Real-world evidence of improved patient outcomes with reslizumab in adults with severe eosinophilic asthma (SEA)

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RATIONALE AND AIMS

- Reslizumab is an IgG4 kappa humanized monoclonal antibody targeting interleukin-5, to disrupt the maturation, activation, and survival of eosinophils.[1]
- Reslizumab was approved in the U.S. and internationally as add-on maintenance therapy for adult patients with severe eosinophilic asthma based on two Phase 3 clinical trials, which demonstrated that intravenous (IV) reslizumab 3 mg/kg once every 4 weeks was associated with a significant improvements in asthma control, lung function, quality of life, and reduction in the risk of clinical asthma exacerbations (CAEs) in patients with inadequately controlled eosinophilic asthma, and a history of asthma exacerbations.[2–4]
- Real-world evidence is becoming increasingly important to inform prescribers and healthcare decision makers about the effectiveness of reslizumab in daily practice. This study aimed to examine outcomes associated with reslizumab treatment in a sample of patients from U.S. clinical practice.

METHODS

Study design and patients

- Multicenter, observational, retrospective chart review conducted to collect patient level data on reslizumab-naïve adults with severe eosinophilic asthma treated with reslizumab ≥7 months in U.S. clinical practice, not as part of a clinical trial, and with 6 months data available prior to the index date (date of reslizumab initiation).

Outcome measures

- The primary outcome was proportion of patients responding to reslizumab, assessed using a 4-category composite measure designed by clinical experts to categorize patients into mutually exclusive and exhaustive groups **(Table 1)**.
- Other outcomes assessed, pre- and post-reslizumab initiation, included:
  - Patients experiencing any CAEs and number of CAEs per patient
  - Lung function (FEV_1 % predicted, forced vital capacity [FVC], FEV_1/FVC ratio)
  - Patient reported asthma control (Asthma Control Test [ACT], Asthma Control questionnaire [ACQ]).

Statistics

- All analyses were performed on the full study sample, and statistical comparisons were restricted to patients with pre- and post-reslizumab initiation data for the given outcome measure.
- For outcomes measured as rates across a specific time period, comparable exposure periods were applied pre- and post-reslizumab.
- The first month post-reslizumab treatment was excluded to allow time for treatment benefits to take effect.
- Differences between pre- and post-reslizumab initiation were assessed using a generalized linear model, accounting for repeated observations and physician level clustering of observations.

Table 1: Response categories as defined in composite measure

Response category	Definition
1. **Excellent response**	Zero CAEs during months 2–7 post-reslizumab initiation
2. **Clinically meaningful response**	Did not meet criteria for category 1 ≥50% reduction in CAEs **and** any of the following: – ≥50% reduction in average maintenance OCS dose (mg/day) or discontinued maintenance OCS use – ≥5% improvement in FEV_1 % predicted – ≥3 point improvement in ACT score – ≥0.5 point improvement in ACQ score
3. **Partial response**	Did not meet criteria for categories 1 or 2, **and** achieved any reduction in CAEs ***or*** reduction or discontinuation of maintenance OCS use, ***or*** improvement in FEV_1 % predicted, ***or*** improvement in ACT or ACQ scores.
4. **Non-response/ treatment failure**	Lack of improvement in CAEs, average maintenance OCS dose (mg/day), FEV_1 % predicted, ACT or ACQ scores, ***or*** discontinuation due to any AE

ACQ; Asthma Control Questionnaire; ACT, Asthma Control Test; AE, adverse event; CAE, clinical asthma exacerbation; FEV_1, forced expiratory volume in 1 second; OCS, oral corticosteroid.

RESULTS

Patient characteristics

- 215 patient charts were collected from December 4th 2018 to March 8th 2019.
- Baseline patient demographics and clinical characteristics are shown in **Table 2**.

Table 2: Baseline demographics and clinical characteristics

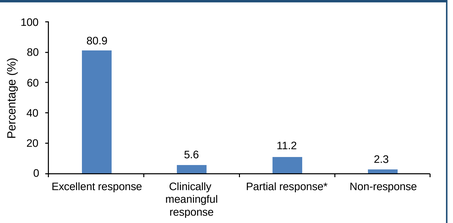
Characteristics	Patients (N=215)
Age (years), mean±SD	45.2±11.9
Male sex, n (%)	121 (56.3%)
Smoking status at index date*	
Never smoked, n (%)	174 (80.9%)
Former smoker, n (%)	37 (17.2%)
Current smoker, n (%)	3 (1.4%)
Selected clinical characteristics at index date (or within 6 months prior)	
BMI (kg/m^2), mean±SD	27.6±5.0
Proportion overweight (BMI ≥25), n (%)	141 (65.6%)
Proportion obese (BMI ≥30), n (%)	53 (24.7%)
Selected clinical characteristics at index date (or within 3 months prior)	
Blood EOS level (cells/μL), mean±SD	464±294 (n=172)
FEV_1 pre-bronchodilation (L), mean±SD	2.2±0.7
FEV_1 % predicted, (pre-bronchodilation), mean±SD	65.1%±20.5%
FVC pre-bronchodilation (L), mean±SD	3.2±1.0 (n=136)
FEV_1/FVC ratio, mean±SD	0.68±0.13 (n=128)
Airway reversibility, mean±SD	20.2%±21.9% (n=104)
Patient-reported outcomes at index date (or within 3 months prior)	
ACT score, mean±SD	13.8±4.2 (n=110)
ACQ score, mean±SD	2.69±1.14 (n=12)
CAEs during index period	
≥1 CAE during the index period (%)	137 (63.7%)

*Data unavailable for one patient. ACQ, Asthma Control Questionnaire; ACT, asthma control test; BMI, body mass index; EOS, eosinophil; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

Clinical response

- 80.9% of patients were 'excellent' responders, 5.6% of patients had a 'clinically meaningful' response, 11.2% had a 'partial' response, and 2.3% were classified as 'non-response' **(Figure 1)**.

Figure 1: Treatment response categories for the full study sample

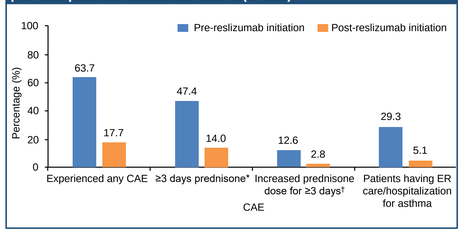


*'Partial responders' were sub-categorized as 'therapeutic responders'† (80.0%), 'physiologic responders'‡ (87.5%), and/or 'patient reported outcome responders'§ (91.7%).
†Reduction in average maintenance OCS dose [mg/day]; ‡Reduction in CAEs or improvement in FEV_1 % predicted; §Improvement in ACT or ACQ score.
ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; CAE, clinical asthma exacerbation; FEV_1, forced expiratory volume in one second; OCS, oral corticosteroid.

CAEs pre- and post-reslizumab initiation

- 36.3% of patients had no CAEs at baseline.
- There was a significant reduction in the proportion of patients experiencing CAEs, post-reslizumab (63.7% versus 17.7%; p<0.001) **(Figure 2)**.
- A numerical decline (46.0% to 28.9%) was observed in the proportion of patients experiencing a CAE-related emergency room (ER) visit or hospitalization.
- Mean number of CAEs per patient were significantly reduced post-reslizumab initiation (1.03±0.99 versus 0.22±0.59; p<0.001).

Figure 2: Proportion of patients experiencing any CAE pre- and post-reslizumab treatment (N=215)

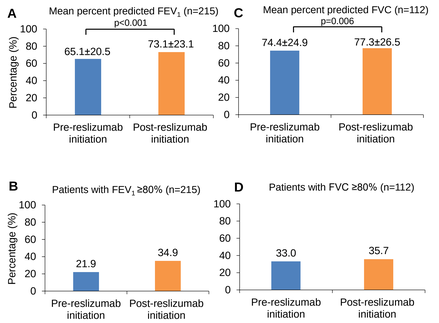


*If patient was not on prednisone; †if patient was on prednisone.
CAE, clinical asthma exacerbation; ER, emergency room.

Lung function

- At 5.5 months post-reslizumab treatment, improvements in lung function parameters were reported **(Figure 3)**.
  - Mean FEV_1/FVC ratio increased from 0.66±0.11 to 0.75±0.16 (n=32; p<0.001).

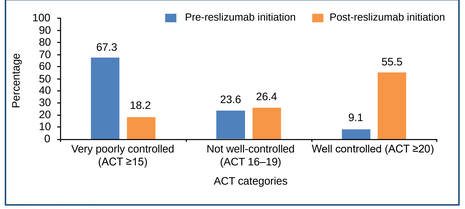
Figure 3: Lung function outcomes



Asthma control

- For patients with available ACT scores, 71.8% had an improvement of ≥3 points, 13.6% had an improvement of 1 or 2 points, and 14.5% had no improvement.
- Mean ACT score improved from 13.8±4.2 pre-index to 18.6±4.0 (p<0.001) at 5.5 months post-reslizumab treatment.
- The proportion of patients with 'very poorly controlled disease' numerically decreased from 67.3% to 18.2%, while those with 'well-controlled disease' numerically increased from 9.1% to 55.5% **(Figure 4).**

Figure 4: Patient ACT score categories pre- and post-reslizumab (N=110)



ACT, Asthma Control Test

- Among the 12 patients for whom ACQ score data were available, mean ACQ score numerically decreased from 2.69±1.14 pre-reslizumab to 2.29±1.28 (p=0.221) at 5.5 months post-reslizumab treatment.

CONCLUSIONS

- This is the largest real-world study investigating IV reslizumab to date, and has demonstrated that this treatment is associated with significant clinical and quality of life improvements in clinical practice generalizable to the U.S.
- ≥80% of the severe eosinophilic asthma patients receiving reslizumab achieved an 'excellent response,' as defined by an expert committee.
- IV reslizumab was associated with reduction in CAEs, improved lung function, and clinically meaningful improvements in patient-reported asthma control
  - While one third of patients did not experience a CAE prior to reslizumab treatment, ACT scores for these patients suggested a high symptom burden. Despite not all patients having CAEs at baseline, there was a significant reduction in the proportion of patients experiencing a CAE and the number of CAEs reported pre- versus post-reslizumab
  - The proportion of patients experiencing a reduction in CAE-related ER visits or hospitalization numerically declined, suggesting reductions in CAE severity, which may have potential clinical and economic implications
  - These real-world data confirm outcomes from Phase 3 studies on CAE rate reduction and other asthma-related outcome measures.

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