Poster #1897

Real-world associations between baseline biomarkers and clinical outcomes in severe asthma patients treated with biologics

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Introduction

- Clinical trial evidence suggests biologic efficacy vs placebo is related to biomarkers[1-4], but their value when selecting treatments in real-world clinical practice is unclear.
- Different classes of biologics have different modes of action, so biomarkers (individually or in combination) may help discriminate which biologic class a patient would be expected to benefit from most.
- The International Severe Asthma Registry (ISAR) collects data from 23 countries and provides an unequalled opportunity to study associations between biomarkers and clinical outcomes in clinical practice.

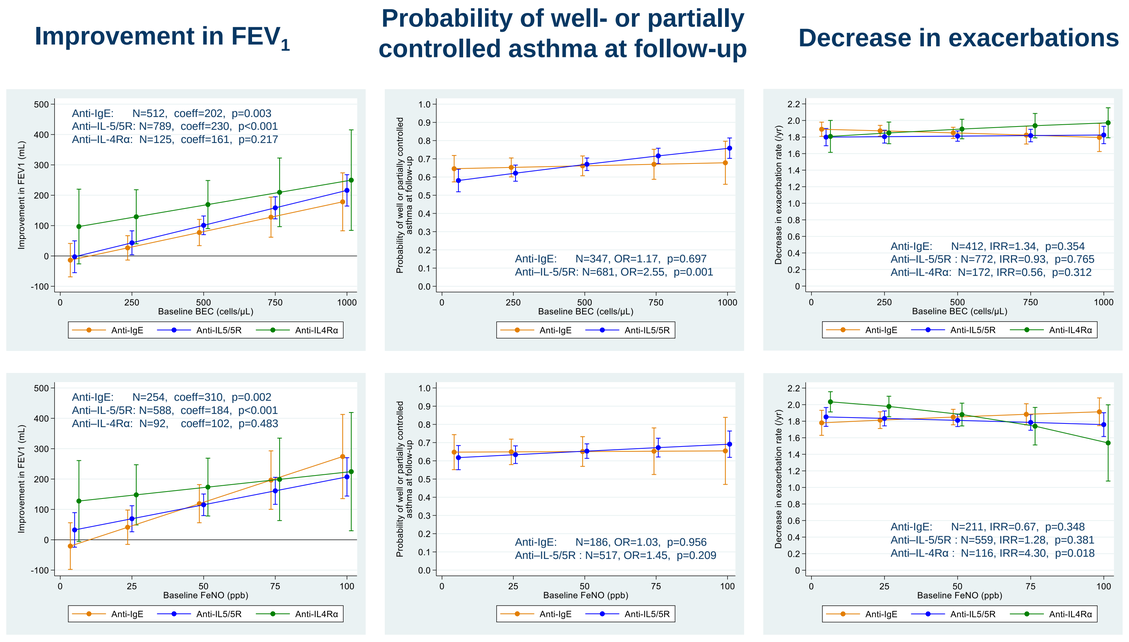
Aim

- To determine if pre-biologic measurements of biomarkers (blood eosinophil count [BEC], fractional exhaled nitric oxide [FeNO] and total immunoglobulin-E [IgE]) were associated with clinical outcomes in severe asthma patients following treatment with anti–IL-5/5R, anti–IL-4Rα or anti-IgE biologics in real-world settings.

Methods

- ISAR patients aged ≥18 years with pre-biologic data available on biomarkers (BEC, FeNO or IgE) and outcome data before and after biologic initiation (FEV_1, asthma control, or exacerbation rates) were evaluated.
- Associations between highest pre-biologic (baseline) biomarker levels and outcomes one year after biologic initiation were examined using regression models, adjusting for baseline measurement of relevant outcome.
- Linear regression was used for FEV_1, logistic regression for asthma control, and negative binomial regression for exacerbation rates.
- Adjusted predictions from the models were presented graphically for mean baseline level of FEV_1 or exacerbations and, for asthma control, for a population with same proportion of well- or partially controlled asthma as for biologic patients in ISAR.
- Potential benefit of including multiple biomarkers to predict the outcomes was investigated by adding additional biomarkers to the models and testing for an improvement in model fit using likelihood ratio tests.

Figure. Associations between highest pre-biologic biomarker levels and clinical outcomes one year after biologic initiation



FEV_1 – Graphs show point estimates from the regression models of the change in FEV_1 compared to baseline for a patient with baseline FEV_1 = 2.1 L (mean baseline FEV_1 for the biologic patients in ISAR). Coefficients are the estimated increase in follow-up FEV_1 (mL) per 1000 cells/µL (BEC) or per 100 ppb (FeNO).
Asthma control – Graphs show point estimates from the regression models of the probability of well- or partially controlled asthma (vs uncontrolled asthma) with each biologic class for a population with 32% of patients with well- or partially controlled asthma at baseline (overall proportion in biologic patients in ISAR). Insufficient patients on anti–IL-4Rα with this outcome were available. Odds ratios (OR) are for the estimated change in odds of well- or partially controlled asthma at follow-up per 1000 cells/µL (BEC) or per 100 ppb (FeNO).
Exacerbation rates – Graphs show point estimates from the regression models of the change in exacerbation rate compared to baseline for a patient with baseline exacerbation rate = 2.2 per year (mean baseline exacerbation rate for the biologic patients in ISAR). Incidence rate ratios (IRR) are for the estimated change in incidence rate of exacerbations (/yr) at follow-up per 1000 cells/µL (BEC) or per 100 ppb (FeNO).
P-values are for tests of association between the outcomes after treatment and baseline levels of the biomarkers (adjusted for baseline level of the outcome).

Table. Comparison of model fit using different combinations of baseline FEV_1, BEC and FeNO to predict FEV_1 one year after biologic initiation

	Predictors in the model			
	Baseline FEV_1 only	Baseline FEV_1 + BEC	Baseline FEV_1 + FeNO	Baseline FEV_1 + BEC + FeNO
Adjusted R^2	0.737	0.747	0.743	0.751
P-value‡		<0.001	<0.001	0.005
				<0.001

‡ P-value for likelihood ratio test comparing the fit of the models

Results

- Higher baseline BEC and FeNO were associated with greater post-treatment improvement in FEV_1 with both anti-IgE and anti–IL-5/5R.
- Higher baseline BEC was also associated with greater odds of well or partially controlled asthma with anti–IL-5/5R.
- Baseline total IgE showed little association with FEV_1 or asthma control for any biologic class (p>0.40 in all cases).
- Follow-up exacerbation rates varied little across the ranges of the biomarkers though there was a statistically significant association in anti–IL-4Rα patients, with greatest decreases in exacerbations seen amongst patients with low FeNO. Baseline IgE showed a significant association with exacerbation rates in anti–IL-5/5R patients (p=0.047), although the effect was small (at baseline IgE=50 IU/mL estimated decrease in annual exacerbations=1.86; at baseline IgE=800 IU/mL estimated decrease in exacerbations=1.67).
- A combination of BEC and FeNO gave statistically significant improvement in regression model fit to predict follow-up FEV_1 (Table). No other combinations of biomarkers improved model fit.

Conclusions

- These results from ISAR support the use of BEC and FeNO to help identify patients who will benefit most from biologics in real-world clinical practice. Combinations of biomarkers (such as BEC and FeNO) may also be useful when selecting the best treatment for patients.

References

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Disclosures

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