



Refractory Asthma  
Stratification Programme

July 2018

# Breathe Deep: Issue 6

Welcome to the sixth issue of the Refractory Asthma Stratification Programme (RASASP-UK) newsletter!

**Save the date for the 2018 General Assembly Meeting - Inside**

## Inside:

- Highlights since the 2017 General Assembly
- Update on work-strand progress
- Upcoming Events
- Feedback from the MRC Stratified Medicines Monitoring Group

promoting research into severe asthma

# Welcome to the sixth Refractory Asthma Stratification Programme - UK Newsletter

by **Gabrielle Gainsborough, Consortium Manager**

Welcome to the latest issue of the Refractory Asthma Stratification Programme (RASP-UK) newsletter. It was encouraging to see so many partners at the 2017 General Assembly meeting last December, including several new faces from our new partners. Since then we have seen significant progress across all work-strands which we'll share with you in this edition.

We are now half way through our third year of the programme. Our Executive Management Team is starting to focus on plans for the reporting of RASP-UK outputs and looking at the legacy we leave behind. We hope to be able to share more information at the 2018 General Assembly meeting which will be held on Tuesday 04 Dec 18.



We hope you enjoy this newsletter. As always, we would be delighted to hear from you if you would like to share any relevant news with the consortium through this newsletter or if you have any suggestions or comments on the RASP-UK programme. You may even like to contribute a short article. So please get in touch with me, Gabrielle Gainsborough, at Niche Science & Technology Ltd . [gabrielle.gainsborough@niche.org.uk](mailto:gabrielle.gainsborough@niche.org.uk)

## Highlights since the 2017 General Assembly Meeting...

- Positive feedback from the RASP-UK Trial Steering Committee and MRC Stratified Medicines Monitoring Group
- SoMOSA has completed recruitment! Read more (p 8)
- Biostratification Study – screening complete! (p 6)
- Three new studies commence under the WS4 umbrella. Learn about the GSK Adherence Study, MEX and MAPLE

# Highlights since the last Newsletter...

## Feedback from the MRC Stratified Medicines Monitoring Group



RASP-UK underwent its latest progress review by the MRC on 03 May 18. As the consortium was judged to be on target in the Nov 17 review, we were only required to submit a progress report to the committee. The feedback from the meeting was succinct and positive:

‘The Group thanked the Team for their update, and were reassured of the consortium’s progress. In the next report, the Group would appreciate the Team including more description of the patient and public involvement (PPI) activities that the consortium is engaged in’.

Our next review will be held on 15 Nov 18 and we hope to have the feedback before the 2018 General Assembly meeting.

## Feedback from the RASP-UK Trial Steering Committee

The Trial Steering Committee (TSC) were due to meet on 01 Mar 18. However, the meeting was sadly cancelled when storm Emma gripped the UK. Review was completed by email. The committee’s first responsibility was to note with great sadness the untimely death of our patient representative Mark Stafford-Watson, from Southampton. Mark was greatly admired in Southampton and more widely for his tireless engagement in research as an expert patient. The team have sent condolences to Mark’s family.

The committee had no safety concerns on our WS1, WS2 or WS3 components and will meet to review again in Sep 2018. We extend thanks to our Chair, Martyn Partridge, and our other TSC members Ann Millar and Mike Morgan for giving their time to the TSC.



# Update on the Patient Input Platform

By Dr Jasmine Parkinson  
Asthma UK

RASP-UK's Patient Input Platform (PIP) continues to ensure that this programme's studies are patient-centred. Coordinated through Asthma UK, the PIP is formed of seven people affected by severe asthma who have brought a diverse range of experiences to the table and helped to steer focus on the outcomes that matter the most to people with this condition.



*Dr Jasmine Parkinson*

Since presenting the results of the Delphi exercise on meaningful steroid reduction at the General Assembly Meeting in December, the PIP have jointly reviewed the draft research letter of this work that has now been submitted to the European Respiratory Journal Open Research. In addition, the PIP have assisted in the design and preparation of the patient-facing materials for the WS4 study "Inflammation following mepolizumab and prednisolone in severe asthma" (MAPLE).

Drawing upon their own experiences and perspectives they have helped to edit the patient information sheets and consent forms so these documents are simple to read and understand. They have also reviewed the trial diary cards so they are practical to use, increasing the likelihood that participants will complete them frequently and thoroughly.

Researchers are always welcome to approach the PIP with requests for patient-perspective consultation on RASP materials and methods. To get in touch, please email Dr Jasmine Parkinson at Asthma UK at [jparkinson@asthma.org.uk](mailto:jparkinson@asthma.org.uk).





# Update on work strand progress

## Work-strand 1 INCA-SUN adherence intervention study

By Dr Joanne Walsh, Research Nurse

The INCA-SUN team have been actively screening and recruiting patients for their study across five severe asthma centres: Beaumont Hospital, Belfast City Hospital, St. Vincent's University Hospital, Cork University Hospital and Connolly Hospital.

The study is looking to recruit 220 patients in total. To date they have successfully enrolled a total of 130 patients, of which 100 patients have successfully completed the 8 month INCA Sun Study. The breakdown of this recruitment figure is as follows:

Site	Number Recruited	Number Complete
Beaumont Hospital	98	81
Belfast City Hospital	7	3
Connolly hospital	6	4
Cork University Hospital	13	10
St. Vincent's University Hospital	6	2

The Team have recently secured additional funding from the Cross-border Healthcare Intervention Trials in Ireland Network (CHITIN). This is a partnership application between QUB and RCSI (led by RCSI) to provide support funding to the INCA-SUN study to establish additional cross-border sites in Ireland: <http://www.research.hscni.net/cross-border-healthcare-intervention-trials-ireland-network-chitin-0>



**INCA**

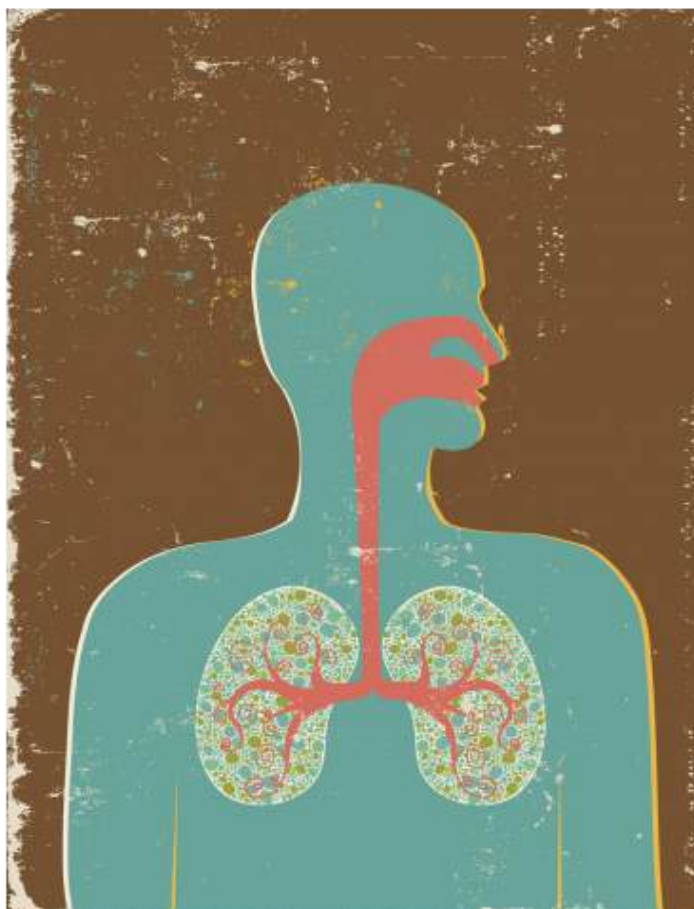
Inhaler  
Compliance  
Assessment



**RCSI**



GlaxoSmithKline



# Update on work strand progress (cont.)

## Work-strand 1: Biostratification Study

By Dr Avril Horn, Work- Strand 1 Project Manager

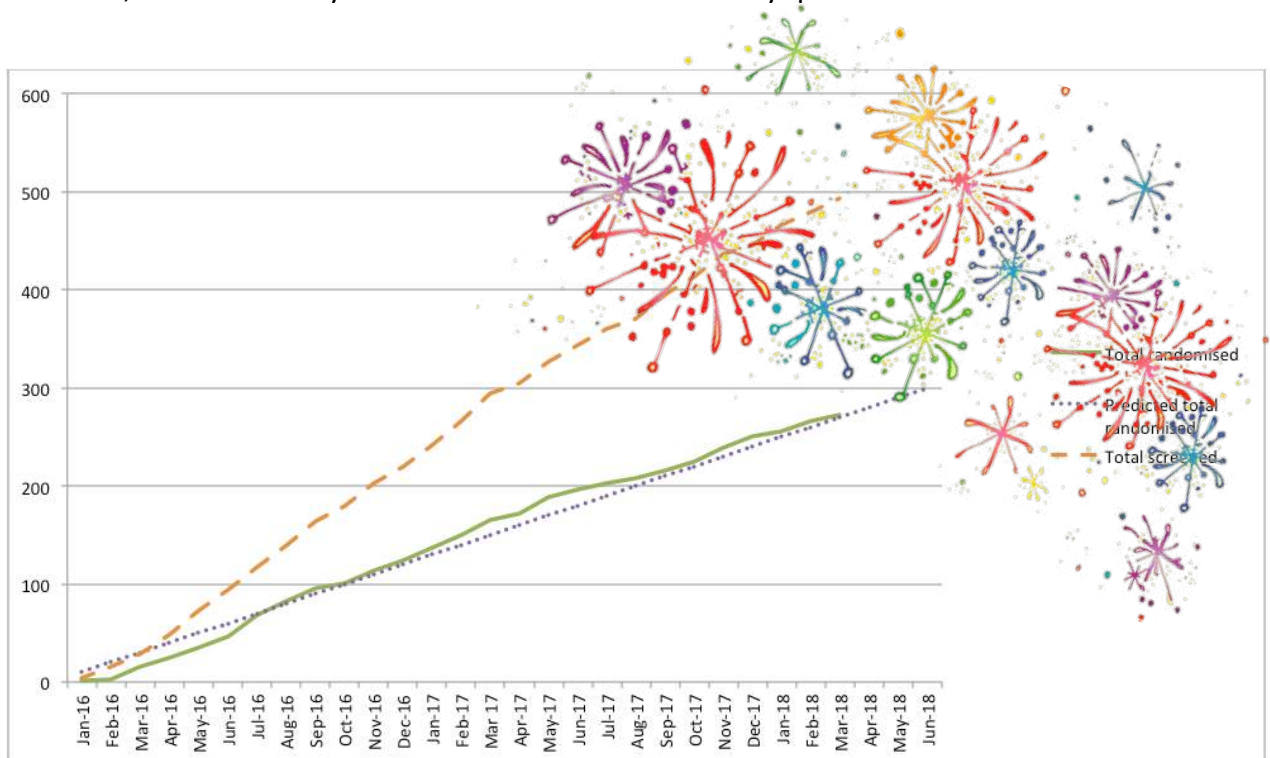
I am writing this on the afternoon of 29th June 2018. While I write I received an email confirming the randomisation of our 300<sup>th</sup> patient. This is a superb finish to our screening period and is due to the enormous efforts that you have all made at site.



It seems a rather long time since January 2016 when we had the excitement of our first patient randomised. Since then, there have been some ups and downs in the study. We have weathered and overcome some management challenges. You have all helped deliver a cohort of patients whose data will answer several questions about the potential benefit of biomarkers in asthma to personalise treatment with steroids.

In addition to routine monitoring visits to review and clarify data, we are now working closely with the study statistician to review listings of study data. Please bear with us if we contact you about data clarifications as a result of this activity. The more we can clarify now, the less we will be trying to resolve at the end of the study in July 2019.

As ever, the Niche study team are available to answer any questions.

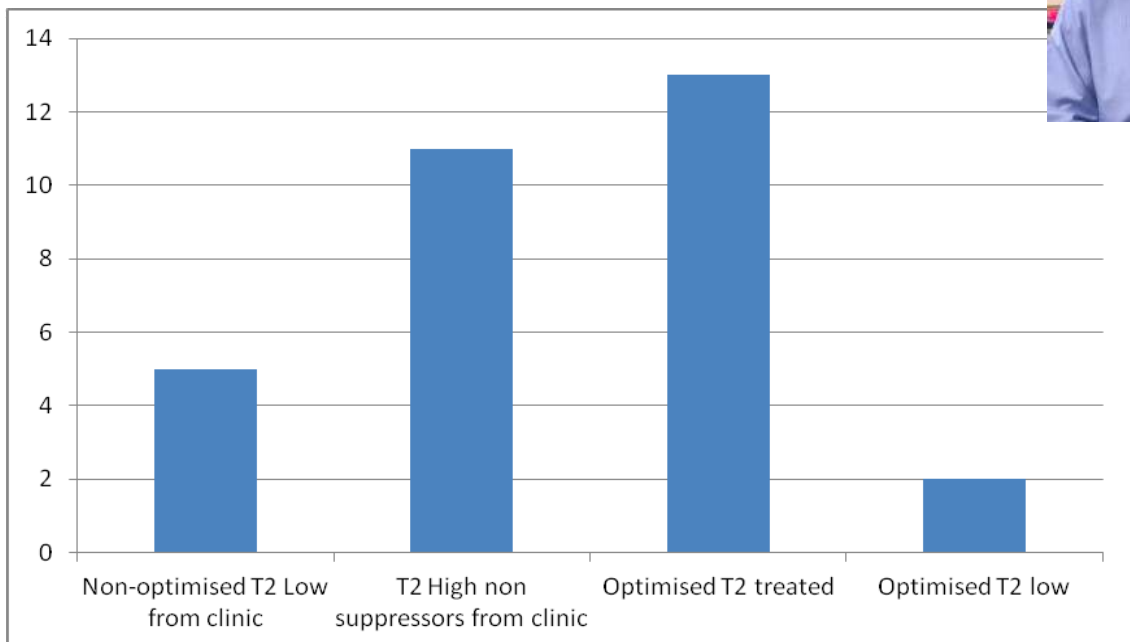


# Update on work strand progress (cont.)

## Work-strand 2: Bronchoscopy Study

By Peter Bradding, Work Strand 2 Lead and Bev Hargadon, Clinical Manager, NIHR Leicester Biomedical Research Centre

All sites now have sponsor green light. Thirty-one patients have undergone bronchoscopy to date. There are an additional 23 biopsies from non-optimised T2 (biomarker)-low patients, collected using an SOP identical to that employed by Genentech/Roche and Leicester (n=23), and a Southampton cohort (n=11) will form an initial training set in the non-optimised T2-Low group.



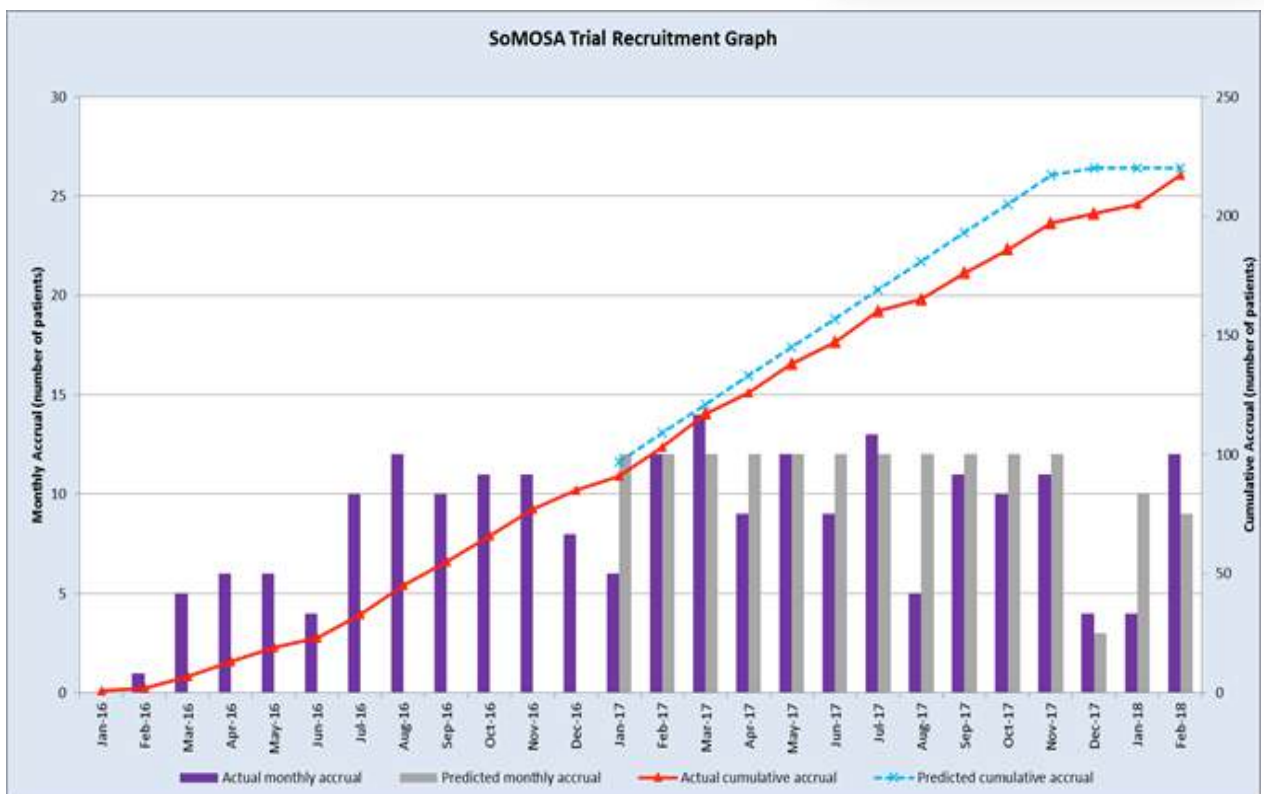
The analysis will be informed further with the results of a bronchoscopy study just completed by Pete Bradding with Genentech, where healthy volunteers have been treated with high dose inhaled corticosteroid for 1 month to determine the “steroid signature”.

# Update on work strand progress (cont.)

## Work Strand 3 The Study of Mechanisms of Action of Omalizumab in Severe Asthma (SoMOSA)

By Ratko Djukanovic, SoMOSA  
Chief Investigator and Work Strand 3  
Lead and, SoMOSA Project Manager

Congratulations to the Work Strand 3 SoMOSA team.  
Recruitment was completed in Feb 18 with  
217 subjects enrolled.



The WS3 team continue to closely monitor the ratio of responders to non responders as well as the drop- out rate. The study is powered for a 10% drop-out rate. The team at Southampton CTU are working with all sites to encourage patient retention. We'd like to thank all the SoMOSA teams for their continued hard work over the course of the study.



# Update on work strand progress (cont.)

## Work-strand 4 Progress Update

By Rekha Chaudhuri

At the 2017 General Assembly, we saw an overview of the planned WS4 studies. Since the meeting, the MEX study has commenced recruitment and plans for two further studies are well underway.

**MEX – Study of Exacerbation Events in patients on Mepolizumab.**

**Sponsor:** Queen’s University, Belfast

**Status:** All 4 planned sites have approval and are recruiting.

**Study Started:** January 2018

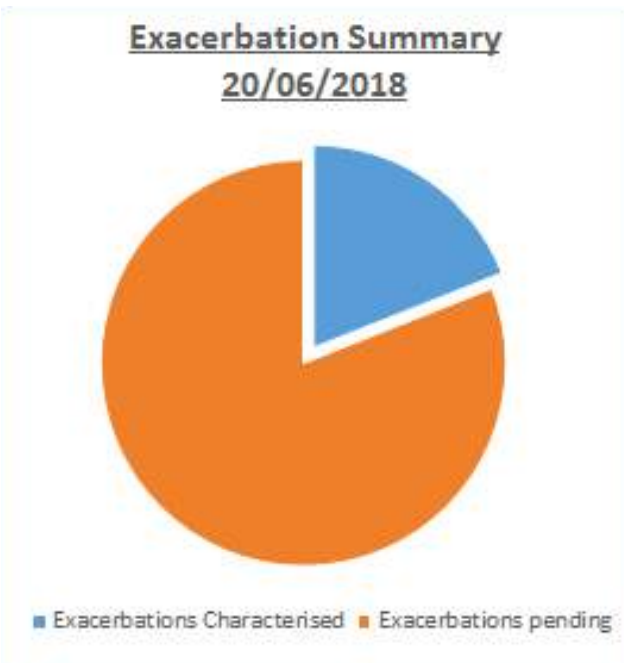
**Target for enrolment:** 150 subjects

**Target for exacerbation events:** 100

A summary of recruitment on the 20 June 18 is provided in the table below.

We enrolled 87 patients from January to June 2018. This represents 58% of our target and collected 19 exacerbation events [19% of our target].

	Established	New	Exacerbations
Oxford	4	4	0
Leicester	14	1	6
Belfast	18	15	6
Glasgow	23	8	7
Totals:	59	28	19
Total recruited:	87		



# Update on work strand progress (cont.)

**MAPLE – Study of adding high dose oral prednisolone for 2 weeks versus placebo in a crossover fashion to measure additional benefits of steroids when established on mepolizumab.**

**Sponsor:** Greater Glasgow and Clyde Health Board

**Study Status:** Ethics approval received; contracts and R&D approval Awaited.

**Target:** 24 patients who get initiated on mepolizumab who are not on maintenance OCS at baseline

**Sites:** Glasgow, Belfast, Leicester, Oxford

**Aim to start:** July 2018

**Aim to complete:** June 2019

**BenRex - Study of exacerbation events while on benralizumab, outcomes in real world patients and predictors of response.**

**Target:** 150 patients across 14 sites

**Drug Supply:** by AstraZeneca for 12-18 months [first 75 patients get offered 18 months]

**Sponsor:** Greater Glasgow and Clyde Health Board

**Status:** Awaiting confirmation of funding following final protocol review by AstraZeneca.

## GSK Adherence Study

In the last newsletter we heard from Professor Barnes, Head of the Respiratory Medical Franchise at GSK, about their planned adherence study. Alison Moore from GSK gives a brief update on how this study is progressing.

GSK is carrying out a clinical study to evaluate the effect of a connected inhaler system on an asthmatic's adherence to maintenance medication. The connected inhaler system consists of sensors on

inhalers to measure when the inhaler is used and this data is fed back to patients through an app and to health care practitioners (HCPs) through a dashboard. It is hoped that such a system will enable asthmatic patients to be more empowered in their asthma and allow patients and HCPs to have more informed discussions on a patient's treatment.



*Alison Moore, GSK*

The study assesses the impact of feeding information back to HCPs in addition to patients and feeding back data on maintenance medication or maintenance as well as rescue medication. The treatment duration for the study after the run-in period is 6 months. The primary objective of the study is adherence to maintenance medication and secondary objectives include rescue medication use and the asthma control test (ACT). The study is being carried out in 7 countries: US, Canada, UK, The Netherlands, Italy, Germany, Spain and recruitment has now completed with just over 500 patients being included in the run-in phase of the study.

# Publications

The consortium has had the following manuscript published in 2018:

*A randomised pragmatic trial of corticosteroid optimization in severe asthma using a composite biomarker algorithm to adjust corticosteroid dose versus standard care: study protocol for a randomised trial* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5753571/>

Manuscript currently under review:

Biomarker-based corticosteroid adjustment in severe asthma: a modified Delphi consensus

Change in type-2 biomarkers and cytokines with high dose prednisolone treatment in severe oral corticosteroid dependent asthmatics: an interventional open-label study

Remotely monitored therapy and nitric oxide suppression identifies non-adherence in severe asthma

# Upcoming RASP-UK Events

Next Trial Steering Committee – **13<sup>th</sup> September 2018**

MRC Stratified Medicines Review – **15<sup>th</sup> November 2018**

RASP-UK 2017 General Assembly Meeting - **4<sup>th</sup> December 2018**

## RASP Website

The RASP-UK website holds copies of all relevant study documents through the secure login portal at <http://www.rasp.org.uk/>.

If you would like to add any documents to the website or if you have any questions or comments on the website, please contact Gabrielle at Niche Science & Technology Ltd ([gabrielle.gainsborough@niche.org.uk](mailto:gabrielle.gainsborough@niche.org.uk))

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