Eligibility for newer biologic therapies in severe asthma, re-analysis of the IDEAL study

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Background

- The Identification and Description of sEvere Asthma patients in a cross-sectionaL (IDEAL) study[1] was a single-visit, cross-sectional, observational study in six countries (Australia, Canada, France, Germany, the UK and USA) that enrolled patients with severe asthma from routine clinical practice between December 2014 and May 2015.
- The aim of the original IDEAL study[1] was to describe treatment eligibility and overlaps in eligibility for mepolizumab (anti-IL-5), omalizumab (anti-IgE) and reslizumab (anti-IL-5).
- Since the initial IDEAL publication[1], labels for mepolizumab and reslizumab, along with an additional biologic therapy (benralizumab, anti-IL-5), have been approved.

Aim

- This *post-hoc* analysis of the IDEAL data aimed to update the eligibility and overlap in eligibly for severe asthma biologic therapies, approved as of mid-2018.

Methods

- Of the 748 subjects enrolled in IDEAL, 669 met criteria for this post-hoc analysis (non-missing data on necessary variables).
- Each biologic was assessed according to their approved US labels (**Table 1**).
  - Exacerbation criteria were assessed in the 12 months immediately prior to but exclusive of the IDEAL study visit, and eosinophil (eos) criteria were assessed in the 12 months immediately prior to and inclusive of the IDEAL study visit.

Table 1. Label criteria for included biologic therapies

Treatment	Exacerbations in past year	Blood eosinophil count	Other
Mepolizumab	≥ 2	≥ 150 cells/µL (past 6 weeks), or ≥ 300 cells/µL (past 12 months)	
Omalizumab†	≥ 1		FEV_1 < 80% predicted; RAST positive; IgE / weight per label‡
Reslizumab	≥ 1	≥ 400 cells / µL	
Benralizumab	≥ 2	≥ 300 cells / µL	

FEV_1 = forced expiratory volume in one second; IgE = immunoglobulin E; RAST = radioallergosorbent test; † Current omalizumab users were assumed eligible *a priori*; ‡ IgE / weight dosing criteria per label criteria for the USA

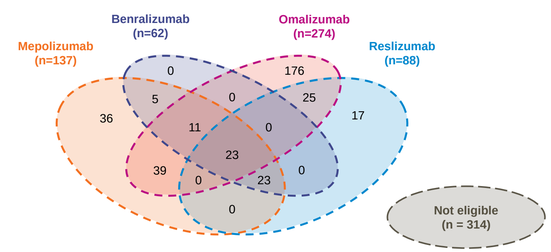
- Eligibility was assessed in the overall analysis population, as well as the population with ≥ 1 exacerbation to reflect severe asthma patients who would most likely warrant the addition of biologic therapy.

Results

Overall Analysis Population

- 355 (53%) out of 669 subjects were eligible for any of the biologics. (**Figure 1**)
- 20%, 9%, 13% and 41% were eligible for mepolizumab, benralizumab, reslizumab, and omalizumab, respectively.
  - Only 23 patients (6% of all subjects) were eligible for all four treatments.
  - Among the anti-IL-5 biologics, 45% and 34% of mepolizumab-eligible subjects were also eligible for benralizumab and reslizumab, respectively.
  - 100% of benralizumab-eligible and 52% of reslizumab-eligible subjects were eligible for mepolizumab.

Figure 1. Eligibility among all subjects



Numbers represent counts, not percentages, of patients; Full analysis cohort (n=699)

- Biologic eligible subjects were similar regarding age and BMI, with minor differences on gender and smoking status, though based on small numbers. (**Table 2**)
- Subjects eligible for anti-IL-5 biologics tended to be similar regarding maintenance OCS and current/prior omalizumab use.
- Omalizumab eligible subjects tended to have less severe disease (less frequently treated with maintenance OCS, less airflow limitation and more controlled patients) relative to the newer biologics.
- Exacerbation frequencies and eosinophil counts were associated with biologic eligibility criteria.
  - Current omalizumab users were assumed eligible *a prioi*, therefore 25% of omalizumab eligible subjects did not have an exacerbation in the prior year.

Table 2. Demographics and clinical characteristics

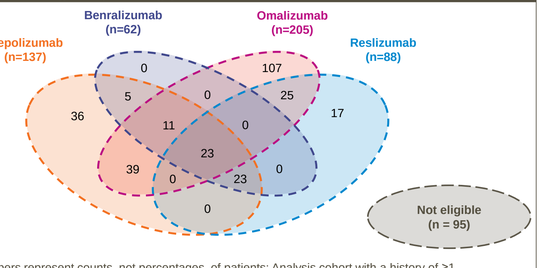
N (%)	All	Mepolizumab eligible	Omalizumab eligible	Reslizumab eligible	Benralizumab eligible
	N= 669	N= 137	N= 274	N= 88	N= 62
Age (y), mean (SD)	50.5 (15.6)	48.0 (15.3)	47.8 (15.7)	51.7 (15.9)	47.3 (14.9)
Female	414 (61.9)	85 (62.0)	175 (63.9)	48 (54.5)	37 (59.7)
BMI, mean (SD)	29.9 (7.4)	30.7 (7.9)	29.8 (6.9)	28.4 (6.5)	30.1 (6.9)
Smoking Status					
Never	427 (63.8)	76 (55.5)	178 (65.0)	51 (58.0)	38 (61.3)
Current	52 (7.8)	9 (6.6)	21 (7.7)	5 (5.7)	2 (3.2)
Ex-	190 (28.4)	52 (38.0)	75 (27.4)	32 (36.4)	22 (35.5)
Pack-years, mean (SD)	13.1 (16.9)	13.9 (16.6)	12.3 (14.0)	12.2 (15.3)	10.5 (12.3)
Current / prior maintenance OCS	152 (22.7)	46 (33.6)	72 (26.3)	31 (35.2)	21 (33.9)
Current / prior omalizumab use	186 (27.8)	44 (32.1)	174 (63.5)	26 (29.5)	20 (32.3)
FEV_1 <80% predicted	470 (70.3)	107 (78.1)	184 (67.2)	73 (83.0)	51 (82.3)
≥12% reversibility	268 (40.1)	67 (48.9)	108 (39.4)	41 (46.6)	34 (54.8)
ACQ ≥ 1.5	431 (64.4)	102 (74.5)	171 (62.4)	65 (73.9)	49 (79.0)
Exacerbations					
0	288 (43.0)	0 (0.0)	69 (25.2)	0 (0.0)	0 (0.0)
1	184 (27.5)	0 (0.0)	99 (36.1)	42 (47.7)	0 (0.0)
2	92 (13.8)	59 (43.1)	54 (19.7)	25 (28.4)	32 (51.6)
≥3	105 (15.7)	78 (56.9)	52 (19.0)	21 (23.9)	30 (48.4)
Historical eos					
< 300	123 (18.4)	18 (13.1)	57 (20.8)	9 (10.2)	3 (4.8)
≥ 300	106 (15.8)	43 (31.4)	52 (19.0)	21 (23.9)	16 (25.8)
Eos at study visit					
<150	244 (36.5)	12 (8.8)	95 (34.7)	0 (0.0)	0 (0.0)
≥150 – 300	211 (31.5)	63 (46.0)	89 (32.5)	0 (0.0)	0 (.0)
≥300	214 (32.0)	62 (45.3)	90	88 (100)	62 (100)

ACQ = asthma control questionnaire; BMI = body mass index; Eos = eosinophils; FEV_1 = forced expiratory volume in one second; Values presented as N(%) unless otherwise specified.

Population with ≥1 exacerbation

- 57% of all subjects had an exacerbation in the year prior to the IDEAL study visit. (**Table 2**)
- Of the exacerbating population (n=381), 286 patients (75%) were eligible for ≥ 1 biologic therapy. (**Figure 2**)
- In the exacerbating population, the same absolute counts of patients with overlapping eligibility between anti-IL-5 treatments were observed.
  - This follows from the use of exacerbations as an eligibility criterion for these treatments.

Figure 2. Eligibility among patients with ≥ 1 exacerbation



Numbers represent counts, not percentages, of patients; Analysis cohort with a history of ≥1 exacerbation(n=381)

Conclusions

- Treatment eligibility was higher for mepolizumab and omalizumab, relative to newer anti-IL-5 biologics, with 75% of the exacerbating severe asthma population eligible for at least one biologic.
- There is considerable eligibility overlap between the anti-IL-5 biologics, as these therapies target a similar severe asthma phenotype.
- Nearly 50% of all severe asthmatics in this analysis (and 25% of exacerbating patients) were not eligible for biologic therapy.
- There is an unmet need among exacerbating patients not eligible for any of the current therapies and further study will be required to understand if future biologics address this need.

References

1. Albers FC et al. J Asthma 2018;55(2):152-160

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