Biologic Responders And Super-responders in the International Severe Asthma Registry

Poster #P607

Eve Denton[1,2], Mark Hew[1,2], Ruth Murray[3], Lakmini Bulathsinhala[3,49], Trung N. Tran[4], Neil Martin[4,5], Mona Al-Ahmad[6], Alan Altraja[7], Carlos Andrés Celis-Preciado[8], Riyad Al-Lehebi[9], Celine Bergeron[10], Mohit Bhutani[11], Sinthia Bosnic-Anticevich[12], Arnaud Bourdin[13], Guy Brusselle[14], John Busby[15], Giorgio Walter Canonica[16], Jérémy Charriot[13], Kenneth R. Chapman[17], George C. Christoff[18], Li Ping Chung[19], Borja G. Cosio[20], Richard W. Costello[21], Breda Cushen[22], João A. Fonseca[23], Peter G. Gibson[24], Liam G. Heaney[25], Takashi Iwanaga[26], Mariko Siyue Koh[27], Lauri Lehtimäki[28], Jorge Máspero[29], Bassam Mahboub[30], Patrick Mitchell[31], Nikolaos Papadopoulos[32], Luis Perez-De-Llano[33], Diahn-Warng Perng[34], Matthew Peters[35], Paul E. Pfeffer[36], Todor A. Popov[37], Celeste M. Porsbjerg[38], Chin Kook Rhee[39], Nicolas Roche[40], Mohsen Sadatsafavi[41], Sundeep Salvi[42], Chau-Chyun Sheu[43], Carlos A. Torres-Duque[44], Charlotte S. Ulrik[45], John Upham[46], Eileen Wang[47], Michael E. Wechsler[48], David B. Price[49,50], on behalf of the LUMINANT Working Group.

[1]Allergy, Asthma & Clinical Immunology, Alfred Health, Melbourne, Australia, [2]Public Health and Preventive Medicine, Monash University, Australia, [3]Optimum Patient Care, Cambridge, United Kingdom, [4]BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD, United States, [5]University of Leicester, Leicester, United Kingdom, [6]Microbiology Department, College of Medicine, Kuwait University, Al-Rashed Allergy Center, Ministry of Health, Kuwait, [7]Department of Pulmonology, University of Tartu and Lung Clinic, Tartu University Hospital, Tartu, Estonia, [8]Pulmonary Unit, Hospital Universitario San Ignacio, Bogota, Colombia, [9]Department of Pulmonology, King Fahad Medical City, Toronto, Toronto, Canada, [10]Vancouver General Hospital and University of British Columbia, Vancouver, Canada, [11]Division of Pulmonary Medicine, Department of Medicine, University of Alberta, Alberta, Canada, [12]Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia, [13]PhyMedExp, Univ Montpellier, CNRS, INSERM, CHU Montpellier, Montpellier, France, [14]Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium, [15]Centre for Public Health, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, [16]Personalized Medicine, Asthma and Allergy, Humanitas Clinical and Research Center IRCCS, Milan, Italy, [17]University of Toronto, Toronto, Canada, [18]Medical University, Sofia, Bulgaria, [19]Fiona Stanley Hospital, Perth, Australia, [20]Son Espases University Hospital-IdISBa-Citeres, Mallorca, Spain, [21]Clinical Research Centre, Smurfit Building Beaumont Hospital, Department of Respiratory Medicine, RCSI, Dublin, Ireland, [22]Department of Respiratory Medicine, Beaumont Hospital, Dublin, Ireland, [23]CINTESIS1@RISE, MEDCIDS, Faculty of Medicine, University of Porto, Porto, Portugal, [24]Australian Severe Asthma Network, Priority Research Centre for Healthy Lungs, University of Newcastle, Newcastle, Australia, [25]Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, United Kingdom, [26]Kindai University Hospital, Osakasayama, Japan, [27]Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore, Singapore, [28]Allergy Centre, Tampere University Hospital; Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland, [29]Clinical Research for Allergy and Respiratory Medicine, CIDEA Foundation, Buenos Aires, Argentina, [30]Rashid hospital, Dubai Health Authority (DHA), Dubai, United Arab Emirates, [31]School of Medicine, Trinity College, Dublin, Ireland, [32]Division of Infection, Immunity & Respiratory Medicine, University of Manchester, Manchester, United Kingdom, [33]Pneumology Service. Lucus Augusti University Hospital. EOXI Lugo, Monforte, Cervo, Spain, [34]School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, [35]Department of Thoracic Medicine, Concord Hospital, Sydney, Australia, [36]Dept of Respiratory Medicine, Barts Health NHS Trust, London, United Kingdom, [37]University Hospital "Sv. Ivan Rilski", Sofia, Bulgaria, [38]Department of Respiratory Medicine and Infections Diseases, Research Unit, Bispebjerg Hospital, Copenhagen, Denmark, [39]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea, [40]Department of Respiratory Medicine, APHP-Centre University Paris Cité, Cochin Hospital and Institute (UMR1016), Paris, France, [41]Faculty of Pharmaceutical Sciences, The University of British Columbia, North Vancouver, BC, Canada, [42]Pulmocare Research and Education Foundation, Pune, India, [43]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [44]Fundacion Neumologica Colombiana, Bogota, Colombia, [45]Department of Respiratory Medicine, Copenhagen University Hospital, Hvidovre, Denmark, [46]Diamantina Institute & PA-Southside Clinical Unit, The University of Queensland, Brisbane, Australia, [47]Division of Allergy and Clinical Immunology, Department of Medicine, National Jewish Health, Denver, CO, United States, [48]NJCohen Family Asthma Institute, Department of Medicine, National Jewish Health, Denver, CO, United States, [49]Observational and Pragmatic Research Institute, Singapore, Singapore, [50]Centre of Academic Primary Care, Division of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom.

Introduction

- Randomised, controlled trials confirm the efficacy of severe asthma biologics in a selected sample of patients, but real-world effectiveness data help further guide clinical practice in the broader population

Aims

- The LUMINANT study describes an international, real-world population who initiate biologic medications and to explore response and super-response across four individual asthma outcomes
- Patients not initiating biologics were also examined for comparison

Methods

- Patients with severe asthma enrolled in the International Severe Asthma Registry (ISAR) with ≥ 24 weeks of follow-up data were included
- Patient that initiated biologics were compared to those that did not
- Response was examined as per **Table 1**

Table 1. Single domain definition of response and super-response in patients with severe asthma between baseline and month 12 visit

Domain	Definition of responders	Definition of super-responders	Excluded from analysis
Asthma exacerbations	≥ 50% reduction in annualised exacerbation rate	Exacerbation elimination	Zero annualised exacerbations at baseline
FEV_1	≥ 100 mL improvement in post bronchodilator FEV_1	≥ 500 mL improvement in post bronchodilator FEV_1	Not applicable
Asthma control	Improved asthma control by category (controlled, partial, poor)	New attainment of well-controlled asthma	Well-controlled asthma at baseline
Long-term oral corticosteroid (LTOCS) burden	Reduction in LTOCS (mg)	Cessation of LTOCS or weaning to adrenal insufficiency dose ≥ 5 mg	Not on LTOCS at baseline

Results

- 2116 participants initiated biologics (5.3% met criteria for clinical trials) and 6335 did not
- Biologic initiators had worse baseline asthma status than non-initiators, although biomarkers were similar between groups (**Table 2**)

Table 2: Baseline characteristics of the total LUMINANT cohort, those who were initiated on biologics and those who were not

	Biologic n = 2116	Non-biologic n = 6330	P-value
DEMOGRAPHICS			
Sex (female), % (n/N)	62% (1311 / 2116)	62% (3893 / 6330)	0.71
White race, % (n/N)	78% (1471 / 1876)	79% (4380 / 5573)	
Age (years), mean ± SD (n)	53 ± 15 (2115)	58 ± 17 (6335)	<0.001
BMI, mean ± SD (n)	29.1 ± 7 (1862)	29.6 ± 8 (4995)	0.03
Smoking status never smoker, % (n/N)	62% (1309 / 2116)	45% (2858 / 6335)	<0.001
Asthma onset, mean ± SD (n)	29 ± 19 (1449)	31 ± 20 (2126)	<0.001
ASTHMA STATUS			
Baseline FEV_1 pre-bronchodilator, mean ± SD (n)	1.9 ± 0.8 (1516)	2.1 ± 0.8 (3678)	<0.001
FEV_1 reversibility, % (n)	16% (178)	12% (346)	<0.001
Poor asthma control, % (n/N)	75% (973 / 1299)	56% (1277 / 2268)	<0.001
Baseline annualised exacerbations, mean ± SD (n)	3.8 ± 4 (1711)	1.6 ± 2 (2688)	<0.001
Baseline annualised exacerbations (categorical), %			
0	11%	30%	<0.001
1–3	48%	58%	
4–5	20%	7%	
≥ 6	21%	5%	
LTOCS, % (n/N)	43% (901 / 2116)	14% (878 / 6335)	<0.001
Anti-IgE, % (n)	38% (809)	N/A	
Anti–IL-5/5R, % (n)	59% (1242)	N/A	
Anti–IL-4/13, % (n)	3% (63)	N/A	
BIOMARKERS			
Blood eosinophil count, mean ± SD (n)	598 ± 893 (504)	617 ± 820 (954)	0.7
FeNO (ppb), mean ± SD (n)	49 ± 46 (800)	47 ± 46 (1532)	0.3
IgE, mean ± SD (n)	443 ± 1003 (1273)	417 ± 1306 (2441)	0.5
Sensitised to perennial allergens, % (n/N)	39% (671 / 1724)	44% (1844 / 4177)	0.001

- Response was more frequently achieved among participants initiating biologics versus those not initiating biologics (**Figure 1**, **Table 3**)
  - FEV_1 (54% versus 34%, p<0.001), asthma control (49% versus 42%, p=0.007), exacerbation reduction (59% versus 44%, p<0.001), and LTOCS reduction (49% versus 28%, p<0.001)
- Super-response was more frequent in each domain among biologic initiators
- Compared to participants initiating an anti-IgE agent, participants initiating anti–IL-5 agents had worse baseline impairment but experienced greater improvement in exacerbations and LTOCS (**Figure 2**)

Figure 1. Proportion of responders (orange), super-responders (yellow) and non-responders (blue) across single domains in those initiated on biologics, with ≥ 24 weeks follow up, and those who were not initiated on biologics

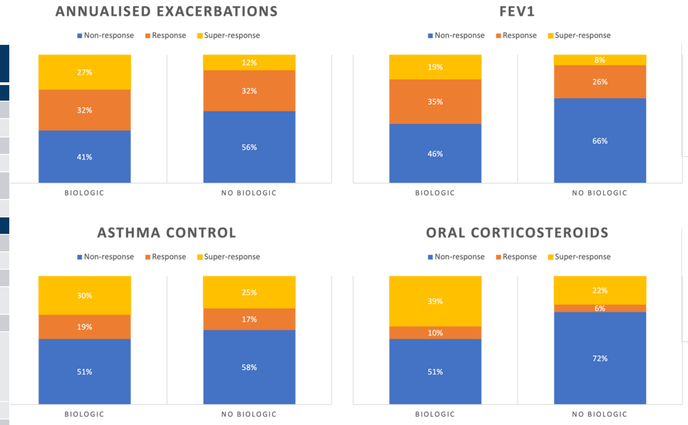

Figure 2. Domains of response (unadjusted) according to biologic class at baseline and follow-up of ≥ 24 weeks

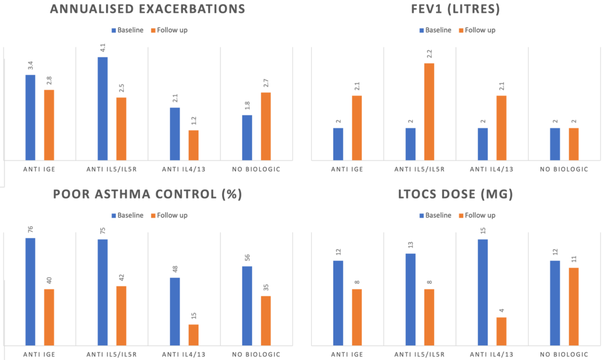

Table 3. Proportion of patients that met the criteria of a single domain of response among those who did and did not initiate a biologic medication between the baseline and follow-up visit

	Biologic	Non-biologic	p-value
RESPONSE, % (n/N)			
Exacerbation reduced ≥ 50%	59% (806 / 1375)	44% (359 / 814)	<0.001
FEV_1 improved ≥ 100 mL	54% (358 / 665)	34% (354 / 1048)	<0.001
Asthma control improved	49% (524 / 1072)	42% (299 / 706)	0.007
LTOCS dose reduced	49% (255 / 517)	28% (32 / 112)	<0.001
SUPER-RESPONSE, % (n/N)			
Exacerbation elimination	27% (442 / 1620)	12% (242 / 1967)	<0.001
FEV_1 improved ≥ 500 mL	19% (124 / 665)	8% (86 / 1048)	<0.001
New good asthma control	30% (318 1072)	25% (196 / 706)	0.016
LTOCS super-response	39% (200 / 517)	22% (25 / 112)	<0.001

Conclusions

- Patients with severe asthma who initiated biologics had greater disease severity at baseline than those who did not initiate biologics, but biomarker levels were similar
- Only 5.3% of study participants met even basic criteria for clinical trials
- Clinical response and super-response to biologics was observed in all four domains
- Super-response was more frequent amongst biologic initiators than non-initiators
- In the context of differing baseline impairment, response to biologics may differ by biologic class

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Abbreviations

BMI, body mass index; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in one second; IgE, immunoglobulin E; IL-4/13, interleukin-4/13; IL-5, interleukin-5; IL-5R, interleukin-5 receptor; ISAR, International Severe Asthma Registry; LTOCS, long-term oral corticosteroids; ppb, parts per billion; SD, standard deviation

Additional COI disclosures

Electronic copy of the poster

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