Phone: +44 123 967855
Email: info@isaregistries.org
Address: 5 Coles Lane Oakington Cambridgeshire CB24 3BA

ERS2021 e-Poster live discussion, 5th September 2021, 13:15 - 14:15 (CEST)
Session: Severe asthma: evaluation using patient-reported outcome measures (PROMs) and biomarkers, comorbidities and treatments

Recording link: https://drive.google.com/file/d/1WeZiAvQXSzpOOKgtbhOZj-rF5mSSMCbY/view?usp=sharing

ISAR FIRE e-Poster

Time Stamp: 39:00

Discussion Question 1:

- What is the justification for the use of anti-IgE – despite it being half as effective than other biologics, costing twice as much, and without any predictive biomarkers?
- The audience would be interested in the abstract looking into both severity of patients getting anti-IL5 (patients on anti-IL5 tended to be more severe) and the response to the treatment.

Responses:

- **Nasloon:** ISAR has a lot of anti-IgE patients, but we were specifically looking into the group who were eligible for both anti-IgE and anti-IL5. Even though anti-IL5 had more severe symptoms at baseline, we looked at patients who were comparable between these two biologics groups at baseline and then try to see how their outcomes were post therapy (at least 24 weeks after being on biologics).
    - It was noticed that amongst patients eligible for both biologics (anti-IgE and anti-IL5), anti-IL5 patients tended to have a lower incidence rate of exacerbations. While both biologics tended to have better outcomes post-therapy, they perform better in terms of having new incidences of exacerbations.
- **David:** Patients with anti-IgE did very well with both biologics. But anti-IL5 is more effective, not twice as effective (as suggested by the host), but there was an edge for anti-IL5.

Discussion Question 2:

It is still surprising that there is still a market for anti-IgE due to weight-based dosing and the requirement for allergy and serum IgE levels which are not shown to be predictive biomarkers.

Responses:

- **Renaud Louis:** Anti-IgE is a very good anti-allergic drug, but it is not very good for severe asthma because it has become clearer that the IgE-mediated process is not strongly linked to the severity of asthma. Anti-IgE is a valid drug, but it should be replaced in the market toward different types of disease. **Host response:** William Busse's study[1] published in the *New England Journal of Medicine,* shown very good outcomes in young adolescents during the full asthma period.

- **Andrew Menzies-Gow:** Omalizumab was the first biologic, hence people have learnt from their mistakes in terms of drug development. ISAR looks around the world and in some countries, not all 5 biologics are available. Hence, there will be issues when potentially comparing dupilumab with omalizumab.
    - If all drugs are not available, omalizumab does have a place – however its place is smaller than it used to be. ISAR very important in that point of view.
    - It has been learnt from ISAR that people tend to stay on the first biologic they are put on, which can be an issue. Super-responders, medium-responders and no-responders were mentioned, and we should think of looking at switching biologics for individuals who are not super-responders particularly to older biologics like anti-IgE.

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- **Aten Brinke (Dutch):** As soon as other biologics are available, it is noticed that the starting of Omalizumab will go down, but there is still a large proportion of patients who are happy with starting Omalizumab 15 years ago.
    - Doubt whether they could handle without because several of these patients' have started biologics at the period where biologics were not secure in defining "what is a severe asthma patient" and a strict criterion.
    - There are many patients around our country and in several countries that are on Omalizumab. They might do very well without, or if they went wrong, then they might do better with another biologic.
- **Angira Dasgupta:** Comparison between two anti-IL5 (Benralizumab and Mepolizumab) is not heard in the literature.
  Host response: Benralizumab will reduce eosinophils to a lower level and more quickly than Mepolizumab. Will this translate to a disadvantage or are people still convinced they are roughly the same?

- **Aten Brinke:** Both biologics are roughly the same and there may be more opportunities for quickly acting Benralizumab, if used in an exacerbation setting.
  Host response: Supportive of what has been mentioned however data is required. Patients who present with acute severe asthma, with a peak flow of 30% predicted respiratory failure and eosinophilic count of 600, nearly died as a result of a biological process (type 2 airway inflammation). Our strategy is to suppress it for 5 days with Prednisolone and let it come back. Imagine a young person that has nearly died from a highly treatable biological process (type 2 airway inflammation) – can you imagine the cardiologist being happy with that? It does make a lot of sense to give something that will suppress that process for a reasonable period of time (in particular Benralizumab would). There is an ongoing clinical trial looking at Benralizumab as an alternative/adjunct to prednisolone in acute eosinophilic asthma.

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ISAR BEAM e-Poster

Time Stamp: 49:33

Discussion question 1:

- **Dr Renaud Louis:** We did an open-label extension of the ANDHI[2] study to reduce background medications of patients and investigate if GINA step reduction can be achieved in patients receiving Benralizumab versus control. The main findings were that almost half of patients had significant reduction in background treatments, and around half of patients who were using OCS as chronic maintenance treatment and stopped OCS use maintained good asthma control. This shows it is possible to reduce background medication such as OCS in patients receiving Benralizumab.
- Dr Perez de Llano, you had an abstract on baseline characteristics of people with oral steroids dependent asthma. I'd be very interested in hearing your response to study mentioned by Dr Renaud.

Responses:

- **Luis Perez de Llano (Group chat comments)**: We can rescue patients with Benralizumab and prior failure to mepolizumab, but the opposite has not been shown.
- **Luis Perez de Llano:** There is quite a large difference between Benralizumab and Mepolizumab, as we can rescue patients who fail with Mepolizumab by switching to Benralizumab. The opposite has not been shown. I am not aware of patients who fail with Benralizumab and improve after switching to Mepolizumab. That is a very important point. In some patients on mepolizumab there is some persistent eosinophilic inflammation in the airways, which is not the case in patients who fail Benralizumab treatment.
  Host response: When it comes to withdrawing background treatment, Benralizumab might be more successful. What was mentioned by Luis may well be correct, but we do not have good solid data. Mepolizumab came before Benralizumab and there is a lot of people swapping that way and not the other way. Patients who are not achieving super-responders' status on Mepolizumab and are keen to swap, should be offered the opportunity of being randomised in a double-blind fashion to swapping to Benralizumab or continuing on Mepolizumab. We can look at predictors – persistent eosinophilic airway inflammation might identify people who will do well with Benralizumab; however, this needs to be demonstrated.

Discussion question 2:

Tell us about your baseline data in severe asthma.

Responses:

- **Luis Perez de Llano:** This study is the first step to find and characterise responders to biologics and it aims to describe baseline characteristics of severe asthma patients initiating biologic treatment. This is part of another initiative of the BEAM study to classify responders to biologic treatment by clinical and functional endpoints and describe their characteristics overall by their biologic class.
  - This is a snapshot of the baseline condition of the patients included in this study. In this study, only patients who receive anti-IL5 or Omalizumab were included (just anti-IL5 or anti-IgE).

  Host response: Existing literature has shown that patients with oral steroid-dependent severe asthma had greater disease severity and had increased eosinophilic airway inflammation noticed from bronchial biopsy. Is that a routine part of your assessment of these severe patients?

- **Luis Perez de Llano:** In my clinical practice, bronchoscopy is not performed to all severe asthma patients starting biologics, only just in case they suspect, for instance a chronic infection. Bronchoscopy is performed in many patients who fail with biologics because the reason for failure is an infection as we have diagnosed pneumocystis pneumonia in patients treated with Benralizumab. Thus, it is crucial to rule out ongoing infections in patients who fail to respond.
  Host response: Pneumocystis link to oral steroids use or suggesting Benralizumab might have been.
  Luis: Yes, Benralizumab plus oral corticosteroids.

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- **Vitina:** It is crucial to process inflammatory pathway that can characterise this condition (severe asthma), for example OCS-dependent asthma.
    - Despite T2 high inflammation, these patients did not respond to oral corticosteroids. This could be addressed with alternative therapy, for example using biologics that is more effective and efficient for these patients.

ISAR GLITTER e-Poster

Time Stamp: 55:25

Discussion question 1:

Many patients are supposed to be on biologics but are not getting the opportunity, is that a correct interpretation?

Responses:

- **Wenjia:** This study uses the same ISAR cohort as the BEAM study but focused on a more restricted subgroup who had high exposure to OCS – either remaining on long term OCS for one year or had at least 4 times of rescue OCS used in the past 12 months. Even in this subgroup of patients who required biologics, 1/3 of them still did not receive biologics.
    - There is great variation across geographical areas with regards to the initiation of biologics. Additionally, the findings were consistent with the previous findings in BEAM, that those who decided to initiate biologics was a step up to high exposure to OCS and those who initiated biologics in addition to country variation were more likely to be eosinophilic, allergic, and tend to be more severe.

  Host response: We need to think of strategies for reaching these patients that are not getting the opportunity to consider biologics. If we are giving the right person these drugs, we will clearly have a big impact.

- **Aten Brinke:** Another abstract also presented at ERS checked for the cumulative OCS dose in two years prior to starting anti-IL5 and the following two years. It was noticed that patients most successful in reducing and stopping OCS after anti-IL5 were the ones with the shortest period of time with OCS prior to starting anti-IL5.
  Host response: They didn't have many people [with airway] remodelling?

- **Aten Brinke:** I think so. All factors may have influenced that, but it should be earlier.
  Host response: That's probably another area where we need more data to make the case that you accumulate a burden over time, and try to quantify that:
    - To determine how much of that could be linked to the treatable trait (type 2 airway inflammation)
    - To determine how much might be due to medication that is used to treat other factors.

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References

1. Busse WW, Morgan WJ, Gergen PJ, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. N Engl J Med. 2011 Mar 17;364(11):1005-15. doi: 10.1056/NEJMoa1009705.
2. Harrison TW, et al. ANDHI study investigators. Onset of effect and impact on health-related quality of life, exacerbation rate, lung function, and nasal polyposis symptoms for patients with severe eosinophilic asthma treated with Benralizumab (ANDHI): a randomised, controlled, phase 3b trial. *Lancet Respir Med 2021*;9(3):260-274