Refractory Asthma Stratification Programme

September 2017

Breathe Deep: Issue 5

Welcome to the fifth issue of the Refractory Asthma Stratification Programme (RASP-UK) newsletter!

Inside:

promoting research into severe asthma

Welcome to the fifth 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.

Recruitment remains our main focus this year across the five active studies:

Work-strand 1 (Adherence, INCA-SUN and Biomarker Stratification Study);
Work-strand 2 Bronchoscopy Study and
Work-strand 3 SoMOSA.

In this edition we'll bring you all the latest updates on the programme.

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

In this issue we cover…

- Highlights since the last Newsletter
- New members to the Consortium
- Medication adherence in asthma
- Update on work-strand progress
- Upcoming events

Highlights since the last Newsletter…

Feedback from the MRC Stratified Medicines Monitoring Group

RASP-UK underwent its third progress review by the MRC on 19 May 17. Recruitment was high up on the list of topics discussed but the Group were reassured by the plans which each of the work-strand teams have put in place around recruitment.

The Group was pleased to see the addition of new partners and impressed by the patient involvement within the consortium. There were also discussions on data collection and curation and how the team plan to adopt learnings from previous MRC programmes.

In conclusion, the Group agreed that the consortium was progressing well and that we are on target to deliver the programme.

Welcome...and farewell

We'd like to welcome **Boehringer Ingelheim** to the consortium who joined the programme in May 2017.

We look forward to meeting you at the next General Assembly Meeting.

Dr Jasmine Parkinson

In June, we said goodbye to **Nile Amos** from Asthma UK, who has been looking after the Patient Input Platform. Nile has moved onto pastures new and we thank him for his help with RASP-UK.

We are also sad to say goodbye to **Dr Nicola Gallagher** our Statistician at QUB who has been supporting RASP-UK over the last year. Welcome to **John Busby** who is taking over from Nicola next month.

Our new Research Operations Officer is **Dr Jasmine Parkinson** – welcome to the team Jasmine!

Medication adherence in Asthma

By Professor Neil Barnes
Head of the Respiratory Medical Franchise at GSK

GSK has great interest in the RASP-UK programme and the questions it tries to address. In particular, GSK recognises that whilst we have many medicines and inhalers available today for the treatment of asthma and COPD with proven efficacy in traditional clinical trials, the reality in clinical practice is that the burden of asthma remains high with only around 20% achieving well controlled asthma and 24% being hospitalised in the last year.

Professor Neil Barnes

At least one of the reasons for this is the fact that patients fail to take their medicines as prescribed. As a physician it is hard to know whether a patient who presents with asthma symptoms is deteriorating in their disease status or simply not taking their medication.

Technologies such as inhaler sensors which allow accurate recording of inhaler use together with patient apps which allow such data to be collected together with the level of asthma symptoms can help to better understand adherence at an individual patient level and allow for a better dialogue between the physician and patient thereby enabling a change in patient behaviour, improved adherence and better clinical outcomes.

GSK is committed to evaluate such technologies and understand which elements offer the greatest benefit and in which types of patient.

Update on work strand progress

Work-strand 1 INCA-SUN adherence intervention study

The INCA-Sun study is still in the recruitment phase. Ninety-three patients have been enrolled, ninety-two of which have been randomised into the two study arms. Forty-five are in the INCA feedback group and forty-seven are in the standard care group. To date, forty-eight patients have completed the study.

Our challenge at the moment is to increase recruitment. In order to do this we ran a country wide advertising campaign to allow patients to self-refer to the study. The recruitment phase has been extended to December 2017.

For updates on the latest INCA technology news follow us on twitter: @INCA_team or visit our website: http://www.incadevice.com/

Update on work strand progress

Work-strand 1: Biostratification Study – summary of the Delphi exercise

By Nicola Gallagher, QUB Statistician

Since the last newsletter we have extended the survey to reach consensus on aspects of biomarker based corticosteroid adjustment in severe asthma to UK severe asthma physicians out with RASP-UK, as well as members and collaborators with the European Severe Asthma Clinical Research Collaboration Severe Heterogenous Asthma Research collaboration, Patient-centered (SHARP) and patients with severe asthma from Asthma UK's network.

The survey is currently being extended to Australian respiratory physicians. A brief summary of the results to date are provided below.

Current biomarker use in adjustment of corticosteroid dose

Approximately 70% of UK physicians with a specialist interest in asthma (both within the RASP-UK programme and non-RASP-UK physicians) believe biomarker-based adjustment of corticosteroid dose is currently optimal to symptom based adjustment in patients with severe asthma, compared to ~40% of European physicians who support this strategy. Biomarker based adjustment of treatment is used less commonly in routine clinical care in Europe than in the UK.

Clinically meaningful reduction in oral and inhaled corticosteroid treatment

All three physician groups agreed that at least a 5 mg reduction in daily oral prednisolone would be regarded as clinically meaningful. RASP-UK physicians agreed that at least a 500 mcg reduction in daily inhaled corticosteroid treatment would be regarded as clinically meaningful. The other two groups thought that at least a 250 mcg reduction would be clinically meaningful. The majority of patients felt that any reduction in oral (60%) or inhaled (67%) steroid dose would make routine use of easily measurable blood and breath tests worthwhile if it led to a reduction in the dose of their treatment.

Clinically meaningful reduction in asthma exacerbations

RASP-UK physicians agreed that at least a 30% reduction in asthma exacerbations per year would justify routine use of biomarker-based corticosteroid treatment adjustment, whereas the other two physician groups agreed that at least a 20% reduction in asthma exacerbations per year would justify routine use of biomarker-based corticosteroid treatment adjustment. The majority of patients (83%) thought that if even a single exacerbation could be reduced having regular blood and breath tests would be worthwhile.

Work-strand 1

Biostratification Study update

By Avril Horn,
Work-strand 1 Project Manager

We are now just over two thirds of the way towards our target of 300 patients randomised. To date, we have 216 confirmed patients randomised from 395 patients screened.

Our dropout rate continues to be low, at around 10%, and we now have over 60 patients who have completed the study. Our target is 300 patients randomised by the end of December 2017.

Site	Total Screened	Total Randomised
Belfast	48	36
Leicester	49	30
Glasgow, Gartnavel	46	28
Oxford	34	24
Glasgow, Stobhill	39	18
Birmingham	39	16
Southampton	31	14
Manchester	27	13
Newcastle	35	13
Brompton, London	20	9
UCL, London	10	8
Nottingham	17	7
Total	**395**	**216**

Thank you all for your efforts in entering data promptly into the eCRF.

The study management team at Niche are now processing data queries that have been raised during monitoring. This may lead to further queries as we review data across centres and I hope you will bear with us during that effort.

Addressing queries now means that there will be less time required for query resolution during the end stages of the study.

Work-strand 1

Biostratification Study update, cont'd…

As a result of the processing of data queries, I would like to remind teams of three study and data requirements:

1. All asthma exacerbations must also be recorded as adverse events
2. Every change in asthma medication must be recorded as a separate line entry. This can be cumbersome for those patients that taper the dose of their oral steroids, but is essential to ensure that one of our endpoints is assessed correctly
3. Any protocol deviations regarding missed or damaged samples, missed visits or missed assessments must be recorded on the protocol deviations log in the study file

…and two reminders regarding operational aspects of the study:

1. Patients can be rescreened up to three times, particularly if they fail screening due to high FeNO, or lack of documented lung function variability / reversibility.
2. Exacerbation visits are very important to give us relevant data on these patients during an episode of asthma worsening.

Please contact me if any of this is unclear, and carry on screening as many patients as possible.

Work-strand 2

Bronchoscopy Study update

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

All of the eight sites are now open to recruitment. Twenty patients have completed and there are serveral with appointments booked.

The work-strand 2 team also have access to thirty six biomarker-low non-optimised legacy samples (19 at Genentech, 11 in Southampton, and 4 in Leicester) that will also be analysed.

These have appropriate clinical metadata and were collected using the same protocols as those used for RASP-UK.

Work-strand 3

The Study of Mechanisms of Action of Omalizumab in Severe Asthma (SoMOSA) Update

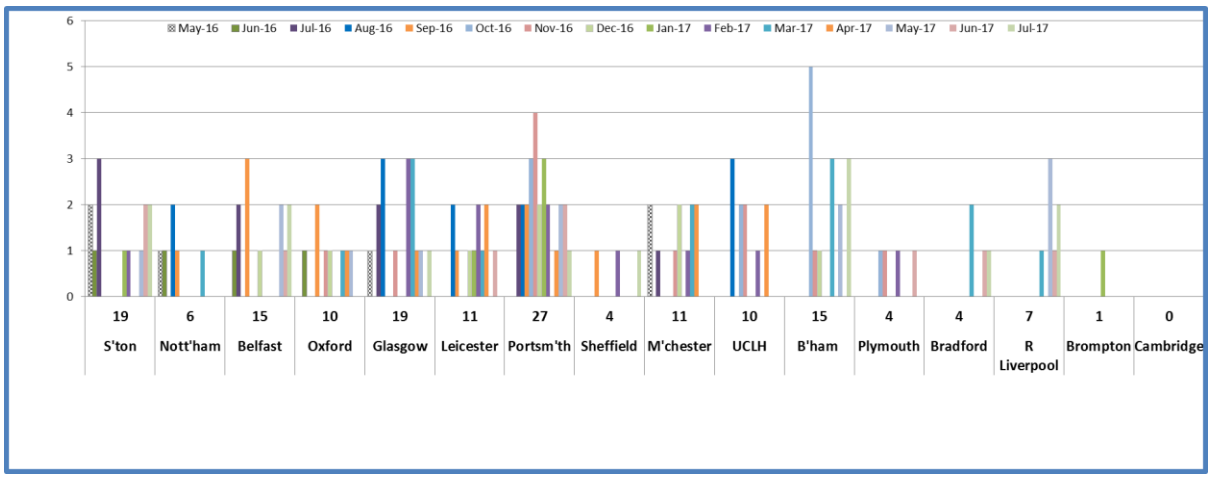
By Ratko Djukanovic, SoMOSA Chief Investigator & WS3 lead and, SoMOSA Project Manager

Where are we now?
Guy's and St Thomas's Hospital has now joined us as the final site to open in the SoMOSA trial, and after a bumpy start are up and screening.

With all 18 sites now open, recruitment has kicked into overdrive prior to our looming recruitment deadline of December 2017.

July saw 13 participants joining the study and previous months have hovered around our expected figure of 12 patients, which is promising.

Thanks to the hard work of the SoMOSA teams at site, we are hoping that this good recruitment climate continues as we run into our final 4 months.

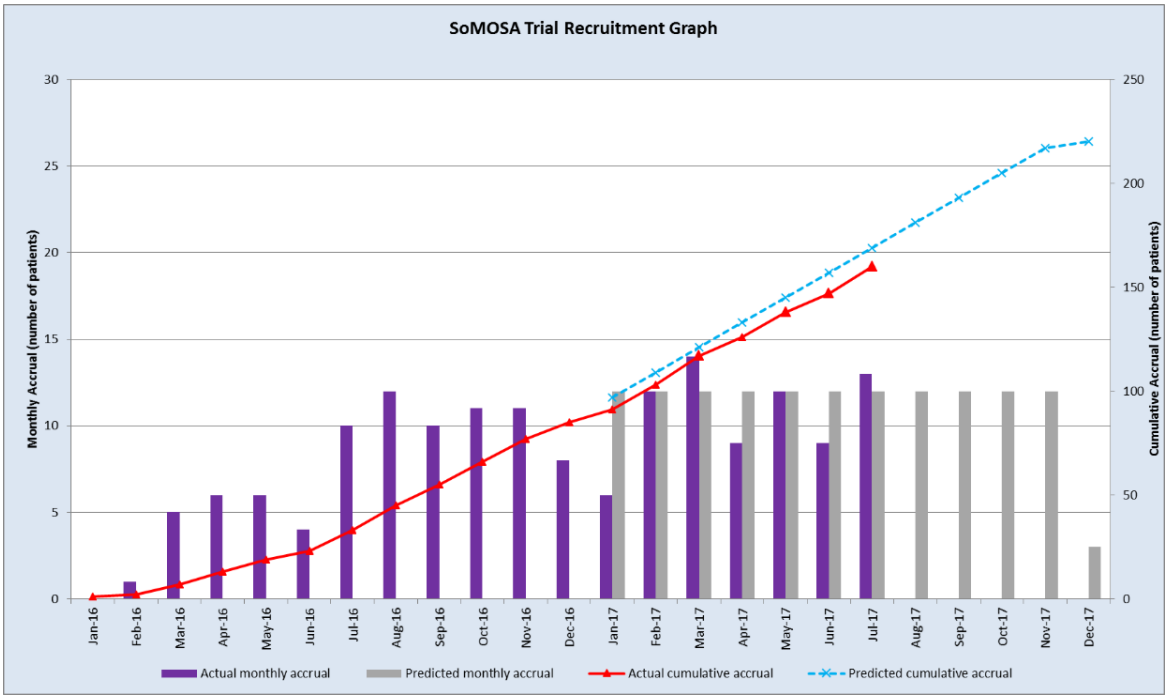


When it comes to individual site recruitment, Portsmouth is going strong with a healthy lead of 27 recruited participants, followed up by Glasgow and Southampton with 19 patients apiece. Belfast have also shot up the charts with 7 patients recruited in the last 4 months alone, bringing their total to 15.

Although we are currently looking at a deficit of 9 patients at this stage of the study, current numbers of identified potential patients indicate that this gap could soon close.

Work-strand 3

The Study of Mechanisms of Action of Omalizumab in Severe Asthma (SoMOSA) Update, cont'd…



Current Tasks

Many thanks to everyone for getting in contact with issues and questions. Due to quick communication, these have been dealt with in a timely manner and have allowed the study to continue moving along smoothly. We would also like to thank all those who attend our monthly Trial Forum TC (usually the final Tuesday of the month) and invite anyone with queries or comments to join in.

A prevailing point to make is sample storage and freezer space at sites. Currently the UoS and SCTU team are in the process of reconciling sample collection between the two databases, which is required before shipments can be authorised. While this has been given priority to prevent any further holdup, we thank sites for their patience in this matter and will be in position to authorise sample shipments shortly. Should freezer space become an urgent issue, please continue to get in touch.

Again, we'd like to thank all the SoMOSA teams for their continued hard work over the course of the study. With our imminent recruitment deadline of December fast approaching, please raise any recruitment issues with SCTU so that we can work through them ASAP.

Work-strand 4

Our first Work-strand 4 study has just received ethical approval. The mepolizumab exacerbation study is an investigator led study sponsored by QUB and funded using the additional contribution received by RASP-UK when the new industrial partners joined the programme.

This study was considered on 07 Sept 17 and there were no objections. In this study, we hope to characterise events of worsening asthma in patients taking mepolizumab to try and establish if they have evidence of inflammation which may respond to oral corticosteroids when their asthma symptoms worsen.

The study aims to recruit 150 patients established on mepolizumab in order to obtain 100 exacerbation events. The study will run at Belfast, Glasgow, Leicester and Oxford.

The RASP-UK Executive Management Team are working with a number of the Consortium Industry partners to set up other studies within this work-strand. We will update you as soon as we have any more details.

Upcoming RASP-UK Events

Next Trial Steering Committee – **21st September 2017**

MRC Stratified Medicines Review – **16th November 2017**

RASP-UK 2017 General Assembly Meeting - **5th December 2017**

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 and questions or comments on the website, please contact Gabrielle at Niche Science & Technology Ltd (gabrielle.gainsborough@niche.org.uk)

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