only mostly descriptive statistics or listings could be presented. It was not possible to conduct any powered statistical hypothesis testing/modelling, as originally planned in the protocol, due to a lack of data.

The primary analysis of the primary and secondary outcomes was conducted using the Intention-to-treat (ITT) population on a complete case basis.

The populations defined for statistical analyses are as follows:

ITT population: includes all participants who were randomised into the Trial. Participants were analysed based on the treatment to which they were randomly allocated, regardless of the treatment received or any protocol deviations.

Per-Protocol: includes all participants who were randomised into the Trial, except for those that have a major protocol deviation.

Safety population: includes all participants who had treatment administered. Participants were considered to be in the treatment arm corresponding to the intervention they received the majority of the time, regardless of their randomised allocation.

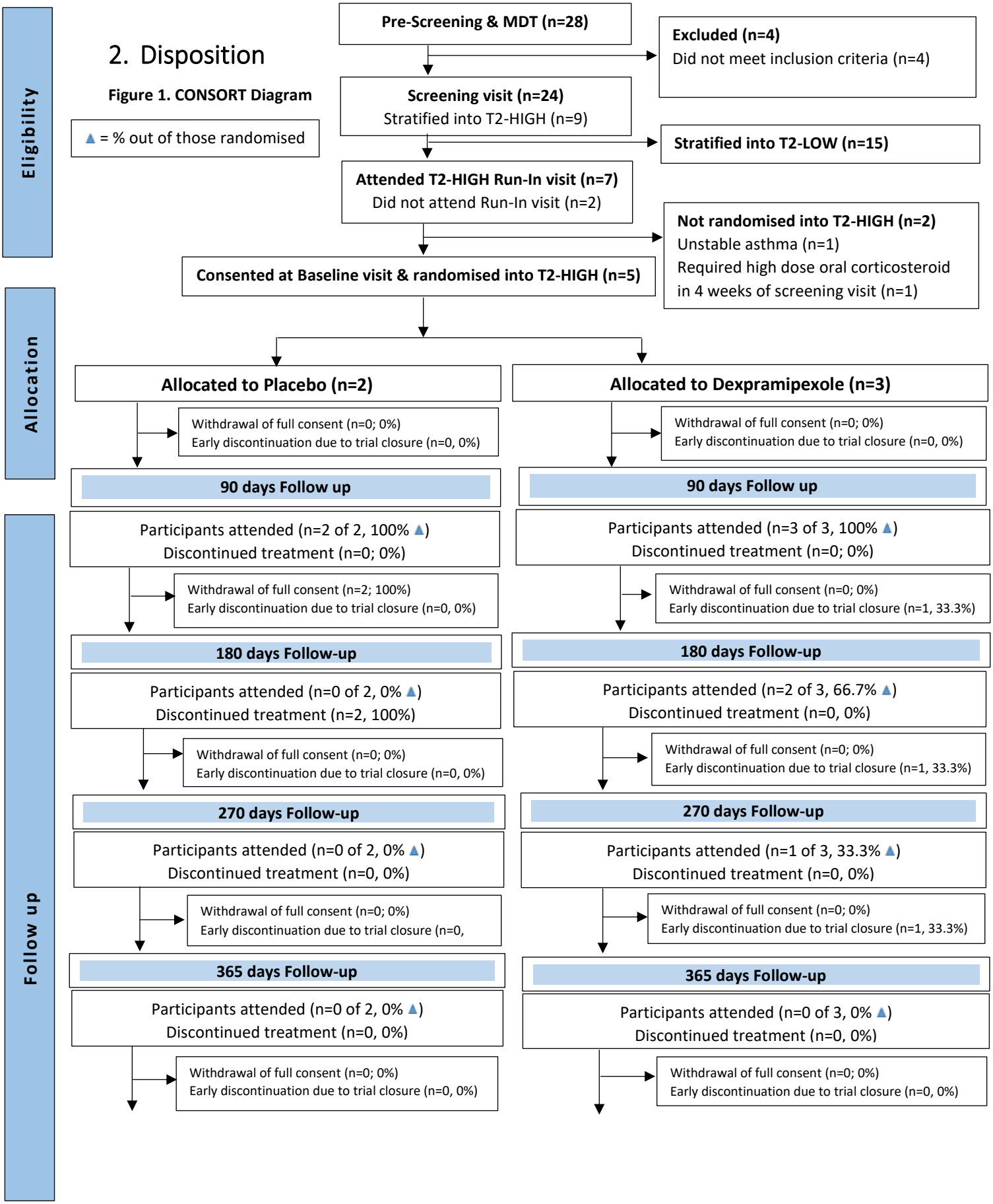
Deviations from the SAP

- The planned descriptive statistics of the Mechanistic Outcomes were not calculated due to the lack of both sputum and nasal swabs/nasosorption data.
- The planned correlations between the Exploratory Outcomes were not calculated as no nasal swabs, nasosorption or sputum data were analysed.

2. Disposition

Figure 1. CONSORT Diagram

▲ = % out of those randomised



Safety Follow-up	Safety Follow-up
Participants attended (n=1 of 2, 50% ▲)	Participants attended (n=3 of 3, 100% ▲)
Analyses of the Primary Outcome Participants included in the Primary (ITT) analysis (n=2) Participants included in the Per Protocol analysis (n=2) Participants included in the Safety analysis (n=2)	**Analyses of the Primary Outcome** Participants included in the Primary (ITT) analysis (n=3) Participants included in the Per Protocol analysis (n=3) Participants included in the Safety analysis (n=3)

Please note the following:

- Pre-Screening & MDT figures and reasons for exclusion were obtained from the Screening Logs provided by sites to the LCTU.
- Run-In visit, reasons for non-attendance (n=2): one of the individuals failed the screening while the other was found not eligible. The latter was obtained from the Screening Logs provided by sites to the LCTU.
- Discontinuation of treatment: figures reported correspond to participants who discontinued their allocated treatment in the period prior to the visit (i.e. between previous and indicated visit).
- Safety Follow-up visits were required to ensure the participants' safety. Participants may have attended their Safety Follow-up visit after withdrawing their full consent.

Recruitment

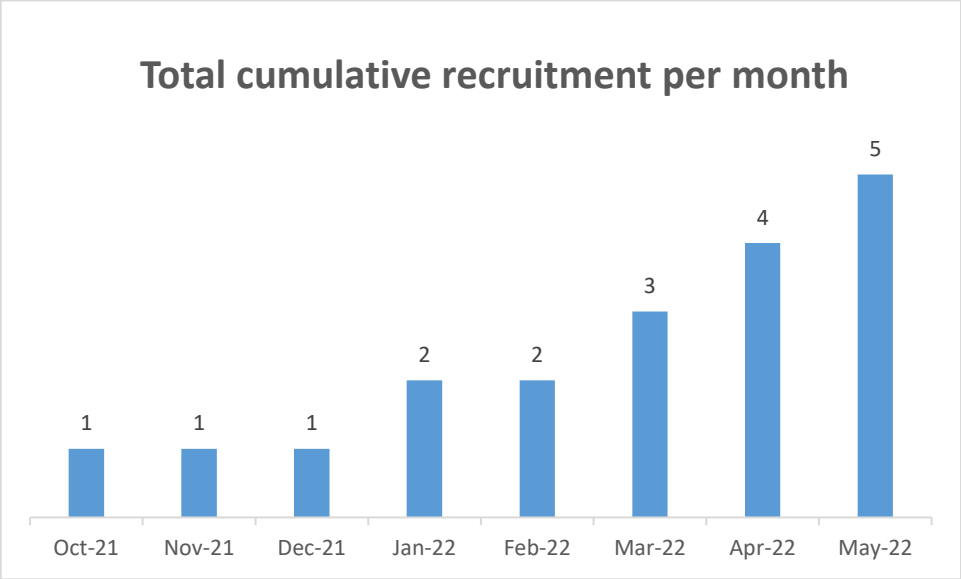


Table 1. T2-HIGH Recruitment Figures per Site

Site	Participants recruited into T2-HIGH Treatment Cohort
Leicester	3
Nottingham	2
Total	5

Table 2. Disposition of participants and withdrawals

		Placebo n=2	Dexpramipexole n=3	Total n=5
At Baseline	Provided consent, n(%)	2 (100%)	3 (100%)	5 (100%)
	Entered trial and provided data, n(%)	2 (100%)	3 (100%)	5 (100%)
At 90 days follow-up	Attended and provided data, n(%)	2 (100%)	3 (100%)	5 (100%)
At 180 days follow-up	Attended and provided data, n(%)	0 (0%)	2 (66.7%)	2 (40%)
At 270 days follow-up	Attended and provided data, n(%)	0 (0%)	1 (33.3%)	1 (20%)
At 365 days follow-up	Attended and provided data, n(%)	0 (0%)	0 (0%)	0 (0%)
Safety Follow-up	Attended and provided data, n(%)	1 (50%)	3 (100%)	4 (80%)
Discontinued treatment early, n(%)		2 (100%)	0 (0%)	2 (40%)
Ceased all physical participation but did not withdraw full consent, n(%)		0 (0%)	0 (0%)	0 (0%)
Withdrew full consent from the trial, n(%)		2 (100%)	0 (0%)	2 (40%)
Early discontinuation due to Trial's early closure, n(%)		0 (0%)	3 (100%)	3 (60%)

NB: Figures for provision of data account for participants who completed and provided any data at each individual time point. Please note that participants randomised into the trial had the option to withdraw their consent for one or more than one trial activity at the same time or at a different time point. Participants who withdrew full consent may have also ceased all physical participation.

3 Demographics and Screening data Summary

A total of 38 eligible individuals attended the Screening visit and consented to have their blood analysed for stratification with a view to participating in either the T2-LOW or T2-HIGH treatment cohorts. Of these individuals, 29 had their severe asthma subtype classed as T2-LOW and 9 as T2-HIGH. Data corresponding to all participants screened is reported in this section of the report.

Table 3. Demographics and Screening data summary

		Total (n=38)
Demographics		
Age (years)	N	38
	Mean (SD)	52.3 (11.2)
	Median (IQR)	52 (46, 62)
	Min, Max	28, 76
Sex	Male, n(%)	10 (26.3%)
	Female, n(%)	28 (73.7%)
Ethnicity	White, n(%)	36 (94.7%)
	Asian/Asian British, n(%)	1 (2.6%)
	Black/African/Caribbean/Black British, n(%)	1 (2.6%)
	Mixed/Multiple Ethnic Groups, n(%)	0 (0%)
	Other Ethnic Group, n(%)	0 (0%)
Asthma History		
Asthma confirmed by one or more of the following objective criteria ***(recorded within a 10 year period of screening)***		
A positive treatment trial to an inhaled steroids recorded by the treating clinician or GP (defined as 200ml improvement in FEV1 and 12% in FEV1 following initiation with inhaled steroids), n(%)		6 (15.8%)
i) Peak flow variation of ≥20% over a two-week period, n(%)		11 (28.9%)
ii) A methacholine or histamine PC20 of ≤8mg/ml, mannitol PD15 achieved after <635mg of cumulative dosing, n(%)		4 (10.5%)
iii) Bronchodilator reversibility of at least 200mls (FEV1) and 12% following the administration of 400mcg of Salbutamol or an equivalent bronchodilator, n(%)		14 (36.8%)
iv) Variability of FEV1 of ≥200ml and 12% between stable asthma spirometry records over a two-year period prior to screening, n(%)		9 (23.7%)
A positive response to an oral steroid trial defined as an improvement in lung function of at least 200mls and 12% (FEV1) after treatment with systemic steroids at any dose over a period of ≥10 days, n(%)		4 (10.5%)
Participant's GINA treatment intensity category:		
	Step 3, n(%)	0 (0%)
	Step 4, n(%)	11 (28.9%)
	Step 5, n(%)	26 (68.4%)
	Missing, n(%)	1 (2.6%)
Has the participant had a severe asthma diagnosis confirmed by the MDT or non-English equivalent trial team?		
	Yes, n(%)	37 (97.4%)

	Total (n=38)
MDT or non-English equivalent trial team confirmed adherence to current asthma therapies using one or more of the following criteria:	
Prescription refill records (≥75% adherence to ICS, ICS/LABA therapy) within 365 days of screening, n(%)	34 (89.5%)
BOTH recordable serum prednisolone and supressed cortisol levels (as determined at the discretion of the Investigator) in patients taking regular systemic corticosteroids. We will capture whether local tests evaluating serum prednisolone and cortisol levels are performed via High Performance Liquid Chromatography (HPLC) or non-HPLC, n(%)	1 (2.6%)
Testing method used:	
HPLC, n(%)	1 (2.6%)
Non-HPLC, n(%)	0 (0%)
A FeNO of <45ppb at screening or a negative FeNO suppression testing in selected patients (FeNO ≥45ppb). FeNO suppression testing can be delivered according to local service level arrangements, including INCA based monitoring, other SMART devices or directly observed inhaler therapy, n(%)	16 (42.1%)
Does the participant have a family history of asthma?	
Yes, n(%)	30 (78.9%)
Have there been any deaths in the family due to asthma?	
Yes, n(%)	1 (2.6%)
Does the participant have an asthma action plan?	
Yes, n(%)	30 (78.9%)
Does the participant have any of the following:	
Allergies (to common seasonal or perennial allergens (confirmed by either skin prick test or immunocap testing/equivalent within 10 years of screening), n(%)	14 (36.8%)
Triggers: Participant reported triggers for asthma exacerbations e.g. aspirin/NSAIDS, grass pollen, dust exposure, etc., n(%)	37 (97.4%)
Polyps: Nasal polyps confirmed by visual nasal examination, nasendoscopy or CT sinus imaging, n(%)	4 (10.5%)
Has the participant had any previous nasal polyp resection surgery?	
Yes, n(%)	3 (7.9%)
Aspirin/NSAID sensitivity	
Yes, n(%)	10 (26.3%)
In the 365 days prior to screening, has the participant:	
Had courses of oral steroids?	
Yes, n(%)	37 (97.4%)
Had any unscheduled visits to their GP/A&E due to airways disease?	
Yes, n(%)	25 (65.8%)
Had any ITU admissions due to airways disease?	
Yes, n(%)	2 (5.3%)

		Total (n=38)
Has the participant received treatment with a biologic (s) within 4 months prior to screening?		
	No, n(%)	38 (100%)
Has the participant received/completed bronchial thermoplasty treatment within 180 days of screening?		
	No, n(%)	38 (100%)
Is the participant currently receiving long term treatment (≥90 days) with macrolides for asthma?		
	No, n(%)	38 (100%)
Smoking History		
Has the participant ever smoked (including e-cigarettes)?		
	Yes, n(%)	12 (31.6%)
How many years did the participant smoke for (including e-cigarettes)?		
	N	12
	Mean (SD)	8.7 (6.7)
	Median (IQR)	6 (3.5, 14)
	Min, Max	1, 22
How many cigarettes did the participant smoke per day?		
	N	12
	Mean (SD)	10 (5.8)
	Median (IQR)	10 (7.5, 11)
	Min, Max	1, 20
Number of pack-years previously smoked		
	N	12
	Mean (SD)	5.1 (4.4)
	Median (IQR)	3.5 (1.5, 8)
	Min, Max	0, 14
Highest Blood Eosinophil Level (if known, in the year prior to screening)		
Blood eosinophil result ($x10^9$ L cells)		
	N	32
	Mean (SD)	0.2 (0.2)
	Median (IQR)	0.1 (0.1, 0.3)
	Min, Max	0.0, 0.9
Medical History		
COPD, n(%)		0 (0%)
Atopic dermatitis, n(%)		4 (10.5%)
Bronchiectasis (reported by CT imaging), n(%)		5 (13.2%)
Allergic Bronchopulmonary Aspergillosis (ABPA), n(%)		1 (2.6%)
Urticaria (e.g. Idiopathic, autoimmune), n(%)		2 (5.3%)
Previous anaphylaxis or angioedema, n(%)		4 (10.5%)
EpiPen usage, n(%)		3 (7.9%)

		Total (n=38)
Eosinophilic esophagitis, n(%)		0 (0%)
Seasonal or perennial rhinitis, n(%)		28 (73.7%)
	Seasonal rhinitis	19 (50%)
	Perennial rhinitis	9 (23.7%)
Immunodeficiency (CVID or specific antibody deficiency confirmed by immunology services, n(%)		0 (0%)
Ischaemic Heart disease, n(%)		2 (5.3%)
Previous Myocardial infarction, n(%)		0 (0%)
Previous Stroke (ischaemic or haemorrhagic), n(%)		0 (0%)
Diabetes, n(%)		4 (10.5%)
	Type 2	4 (10.5%)
Hypertension, n(%)		13 (34.2%)
Pulmonary hypertension, n(%)		0 (0%)
Epilepsy, n(%)		0 (0%)
High cholesterol, n(%)		9 (23.7%)
Chronic kidney disease, n(%)		0 (0%)
Liver Disease, n(%)		1 (2.6%)
Depression, n(%)		12 (31.6%)
Anxiety, n(%)		15 (39.5%)
GORD, n(%)		21 (55.3%)
Blindness/Glaucoma, n(%)		2 (5.3%)
Malignancy, n(%)		3 (7.9%)
Drug allergy, n(%)		18 (47.4%)
Other medical conditions, n(%)		29 (76.3%)
Total IgE (if assessment done, within the previous 365 days prior to Screening)		
Total IgE (kU/L)		
	N	19
	Mean (SD)	76.8 (182.3)
	Median (IQR)	30.0 (8.0, 55.0)
	Min, Max	2.0, 813.0

		Total (n=38)
COVID-19 Status		
Has the participant previously had COVID-19 based on a PCR test?		
	Yes, n(%)	18 (47.4%)
Has the participant received a COVID-19 vaccine?		
	Yes, n(%)	37 (97.4%)
Has the participant had (or will be receiving) a second dose of a COVID-19 vaccine?		
	Yes, n(%)	36 (94.7%)
Has the participant received any further COVID-19 'booster' vaccinations?		
	Yes, n(%)	34 (89.5%)
Has the participant been shielding due to COVID-19 at any point in the last 365 days?		
	Yes, n(%)	10 (26.3%)
If Yes, approximately, how many months has the participant been shielding for within the last 365 days?		
	N	10
	Mean (SD)	6.9 (4.6)
	Median (IQR)	6 (2, 12)
	Min, Max	2, 12
Blood Stratification Sample Result		
BEAT-SA Central Management Team confirmed Eosinophil level (x10^9 L cells)		
	N	38
	Mean (SD)	0.2 (0.2)
	Median (IQR)	0.1 (0.1, 0.3)
	Min, Max	0.0, 0.8
BEAT-SA Central Management Team confirmed severe asthma sub-type according to eosinophil level		
	T2-HIGH, n(%)	9 (23.7%)
	T2-LOW, n(%)	29 (76.3%)

4 Run-In data Summary of T2-HIGH Cohort

Of the 9 individuals whose severe asthma sub-type was confirmed as T2-HIGH at the Screening stage, 2 of them did not attend the Run-In visit. One of the individuals failed the screening while the other was found not eligible.

Table 4. Run-In data Summary

		Total (n=7)
Participant Information Sheet		
Has the participant been provided with the relevant Stage 2 Participant Information Sheet? V4.0, Date 18/01/2021		
	Yes, n(%)	7 (100%)
Stable Disease Assessment		
Is the participant currently exacerbating?		
	Yes, n(%)	0 (0%)
Asthma Action Plan Review		
Has the participant's asthma action plan been clinically reviewed by a trained practitioner?		
	Yes, n(%)	7 (100%)
Is the Research Nurse/treating Clinician satisfied that the participant understands how to identify, manage and report exacerbations?		
	Yes, n(%)	7 (100%)
ICS, ICS/LABA Assessment		
Has the participant's maintenance ICS, ICS/LABA technique been clinically reassessed by a trained practitioner/trial team?		
	Yes, n(%)	7 (100%)
Has the participant's ICS, ICS/LABA technique been clinically confirmed as adequate by a trained practitioner/trial team?		
	Yes, n(%)	7 (100%)
Micro Diary		
The participant has been trained in how to use the micro diary		
	Yes, n(%)	7 (100%)
The participant has been provided with the micro diary questions and user guide		
	Yes, n(%)	7 (100%)

5 Baseline data Summary of T2-HIGH Cohort

Table 5. Baseline data Summary

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Vital Signs				
Height, cm	N	2	3	5
	Mean (SD)	163.5 (3.5)	167.3 (7.8)	165.8 (6.1)
	Median (IQR)	163.5 (161.0, 166.0)	165.0 (161.0, 176.0)	165.0 (161.0, 166.0)
	Min, Max	161.0, 166.0	161.0, 176.0	161.0, 176.0
Weight, kg	N	2	3	5
	Mean (SD)	94.9 (8.3)	73.7 (14.2)	82.2 (15.9)
	Median (IQR)	94.9 (89.0, 100.8)	70.3 (61.5, 89.2)	89.0 (70.3, 89.2)
	Min, Max	89.0, 100.8	61.5, 89.2	61.5, 100.8
BMI, kg/m^2	N	2	3	5
	Mean (SD)	35.5 (4.6)	26.4 (5.6)	30.1 (6.8)
	Median (IQR)	35.5 (32.3, 38.8)	23.7 (22.7, 32.8)	32.3 (23.7, 32.8)
	Min, Max	32.3, 38.8	22.7, 32.8	22.7, 38.8
Respiratory Rate, breaths/min	N	2	3	5
	Mean (SD)	19.0 (1.4)	18.3 (3.2)	18.6 (2.4)
	Median (IQR)	19.0 (18.0, 20.0)	17.0 (16.0, 22.0)	18.0 (17.0, 20.0)
	Min, Max	18.0, 20.0	16.0, 22.0	16.0, 22.0
Oxygen Saturation, %	N	2	3	5
	Mean (SD)	96.0 (0.0)	97.0 (2.6)	96.6 (1.9)
	Median (IQR)	96.0 (96.0, 96.0)	98.0 (94.0, 99.0)	96.0 (96.0, 98.0)
	Min, Max	96.0, 96.0	94.0, 99.0	94.0, 99.0
Systolic BP, mmHg	N	2	3	5
	Mean (SD)	129.0 (5.7)	134.7 (4.0)	132.4 (5.1)
	Median (IQR)	129.0 (125.0, 133.0)	137.0 (130.0, 137.0)	133.0 (130.0, 137.0)
	Min, Max	125.0, 133.0	130.0, 137.0	125.0, 137.0
Diastolic BP, mmHg	N	2	3	5
	Mean (SD)	88.0 (1.4)	86.0 (2.6)	86.8 (2.3)
	Median (IQR)	88.0 (87.0, 89.0)	87.0 (83.0, 88.0)	87.0 (87.0, 88.0)
	Min, Max	87.0, 89.0	83.0, 88.0	83.0, 89.0
Heart Rate, beats/min	N	2	3	5
	Mean (SD)	78.5 (3.5)	77.7 (13.7)	78.0 (9.8)
	Median (IQR)	78.5 (76.0, 81.0)	84.0 (62.0, 87.0)	81.0 (76.0, 84.0)
	Min, Max	76.0, 81.0	62.0, 87.0	62.0, 87.0

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Temperature, ^{0}C	N	2	3	5
	Mean (SD)	37.2 (0.6)	36.9 (0.2)	37.0 (0.4)
	Median (IQR)	37.2 (36.8, 37.7)	36.8 (36.7, 37.1)	36.8 (36.8, 37.1)
	Min, Max	36.8, 37.7	36.7, 37.1	36.7, 37.7
COVID-19				
Has the participant received a positive PCR COVID-19 test result since their previous visit?				
	No, n(%)	2 (100%)	3 (100%)	5 (100%)
Exacerbation History (since the previous Run-In visit)				
Treatment duration, days	N	1 [a]	0	1
	Mean (SD)	5.0 (.)	-	5.0 (.)
	Median (IQR)	5.0 (5.0, 5.0)	-	5.0 (5.0, 5.0)
	Min, Max	5.0, 5.0	-	5.0, 5.0
Treatment	Antibiotics, n(%)	1 (50%)	0 (0%)	1 (20%)
	Steroids, n(%)	1 (50%)	0 (0%)	1 (20%)
	Antibiotics and Steroids, n(%)	1 (100%)	-	1 (100%)
Dose, mg of prednisolone	N	1	0	1
	Mean (SD)	40.0 (.)	-	40.0 (.)
	Median (IQR)	40.0 (40.0, 40.0)	-	40.0 (40.0, 40.0)
	Min, Max	40.0, 40.0	-	40.0, 40.0
Admission	Hospital, n(%)	0 (0%)	-	0 (0%)
	Emergency Department, n(%)	0 (0%)	-	0 (0%)
	Hospital and Emergency Department, n(%)	-	-	-
Confirmation of Severe Asthma				
	Patient Confirmed, n(%)	1 (100%)	-	1 (100%)
	Patient confirmed and verified, n(%)	0 (0%)	-	0 (0%)
Physical Examination				
General appearance	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
	Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
	Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
	Clinically significant (if abnormal), n(%)	-	-	-
Skin	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
	Normal, n(%)	2 (100%)	2 (66.7%)	4 (80%)
	Abnormal, n(%)	0 (0%)	1 (33.3%)	1 (20%)
	Clinically significant (if abnormal), n(%)	-	0 (0%)	0 (0%)
Head (eyes, ears, nose, mouth and throat)	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
	Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
	Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
	Clinically significant (if abnormal), n(%)	-	-	-

[a] Only one participant reported 1 exacerbation at the Baseline visit

			Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Lymph nodes		Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
		Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
		Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Clinically significant (if abnormal), n(%)	-	-	-
Musculoskeletal		Not done, n(%)	0 (0%)	1 (33.3%)	1 (20%)
		Normal, n(%)	1 (50%)	2 (66.7%)	3 (60%)
		Abnormal, n(%)	1 (50%)	0 (0%)	1 (20%)
		Clinically significant (if abnormal), n(%)	0 (0%)	-	0 (0%)
Cardiovascular		Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
		Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
		Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Clinically significant (if abnormal), n(%)	-	-	-
Respiratory		Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
		Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
		Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Clinically significant (if abnormal), n(%)	-	-	-
Gastrointestinal		Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
		Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
		Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Clinically significant (if abnormal), n(%)	-	-	-
Neurological		Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
		Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
		Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Clinically significant (if abnormal), n(%)	-	-	-
Other		Not done, n(%)	1 (50%)	1 (33.3%)	2 (40%)
		Normal, n(%)	0 (0%)	0 (0%)	0 (0%)
		Abnormal, n(%)	0 (0%)	1 (33.3%)	1 (20%)
		Not applicable, n(%)	1 (50%)	1 (33.3%)	2 (40%)
		Clinically significant (if abnormal), n(%)	-	0 (0%)	0 (0%)
FeNO					
Assessment performed?	Yes, n(%)		2 (100%)	3 (100%)	5 (100%)
Result 1, ppb		N	2	3	5
		Mean (SD)	45.5 (0.7)	52.0 (40.8)	49.4 (29.1)
		Median (IQR)	45.5 (45.0, 46.0)	38.0 (20.0, 98.0)	45.0 (38.0, 46.0)
		Min, Max	45.0, 46.0	20.0, 98.0	20.0, 98.0
Result 2, ppb		N	2	3	5
		Mean (SD)	46.0 (1.4)	49.3 (41.6)	48.0 (29.5)
		Median (IQR)	46.0 (45.0, 47.0)	31.0 (20.0, 97.0)	45.0 (31.0, 47.0)
		Min, Max	45.0, 47.0	20.0, 97.0	20.0, 97.0

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Average Result (only recorded if participant was unable to produce two measurements within 10%) (ppb)	N	0	1	1
	Mean (SD)	-	34.0 (.)	34.0 (.)
	Median (IQR)	-	34.0 (34.0, 34.0)	34.0 (34.0, 34.0)
	Min, Max	-	34.0, 34.0	34.0, 34.0
Number of duplicate measurements not within 10% of one another	N	1	1	2
	Mean (SD)	0.0 (.)	2.0 (.)	1.0 (1.4)
	Median (IQR)	0.0 (0.0, 0.0)	2.0 (2.0, 2.0)	1.0 (0.0, 2.0)
	Min, Max	0.0, 0.0	2.0, 2.0	0.0, 2.0
Best Post-Bronchodilator Spirometry (if assessment done)				
FEV_1, L	N	2	3	5
	Mean (SD)	1.8 (0.7)	2.2 (1.1)	2.0 (0.9)
	Median (IQR)	1.8 (1.3, 2.3)	1.8 (1.4, 3.5)	1.8 (1.4, 2.3)
	Min, Max	1.3, 2.3	1.4, 3.5	1.3, 3.5
% Predicted FEV_1	N	2	3	5
	Mean (SD)	69.0 (24.0)	73.7 (18.6)	71.8 (18.0)
	Median (IQR)	69.0 (52.0, 86.0)	65.0 (61.0, 95.0)	65.0 (61.0, 86.0)
	Min, Max	52.0, 86.0	61.0, 95.0	52.0, 95.0
FVC, L	N	2	3	5
	Mean (SD)	2.5 (1.1)	3.7 (1.1)	3.2 (1.1)
	Median (IQR)	2.5 (1.8, 3.3)	3.7 (2.5, 4.7)	3.3 (2.5, 3.7)
	Min, Max	1.8, 3.3	2.5, 4.7	1.8, 4.7
% Predicted FVC	N	2	3	5
	Mean (SD)	82.0 (35.4)	102.7 (9.7)	94.4 (22.1)
	Median (IQR)	82.0 (57.0, 107.0)	105.0 (92.0, 111.0)	105.0 (92.0, 107.0)
	Min, Max	57.0, 107.0	92.0, 111.0	57.0, 111.0
PEF, L/min	N	2	3	5
	Mean (SD)	368.5 (136.5)	388.3 (245.9)	380.4 (187.1)
	Median (IQR)	368.5 (272.0, 465.0)	291.0 (206.0, 668.0)	291.0 (272.0, 465.0)
	Min, Max	272.0, 465.0	206.0, 668.0	206.0, 668.0
% Predicted PEF	N	2	3	5
	Mean (SD)	96.5 (33.2)	85.3 (36.1)	89.8 (31.1)
	Median (IQR)	96.5 (73.0, 120.0)	73.0 (57.0, 126.0)	73.0 (73.0, 120.0)
	Min, Max	73.0, 120.0	57.0, 126.0	57.0, 126.0
% FEV_1/FVC	N	2	3	5
	Mean (SD)	74.0 (7.1)	58.7 (13.2)	64.8 (13.0)
	Median (IQR)	74.0 (69.0, 79.0)	56.0 (47.0, 73.0)	69.0 (56.0, 73.0)
	Min, Max	69.0, 79.0	47.0, 73.0	47.0, 79.0

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
% Predicted FEV_1/FVC	N	2	3	5
	Mean (SD)	89.0 (2.8)	75.3 (17.6)	80.8 (14.6)
	Median (IQR)	89.0 (87.0, 91.0)	73.0 (59.0, 94.0)	87.0 (73.0, 91.0)
	Min, Max	87.0, 91.0	59.0, 94.0	59.0, 94.0
Bronchodilator Reversibility FEV_1, %	N	1	0	1
	Mean (SD)	10.2 (.)	-	10.2 (.)
	Median (IQR)	10.2 (10.2, 10.2)	-	10.2 (10.2, 10.2)
	Min, Max	10.2, 10.2	-	10.2, 10.2
	Not available, N	1	2	3
	Missing, N	0	1	1
Bronchodilator Reversibility FEV_1, mls	N	1	0	1
	Mean (SD)	120.0 (.)	-	120.0 (.)
	Median (IQR)	120.0 (120.0, 120.0)	-	120.0 (120.0, 120.0)
	Min, Max	120.0, 120.0	-	120.0, 120.0
	Not available, N	1	2	3
	Missing, N	0	1	1
Sputum Induction				
Sputum induction performed?	Yes, n(%)	1 (50%)	0 (0%)	1 (20%)
Sputum production spontaneous (S) or induced (I)?				
	Spontaneous, n(%)	1 (100%)	-	1 (100%)
	Induced, n(%)	0 (0%)	-	0 (0%)
Sample collected?	Yes, n(%)	1 (50%)	-	1 (20%)
Sample taken for differential cell count?	Yes,			
	Yes, n(%)	1 (50%)	-	1 (20%)
Sample taken for qPCR?	Yes, n(%)	1 (50%)	-	1 (20%)
Sample taken for routine NHS microbiological culture?				
	No, n(%)	1 (50%)	-	1 (20%)
Biochemistry				
Sodium (mmol/L)	N	2	3	5
	Mean (SD)	139.0 (4.2)	140.7 (1.2)	140.0 (2.4)
	Median (IQR)	139.0 (136.0, 142.0)	140.0 (140.0, 142.0)	140.0 (140.0, 142.0)
	Min, Max	136.0, 142.0	140.0, 142.0	136.0, 142.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Potassium (mmol/L)	N	2	3	5
	Mean (SD)	4.3 (0.1)	4.2 (0.3)	4.2 (0.2)
	Median (IQR)	4.3 (4.2, 4.4)	4.3 (3.9, 4.4)	4.3 (4.2, 4.4)
	Min, Max	4.2, 4.4	3.9, 4.4	3.9, 4.4
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Urea (mmol/L)	N	2	3	5
	Mean (SD)	4.3 (0.2)	5.2 (1.3)	4.9 (1.1)
	Median (IQR)	4.3 (4.2, 4.5)	5.9 (3.7, 6.1)	4.5 (4.2, 5.9)
	Min, Max	4.2, 4.5	3.7, 6.1	3.7, 6.1
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Creatinine (mmol/L)	N	2	3	5
	Mean (SD)	61.0 (12.7)	77.0 (19.9)	70.6 (17.8)
	Median (IQR)	61.0 (52.0, 70.0)	66.0 (65.0, 100.0)	66.0 (65.0, 70.0)
	Min, Max	52.0, 70.0	65.0, 100.0	52.0, 100.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
eGFR (mL/min)	N	2	3	5
	Mean (SD)	86.5 (4.9)	83.7 (7.8)	84.8 (6.2)
	Median (IQR)	86.5 (83.0, 90.0)	86.0 (75.0, 90.0)	86.0 (83.0, 90.0)
	Min, Max	83.0, 90.0	75.0, 90.0	75.0, 90.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
C-Reactive Protein (mg/L)	N	2	3	5
	Mean (SD)	5.5 (4.9)	4.0 (1.7)	4.6 (2.9)
	Median (IQR)	5.5 (2.0, 9.0)	5.0 (2.0, 5.0)	5.0 (2.0, 5.0)
	Min, Max	2.0, 9.0	2.0, 5.0	2.0, 9.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Alanine Transaminase (U/L)	N	2	3	5
	Mean (SD)	27.5 (2.1)	21.3 (9.7)	23.8 (7.7)
	Median (IQR)	27.5 (26.0, 29.0)	19.0 (13.0, 32.0)	26.0 (19.0, 29.0)
	Min, Max	26.0, 29.0	13.0, 32.0	13.0, 32.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Total Bilirubin (µmol/L)	N	2	3	5
	Mean (SD)	17.5 (17.7)	7.7 (1.5)	11.6 (10.4)
	Median (IQR)	17.5 (5.0, 30.0)	8.0 (6.0, 9.0)	8.0 (6.0, 9.0)
	Min, Max	5.0, 30.0	6.0, 9.0	5.0, 30.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Albumin (g/L)	N	2	3	5
	Mean (SD)	41.0 (2.8)	44.0 (4.0)	42.8 (3.6)
	Median (IQR)	41.0 (39.0, 43.0)	44.0 (40.0, 48.0)	43.0 (40.0, 44.0)
	Min, Max	39.0, 43.0	40.0, 48.0	39.0, 48.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Adjusted Calcium (mmol/L)	N	2	3	5
	Mean (SD)	2.3 (0.0)	2.3 (0.0)	2.3 (0.0)
	Median (IQR)	2.3 (2.3, 2.4)	2.3 (2.3, 2.3)	2.3 (2.3, 2.3)
	Min, Max	2.3, 2.4	2.3, 2.3	2.3, 2.4
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Inorganic Phosphate [a] (mmol/L)	N	2	2	4
	Mean (SD)	1.10 (0.14)	1.19 (0.02)	1.14 (0.10)
	Median (IQR)	1.10 (1.00, 1.20)	1.19 (1.17, 1.20)	1.19 (1.08, 1.20)
	Min, Max	1.00, 1.20	1.17, 1.20	1.00, 1.20
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
	Unverified, N	0	1	1
Alkaline Phosphatase (lμ/L)	N	2	3	5
	Mean (SD)	69.5 (17.7)	80.0 (7.2)	75.8 (11.7)
	Median (IQR)	69.5 (57.0, 82.0)	82.0 (72.0, 86.0)	82.0 (72.0, 82.0)
	Min, Max	57.0, 82.0	72.0, 86.0	57.0, 86.0
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Cholesterol (mmol/L)	N	2	3	5
	Mean (SD)	4.1 (0.1)	5.1 (0.7)	4.7 (0.7)
	Median (IQR)	4.1 (4.1, 4.2)	5.1 (4.5, 5.8)	4.5 (4.2, 5.1)
	Min, Max	4.1, 4.2	4.5, 5.8	4.1, 5.8
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Triglycerides (mmol/L)	N	2	3	5
	Mean (SD)	2.2 (1.9)	1.3 (1.0)	1.6 (1.3)
	Median (IQR)	2.2 (0.9, 3.5)	0.7 (0.7, 2.4)	0.9 (0.7, 2.4)
	Min, Max	0.9, 3.5	0.7, 2.4	0.7, 3.5
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
HDL Cholesterol (mmol/L)	N	2	3	5
	Mean (SD)	1.4 (0.7)	1.7 (0.2)	1.6 (0.4)
	Median (IQR)	1.4 (0.9, 1.9)	1.7 (1.5, 1.8)	1.7 (1.5, 1.8)
	Min, Max	0.9, 1.9	1.5, 1.8	0.9, 1.9
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
Total Cholesterol: HDL Ratio (mmol/L)	N	2	3	5
	Mean (SD)	3.4 (1.7)	3.1 (0.1)	3.2 (0.9)
	Median (IQR)	3.4 (2.2, 4.6)	3.0 (3.0, 3.2)	3.0 (3.0, 3.2)
	Min, Max	2.2, 4.6	3.0, 3.2	2.2, 4.6
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)
LDL Cholesterol (mmol/L)	N	2	3	5
	Mean (SD)	1.8 (0.2)	2.9 (0.7)	2.4 (0.8)
	Median (IQR)	1.8 (1.6, 1.9)	2.7 (2.3, 3.7)	2.3 (1.9, 2.7)
	Min, Max	1.6, 1.9	2.3, 3.7	1.6, 3.7
	Not done, n(%)	0 (0%)	0 (0%)	0 (0%)

[a] Inorganic Phosphate data reported in this section was provided by sites in an Excel document as data captured in the MACRO database was not measured in mmol/L

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
Related Case Report				
Has the participant experienced any adverse events or serious adverse events since their last visit?				
	Yes, n(%)	1 (50%)	1 (33%)	2 (40%)
Has the participant reported any changes/additions/cessations in concomitant medications?				
	Yes, n(%)	1 (50%)	1 (33%)	2 (40%)
Informed Consent for Samples				
Has the participant provided their informed consent to allow their samples to be used for ethically approved research?				
	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Micro Diary				
Is the participant using a Micro Diary during the trial?				
	Yes, n(%)	2 (100%)	2 (66.7%)	4 (80%)
Participant declined to use the Micro Diary during the trial, it was due to:				
	High technical demand/load, n(%)	-	0 (0%)	0 (0%)
	High level of inconvenience to recording data, n(%)	-	0 (0%)	0 (0%)
	Did not want to undertake the Micro Diary component, n(%)	-	0 (0%)	0 (0%)
	Manual dexterity, n(%)	0 (0%)	1 (33.3%)	1 (20%)
	Other, n(%)	-	0 (0%)	0 (0%)
If the participant is not using the Micro Diary, have they have been provided with paper copies of the BEAT-SA Participant Asthma Diary and a PEF meter?				
	Yes, n(%)	0 (0%)	1 (33.3%)	1 (20%)
FEV_1 via Micro Diary (if used)				
FEV1	Not done, n(%)	1 (50%)	3 (100%)	4 (80%)
FEV_1 (L)	N	1	0	1
	Mean (SD)	1.3 (.)	-	1.3 (.)
	Median (IQR)	1.3 (1.3, 1.3)	-	1.3 (1.3, 1.3)
	Min, Max	1.3, 1.3	-	1.3, 1.3
FEV_1 (L)	N	1	0	1
	Mean (SD)	1.2 (.)	-	1.2 (.)
	Median (IQR)	1.2 (1.2, 1.2)	-	1.2 (1.2, 1.2)
	Min, Max	1.2, 1.2	-	1.2, 1.2
FEV_1 (L)	N	1	0	1
	Mean (SD)	1.0 (.)	-	1.0 (.)
	Median (IQR)	1.0 (1.0, 1.0)	-	1.0 (1.0, 1.0)
	Min, Max	1.0, 1.0	-	1.0, 1.0
Pregnancy Test (Urine) – WOCBP Only				
Pregnancy test performed	No, n(%)	2 (100%)	2 (100%)	4 (100%)
Result	Negative, n(%)	-	-	-
	Positive, n(%)	-	-	-

		Placebo (n=2)	Dexpramipexole (n=3)	Total (n=5)
12-Lead ECG				
12-Lead ECG performed?	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Rhythm	Normal, n(%)	2 (100%)	3 (100%)	5 (100%)
	Abnormal, n(%)	0 (0%)	0 (0%)	0 (0%)
Heart Rate (beats/min)	N	2	3	5
	Mean (SD)	69.0 (1.4)	72.0 (7.9)	70.8 (5.9)
	Median (IQR)	69.0 (68.0, 70.0)	75.0 (63.0, 78.0)	70.0 (68.0, 75.0)
	Min, Max	68.0, 70.0	63.0, 78.0	63.0, 78.0
PR Interval (seconds)	N	2	3	5
	Mean (SD)	0.2 (0.0)	0.2 (0.0)	0.2 (0.0)
	Median (IQR)	0.2 (0.2, 0.2)	0.2 (0.1, 0.2)	0.2 (0.2, 0.2)
	Min, Max	0.2, 0.2	0.1, 0.2	0.1, 0.2
QRS Complex Width (seconds)	N	2	3	5
	Mean (SD)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)
	Median (IQR)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
	Min, Max	0.1, 0.1	0.1, 0.1	0.1, 0.1
QT Interval (corrected) Friedericia's correction (QTcF) (milliseconds)	N	2	3	5
	Mean (SD)	416.0 (31.1)	404.0 (17.8)	408.8 (21.1)
	Median (IQR)	416.0 (394.0, 438.0)	410.0 (384.0, 418.0)	410.0 (394.0, 418.0)
	Min, Max	394.0, 438.0	384.0, 418.0	384.0, 438.0
12-Lead ECG reviewed by treating clinician?	Yes,			
	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Blood and Bio-banking samples taken				
Full Blood Count	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Plasma	Yes, n(%)	2 (100%)	2 (66.7%)	4 (80%)
Serum	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
DNA	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Urine	Yes, n(%)	2 (100%)	3 (100%)	5 (100%)
Nasosorption	Yes, n(%)	1 (50%)	2 (66.7%)	3 (60%)
Nasopharyngeal swab	Yes, n(%)	1 (50%)	2 (66.7%)	3 (60%)

6 Primary Analysis of the Primary Outcome – Annual Rate of Severe Exacerbations

A line listing including participant ID, treatment group and the primary outcome defined as the annual rate of severe exacerbations was produced using the Intention-to-treat population. The primary outcome was calculated as the sum of severe asthma exacerbations reported by each participant divided by the sum of follow-up time (measured in years). The number of severe exacerbations reported at visits 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14 (and 15 where visit 14 and/or others are missed due to early discontinuation) was calculated using the following variables from the Exacerbation History: date started, treatment duration (days), antibiotics treatment (yes), steroid treatment (yes), hospital admission (yes) or emergency department attendance (yes). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the listing below. The line listing presented below assumes that missing primary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised primary outcome data up until the last known point for each participant prior to 372 days.

Table 6. Listing of Primary Outcome data: Annual Rate of Severe Exacerbations

Participant ID	Treatment group	Total number of Severe Exacerbations	Follow-up time (years)	Annual Rate of Severe Exacerbations
T2H006-701	Dexpramipexole	0	1.018481	0
T2H006-703	Dexpramipexole	3	0.7446954	4.03
T2H006-704	Placebo	1	0.2683094	3.73
T2H008-702	Placebo	2	0.421629	4.74
T2H008-705	Dexpramipexole	0	0.495551	0

7 Primary Analysis of Secondary Outcomes

7.1 Time to first Severe Exacerbation

A line listing including participant ID, treatment group and the time to first severe exacerbation defined as the time (measured in days) from randomisation to the first severe asthma exacerbation was produced using the Intention-to-treat population. The date of randomisation as well as the date of the first severe exacerbation were used to calculate the time to event. The first severe exacerbation reported at 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 365 days follow-up or Safety Follow-up was derived using the following criteria: date started, date of treatment duration (days), antibiotics treatment (yes), steroid treatment (yes), hospital admission (yes) or emergency department attendance (yes). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the summary below. The line listing presented below assumes that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant prior to 372 days.

Table 7. Listing of Secondary Outcome data: Time to first Severe Exacerbation

Participant ID	Treatment group	Time to first Severe Exacerbation (days)
T2H006-701	Dexpramipexole	372 [a]
T2H006-703	Dexpramipexole	39
T2H006-704	Placebo	25
T2H008-702	Placebo	26
T2H008-705	Dexpramipexole	182 [a]

Censored ([a]): no severe exacerbations were reported for participant T2H008-705, therefore their time to first severe exacerbation was replaced with their follow-up time. Additionally, the time to first severe exacerbation of participant T2H006-001 was capped at 372 days as they did not report any severe exacerbations within the first 12 months.

7.2 Annual Rate of Severe Exacerbations defined as the use of systemic steroid only

A line listing including participant ID, treatment group and the annual rate of severe exacerbations was produced using the Intention-to-treat population. The secondary outcome was calculated as the sum of severe asthma exacerbations reported by each participant divided by the sum of follow-up time (measured in years). The number of severe exacerbations reported at 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 365 days follow-up or Safety Follow-up was calculated using the following variables from the Exacerbation History: date started, treatment duration (days), steroid treatment (yes) and antibiotic treatment (no). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the listing below. The line listing presented below assumes that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised primary outcome data up until the last known point for each participant prior to 372 days.

Table 8. Listing of Secondary Outcome data: Annual Rate of Severe Exacerbations | Systemic Steroid only

Participant ID	Treatment group	Total number of Severe Exacerbations	Follow-up time (years)	Annual Rate of Severe Exacerbations
T2H006-701	Dexpramipexole	1	1.018481	0.98
T2H006-703	Dexpramipexole	2	0.7446954	2.69
T2H006-704	Placebo	0	0.2683094	0
T2H008-702	Placebo	0	0.421629	0
T2H008-705	Dexpramipexole	0	0.495551	0

7.3 Annual Rate of Severe Exacerbations defined as the use of antibiotic only

A line listing including participant ID, treatment group and the annual rate of severe exacerbations was produced using the Intention-to-treat population. The secondary outcome was calculated as the sum of severe asthma exacerbations reported by each participant divided by the sum of follow-up time (measured in years). The number of severe exacerbations reported at 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 365 days follow-up or Safety Follow-up was calculated using the following variables from the Exacerbation History: date started, treatment duration (days), steroid treatment (no) and antibiotic treatment (yes). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the listing below. The line listing presented below assumes that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised primary outcome data up until the last known point for each participant prior to 372 days.

Table 9. Listing of Secondary Outcome data: Annual Rate of Severe Exacerbations | Antibiotic only

Participant ID	Treatment group	Total number of Severe Exacerbations	Follow-up time (years)	Annual Rate of Severe Exacerbations
T2H006-701	Dexpramipexole	0	1.018481	0
T2H006-703	Dexpramipexole	0	0.7446954	0
T2H006-704	Placebo	0	0.2683094	0
T2H008-702	Placebo	0	0.421629	0
T2H008-705	Dexpramipexole	0	0.495551	0

7.4 Annual Rate of Severe Exacerbations defined as the use of systemic steroid and antibiotic only

A line listing including participant ID, treatment group and the annual rate of severe exacerbations was produced using the Intention-to-treat population. The secondary outcome was calculated as the sum of severe asthma exacerbations reported by each participant divided by the sum of follow-up time (measured in years). The number of severe exacerbations reported at 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 365 days follow-up or Safety Follow-up was calculated using the following variables from the Exacerbation History: date started, treatment duration (days), steroid treatment (yes) and antibiotic treatment (yes). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the listing below. The line listing presented below assumes that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised primary outcome data up until the last known point for each participant prior to 372 days.

Table 10. Listing of Secondary Outcome data: Annual Rate of Severe Exacerbations | Systemic Steroid and Antibiotic only

Participant ID	Treatment group	Total number of Severe Exacerbations	Follow-up time (years)	Annual Rate of Severe Exacerbations
T2H006-701	Dexpramipexole	1	1.018481	0.98
T2H006-703	Dexpramipexole	1	0.7446954	1.34
T2H006-704	Placebo	1	0.2683094	3.73
T2H008-702	Placebo	2	0.421629	4.74
T2H008-705	Dexpramipexole	0	0.495551	0

7.5 Annual Rate of Severe Exacerbations defined as admission to Hospital or Emergency Department

A line listing including participant ID, treatment group and the annual rate of severe exacerbations was produced using the Intention-to-treat population. The secondary outcome was calculated as the sum of severe asthma exacerbations reported by each participant divided by the sum of follow-up time (measured in years). The number of severe exacerbations reported at 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 365 days follow-up or Safety Follow-up was calculated using the following variables from the Exacerbation History: date started, treatment duration (days), hospital admission (yes) or emergency department admission (yes). Data was capped at 372 days, if a severe exacerbation occurred after 372 days following randomisation it wasn't included in the listing below. The line listing presented below assumes that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised primary outcome data up until the last known point for each participant prior to 372 days.

Table 11. Listing of Secondary Outcome data: Annual Rate of Severe Exacerbations | Hospital or Emergency Department admission

Participant ID	Treatment group	Total number of Severe Exacerbations	Follow-up time (years)	Annual Rate of Severe Exacerbations
T2H006-701	Dexpramipexole	0	1.018481	0
T2H006-703	Dexpramipexole	1	0.7446954	1.34
T2H006-704	Placebo	1	0.2683094	3.73
T2H008-702	Placebo	0	0.421629	0
T2H008-705	Dexpramipexole	0	0.495551	0

7.6 Change in Juniper Asthma Control Questionnaire 6 – Interviewer Administered (ACQ 6-IA) Score from Baseline to 90, 180, 270 and 365 days follow-up

The ACQ 6-IA score at each individual time point was calculated as the mean of the 7 questions of the questionnaire, with each question being scored on a 7-point scale (0=no impairment, 6=maximum impairment) and the total ACQ 6-ia score ranging between 0 (totally controlled asthma) and 6 (severely uncontrolled asthma). Line listings including participant ID, treatment group and this secondary outcome defined as the change in ACQ 6-IA score from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the score recorded at each of the follow-up visits and the score reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 12. Listing of ACQ 6-IA score data

Participant ID	Treatment group	ACQ 6-IA score				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	1.8	1	0.8	0.2	-
T2H006-703	Dexpramipexole	2	1.3	0.7	-	-
T2H006-704	Placebo	2.7	1.7	-	-	-
T2H008-702	Placebo	5.5	5.2	-	-	-
T2H008-705	Dexpramipexole	3.4	1	-	-	-

Table 13. Listing of Secondary Outcome data: Change in ACQ 6-IA score from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in ACQ 6-IA score from Baseline to 90 days
T2H006-701	Dexpramipexole	-0.8
T2H006-703	Dexpramipexole	-0.7
T2H006-704	Placebo	-1
T2H008-702	Placebo	-0.3
T2H008-705	Dexpramipexole	-2.4

Table 14. Listing of Secondary Outcome data: Change in ACQ 6-IA score from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in ACQ 6-IA score from Baseline to 180 days
T2H006-701	Dexpramipexole	-1
T2H006-703	Dexpramipexole	-1.3
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 15. Listing of Secondary Outcome data: Change in ACQ 6-IA score from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in ACQ 6-IA score from Baseline to 270 days
T2H006-701	Dexpramipexole	-1.6
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 16. Listing of Secondary Outcome data: Change in ACQ 6-IA score from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in ACQ 6-IA score from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.7 Change in Juniper Asthma Quality of Life Questionnaire – Interviewer Administered (AQLQ S-IA) Score from Baseline to 90, 180, 270 and 365-days follow-up

The AQLQ S-IA score at each individual time point was calculated as the mean of the 32 questions of the questionnaire, with each question being scored on a 7-point scale (1=maximal impairment, 7=no impairment) and the total AQLQ S-IA score ranging between 1 (severely impaired) and 7 (not impaired at all). Line listings including participant ID, treatment group and this secondary outcome defined as the change in AQLQ S-IA score from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the score recorded at each of the follow-up visits and the score reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 17. Listing of AQLQ S-IA score data

Participant ID	Treatment group	AQLQ S-IA score				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	5.4	6.2	6.2	6.6	-
T2H006-703	Dexpramipexole	5	5.1	5.8	-	-
T2H006-704	Placebo	4.3	4.4	-	-	-
T2H008-702	Placebo	1.8	2.6	-	-	-
T2H008-705	Dexpramipexole	3.3	6	-	-	-

Table 18. Listing of Secondary Outcome data: Change in AQLQ S-IA score from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in AQLQ S-IA score from Baseline to 90 days
T2H006-701	Dexpramipexole	0.8
T2H006-703	Dexpramipexole	0.1
T2H006-704	Placebo	0.1
T2H008-702	Placebo	0.8
T2H008-705	Dexpramipexole	2.7

Table 19. Listing of Secondary Outcome data: Change in AQLQ S-IA score from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in AQLQ S-IA score from Baseline to 180 days
T2H006-701	Dexpramipexole	0.8
T2H006-703	Dexpramipexole	0.8
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 20. Listing of Secondary Outcome data: Change in AQLQ S-IA score from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in AQLQ S-IA score from Baseline to 270 days
T2H006-701	Dexpramipexole	1.2
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 21. Listing of Secondary Outcome data: Change in AQLQ S-IA score from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in AQLQ S-IA score from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.8 Change in Post-Bronchodilator FEV_1 measured via remote digital asthma spirometry (and post-bronchodilator FEV_1/FVC at Baseline and week 52 only, subject to feasibility of testing at trial sites during COVID-19) from Baseline to 365 days follow-up

Line listings including participant ID, treatment group and this secondary outcome defined as the change in Post-Bronchodilator FEV_1 from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the FEV_1 value recorded at each of the follow-up visits and the FEV_1 value reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 22. Listing of Post-Bronchodilator FEV_1 and FEV_1/FVC data

Participant ID	Treatment group	Post-Bronchodilator FEV_1		Post-Bronchodilator FEV_1/FVC	
		Baseline	365 days	Baseline	365 days
T2H006-701	Dexpramipexole	3.45	-	73	-
T2H006-703	Dexpramipexole	1.42	-	56	-
T2H006-704	Placebo	2.27	-	69	-
T2H008-702	Placebo	1.29	-	79	-
T2H008-705	Dexpramipexole	1.75	-	47	-

Table 23. Listing of Secondary Outcome data: Change in Post-Bronchodilator FEV_1 from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in Post-Bronchodilator FEV_1 from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 24. Listing of Secondary Outcome data: Change in Post-Bronchodilator FEV_1/FVC from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in Post-Bronchodilator FEV_1/FVC from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.9 Change in Absolute Blood Eosinophil and Neutrophil levels from Baseline to 90, 180, 270 and 365 days follow-up

Line listings including participant ID, treatment group and this secondary outcome defined as the change in absolute blood eosinophil and neutrophil levels from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the absolute blood eosinophil and neutrophil levels recorded at each of the follow-up visits and the absolute levels reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 25. Listing of Absolute Blood Eosinophil level data

		Absolute Blood Eosinophil level				
Participant ID	Treatment group	Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	0.33	0.3	0.01	0.3	-
T2H006-703	Dexpramipexole	0.35	0.48	0.16	-	-
T2H006-704	Placebo	0.34	0.26	-	-	-
T2H008-702	Placebo	0.36	0.04	-	-	-
T2H008-705	Dexpramipexole	0.5	0	-	-	-

Table 26. Listing of Secondary Outcome data: Change in absolute Blood Eosinophil level from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Eosinophil level from Baseline to 90 days
T2H006-701	Dexpramipexole	-0.03
T2H006-703	Dexpramipexole	0.13
T2H006-704	Placebo	-0.08
T2H008-702	Placebo	-0.32
T2H008-705	Dexpramipexole	-0.5

Table 27. Listing of Secondary Outcome data: Change in absolute Blood Eosinophil level from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Eosinophil level from Baseline to 180 days
T2H006-701	Dexpramipexole	-0.32
T2H006-703	Dexpramipexole	-0.19
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 28. Listing of Secondary Outcome data: Change in absolute Blood Eosinophil level from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Eosinophil level from Baseline to 270 days
T2H006-701	Dexpramipexole	-0.03
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 29. Listing of Secondary Outcome data: Change in absolute Blood Eosinophil level from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Eosinophil level from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 30. Listing of Absolute Blood Neutrophil level data

Participant ID	Treatment group	Absolute Blood Neutrophil level				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	4.95	4.14	3.97	2.86	-
T2H006-703	Dexpramipexole	11.84	7.69	9.46	-	-
T2H006-704	Placebo	4.05	4.65	-	-	-
T2H008-702	Placebo	5.34	6.86	-	-	-
T2H008-705	Dexpramipexole	4.19	3.04	-	-	-

Table 31. Listing of Secondary Outcome data: Change in absolute Blood Neutrophil level from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Neutrophil level from Baseline to 90 days
T2H006-701	Dexpramipexole	-0.81
T2H006-703	Dexpramipexole	-4.15
T2H006-704	Placebo	0.6
T2H008-702	Placebo	1.52
T2H008-705	Dexpramipexole	-1.15

Table 32. Listing of Secondary Outcome data: Change in absolute Blood Neutrophil level from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Neutrophil level from Baseline to 180 days
T2H006-701	Dexpramipexole	-0.98
T2H006-703	Dexpramipexole	-2.38
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 33. Listing of Secondary Outcome data: Change in absolute Blood Neutrophil level from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Neutrophil level from Baseline to 270 days
T2H006-701	Dexpramipexole	-2.09
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 34. Listing of Secondary Outcome data: Change in absolute Blood Neutrophil level from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in Absolute Blood Neutrophil level from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.10 Change in Fractional Exhaled Nitric Oxide Levels (FeNO) from Baseline to 90, 180, 270 and 365 days follow-up

The FeNO measured at each individual time point was calculated as the average of the 1st and 2nd FeNO result. Line listings including participant ID, treatment group and this secondary outcome defined as the change in FeNO from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the FeNO value recorded at each of the follow-up visits and the FeNO value reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 35. Listing of FeNO data

Participant ID	Treatment group	FeNO				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	20	15.5	22.5	42.5	-
T2H006-703	Dexpramipexole	97.5	104	82.5	-	-
T2H006-704	Placebo	46	48.5	-	-	-
T2H008-702	Placebo	45.5	121	-	-	-
T2H008-705	Dexpramipexole	34.5	14.5	-	-	-

Table 36. Listing of Secondary Outcome data: Change in FeNO from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in FeNO from Baseline to 90 days
T2H006-701	Dexpramipexole	-4.5
T2H006-703	Dexpramipexole	6.5
T2H006-704	Placebo	2.5
T2H008-702	Placebo	75.5
T2H008-705	Dexpramipexole	-20

Table 37. Listing of Secondary Outcome data: Change in FeNO from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in FeNO from Baseline to 180 days
T2H006-701	Dexpramipexole	2.5
T2H006-703	Dexpramipexole	-15
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 38. Listing of Secondary Outcome data: Change in FeNO from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in FeNO from Baseline to 270 days
T2H006-701	Dexpramipexole	22.5
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 39. Listing of Secondary Outcome data: Change in FeNO from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in FeNO from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.11 Change in Sino-nasal Outcome Test (SNOT-22) Score from Baseline to 90, 180, 270 and 365 days follow-up

The SNOT-22 score at each individual time point was calculated as the sum of the score for all items of the questionnaire, with the total score ranging between 0 and 110 noting that higher scores indicate greater rhinosinusitis-related health burden. Line listings including participant ID, treatment group and this secondary outcome defined as the change in SNOT-22 score from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the SNOT-22 score recorded at each of the follow-up visits and the SNOT-22 score reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 40. Listing of SNOT-22 score data

Participant ID	Treatment group	SNOT-22 score				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	14	11	12	18	-
T2H006-703	Dexpramipexole	19	35	43	-	-
T2H006-704	Placebo	42	49	-	-	-
T2H008-702	Placebo	51	53	-	-	-
T2H008-705	Dexpramipexole	41	41	-	-	-

Table 41. Listing of Secondary Outcome data: Change in SNOT-22 score from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in SNOT-22 score from Baseline to 90 days
T2H006-701	Dexpramipexole	-3
T2H006-703	Dexpramipexole	16
T2H006-704	Placebo	7
T2H008-702	Placebo	2
T2H008-705	Dexpramipexole	0

Table 42. Listing of Secondary Outcome data: Change in SNOT-22 score from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in SNOT-22 score from Baseline to 180 days
T2H006-701	Dexpramipexole	-2
T2H006-703	Dexpramipexole	24
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 43. Listing of Secondary Outcome data: Change in SNOT-22 score from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in SNOT-22 score from Baseline to 270 days
T2H006-701	Dexpramipexole	4
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 44. Listing of Secondary Outcome data: Change in SNOT-22 score from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in SNOT-22 score from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.12 Change in Visual Analogue Scale (VAS) Score for cough, shortness of breath and wheeze from Baseline to 90, 180, 270 and 365 days follow-up

The VAS score at each individual time point was calculated as the sum of the score recorded for each of the 4 items, with each item being scored on a 0-100mm scale noting that higher scores indicate greater severity of breathlessness. Line listings including participant ID, treatment group and this secondary outcome defined as the change in VAS score from Baseline to 90, 180, 270 and 365 days follow-up were produced using the Intention-to-treat population. The secondary outcome was calculated as the difference between the VAS score recorded at each of the follow-up visits and the VAS score reported at Baseline. The line listings presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

Table 45. Listing of VAS score data

Participant ID	Treatment group	VAS score				
		Baseline	90 days	180 days	270 days	365 days
T2H006-701	Dexpramipexole	5	4	1	1	-
T2H006-703	Dexpramipexole	5	6	5	-	-
T2H006-704	Placebo	18	10	-	-	-
T2H008-702	Placebo	218	217	-	-	-
T2H008-705	Dexpramipexole	254	30	-	-	-

Table 46. Listing of Secondary Outcome data: Change in VAS score from Baseline to 90 days follow-up

Participant ID	Treatment group	Change in VAS score from Baseline to 90 days
T2H006-701	Dexpramipexole	-1
T2H006-703	Dexpramipexole	1
T2H006-704	Placebo	-8
T2H008-702	Placebo	-1
T2H008-705	Dexpramipexole	-224

Table 47. Listing of Secondary Outcome data: Change in VAS score from Baseline to 180 days follow-up

Participant ID	Treatment group	Change in VAS score from Baseline to 180 days
T2H006-701	Dexpramipexole	-4
T2H006-703	Dexpramipexole	0
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 48. Listing of Secondary Outcome data: Change in VAS score from Baseline to 270 days follow-up

Participant ID	Treatment group	Change in VAS score from Baseline to 270 days
T2H006-701	Dexpramipexole	-4
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

Table 49. Listing of Secondary Outcome data: Change in VAS score from Baseline to 365 days follow-up

Participant ID	Treatment group	Change in VAS score from Baseline to 365 days
T2H006-701	Dexpramipexole	Assessment not done at one of the time points
T2H006-703	Dexpramipexole	Assessment not done at one of the time points
T2H006-704	Placebo	Assessment not done at one of the time points
T2H008-702	Placebo	Assessment not done at one of the time points
T2H008-705	Dexpramipexole	Assessment not done at one of the time points

7.13 Change in EuroQol-5D-5L (EQ-5D-5L) Quality of Life Questionnaire from Baseline to Visit 14 (365 days follow-up)

Line listings including data for this secondary outcome are not reported in this section as none of the 5 participants in the T2-HIGH trial completed this assessment at visit 14.

7.14 Change in Work Productivity & Activity Impairment (WPAI) questionnaire Score from Baseline to Visit 14 (365 days follow-up)

The WPAI comprises four main outcomes: work time missed, impairment at work, overall work impairment and activity impairment, with each of these outcomes due to asthma being expressed as percentages.

Line listings including data for this secondary outcome are not reported in this section as none of the 5 participants in the T2-HIGH trial completed this assessment at visit 14.

7.15 Adverse Events

The summary of safety data presented in this section was produced using the Safety population.

A total of 19 adverse events were reported for 4 (80%) participants who were randomised into the T2-HIGH trial and included in the Safety population. Two of the 19 adverse events were reported as serious for 2 participants allocated to the Dexpramipexole group.

7.15.1 Number of participants with Adverse Events

Table 50. Number of participants with Adverse Events | Secondary Outcome: Adverse Events

	Placebo	Dexpramipexole	Total
Randomised participants, n	2	3	5
Participants with Adverse Events, n(%)	2 (100%)	2 (66.7%)	4 (80%)
Participants with no Adverse Events, n(%)	0 (0%)	1 (33.3%)	1 (20%)
Participants with 1 Adverse Events, n(%)	1 (50%)	1 (33.3%)	2 (40%)
Participants with 7 Adverse Events, n(%)	1 (50%)	0 (0%)	1 (20%)
Participants with 10 Adverse Events, n(%)	0 (0%)	1 (33)	1 (20%)

7.15.2 Characteristics of Adverse Events

Table 51. Characteristics of Adverse Events | Secondary Outcome: Adverse Events

	Placebo	Dexpramipexole	Total
Overall number of Adverse Events, n	8	11	19
Severity			
Mild, n(%)	0 (0%)	3 (27.3%)	3 (15.8%)
Moderate, n(%)	6 (75%)	7 (63.6%)	13 (68.4%)
Severe, n(%)	2 (25%)	1 (9.1%)	3 (15.8%)
Fatal, n(%)	0 (0%)	0 (0%)	0 (0%)
Outcome			
Resolved, n(%)	7 (87.5%)	8 (72.7%)	15 (78.9%)
Resolved with sequelae, n(%)	0 (0%)	1 (9.1%)	1 (5.3%)
Continuing, n(%)	0 (0%)	2 (18.2%)	2 (10.5%)
Fatal, n(%)	0 (0%)	0 (0.0%)	0 (0%)
Unknown, n(%)	1 (12.5%)	0 (0.0%)	1 (5.3%)
Treatment			
None, n(%)	3 (37.5%)	2 (18.2%)	5 (26.3%)
Concomitant Medication, n(%)	5 (62.5%)	8 (72.7%)	13 (68.4%)
Non-drug therapy, n(%)	0 (0%)	1 (9.1%)	1 (5.3%)
Concomitant Medication and Non-drug therapy, n(%)	0 (0%)	0 (0%)	0 (0%)
Action taken			
None, n(%)	8 (100%)	11 (100%)	19 (100%)
Study interrupted, n(%)	0 (0%)	0 (0%)	0 (0%)
Study discontinued, n(%)	0 (0%)	0 (0%)	0 (0%)
Relatedness			
Not related, n(%)	8 (100%)	11 (100%)	19 (100%)
Unlikely, n(%)	0 (0%)	0 (0%)	0 (0%)
Possible, n(%)	0 (0%)	0 (0%)	0 (0%)
Probable, n(%)	0 (0%)	0 (0%)	0 (0%)
Definite, n(%)	0 (0%)	0 (0%)	0 (0%)
Serious Adverse Event			
Yes, n(%)	0 (0%)	2 (18.2%)	2 (10.5%)
No, n(%)	8 (100%)	9 (81.8%)	17 (89.5%)
Expectedness			
Yes, n(%)	0 (0%)	0 (0%)	0 (0%)
No, n(%)	8 (100%)	11 (100%)	19 (100%)

7.16 Treatment Adherence and Compliance (patient level drug accountability) reported at 90, 180, 270 and 365 days follow-up

Numbers (with percentages) for binary variables and descriptive statistics of the proportion of missed tablets reported at 90, 180, 270 and 365 days follow-up were produced for this secondary outcome using the Intention-to-treat population. The number of missed tablets reported at each of the aforementioned study visits and the follow-up time (measured in days) were used to calculate the proportion of missed tablets. The summaries presented below assume that missing secondary outcome data are missing at random (MAR) with no deletion or imputation being implemented. This approach utilised secondary outcome data up until the last known point for each participant.

7.16.1 Treatment Adherence and Compliance at 90 days follow-up

Table 52. Descriptive Statistics | Secondary Outcome: Treatment Adherence at 90 days follow-up

	Placebo	Dexpramipexole	Total
Has the participant missed >21 days of treatment?			
No, n(%)	0 (0%)	1 (100%)	1 (100%)
Proportion of missed tablets since their previous visit			
N	2	3	5
Median (IQR)	0.1 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)
Min, Max	0.0, 0.1	0.0, 0.1	0.0, 0.1
Has the participant taken less than 75% of their trial medication since their previous visit?			
No, n(%)	0 (0%)	1 (100%)	1 (100%)

7.16.2 Treatment Adherence and Compliance at 180 days follow-up

Table 53. Descriptive Statistics | Secondary Outcome: Treatment Adherence at 180 days follow-up

	Placebo	Dexpramipexole	Total
Has the participant missed >21 days of treatment?			
No, n(%)	0 (0%)	2 (100%)	2 (100%)
Proportion of missed tablets since their previous visit			
N	0	2	2
Median (IQR)	-	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Min, Max	-	0.0, 0.0	0.0, 0.0
Has the participant taken less than 75% of their trial medication since their previous visit?			
No, n(%)	0 (0%)	2 (100%)	2 (100%)

7.16.3 Treatment Adherence and Compliance at 270 days follow-up

Table 54. Descriptive Statistics | Secondary Outcome: Treatment Adherence at 270 days follow-up

	Placebo	Dexpramipexole	Total
Has the participant missed >21 days of treatment?			
No, n(%)	0 (0%)	1 (100%)	1 (100%)
Proportion of missed tablets since their previous visit			
N	0	1	1
Median (IQR)	-	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Min, Max	-	0.0, 0.0	0.0, 0.0
Has the participant taken less than 75% of their trial medication since their previous visit?			
No, n(%)	0 (0%)	1 (100%)	1 (100%)

7.16.4 Treatment Adherence and Compliance at 365 days follow-up

No participants attended their 365 days follow-up visit.

8 Secondary Analysis of Secondary Outcomes

Line listings of the secondary outcomes were not produced as all participants are included in the Per-Protocol population. This is as a result of no major deviations being recorded for any of the 5 participants who were randomised into the T2-HIGH trial.

9 Mechanistic Outcomes Analysis

The planned descriptive statistics of the mechanistic outcomes were not produced due to lack of both sputum and nasal swabs/nasosorption data.

10 Exploratory Outcomes Analysis

The planned correlations between the exploratory outcomes were not calculated due to lack of both sputum and nasal swabs/nasosorption data.

11 Neutropenia

Sites confirmed that no cases of neutropenia were reported for any of the 5 participants that were randomised into the T2-HIGH trial.

12 Protocol Deviations

A total of 9 Protocol Deviations were reported for 4 (80%) participants who were randomised into the T2-HIGH trial.

12.1 Number of participants with Protocol Deviations

Table 55. Number of participants with Protocol Deviations

	Placebo	Dexpramipexole	Total
Randomised participants, n	2	3	5
Participants with Protocol Deviations, n(%)	2 (100%)	2 (66.7%)	4 (80%)
Participants with no Protocol Deviations, n(%)	0 (0%)	1 (33.3%)	1 (20%)
Participants with 1 Protocol Deviation, n(%)	1 (50%)	1 (33.3%)	2 (40%)
Participants with 3 Protocol Deviations, n(%)	1 (50%)	0 (0%)	1 (20%)
Participants with 4 Protocol Deviations, n(%)	0 (0%)	1 (33.3%)	1 (20%)

12.2 Major Protocol Deviations

Table 56. Breakdown of Major Protocol Deviation reasons by deviation type and Number of Participants affected by deviation type

Major Protocol Deviation Reason	Placebo		Dexpramipexole		Total	
	P	N	P	N	P	N
Participant discovered to be ineligible for entry into trial post-randomisation, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Non-compliance with randomised treatment:						
Participant did not take greater than 75% of trial treatment within the last 90 days, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Participant received incorrect trial treatment, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Participant received prohibited medications, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

P: number of protocol deviations by deviation type, **N:** number participants affected per deviation type Please note the percentage corresponding to the proportion of participants affected per minor deviation type (including the total for each treatment arm and Total) was calculated out of the total number of participants randomised.

12.3 Minor Protocol Deviations

Table 57. Reasons for Minor Protocol Deviations and number of participants affected by deviation type

Minor Protocol Deviation Reason	Placebo		Dexpramipexole		Total	
	P	N	P	N	P	N
Time Window or Assessment deviations for any of the dispensing visits listed below [a]:						
Baseline, n(%)	1 (100%)	1 (100%)	2 (66.7%)	2 (66.7%)	3 (75%)	3 (75%)
Visit 5 (90 days follow-up) [b], n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Visit 8 (180 days follow-up), n(%)	0 (0%)	0 (0%)	1 (33.3%)	1 (33.3%)	1 (25%)	1 (25%)
Visit 11 (270 days follow-up), n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total, n(%)	1 (100%)	1 (50%)	3 (100%)	2 (66.7%)	4 (100%)	3 (60%)

P: number of protocol deviations by deviation type, **N:** number participants affected per deviation type Please note the percentage corresponding to the proportion of participants affected per minor deviation type (including the total for each treatment arm and Total) was calculated out of the total number of participants randomised.

[a] Each one of the visits had a ± 7 day time window. The number of deviations corresponding to each visit was calculated out of participants who attended their visit.
[b] Please note that figures corresponding to one time window deviation are not reported here as the deviation was recorded under the category of "Other deviation".

Please refer to section 8.12 Treatment Adherence and Compliance for the reporting of taking less than 25% of the intended number of tablets also constitutes a minor deviation in accordance with the SAP v2.1.

12.4 Additional Protocol Deviations

A summary of protocol deviations that were not classed as either major or minor is presented in the table below:

Table 58. Reasons for Additional Protocol Deviations and number of participants affected by deviation type

Protocol Deviation Reason	Placebo		Doxycycline		Total	
	P	N	P	N	P	N
Participant did not attend the scheduled drug dispensing visit at 3, 6 or 9 months, n(%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other deviations, n(%)	3 (100%)	1 (100%)	2 (100%)	1 (100%)	5 (100%)	2 (100%)
Total, n(%)	3 (100%)	1 (50%)	2 (100%)	1 (33.3%)	5 (100%)	2 (40%)

P: number of protocol deviations by deviation type, **N:** number participants affected per deviation type Please note the percentage corresponding to the proportion of participants affected per minor deviation type (including the total for each treatment arm and Total) was calculated out of the total number of participants randomised.

13 Appendix

13.1 Medical History reported at Screening visit: Listing of Other medical conditions

Table 59. Listing of Other medical conditions

Screening ID	Description of Other medical condition(s)
BSA010-001	Ibuprofen
BSA013-002	Cerebral Palsy
	Achilles Tendon Shortening (Bilateral)
BSA013-004	Opiates - causes nausea
	Pineapple and Kiwi fruit
BSA013-003	ulcerative colitis
	hysterectomy fibroids
BSA014-001	Previous nephrectomy and hysterectomy, now bladder dysfunction, self-catheterises
	Previous spinal fixation with spinal impact
BSA015-001	Borderline personality disorder
	Migraine
BSA005-001	Hypothyroidism
	total abdominal hysterectomy
BSA006-002	Intermittent headaches
	occasional migraines
BSA006-003	insomnia
	sleep apnoea
BSA006-004	psoriasis
	diverticulitis
BSA006-005	Diverticular disease
	Lower back pain
BSA006-009	Tramadol allergy
	Trimethoprim allergy
BSA008-001	Latex
	Nikel
BSA008-004	Azithromycin
BSA008-002	Doxazosin
BSA008-005	Aminophylline
BSA009-008	Mustard

13.2 Listing of Protocol Deviations

13.2.1 Other

Table 60. Protocol Deviation: Other

Trial ID	Treatment	Deviation date	Deviation reason details
T2H006-701	Dexpramipexole	01/12/2021	Visit 3 occurred out of the visit window due to subject isolating with covid-19
T2H006-704	Placebo	14/07/2022	visit 5 one day out of window as subject was too busy to attend on planned date
T2H006-704	Placebo	13/08/2022	Visit 6 missed
T2H006-704	Placebo	28/10/2022	EARLY DISCONTINUATION VISIT WAS NOT COMPLETED AS SUBJECT WAS LOST TO FOLLOW-UP
T2H006-701	Dexpramipexole	23/11/2022	Participant continued to take trial medication following advice to discontinue study drug at Sponsor's request

13.3 Listing of Adverse Events reported for participants in the Placebo group

Table 61. Listing of Adverse Events reported in the Placebo group

Trial ID	Adverse Event description	Duration (days)	Severity	Outcome	Treatment	Related	Serious	Expected
T2H006-704	Viral upper respiratory tract infection	16	Severe	Resolved	None	Not related	No	No
T2H006-704	Infective exacerbation of asthma	16	Severe	Resolved	Concomitant Medication	Not related	No	No
T2H006-704	Generalised fatigue	50	Moderate	Resolved	None	Not related	No	No
T2H006-704	common cold	5	Moderate	Resolved	None	Not related	No	No
T2H006-704	lower respiratory tract infection	4	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-704	tonsilitis	21	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-704	infective exacerbation of asthma	-	Moderate	Unknown	Concomitant Medication	Not related	No	No
T2H008-702	Community Acquired Pneumonia	9	Moderate	Resolved	Concomitant Medication	Not related	No	No

13.4 Listing of Adverse Events in the Dexpramipexole group

Table 62. Listing of Adverse Events reported in the Dexpramipexole group

Trial ID	Adverse Event	Duration (days)	Severity	Outcome	Treatment	Related	Serious	Expected
T2H006-703	High FeNO	-	Mild	Continuing	None	Not related	No	No
T2H006-703	superficial skin rash on both ankles	15	Mild	Resolved	None	Not related	No	No
T2H006-703	asthma exacerbation	12	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	sinus infection	41	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	asthma exacerbation	10	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	sinus headaches	39	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	Infective diverticulitis	7	Moderate	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	asthma exacerbation	16	Severe	Resolved	Concomitant Medication	Not related	No	No
T2H006-703	oral thrush	-	Moderate	Continuing	Concomitant Medication	Not related	No	No
T2H006-703	Respiratory syncytial virus induced community acquired pneumonia	11	Moderate	Resolved	Concomitant Medication	Not related	Yes	No
T2H008-705	Head Injury following accident at work	95	Mild	Resolved with Sequelae	Non-drug therapy	Not related	Yes	No

13.5 Listing of Serious Adverse Events in the Dexpramipexole group

Table 63. Listing of Serious Adverse Events reported in the Dexpramipexole group

Trial ID	Serious Adverse Event	Duration (days)	Severity	Outcome	Treatment	Related	Expected
T2H006-703	Respiratory syncytial virus induced community acquired pneumonia	11	Moderate	Resolved	Concomitant Medication	Not related	No
T2H008-705	Head Injury following accident at work	95	Mild	Resolved with Sequelae	Non-drug therapy	Not related	No