Global Access for Biologics in The Treatment Of Severe Asthma: A Challenge To Personalized Medicine

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Introduction

- The value of biologics in severe asthma is well documented, including reduction in exacerbation frequency, asthma symptoms, dosage of controller medication and the need for oral corticosteroids.[1,2]
- However, their potential may not be fully realized due to country-specific variations in accessibility.

Aims

- To chart biologic accessibility around the world.
- To highlight country-specific differences in prescription criteria, such as background asthma therapy and exacerbations.

Methods

ISAR

- The International Severe Asthma Registry (ISAR; https://isaregistries.org/) is the largest severe adult asthma registry in the world.[3–5]
- ISAR provides an appropriate platform to address essential research questions, benefiting from the expertise of key thought leaders in severe asthma from all over the world.
  - The ISAR Steering Committee (ISC) comprises 48 experts in severe asthma research from 29 countries and medical experts from AstraZeneca (AZ).

Survey design, dissemination and completion

- A semi-structured survey was designed and sent out to the ISAR network in July 2019 and engaged severe asthma clinicians from 29 countries participating in the ISAR registry in 2019, reflecting the medication access criteria at that time (**Figure 1**).

Figure 1: ISAR countries surveyed

Biologics assessed

- Anti-IgE (omalizumab)
- Anti–IL-5/5R (mepolizumab, reslizumab, benralizumab)
- Anti–IL-4Rα (dupilumab)

Study outcomes

- Biologic reimbursement status (full-, partial- or not-reimbursed).
- Biologic prescription criteria, including exacerbation and background therapy criteria.
  - Background therapy: inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA), add-on to ICS/LABA (e.g. long-acting muscarinic antagonist (LAMA), leukotriene receptor antagonist (LTRA) and/or theophylline) or maintenance OCS (mOCS).

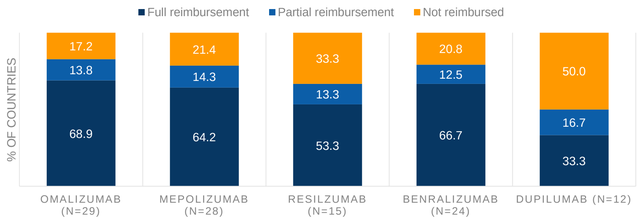
Results

- The survey had a response rate of 100% (29 countries).

Biologic availability: reimbursement

- National reimbursement varied substantially across ISAR countries (**Figure 2**).
  - Omalizumab, mepolizumab, and benralizumab were available in 29, 28, and 24 countries, respectively, and most frequently fully reimbursed (>60% of countries).
  - Dupilumab was available in 12 countries, and most frequently either partially or not reimbursed in these countries (66.7%).
  - Reslizumab was available in 15 countries, with partial/no reimbursement (46.7%).
  - Biologics were not nationally-reimbursed in South Korea, Brazil, the US, and Singapore.
    - To note, reimbursement is insurer-dependent in the US. Measurement of private payment schemes in the US is beyond the scope of the survey.

Figure 2: Number and proportion of countries with full, partial, and non-reimbursement of biologics



Biologic prescribing criteria: exacerbation rate (Table 1)

- Most countries (>65%) currently use total exacerbation number as a biologic prescribing criterion, ranging from 1 exacerbation in Australia to 4 in the UK.
- Omalizumab, mepolizumab, and benralizumab: ≥2 exacerbations are most frequently required for (>40% of countries).
- Reslizumab: ≥1 exacerbation is most frequently required (33.5% of countries).
- Dupliumab: No exacerbation criterion required (50% of countries). Eligibility criteria are under development for 5 (41.7%) of these countries.

Table 1: Proportion of countries which currently use exacerbations experienced in the preceding year as a biologic prescription criterion

	Anti-IgE	Anti–IL-5/5R			Anti–IL-4/13
	Oma	Mepo	Resli	Benra	Dupi
N(%)	29	28	15	24	12
≥ 1	7 (24.1)	8 (28.6)	5 (33.3)	4 (16.7)	2 (16.7)
≥ 2	13 (44.8)	12 (42.9)	4 (26.7)	11 (45.8)	4 (33.3)
≥ 3	1 (3.4)	1 (3.6)	2 (13.3)	2 (8.3)	1 (8.3)
≥ 4	2 (6.9)	2 (7.1)	0 (0.0)	1 (4.2)	0 (0.0)
None	7 (24.1)	6 (21.4)	4 (26.7)	8 (33.3)	6 (50.0)

Results

Biologic prescribing criteria: background therapy (Table 2)

- ICS/LABA background therapy is a prescribing criterion in all countries for currently available biologics.
- Add-on therapy to ICS/LABA (e.g. plus LAMA, LTRA, and/or theophylline) is a biologic prescribing criterion for each of the 5 biologics in approximately 20-25% of countries.
  - In the US, Mexico, and Colombia, health authorities do not require add-on therapy as a criterion; however, private insurance companies may require it.
- 20-30% of all countries require patients to be on mOCS prior to biologic prescription.

Table 2: Proportion of countries that currently use background therapy as a biologic prescription criterion

	Anti-IgE	Anti–IL-5/5R			Anti–IL-4/13
	Oma	Mepo	Resli	Benra	Dupi
N(%)	29	28	15	24	12
ICS + LABA	29 (100.0)	28 (100.0)	15 (100.0)	24 (100.0)	12 (100.0)
+LAMA/LTRA/ Theophylline	6 (20.7)	7 (25.0)	4 (26.7)	6 (25.0)	3 (25.0)
+ mOCS	7 (24.1)	8 (28.6)	3 (20.0)	7 (29.2)	3 (25.0)
None	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	2 (16.7)

Omal: omalizumab: Mepo: mepolizumab; Resliz: reslizumab; Benra: benralizumab; Dupi: dupilumab

Conclusions

- **Currently, access to biologics depends on patient geographic location and is dependent upon country-specific biologic availability, reimbursement and prescription criteria.**
- **Prescription criteria are relatively similar across countries with all countries requiring ICS/LABA as background therapy and majority of countries requiring ≥1 exacerbation.**
- **Global harmonization of these factors would ensure equitable biologics access around the world.**
- **Future studies could explore the effect of both inter- and intra-country variation on biologic use in real-life populations and on outcomes in severe asthma.**

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