Association between pre-biologic T2-biomarker combinations and response to biologics in patients with severe asthma (IGNITE)

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Aim and Methods

Rationale

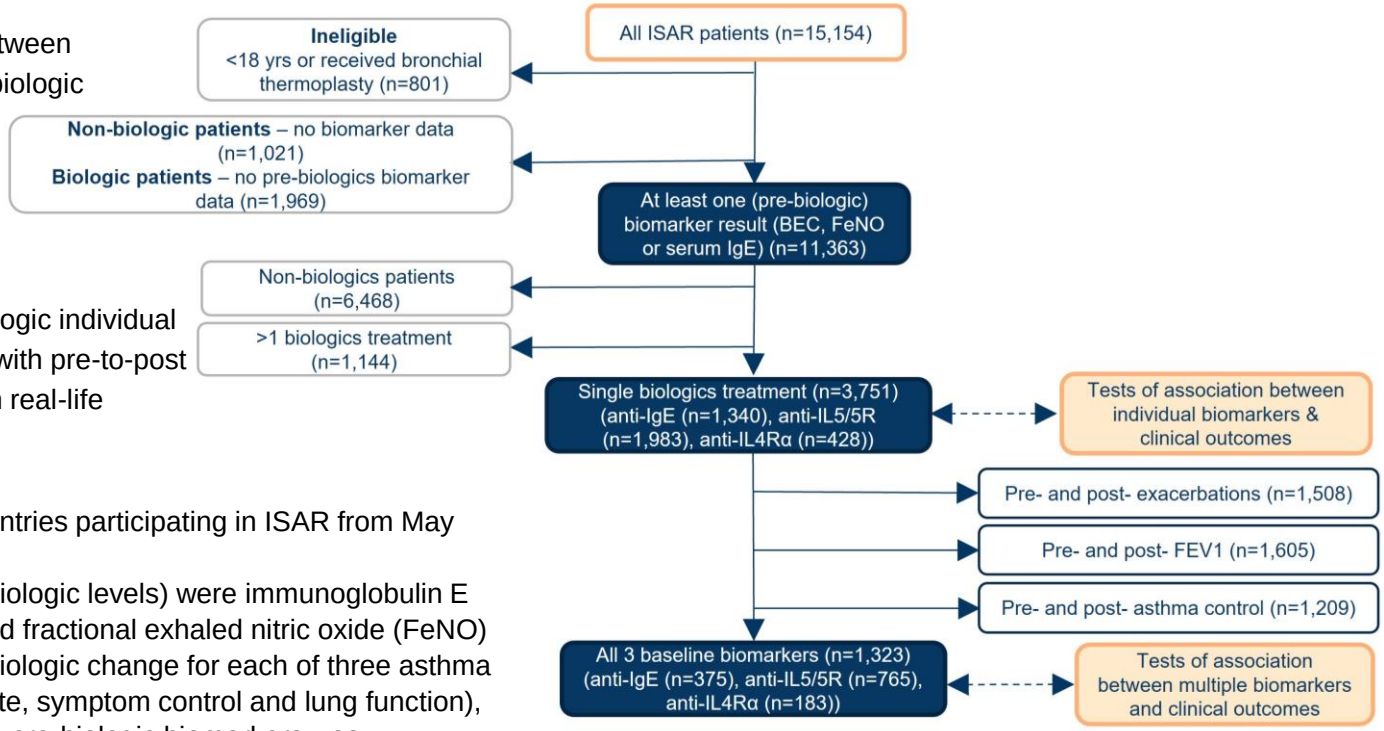
Studies investigating the association between pre-biologic biomarker levels and post-biologic outcomes have been limited to single biomarkers and assessment of biologic efficacy from structured clinical trials

Objective

To elucidate the associations of pre-biologic individual biomarker levels or their combinations with pre-to-post biologic changes in asthma outcomes in real-life

Methods

- Cohort study using data across 23 countries participating in ISAR from May 2017 to February 2023.
- Investigated biomarkers (highest pre-biologic levels) were immunoglobulin E (IgE), blood eosinophil count (BEC) and fractional exhaled nitric oxide (FeNO)
- Pre- to approximately 12-month post-biologic change for each of three asthma outcome domains (i.e. exacerbation rate, symptom control and lung function), and the association of this change with pre-biologic biomarkers was investigated for individual and combined biomarkers



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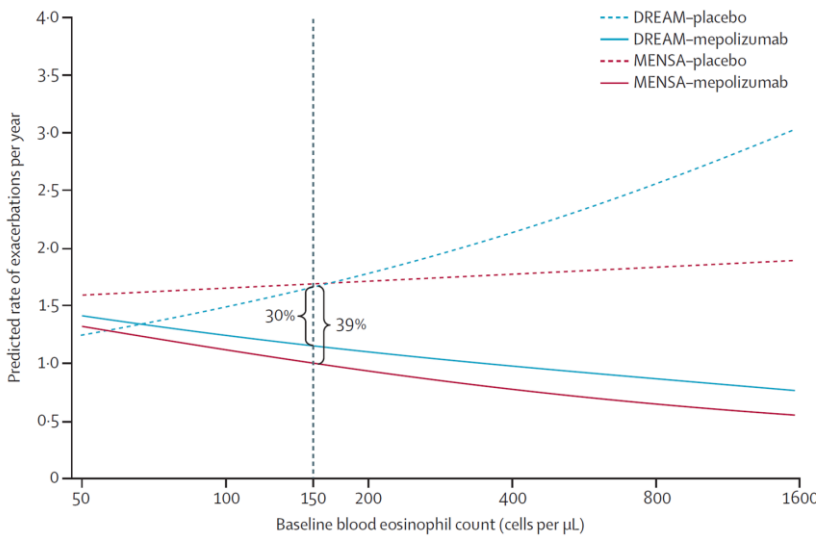
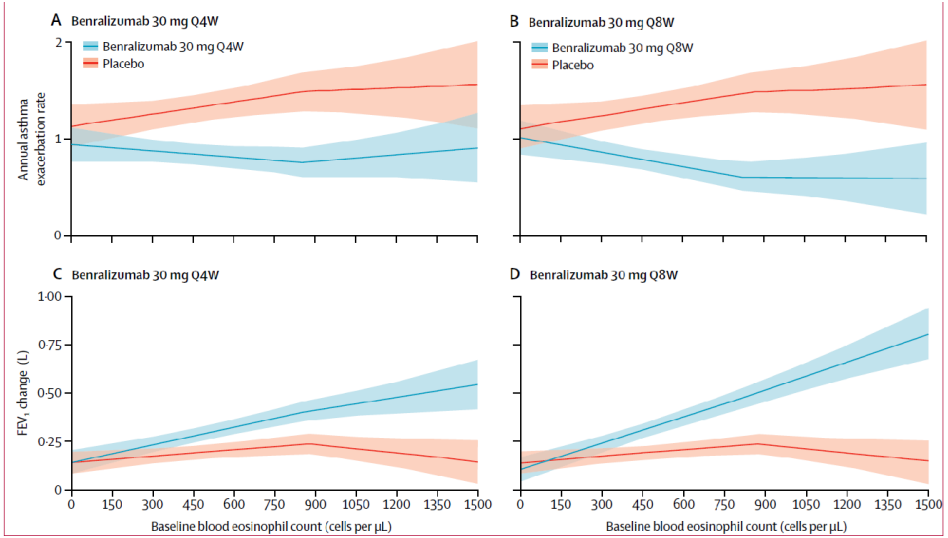
ISAR: International Severe Asthma Registry, Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R, Anti-IL4: Anti-Interleukin 4, FEV1: Forced Expiratory Volume 1 second, FeNO: Fractional exhaled Nitric Oxide, BEC: Blood Eosinophil Count

What is already known? Background and rationale:

BEC predicts less exacerbations with biologics than placebo but little dose response within the active arm

Response to Anti-IL5 Treatment According to Blood Eosinophil Count (evidence from clinical trials)





SIROCCO/CALIMA: Response to Benralizumab Treatment According to Blood Eosinophil Count[2]

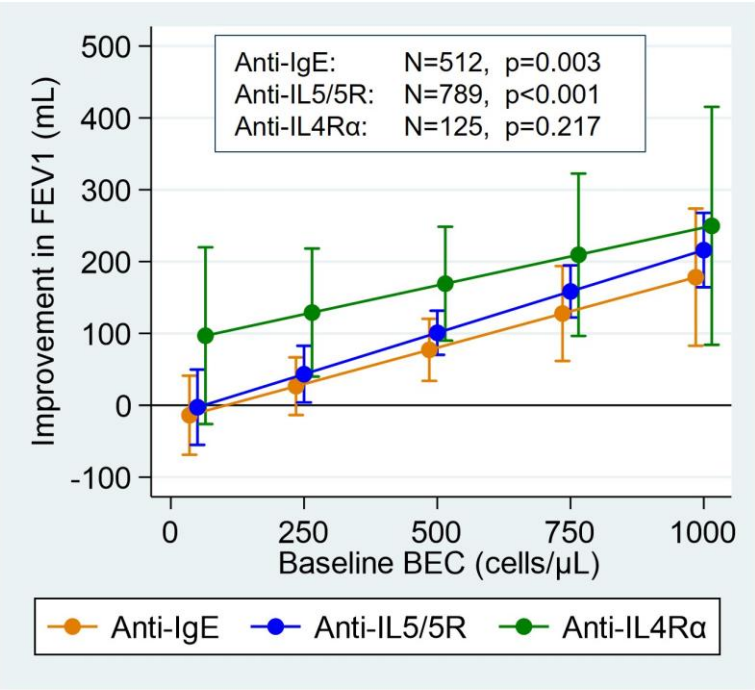
Low association between BEC and exacerbations has been seen in clinical trials of anti-IL5 treatments

Ortega HG, et al. Lancet Respir Med 2016;4(7):549-556
FitzGerald JM, Goldman M, et al. Lancet Respir Med 2018;6(1):51-64

Anti-IL5/5R: Anti-Interleukin 5/5R, BEC: Blood Eosinophil Count

BEC and FeNO significantly associated with degree of lung function improvement following treatment with anti-IL5/5R or anti-IgE biologics

Association between improvement in FEV_1 and highest pre-biologic blood eosinophil count



- **Patients with the highest pre-biologic levels (1000 cells/μL BEC and 100 ppb FeNO) achieved mean improvements of approximately 200 mL in FEV_1**
- **Patients with the lowest levels (<250 cells/μL BEC and <25 ppb FeNO) achieved less than a third of the mean improvement in FEV_1**

Using a combination of pre-biologic BEC + FeNO combined gave a marginal improvement in prediction of FEV1 reduction but probably not of clinical significance.

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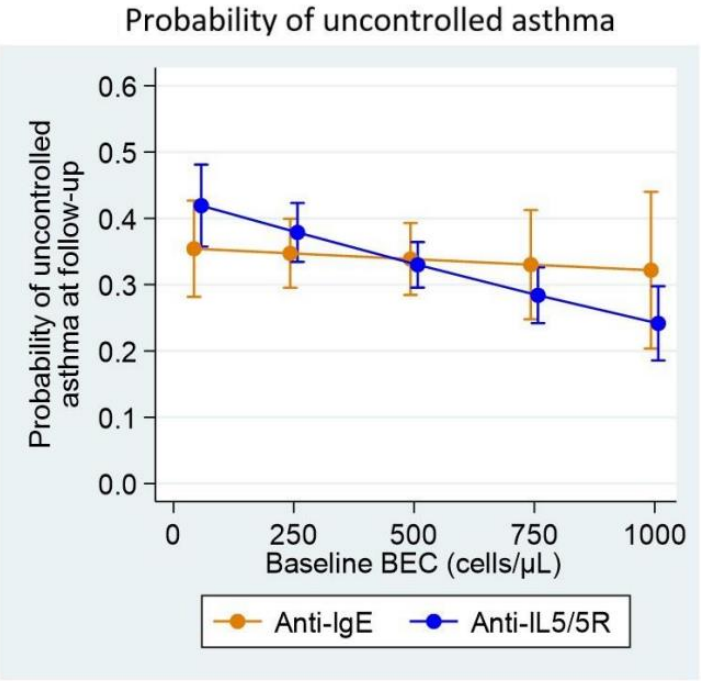
Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R, Anti-IL4: Anti-Interleukin 4, FEV1: Forced Expiratory Volume 1 second, BEC: Blood Eosinophil Count,, FeNO: Fractional exhaled Nitric Oxide

BEC associated with greater asthma control for patients receiving anti-IL5/5R



- Patients with pre-biologic BEC of 1000 cells/µL had a 24% probability of uncontrolled asthma after one year (reduced from 68% before treatment) with anti-IL5/5R treatment
- For patients with a pre-biologic BEC level of 50 cells/µL this was only reduced to 42%
- The improvement in control was consistent across different pre-biologic BEC levels with anti-IgE

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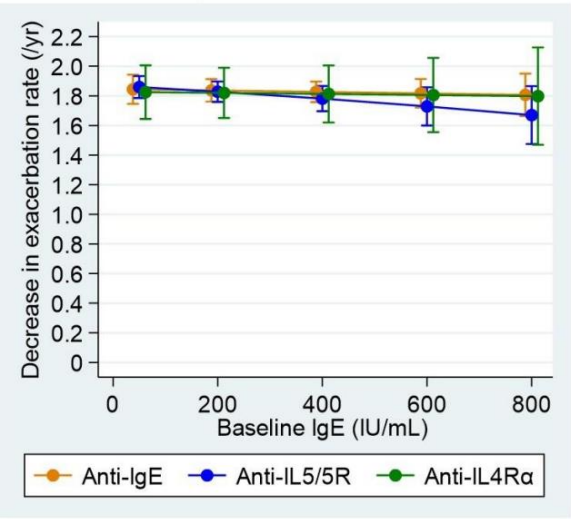
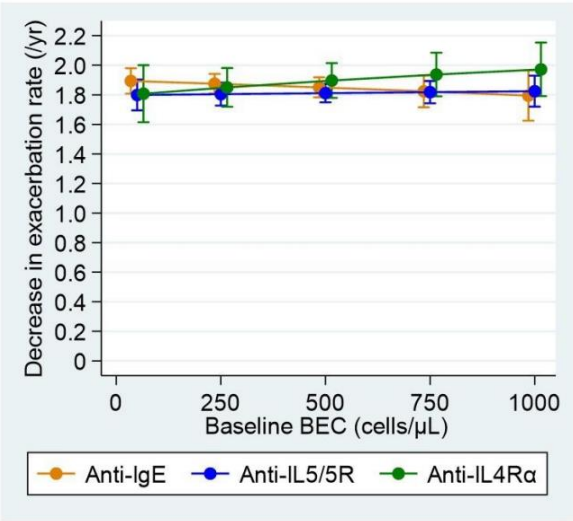
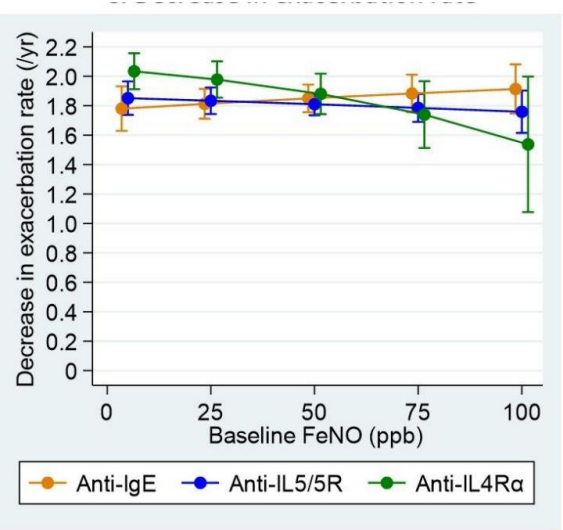
Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R, BEC: Blood Eosinophil Count

Pre-biologic biomarkers not strongly associated with the extent of pre- to post-therapy reduction in exacerbations

Decrease in exacerbation rates:







Most patients in the study achieved a marked decrease one year after initiating any of the biologic treatments studied (anti-IgE, anti-IL5/5R or anti-IL4Rα) irrespective of pre-biologic biomarker levels

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Summary
IGNITE: BEC and FeNO predict effectiveness of biologic therapies in Severe Asthma

BEC and FeNO significantly associated with degree of lung function improvement following treatment with anti-IL5/5R or anti-IgE biologics

BEC associated with greater asthma control for patients receiving anti-IL5/5R

Pre-biologic biomarkers not strongly associated with the extent of pre- to post-therapy reduction in **exacerbations**

Using **BEC and FeNO as biomarkers can give insight** into **which severe asthma patients will benefit most** from treatment with biologics

The ability of higher baseline BEC, FeNO and their combination to predict biologic associated lung function improvement highlights **opportunity for earlier intervention in patients with impaired lung function or at risk of accelerated lung function decline**

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