ROLE OF BIOLOGICS IN ASTHMA

“Asthma Mary Clare McGregor, James G. Krings, Parameswaran Nair, and Mario Castro

ANUSHKA TAKHI
OUTLINE

• Overview on Asthma

• Cause for Asthma: ENDOTYPES (T2-High Asthma and T2-Low Asthma)

• Treatments for Asthma

• Biologics:
  - Omalizumab
  - Mepolizumab
  - Reslizumab
  - Benralizumab
  - Dupilumab

• Conclusions
ASTHMA

Chronic inflammatory disorder of airways.

Characterized by: Bronchial hyperresponsiveness and limited airflow

Heterogeneous disease, caused by endotypes, type 2 (T2) high and low.

Poor quality of life, impaired lifestyle, effects of oral corticosteroids.

Characterized by:
- Bronchial hyperresponsiveness
- Limited airflow

Heterogeneous disease, caused by endotypes, type 2 (T2) high and low.

Poor quality of life, impaired lifestyle, effects of oral corticosteroids.
(High)
T2 inflammation is slightly more common in people with severe asthma.
Caused via interaction of allergens, microbes with airway epithelium.
Sputum, blood eosinophil counts, Serum IgE-BIOMARKERS of T2.

(Low)
Includes neutrophils.
Poorly understood pathophysiology.
Neutrophilic inflammation.
Less responsive to corticosteroids.
T2–High Asthma

Interacts with airway epithelium

Allergens/microbes/pollutants

Bronchoconstriction
Airway hyperresponsiveness
Mucus production
Airway remodeling

ALLERGIC- IgE dependent process.

NON ALLERGIC EOSINOPHILIC- T2 cytokines-inflammation

IL-4
IL-5
IL-13

Attraction and activation

basophils
eosinophils
IgE by B cells
Airway epithelium and smooth muscle
T2-Low Asthma

- Neutrophilic inflammation

- High IL-17A mRNA levels in patients.

- Less responsive to corticosteroids.

- Fewer allergic symptoms

- No approved Biologic

- Controller medications and possible bronchial thermoplasty.
TREATMENTS FOR ASTHMA

**Biologic therapies**

Target inflammatory modulators in T2-High subset of patients.

Inhaled corticosteroids (ICS)
Oral corticosteroids (OCS)

Long-acting Bronchodilator

Treatments for asthma

Bronchial thermoplasty
Approved Biologics for treatment of Moderate to Severe Persistent Asthma - Type2 High phenotype

- Omalizumab
- Benralizumab
- Mepolizumab
- Dupilumab
- Reslizumab
OMALIZUMAB (Allergic asthma)

OMALIZUMAB

- Humanized Anti-IgE monoclonal antibody.
- Prevents the binding of IgE to its receptor on the Basophil/Mast cells.
- Decrease activation of Mast cells and Basophil cells by decreasing serum free IgE.
- IgE is necessary for inflammatory cascade.
- Adverse effects: 0.1-0.2% risk of anaphylaxis.

Omalizumab for severe asthma: toward personalized treatment based on biomarker profile and clinical history. Tabatabaian F, Ledford DK.
MEPOLIZUMAB

• Patients with moderate to severe eosinophilic asthma.

• Characterised by: High sputum (3%)  
  High AEC (>300 cells/µl)

• Anti-IL-5 monoclonal antibody.

• It binds to the IL-5 ligand, prevents IL-5 from binding to its receptor on eosinophil.

• Adverse effects: Activation of zoster  
  Rarely causes hypersensitivity
RESLIZUMAB

- Patients with moderate to severe eosinophilic asthma.

- Characterised by: High sputum (3%)
  High AEC(>400 cells/µl)

- Anti-IL-5 monoclonal antibody.

- Binds to the IL-5 ligand, prevents IL-5 from binding to its receptor on eosinophils.

- Adverse effects: 0.3% risk of Anaphylaxis
BENRALIZUMAB

• Patients with severe eosinophilic asthma.

• Characterised by: High sputum (3%)
  High AEC (>300 cells/μl)

• Anti-IL-5 monoclonal antibody.

• Binds to the IL-5 receptor α, prevents IL-5 from binding to its receptor on eosinophil and Basophils.

• Adverse effects: Rarely causes hypersensitivity reactions.
DUPILUMAB

- Patients with severe eosinophilic asthma.

- Characterised by: High sputum (3%)
  High AEC (>150 cells/µl)

- Anti- IL-4R monoclonal antibody.

- Binds to the IL-4 receptor α, blocks signaling of IL-4 and IL-13

- Adverse effects: Rarely causes hypersensitivity
  Higher incidence of injection site reactions (upto 18%)
  Hypereosinophilia
### Efficacy of Biologics for Treatment of Moderate to Severe Persistent Asthma (Type 2-High Phenotype)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Asthma Exacerbation</th>
<th>Lung Function</th>
<th>Corticosteroid Weaning</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>Reduces by 25%</td>
<td>Minimal or equivocal improvement</td>
<td>Decreases use of ICS, but no data that it helps with OCS weaning</td>
<td>Only s.c. biologic approved for children 6–11 yr old</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>Reduces by ~50%</td>
<td>Inconsistent effect</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (14%)</td>
<td>Standard s.c. dosing has not been shown to decrease sputum eosinophilia; approved at higher dosing for EGPA</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>Reduces by ~50–60%</td>
<td>Improved</td>
<td>Has not been specifically evaluated for this indication</td>
<td>Only weight-based dosing i.v. biologic approved for asthma</td>
</tr>
<tr>
<td>Benralizumab</td>
<td>Reduces by ~25–60%</td>
<td>Improved</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)</td>
<td>Only s.c. biologic that offers every-8-wk dosing</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Reduces by ~50–70%</td>
<td>Improved</td>
<td>Decreases total use of OCS and has been shown to facilitate complete weaning from chronic OCS (50%)</td>
<td>Only biologic that can be self-administered s.c.; showed benefit with $F_{ENO} \geq 25$ ppb regardless of eosinophil count</td>
</tr>
</tbody>
</table>
Role of Biologics in Asthma

Mary Clare McGregor, James G. Krings, Parameswaran Nair, and Mario Castro
Conclusion

• Most of the patients with Asthma do not require Biologic if they are adherent with their usual controller medications.
• Allergic Asthma is aggravated because of elevated level of eosinophil.

• Biologic therapy is used in moderate or severe persistence Asthma.

(T2-High Asthma)

- eosinophilic airway inflammation
- mucus production, smooth muscle contraction, and remodeling (Anti IL-4R mABs therapy)

• Biologics

- IgE activated (allergic response) inflammation (Anti IgE – therapy)

• Non eosinophilic or T2-Low Asthma- Neutrophilic inflammation, no biologic approved yet, poorly understood.
Thank you so much!

Any Questions??