



Refractory Asthma
Stratification Programme

August 2019

Breathe Deep: Issue 7

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

Save the date for the 2019 General Assembly Meeting - Inside

Inside:

- Highlights since the 2018 General Assembly
- Update on work-strand progress
- Upcoming Events
- Feedback from the MRC Precision Medicines 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. We've seen several of our key studies completed over the past few months and we'll share more information in this edition. As we approach the end of our fourth year of the programme, we are looking ahead to sharing the results from our various work-strands and we'll update you on how we plan to do this.



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 .

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Highlights since the 2018 General Assembly Meeting.....

- Positive feedback from the MRC Precision Medicines Group. Read more on page 8.
- WS1 Biostratification Study and WS3 SoMOSA studies complete. Read more on pages 4 and 6.
- WS4 MEX study complete. Read more on pages 6 and 7.

Update on work strand progress

Work-strand 1 INCA-SUN adherence intervention study

By Joanne Walsh, Research Nurse

The INCA-SUN team have been actively screening and recruiting patients for the INCA Sun Study across six sites. The study aims to recruit 220 patients in total. To date they have successfully enrolled a total of 174 patients, of which 135 patients have completed the eight month INCA Sun Study. The breakdown of this recruitment figure is as follows:

Site	Number Recruited	Number Complete
Beaumont Hospital	117	97
Belfast City Hospital	12	8
Connolly Memorial Hospital	14	8
Cork University Hospital	20	14
Craigavon Hospital	3	0
St. Vincent's University Hospital	8	8

In 2018 the team secured additional funding from the Cross-border Healthcare Intervention Trials in Ireland Network (CHITIN): <http://www.research.hscni.net/cross-border-healthcare-intervention-trials-ireland-network-chitin-0>). Since the 2018 General Assembly meeting, three sites have been identified using this initiative: the study is up and running at Craigavon Hospital. Cavan & Our Lady of Lourdes Hospital Drogheda have been initiated and are starting to identify patients. Altnagelvin Hospital is working towards initiation.

In addition the team have opened a site at Guys & Thomas Hospital where the team are now starting to identify patients.

Recruitment to the study is due to continue until December 19 and last patient, last visit is expected in September 20. The team hope to achieve data base lock in December 20 and the final outcome of study is expected in December 21.

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 (cont.)

GSK Connected Inhaler Study

At the 2018 General Assembly Meeting, Alison Moore from GSK gave an overview of the connected inhaler system study. The study, which assesses the impact of feeding information back to health care professionals in addition to patients and feeding back data on maintenance medication or maintenance as well as rescue medication, is now complete. The study management team have had a late breaker abstract accepted for the ERS 19 meeting.



Alison Moore, GSK

Work-strand 1: Biostratification Study

By Dr Avril Horn, Work- Strand 1 Project Manager

The biostratification study was initiated in December 15, and our first patient was randomised on 25 January 16 in Belfast. Our last patient was randomised on 12 July 18 in Oxford. It has taken many hours of effort by site staff, and patients, to bring us to the major milestone of database lock, due on 13 September 19.



As with all clinical research projects, there is a data cleaning stage to ensure that conventions have been applied consistently across sites. Thank you to all of our site staff for your prompt attention to the queries generated as a result of this process, and for bearing with our pleading E:mails as the timeline shortened. The study statistician, John Busby, has really appreciated the effort that has gone in to reviews of steroid dosing, exacerbations and adverse events. By the time you read this, we anticipate that we will be down to the last few queries, and that your inboxes will contain fewer and fewer mails from @niche.org.

The monitoring team at Niche thank you all for your help as we came up to speed on the many combinations of steroid therapy that patients used during the study. We are now much better versed in inhaler technology and on steroid equivalence.

We are all looking forward to seeing the results of the study and improving the lives of patients with severe asthma and we look forward to sharing the results with you in due course.

Update on work strand progress (cont.)

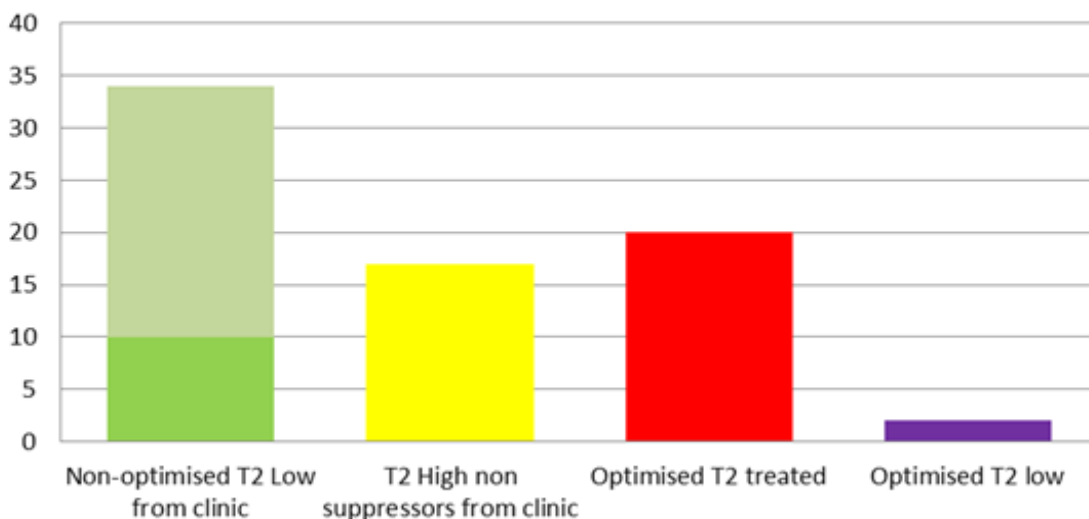
Work-strand 2: Bronchoscopy Study

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

Forty-nine patients have completed bronchoscopy to date. We have an additional 24 non-optimised T2 (biomarker)-low biopsies collected with an identical SOP from Genentech/Roche, Southampton and Leicester (legacy samples) which will form part of our non-optimised T2-Low group. We are aiming to recruit a further six patients into this non-optimised T2-Low group and three into the T2 High non-suppressors from clinic. Recruitment will end in October 19 and we are hoping to lock our database in early 2020.



Recruitment including legacy samples



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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

I am delighted to inform you that the last patient in the SoMOSA study completed their one year treatment in May 19. The programme started with the first patient enrolled in Southampton and also finished in Southampton



I want to thank all the PIs and their teams for seeing this study through. It was a complex study and, therefore, difficult to deliver. This is a pioneer study, with much uncharted waters to sail through, providing the ultimate test for the U-BIOPRED biomarkers. Many thanks to Novartis for trusting us.

Last but not most of all, a big thank you to all the patients who participated in the study. We hope this project will advance our knowledge of severe asthma and biologic treatments.

We hope to share with you soon the omics data which are in the final stage of analysis.

Work-strand 4 Progress Update

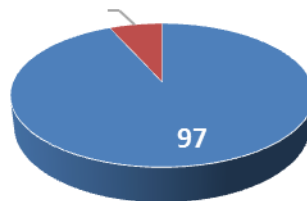
By Rekha Chaudhuri

Work-strand 4 had no pre-specified studies when we started the programme. We now have 3 projects included in this work-strand.

1. The first study in this work-strand was **MEX – a study of exacerbation events in patients receiving mepolizumab treatment**. This study was conducted at four sites and sponsored by Queen's University, Belfast; CI: Liam Heaney and managed by Jane McDowell (research fellow, Belfast). The study closed on 29 May 19, after successfully recruiting 146 patients (Glasgow 46, Belfast 41, Leicester 33, Oxford 26) and a total of 107 exacerbation events studied on mepolizumab (104 prior to steroids, 97 prior to steroids/antibiotics). The study data is now being reviewed and samples being sent for analysis. No results are available as yet, but we hope to be able to share some results later this year.

Update on work strand progress (cont.)

**Mepolizumab exacerbation study:
Exacerbations assessed prior to commencing oral
steroids (n=104).**

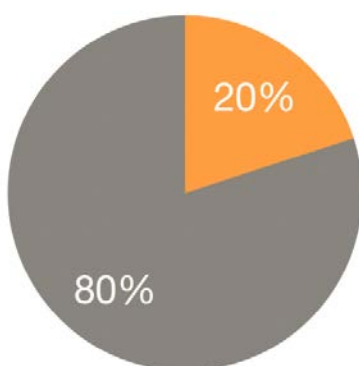


■ Exacerbations assessed pre-treatment
■ Exacerbations assessed after commencing antibiotics only

2. The second study to get approval was MAPLE – a study of the additional effect of 14 days high dose oral corticosteroid compared to placebo in patients established on mepolizumab therapy. In this study participants are randomised after being treated with mepolizumab for at least three months to receive two weeks of prednisolone and placebo in a crossover fashion.

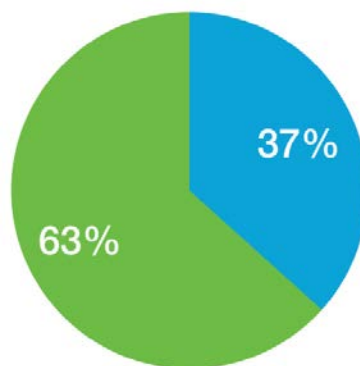
The study is being conducted at four sites. The sponsor is Greater Glasgow and Clyde NHS Board, PI Rekha Chaudhuri and study is managed by Freda Yang (Glasgow asthma research fellow). Target recruitment is 30 and the study currently has 24 enrolled (Glasgow 17, Oxford 3, Leicester 3, Belfast 1); 17 randomised overall and 6 completed. The plan is to end the study by November 19. Vanessa Brown from Belfast is the lead for lab kits and bio-banking of study samples and John Busby is the study statistician. Early results are expected by February 20.

Recruitment



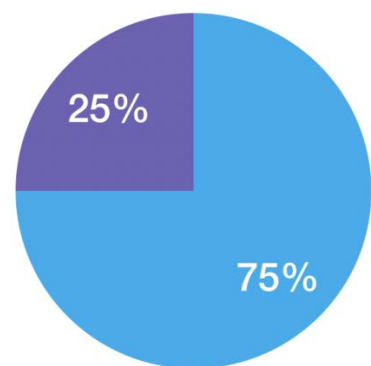
● Needed
● Recruited

Randomisation



● Needed
● Randomised

Completed



● Needed
● Completed

Update on work strand progress (cont.)

3. The last study in work-strand 4 is BenRex – a study of exacerbation events while on benralizumab treatment. This study will also collect data on outcomes and predictors of response with benralizumab treatment and a comparison of different assessment tools of asthma control and quality of life.

The study is sponsored by Greater Glasgow and Clyde Health Board and funded by AstraZeneca (CI Rekha Chaudhuri). Drug supply for 150 participants will be provided by AZ. The study is due to start by end of August 19. MHRA and ethics approvals are in place and final contracts with AZ are being signed. This will be followed by individual site contracts and approvals. Fourteen sites will participate in BenRex from across the UK.



Feedback from the MRC Precision Medicines Group



RASP-UK underwent its latest progress review by the MRC on 08 May 19. As the consortium was judged to be on target in the Nov 18 review, we were only required to submit a progress report to the committee. The feedback from the meeting was succinct and positive:

‘The Precision Medicine Group thanked the Team for their written report. The Group congratulated the consortium on their success in attracting funding from the Innovative Medicines Initiative (IMI)’.

All of the reports we submit to the MRC are available to partners on the RASP-UK website. Our next review will be held on 27 Nov 19.

Publications

The consortium has had the following published in 2019:

Remotely monitored therapy and nitric oxide suppression identifies non-adherence in severe asthma [https://www.jacionline.org/article/S0091-6749\(18\)31662-2/fulltext#sec3](https://www.jacionline.org/article/S0091-6749(18)31662-2/fulltext#sec3)

For details of all publications linked to the programme please visit our news section on the RASP-UK Website.

Upcoming RASP Events

Next Trial Steering Committee Meeting – **17th October 19**

MRC Precision Medicines Group Review – **27th November 19**

RASP-UK 2017 General Assembly Meeting – **3rd December 19**

We are hoping to share the results of our analysis of the WS1 Biostratification study primary endpoint in October 19. We will provide more information over the next few weeks.

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)

RASP on Twitter

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