Real-world evidence of improved patient outcomes with reslizumab in adults with severe eosinophilic asthma (SEA): Subgroup analyses of patients using maintenance oral corticosteroids (OCS) prior to treatment initiation

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Reynold A. Panettieri, Jr,[1] Michael E. Wechsler,[2] Stephen P. Peters,[3] Bradley E. Chipps,[4] Tanisha Hill,[5] Rinat Ariely,[5] Michael DePietro,[5] Maurice T. Driessen,[6] Emi Terasawa,[7] Darren Thomason[7]

[1]Rutgers University, New Brunswick, NJ, USA; [2]National Jewish Health, Denver, CO, USA; [3]Wake Forest School of Medicine, Winston-Salem, NC, USA; [4]Capital Allergy & Respiratory Disease Center, Sacramento, CA, USA; [5]Teva Branded Pharmaceuticals R&D Inc., West Chester, PA, USA; [6]Teva Pharmaceutical Industries Ltd, Amsterdam, The Netherlands; [7]Analysis Group, Inc., New York, NY, USA

Background

- Reslizumab is an IgG4 kappa humanized monoclonal antibody[1] that was approved in the U.S. and internationally as add-on maintenance therapy for adult patients with severe eosinophilic asthma[2,3] based on two Phase 3 clinical trials that demonstrated that intravenous (IV) reslizumab 3 mg/kg administered once every 4 weeks was associated with 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.[4]
- As real-world evidence is limited, data on patients treated with reslizumab in U.S. clinical practice were collected in order to assess the real-world effectiveness of this therapy.
- Here we present data on the subgroup of patients using maintenance oral corticosteroids (OCS) therapy pre- and post-reslizumab treatment.

Methods

Study design and OCS-dependent patient characteristics

- A multicenter, observational, retrospective chart review collected patient-level data on reslizumab-naïve, adult patients (≥18 years) with severe eosinophilic asthma.
- Patients received reslizumab ≥7 months in U.S. clinical practice, not as part of a clinical trial, and had ≥6 months of data available prior to the date of reslizumab initiation (index date).

Outcome measures

- Outcomes assessed, pre- and post-reslizumab initiation, included:
  - Maintenance OCS use
  - CAEs
  - Lung function parameters (forced expiratory volume in 1 second [FEV_1] % predicted, forced vital capacity [FVC], FEV_1/FVC ratio)
  - Patient-reported asthma control (Asthma Control Test [ACT])
  - Healthcare resource utilization (asthma-related admissions/visits).

Statistics

- All analyses were performed on the subgroup of patients with maintenance OCS use at reslizumab initiation.
- Statistical comparisons were restricted to patients with pre- and post-reslizumab initiation data for the given outcome measure.
- Differences between pre- and post-reslizumab initiation were assessed using generalized linear mixed models, accounting for repeated observations and physician level clustering of observations.
- The index date was defined as the first date of reslizumab initiation.
- For outcomes measured as rates across a specific time period, comparable exposure periods were applied pre- and post-reslizumab.
- The first month post-reslizumab initiation was excluded to allow time for treatment benefits to take effect.

Results

Patients

- A subgroup of 37 OCS-dependent patients were identified from the full study sample of 215 patients.
- Patient demographics and clinical characteristics at baseline are presented in **Table 1**
  - Baseline characteristics, including mean blood eosinophil counts of 528±378 cells/μL (N=30) were indicative of patients with greater asthma severity compared to the full study sample (464±294 cells/μL [N=172]).

Table 1 Baseline demographics and clinical characteristics

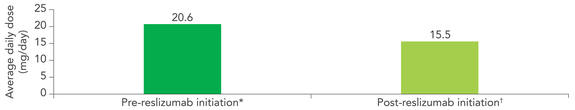
Characteristics	Patients (N=37)
Age (years), mean±SD	45.2±10.8
Sex Male, n (%)	21 (56.8)
Smoking status at index date Never smoked, n (%) Former smoker, n (%) Current smoker, n (%)	28 (75.7) 8 (21.6) 1 (2.7)
Selected clinical characteristics at index date (or within 6 months prior)	
BMI Mean BMI±SD, kg/m^2 Proportion overweight (BMI ≥25), n (%) Proportion obese (BMI ≥30), n (%)	27.7±4.7 26 (70.3) 9 (24.3)
Selected clinical characteristics at index date (or within 3 months prior)	
EOS level at index date Blood EOS level, mean±SD	528±378 (N=30)
FEV_1 (pre-bronchodilation) (L), mean±SD	2.1±0.6
FEV_1 % predicted (pre-bronchodilation), mean±SD	60.2±17.4
FVC (pre-bronchodilation) (L), mean±SD	3.1±0.9 (N=23)
FEV_1/FVC ratio, mean±SD	0.67±0.16 (N=22)
Airway reversibility (%), mean±SD	19.2±15.2 (N=17)
Patient reported outcomes at index date (or within 3 months prior)*	
ACT score, mean±SD	14.4±5.1 (N=20)
CAEs during the index period	
≥1 CAE (%)	78.4

*ACQ score data unavailable. ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; BMI, body mass index; CAE, clinical asthma exacerbation; EOS, eosinophil; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

Maintenance OCS use pre- and post-reslizumab initiation by design

- 37 (100.0%) patients used maintenance OCS at reslizumab initiation
  - 21 (56.8%) continued OCS use at ≥4 months post-initiation with dose information available, but significantly reduced their mean daily OCS dose (**Figure 1**)
  - 19 (53.2%) patients had discontinued OCS therapy by around 10 months post-initiation, adjusting for variable follow-up across patients.

Figure 1 Average daily dose of maintenance OCS therapy in patients (N=21) with continued use ≥4 months post-reslizumab initiation*

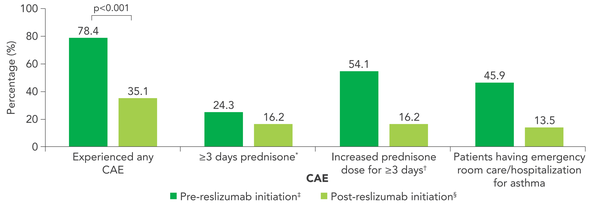


*OCS use, including dose, was recorded for the 3-month period prior to the index date; †Maintenance OCS use, including dose was also recorded for the 3-month period from the start of month 5 through to the end of month 7 following the index date. OCS, oral corticosteroids.

CAEs pre- and post-reslizumab initiation

- The proportion of patients experiencing CAEs was significantly reduced post-reslizumab initiation versus pre-reslizumab (78.4% versus 35.1%; p<0.001) (**Figure 2**).
- The mean number of CAEs per patient was significantly reduced following reslizumab initiation (1.59±1.24 versus 0.49±0.93; p<0.001).
- A numeric decline in the proportion of patients experiencing a CAE-related emergency room visit was observed (45.9% versus 13.5%).

Figure 2 Proportion of patients experiencing any CAE pre- and post-reslizumab initiation (N=37)

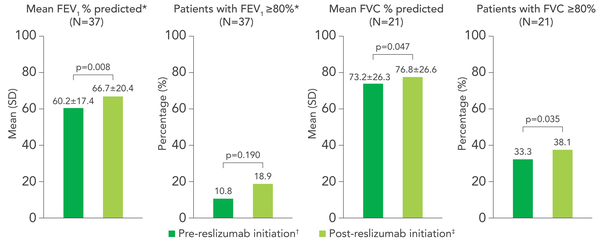


*If patient was not on prednisone at baseline; †If patient was on prednisone at baseline; ‡Results are presented for the 6-month period prior to the index date; §Results were collected during the 6-month period from the start of month 2 to the end of month 7 post-index (data were not collected during the first month to allow reslizumab treatment benefits to take place). CAE, clinical asthma exacerbation.

Lung function

- At 5.5 months post-reslizumab initiation, improvements in lung function parameters were reported (**Figure 3**).

Figure 3 Lung function outcomes



*For FEV_1, all measurements were collected as close to the mid-point of month-6 post-index within a 2-month window after that time point (if available); †Outcomes were collected as close to the reslizumab initiation date as possible within a 3-month window prior to this date; ‡During the study period, outcomes were collected as close to the mid-point of month-6 post-index as possible, within a 45-day window before and after that time point. FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation

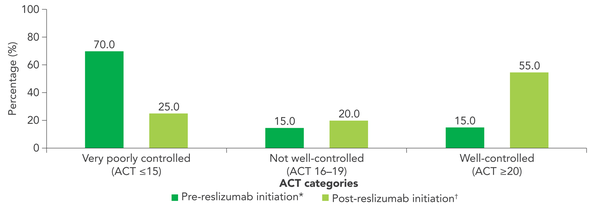
Patient-reported asthma control

- The mean ACT score increased from 14.4±5.1 pre-reslizumab initiation to 18.6±4.8 (p<0.001) post-reslizumab initiation
  - The proportion of patients with 'very poorly controlled disease' decreased from 70.0% to 25.0%, while those with 'well-controlled disease' increased from 15.0% to 55.0% (**Figure 4**).

Asthma-related healthcare resource utilization

- There was a significant reduction in the proportion of patents who experienced a healthcare resource utilization event (asthma-related admission/visit) pre- versus post-reslizumab initiation
  - Inpatient admissions (37.8% versus 2.7%; p<0.001), emergency room visits (73.0% versus 37.8%; p<0.001), urgent care visits (40.6% versus 12.5%; p=0.007), or any unscheduled outpatient visit (75.0% versus 55.6%; p=0.035).

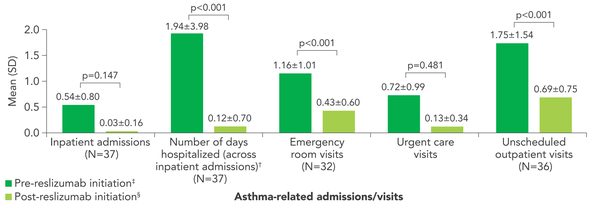
Figure 4 Patient ACT score categories pre- and post-reslizumab initiation (N=20)



*Outcomes were collected as close to the reslizumab initiation date as possible within a 3-month window prior to this date; †During the study period, outcomes were collected as close to the mid-point of month-6 post-index, as possible, within a 45-day window before and after that time point. ACT, Asthma Control Test.

- There was a significant decrease in the mean number of asthma-related inpatient admissions (including the number of days hospitalized across inpatient admissions), emergency room visits, urgent care visits, and unscheduled outpatient visits post-reslizumab versus pre-reslizumab initiation (**Figure 5**).

Figure 5 Number of asthma-related admissions/visits*



*All healthcare resource utilization was deemed asthma-related, but in some cases was not associated with CAE diagnosis. Some patients who were reported as not having CAE pre- and post-reslizumab initiation did experience asthma-related HRU as reported by study sites. †The number of days hospitalized is calculated out of the 33 patients with data on hospitalization available during pre- and post-reslizumab initiation periods; ‡Results are presented for the 6-month period prior to the index date; §Results were collected during the 6-month period from the start of month 2 to the end of month 7 post-index (data were not collected during the first month post-index to allow reslizumab treatment benefits to take place). CAE, clinical asthma exacerbation; SD, standard deviation.

Conclusions

- This study represents the largest real-world study, to date, investigating IV reslizumab, and previous analyses demonstrated that IV reslizumab is associated with significant clinical and quality of life improvements in U.S. clinical practice.
- Baseline blood eosinophil levels in this subgroup were indicative of patients having greater asthma severity compared with the full study sample.
- In this subgroup of OCS-dependent patients, the entire cohort reduced their maintenance OCS dose over the first 4 months of treatment. By around 10 months post-reslizumab initiation, more than half had discontinued OCS therapy completely, suggesting that in the real-world setting, IV reslizumab may be associated with discontinuation or reduced dose of OCS in patients with severe eosinophilic asthma.
- In this subgroup, treatment with reslizumab was associated with a reduction in the proportion of patients experiencing a CAE and improvements in lung function parameters and patient-reported asthma control.

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