Refractory Asthma Stratification Programme

July 2016

Breathe Deep: Issue 2

Welcome to the second issue of the Refractory Asthma Stratification Programme (RASP-UK) newsletter! We hope we will be able to bring you regular updates on the RASP-UK programme and related subjects through the newsletters. With the first patient screenings and randomisations taking place and over the next few months we are looking forward to seeing many more patients being recruited

Inside:

Welcome to the second Refractory Asthma Stratification Programme - UK Newsletter

by Gabrielle Gainsborough, Consortium Manager

Welcome to the second issue of the Refractory Asthma Stratification Programme (RASP-UK) newsletter. We are now 8 months into the programme and working towards our first consortium milestone.

Since the last newsletter, recruitment into Work-strand 1 (Adherence, INCA-SUN and Biomarker Stratification Study) and Work-strand 3 (SoMOSA) continues to be our main focus. Professor Heaney and I attended the first MRC Stratified Medicines Monitoring Group Meeting for RASP-UK and we will share the outcome of this meeting in this edition.

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, by email at Niche Science & Technology Ltd. – gabrielle.gainsborough@niche.org.uk

In this issue we cover…

- MRC Stratified Medicine Monitoring Group Meeting
- Facilitating Unscheduled Visits in the Biomarker study
- Getting new treatments to patients: the RASP-UK Patient Input Platform
- Update on work-strand progress
- Events

MRC Stratified Medicine Monitoring Group Meeting

On 20 May 2016 Professor Heaney and I attended the first RASP-UK review meeting at the MRC. The purpose of the meeting was to report on the progress we have made since RASP-UK officially started on 20 October 2015 and whether or not we were managing to meet our defined programme metrics.

The Monitoring Group agreed that the consortium had made a strong start and had an excellent governance model in place. Members of the group were pleased with the amount of work that we achieved ahead of signing the consortium agreement. The general opinion was that this demonstrated good planning and highlighted the enthusiasm of partners to work together.

The Group noted that our consortium was failing to achieve two of the programmes objectives for Milestone 1 but was reassured by the mitigation plans that were in place to correct for the current issues.

These objectives are:

- Objective 2. Acceptable recruitment to inflammatory biomarker stratification study target
- Objective 4. Identification of novel biomarkers from UBioPred. Acceptable level of recruitment to SoMOSA study

The group questioned the use of our composite T2 biomarker strategy (FeNO, blood eosinophils and periostin) rather than using individual biomarkers. The team explained that as outlined in the initial application, the combination of three factors was more predictive of exacerbation than the individual biomarkers and planned some further analysis of this in other datasets. In further discussion, the members commented that an appropriate health economic assessment will be an important aspect of this defining utility of this type of approach in the clinic.

The Group also noted the following:

- Loss of the cash contribution from Janssen due to their withdrawal from the consortium
- The importance of consortia being sufficiently flexible to appropriately respond to new advances, for example, changes in therapies, technologies, and mechanistic understanding, asking how we might respond to these changes

The Monitoring Group concluded that the consortium appears to function as a coherent and well balanced team and that the project was progressing well.

Our next review meeting will take place on Friday 18 November 2016.

Gabrielle Gainsborough
Consortium Manager

Facilitating Unscheduled Visits in the Biomarker Study

by Professor Liam Heaney and Professor Ian Pavord

Thanks for all your efforts so far on the Biomarker Study. As you know, one of the important aspects of the study is to, where possible, see patients when they become more symptomatic during an exacerbation. This is critical to our capturing events in an adequate number of biomarker-low patients to profile these events and understand the mechanism of any symptomatic deterioration.

Professor Ian Pavord

In centres where we've captured several such episodes, many have been clearly infective in nature with bacterial bronchitis appearing prevalent. Sites have also been able to advise subjects that they did not need to use steroids for such 'exacerbations" based on clinical assessment.

Offering to see and assess subjects on an unscheduled basis, when they have increased symptoms represents a very demanding part of the study and requires considerable commitment from the study team. However the data we collect will be very informative as it will allow biomarker profile and steroid adjustments at scheduled visits to be related to these unscheduled events. We would like to encourage you to be as flexible as you can to facilitate these unscheduled visits.

RASP Refractory Asthma Stratification Programme

Getting new treatments to patients: the RASP-UK Patient Input Platform

By Courtney Coleman, Asthma UK

RASP-UK has the potential to revolutionise the way severe asthma is understood and treated. Affecting around 250,000 people in the UK, we know that severe asthma has a huge impact on an individual's quality of life. Research programmes like RASP-UK are essential to understand and learn how to better tackle this debilitating condition in future.

However, we also know that new, effective treatments for severe asthma don't always reach the people who need them. The Scottish Medicines Consortium recently approved the use of a new drug, mepolizumab, for people with severe eosinophilic asthma in Scotland. However, in England the National Institute for Care and Health Excellence (NICE) has failed to provide approval, despite accepting that the treatment is innovative and has shown benefits to patients in clinical trials. This could have a knock-on effect on decisions for Wales and Northern Ireland, meaning patients could miss out on a potentially life-changing treatment.

The approval process highlights that more needs to be done to demonstrate the tangible impact that new and effective treatments can have on the quality of life of patients. Working in partnership with patients can help researchers and clinicians to optimise the design and delivery of trials, building compelling evidence for implementing new interventions in clinical practice.

RASP-UK's Patient Input Platform (PIP) has worked closely with consortium partners over the last year to ensure that the research is relevant, acceptable and feasible to people with severe asthma, and that the outcomes have the potential to impact on clinical practice.

Coordinated through Asthma UK, the PIP is formed of eight people who are affected by severe asthma. This group of dedicated and well motivated individuals bring a diverse range of experiences to our project. All PIP members are Asthma UK Research and Policy Volunteers – a network of almost 200 people who are trained and supported to work with researchers. These volunteers work on a range of projects, including setting research priorities, feeding into funding applications, and overseeing participant safety in clinical trials.

Continued...

Members of the RASP-UK Patient Input Platform at the 2015 AGM
Left to right – Frankie Gibson, Lehanne Sergison, Rebecca Adams, Val Hudson, Becky Giles

So far, the RASP-UK PIP has reviewed the clinical study protocols for each work strand, suggesting amendments to study design or additional outcome measures. For example, they recommended measuring length of hospital stay in addition to whether or not a participant is admitted. The length of a hospital stay can have a huge impact on a person's life and it's something that patients will be keen to see considered in future publications.

The PIP also worked closely with the bronchoscopy study team to refine the participant information sheets and ethical approval documentation, ensuring that the types of questions or concerns a potential participant might have are addressed up front. After reviewing the protocol for Work Strand 4's NOX4 study, the group expressed concerns over the intensity of the visiting schedule. As a result, they worked with the study leads to develop an exit questionnaire for participants to capture their experience and inform future trial design.

All of these activities help to ensure that RASP-UK's studies are patient-centred, increasing the chances of recruiting and retaining participants within the trials. It also ensures that those data on outcomes that actually matter to people with severe asthma are captured; helping to build the evidence base around quality of life which will become crucial when lobbying for new treatments to be implemented in practice.

If you'd like to know more about the PIP or would like their input, please contact Courtney Coleman at Asthma UK: ccoleman@asthma.org.uk

Work-strand 1

A prospective randomised multicentre study to optimise management of symptomatically uncontrolled asthma patients (INCA-SUn)

By Lorna Lombard and Professor Richard Costello, Royal College of Surgeons in Ireland

The INCA (Inhaler Compliance Assessment) Sun study aims to address the issue of adherence to prescribed inhaled therapy schedules in patients with severe asthma. Adherence is assessed using INCA (Inhaler Compliance Assessment) technology which was developed by the RCSI and Trinity College Dublin research teams and is being manufactured exclusively by Vitalograph, Ireland. The INCA device is an acoustic recording device that records habit of use and inhaler technique.

It has been hypothesised that it is possible to improve adherence by sharing the information collected via the INCA device with patients. We will compare this approach to patient management with generalised teaching, as suggested in the practice guidelines. In addition, with our partners in RASP-UK we will look at the relationship between adherence to therapy, biomarkers and clinical outcomes. In this way, we will get a comprehensive view of the relationship of change in the patient's clinical status and the relationship with prior adherence.

INCA
Inhaler Compliance Assessment

RCSI

HRB
Health Research Board

Work-strand 1

INCA-SUN continued…

This aspect of the programme is funded by the Health Research Board of Ireland and GlaxoSmithKline. The project is being led by Professor Richard Costello and delivered by his research team from the RCSI Clinical Research Centre, Beaumont Hospital.

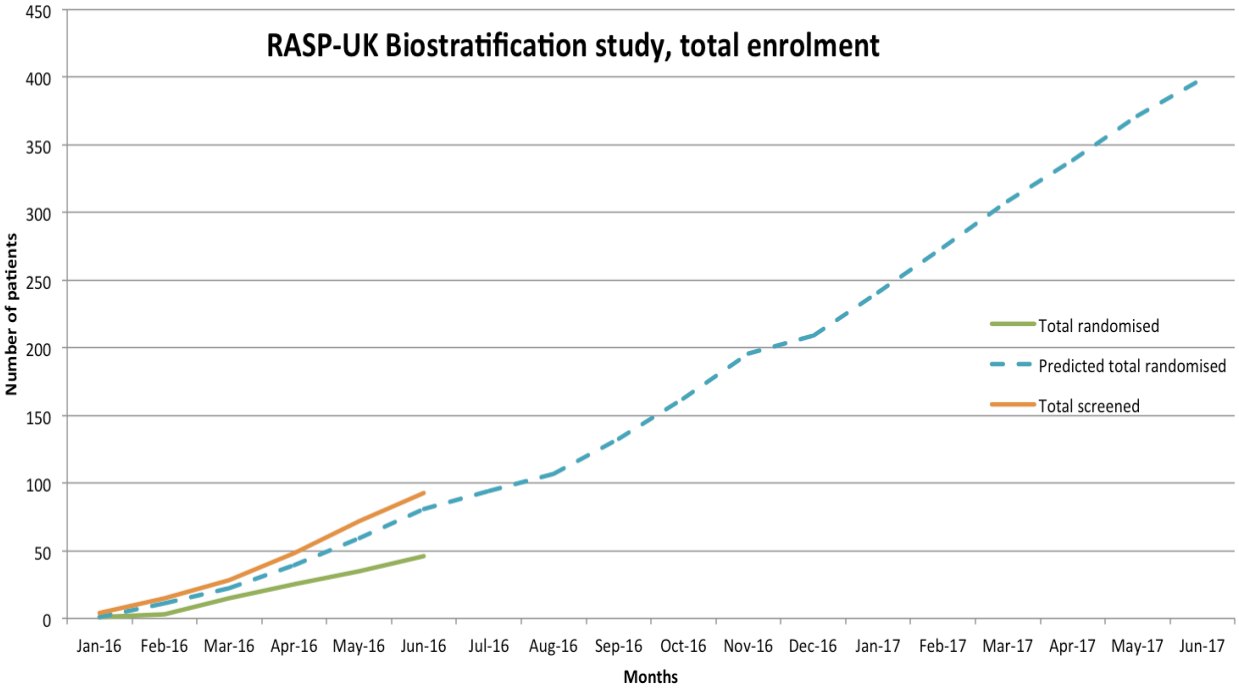
The study is being conducted in multiple centres in Dublin, Cork and Belfast, with a hope to expand to other centres in the future. The study began in November 2015 and we aim to enrol approximately 200 patients with severe asthma by February 2017. Each patient attends six study visits with a research nurse, three of which include a physician review. Data on inhaler education and feedback, quality of life questionnaires, spirometry, FeNO measurements and blood sampling are collected during the visits. To date, 24 patients have been enrolled into the study, two of which have already completed all of the study visits.

Save the date! We are planning the 2016 General Assembly Meeting - Watch this space for further information but please put Tuesday 6th December 2016 in your diaries!

Work-strand 1 Biostratification Study update

By Dr Avril Horn, Study Manager

Recruitment into the study has been slower than anticipated. We currently have 93 screened patients and 46 randomised patients in the study:



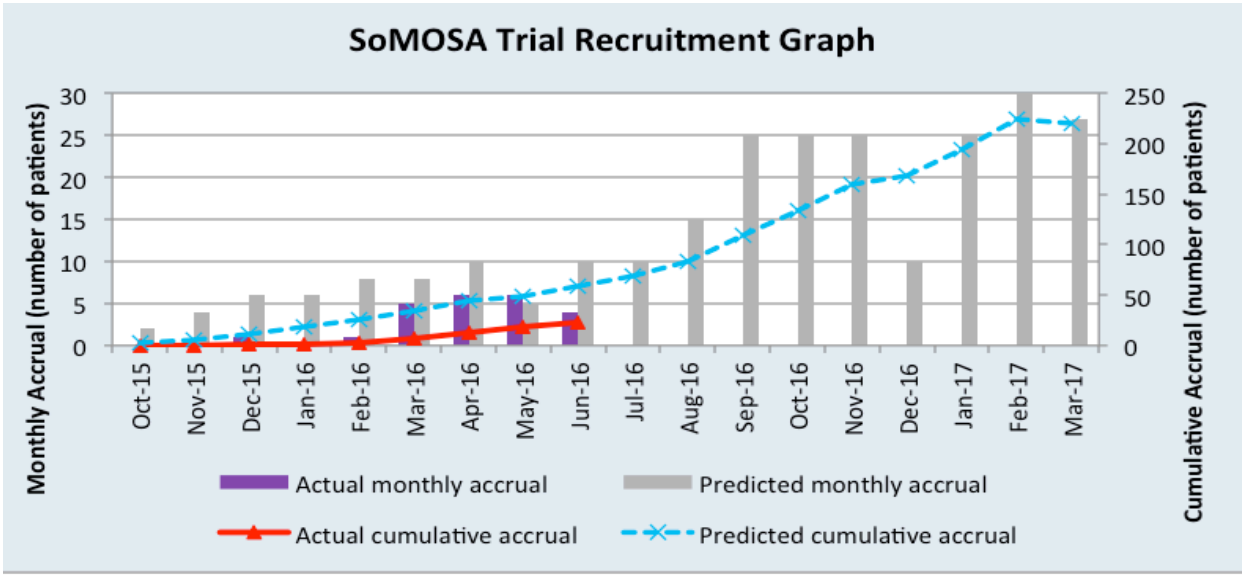
To date, our highest recruiting sites have achieved their level of success by stressing to potential candidates that the study is designed to optimise their steroid dose and minimise side effects, while maintaining control of their asthma. Another aspect of their success has been the ongoing screening of patient's notes conducted by research nurses before every asthma clinic.

We wanted to thank all of the sites for their hard work, commitment and enthusiasm to date. We also want to reiterate that if there is anything that the project team or RASP-UK Executive management team can do to assist with recruitment, then please contact Avril Horn at Niche Science & Technology Ltd (avril.horn@niche.org.uk)

Work-strand 3

SoMOSA Update

Recruitment into the study has been slower than anticipated. We currently have 23 randomised patients in the study. The Work-strand 3 team would like to thank all of the sites for their support and commitment to date.



Work-strand 2

Bronchoscopy Study Update

The bronchoscopy protocol and standard operating procedures for Work-Strand 2 has been submitted for approval.

The study is being reviewed via the new Health Research Authority approval process that brings together the assessment of governance and legal compliance, undertaken by dedicated HRA staff, with the independent Research Ethics Committee opinion provided through the UK Health Departments' Research Ethics Service. It replaces the need for local checks of legal compliance and related matters by each participating organisation in England.

There will be a virtual investigators meeting on 31st August 2016 and we are aiming to see our first patients recruited in September 2016.

RASP UK Events

- EME Discussion Meeting, Asthma UK – 4th August 2016
- WS2 Bronchoscopy Study Virtual Investigators Meeting – 31st August 2016
- SoMOSA Team Dinner, European Respiratory Society – 3rd September 2016
- Trial Steering Committee Meeting, Asthma UK – 7th September 2016
- MRC Stratified Medicine Monitoring Group Meeting – 18th November 2016

Save the date! We are planning the 2016 General Assembly Meeting - Watch this space for further information but please put Tuesday 6th December 2016 in your diaries!

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)

Newsletters

Please let us know if you would like to share any news with the RASP-UK consortium. Your suggestions or comments on the RASP-UK programme are always welcome! Simply contact Gabrielle at Niche.

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