Final Live Outcomes Report

The Role of Biologic Therapy in Severe Asthma: A Shifting Treatment Paradigm

Sanofi Genzyme and Regeneron Pharmaceuticals • IME-2018-13285

October 1, 2019
The Role of Biologic Therapy in Severe Asthma: A Shifting Treatment Paradigm

Learning Gains Across Objectives

<table>
<thead>
<tr>
<th>Learning Objectives</th>
<th>Pre-Test</th>
<th>Post-Test</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>LO 1: Describe the current concepts in the pathophysiology of asthma and type 2 inflammation, and the implications of biologic therapies in the era of precision medicine</td>
<td>36.26%</td>
<td>58.79%</td>
<td>+62.12%*</td>
</tr>
<tr>
<td>LO 2: Discuss the clinical assessment of asthma control and risk factors for poor asthma outcomes</td>
<td>25.96%</td>
<td>48.08%</td>
<td>+85.19%*</td>
</tr>
<tr>
<td>LO 3: Individualize the treatment approach for patients with moderate to severe asthma while recognizing appropriate candidates for biologics and other advanced therapies</td>
<td>3.75 (0.94)</td>
<td>3.62 (1.11)</td>
<td>-6.57%</td>
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<tr>
<td>LO 4: Recognize the impact of comorbid conditions on asthma control and evidence-based approaches to their treatment</td>
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</table>

Classification of interleukin cytokines
On a Knowledge item asking learners to identify key Type 2 cytokines, Post-Test scores were low in spite of substantial gains.

Importance of confirming diagnosis for patients with apparent uncontrolled asthma
On a Competence item asking learners to identify the appropriate next step for a patient with a long history of diagnosed asthma and daily symptoms, learners struggled at Post-Test to correctly identify the need to confirm the asthma diagnosis.

Treatment selection for asthma patients unmanaged by current therapies
On Knowledge and Competence items asking learners to select specific therapies for patients with frequent symptoms in spite of currently being treated for asthma, learners struggled at Post-Test to correctly identify the appropriate agent.

Learners demonstrated strong and significant improvements from Pre- to Post-Test in Knowledge and Competence.

A moderate score (3.6) was measured in learners’ reported propensity to assess patients who have uncontrolled asthma for environmental triggers, inhaler technique, and comorbidities.

Sanofi US and Regeneron Pharmaceuticals
IME-2018-13285
In the evaluation, learners (N = 383) were asked to report how many patients with asthma they see in any clinical setting per week by selecting a range. The resulting distribution of learner responses was then extrapolated to reflect the total number of learners who have attended the onsite and online meetings.

The findings reveal that this education has the potential to impact **273,529** patients with asthma on an annual basis.

4,109–5,269 patients with asthma on a weekly basis
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- Boehringer Ingelheim Pharmaceuticals, Inc.
- Shire
- Sanofi Genzyme and Regeneron Pharmaceuticals
- Mallinckrodt Pharmaceuticals, LLC
Overview
Learning Objectives

- Describe the current concepts in the pathophysiology of asthma and type 2 inflammation, and the implications of biologic therapies in the era of precision medicine

- Discuss the clinical assessment of asthma control and risk factors for poor asthma outcomes

- Individualize the treatment approach for patients with moderate to severe asthma while recognizing appropriate candidates for biologics and other advanced therapies

- Recognize the impact of comorbid conditions on asthma control and evidence-based approaches to their treatment
Clinical Highlights eMonograph

eMonograph, containing key teaching points from the CME activity, was distributed 1 week after the meeting to all attendees.
Outcomes Methodology

Learning outcomes were measured using matched Pre-Test and Post-Test scores for Knowledge, Performance, Confidence, and practice strategy and across all of the curriculum’s Learning Objectives.

<table>
<thead>
<tr>
<th>Outcomes Metric</th>
<th>Definition</th>
<th>Application</th>
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<tbody>
<tr>
<td>Percentage change</td>
<td>This is how the score changes resulting from the education are measured. The change is analyzed as a relative percentage difference by taking into account the magnitude of the Pre-Test average.</td>
<td>Differences between Pre-Test, Post-Test, and PCA score averages</td>
</tr>
<tr>
<td>P value (p)</td>
<td>This is the measure of the statistical significance of a difference in scores. It is calculated using dependent or independent samples t-tests to assess the difference between scores, taking into account sample size and score dispersion. Differences are considered significant for when ( p \leq .05 ).</td>
<td>Significance of differences between Pre-Test, Post-Test, and PCA scores and among cohorts</td>
</tr>
<tr>
<td>Effect size (d)</td>
<td>This is a measure of the strength/magnitude of the change in scores (irrespective of sample size). It is calculated using Cohen's d formula, with the most common ranges of d from 0-1: d ( &lt; .2 ) is a small effect, d= .2-.8 is a medium effect, and d &gt; .8 is a large effect.</td>
<td>Differences between Pre-Test and Post-Test score averages</td>
</tr>
<tr>
<td>Power</td>
<td>This is the probability (from 0 to 1) that the “null hypothesis” (no change) will be appropriately rejected. It is the probability of detecting a difference (not seeing a false negative) when there is an effect that is dependent on the significance (p), effect size (d), and sample size (N).</td>
<td>Differences between Pre-Test and Post-Test score averages</td>
</tr>
<tr>
<td>Percentage non-overlap</td>
<td>This is the percentage of data points at the end of an intervention that surpass the highest scores prior to the intervention. In this report, it will reflect the percentage of learners at Post-Test who exceed the highest Pre-Test scores.</td>
<td>Differences between Pre-Test and Post-Test score averages</td>
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</table>
Level 1 Participation
Demographics
Patient Reach

Participation

468 Total Attendees
1 Activity
Level 1: Demographics and Patient Reach

**Specialty**

- **Primary Care**: 69.74%
- **Other**: 13.16%
- **Pulmonology**: 7.89%
- **Neurology/Psychiatry**: 2.63%
- **Emergency Medicine/Critical Care**: 2.63%
- **Cardiology**: 2.63%

**Patient Care Focus**: 92%

**Patients with asthma seen each week, in any clinical setting:**

- None: 69.74%
- 1-5: 13.16%
- 6-10: 7.89%
- 11-15: 4.72%
- 16-20: 3.77%
- 21-25: 0.94%
- > 25: 0%

**Average number of patients with asthma seen each week per clinician**: 9

**Profession**

- **NP**: 59.43%
- **MD**: 23.58%
- **PA**: 7.55%
- **DO**: 4.72%
- **Other**: 3.77%
- **RN**: 0.94%

**Years in Practice**

- **< 5**: 28.83%
- **5-10**: 16.22%
- **11-20**: 20.72%
- **> 20**: 34.23%

N = 144
Level 2-5: Outcomes Metrics
Learning Objective Analysis

Substantial and significant improvements were measured across all curriculum Learning Objectives, from Pre- to Post-Test.

- Pre- and Post-Test scores were low for all Learning Objectives, due to uniformly low scores on scored Knowledge and Competence questions.
- The highest scoring item, about use of targeted therapies, had an average Post-Test score of 73%.
Learners demonstrated strong and significant improvements from Pre- to Post-Test in Knowledge and Competence.

- In spite of these gains, Post-Test scores in both Knowledge and Competence remained low.
- Though Post-Test scores in Knowledge and Competence were low, over half of learners gave a 4 or 5 rating to the improvement in their confidence in their ability to integrate biologic therapy for patients with severe asthma.
- A moderate score (3.6) was measured in learners’ reported propensity to assess patients who have uncontrolled asthma for environmental triggers, inhaler technique, and comorbidities.

Note: Knowledge and Competence data is matched

*significant at the p ≤ 0.05 level, matched data
Learning Objectives Retention Analysis – 4 weeks

- Substantial and significant gains were retained all of the four curriculum Learning Objectives
- On three of the four Learning Objectives, scores decreased mildly from Post-Test to follow-up
  - Learners’ understanding of assessment of asthma control and risk factors for poor outcomes increased substantially between the Post-Test and follow-up measurements, highlighting ongoing improvements in this area

*(significant at the $p \leq 0.05$ level)

Note: data is matched; learners with a score for the given domain on both the Pre-Test and PCA are included
At follow-up:

- In addition to collecting Confidence and Practice data for the curriculum, the Post Curriculum Assessment (PCA) included questions from the Knowledge and Competence domains.
- A statistically significant net gain was measured from Pre-Test to the Post Curriculum Assessment (PCA) in both Knowledge (71%) and Competence (27%).
- In both Competence, some decrease in score was measured between Post-Test and PCA, reflecting a need for further reinforcement of case-based content.

*Note: data is matched; learners with a score for the given domain on both the Pre-Test and PCA are included.*

*significant at the p ≤ 0.05 level*
Cohort Comparison by Profession: Learning Objectives

<table>
<thead>
<tr>
<th>Learning Objective</th>
<th>Nurse Practitioners</th>
<th>Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Pre-Test</td>
</tr>
<tr>
<td>Describe the current concepts in the pathophysiology of asthma and type 2 inflammation, and the implications of biologic therapies in the era of precision medicine</td>
<td>29</td>
<td>13.79% (25.92%)</td>
</tr>
<tr>
<td>Discuss the clinical assessment of asthma control and risk factors for poor asthma outcomes</td>
<td>36</td>
<td>44.44% (42.13%)</td>
</tr>
<tr>
<td>Individualize the treatment approach for patients with moderate to severe asthma while recognizing appropriate candidates for biologicals and other advanced therapies</td>
<td>39</td>
<td>18.16% (24.74%)</td>
</tr>
<tr>
<td>Recognize the impact of comorbid conditions on asthma control and evidence-based approaches to their treatment</td>
<td>37</td>
<td>22.97% (34.08%)</td>
</tr>
</tbody>
</table>

- Substantial improvements across all Learning Objectives were measured for both nurse practitioners and physicians.
- These gains were greater for nurse practitioners, though physicians had higher or similar Post-Test scores.
- These results should be interpreted with caution due to the small sample size.
## Cohort Comparison by Profession: Learning Domains

<table>
<thead>
<tr>
<th>Learning Domain</th>
<th>Nurse Practitioners</th>
<th>Physicians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$N$</td>
<td></td>
</tr>
<tr>
<td>Knowledge</td>
<td>34</td>
<td>Pre-Test: 32.84% (33.45%)</td>
</tr>
<tr>
<td>Competence</td>
<td>37</td>
<td>Pre-Test: 22.97% (34.08%)</td>
</tr>
</tbody>
</table>

- Substantial improvements in both Knowledge and Competence were measured for both nurse practitioners and physicians.
- These gains were greater for nurse practitioners, though physicians had higher or similar Post-Test scores.
- These results should be interpreted with caution due to the small sample size.
Please select the specific areas of skills, or practice behaviors, you have improved regarding the treatment of patients with asthma since this CME activity. (Select all that apply.)

N=116

- Patient education: 50%
- Disease state awareness: 61%
- Pharmacotherapy: 50%
- Non-pharmacotherapy: 28%
- Timely referral: 45%
- Patient engagement regarding treatment options: 33%
- Screening protocols: 45%
- Diagnostic evaluation: 49%
What specific barriers have you encountered that may have prevented you from successfully implementing strategies for patients with asthma since this CME activity? (Select all that apply.)

N=116

- Medication costs: 34%
- Insurance/financial issues: 34%
- Patient adherence/compliance: 46%
- Lack of knowledge: 27%
- Time constraints: 18%
- Formulary constrictions: 28%
- System constraints: 19%
Identified Learning Gap, 1 of 3: Importance of confirming diagnosis for patients with apparent uncontrolled asthma

On a Competence item asking learners to identify the appropriate next step for a patient with a long history of diagnosed asthma and daily symptoms, learners struggled at Post-Test to correctly identify the need to confirm the asthma diagnosis.

Competence: A 59-year-old obese woman with 20-year history of physician diagnosed asthma presents with daily asthma symptoms, nighttime awakenings 2-3 nights per week, and frequent use of a rescue inhaler. She reports difficulty walking uphill or a flight of stairs. Current medications include high-dose ICS/LABA and LAMA. Which of the following would be the appropriate next step?

Results:

- At Post-Test, 41% of learners correctly answered: “Confirm diagnosis of asthma”
Identified Learning Gap, 2 of 3: *Classification of interleukin cytokines*

On a Knowledge item asking learners to identify key Type 2 cytokines, Post-Test scores were low in spite of substantial gains.

**Knowledge: All of the following are key Type 2 cytokines except:**

**Results:**
- At Post-Test, 69% of learners correctly answered: “IL-8”
Identified Learning Gap, 3 of 3:
*Treatment selection for asthma patients unmanaged by current therapies*

On Knowledge and Competence items asking learners to select specific therapies for patients with frequent symptoms in spite of currently being treated for asthma, learners struggled at Post-Test to correctly identify the appropriate agent.

**Knowledge:** Which of the following add-on therapies would be most appropriate for a patient who has severe uncontrolled asthma despite GINA step 4 therapy and low levels of Type 2 inflammation?

**Results:**
- At Post-Test, only 29% of learners correctly answered: “Bronchial thermoplasty”

**Competence:** 44-y/o man with history of asthma since childhood presents with frequent asthma symptoms despite treatment with high-dose ICS/LABA plus LAMA, and prednisone 10 mg/day. He has required two hospitalizations in the last one year for acute asthma. Comorbidities include atopic dermatitis, poorly controlled with topical agents. Spirometry reveals moderate airflow obstruction with bronchodilator reversibility. Patient demonstrates good inhaler technique and confirms regular use of medications. Serum IgE 20 kU/L. Negative allergen skin testing. Blood eosinophils 450 cells per mcL. Which of the following agents might be most appropriate at this time?

**Results:**
- At Post-Test, only 42% of learners correctly answered: “Dupilumab”
Overall Educational Impact

- Significant and substantial improvements (of 62% and 85%) were seen in both learner Knowledge and Competence
  - Post-Test scores of 59% and 48% were measured in Knowledge and Competence, following low (36% and 26%) Pre-Test scores
  - Final scores on Confidence and practice strategy questions were moderate (3.75 and 3.62), and collected in the Post Curriculum Assessment (PCA)

- Substantial and significant improvements ranging from 36% to 121% were measured across all four Learning Objectives, from Pre-Test to Post-Test, but remained low at Post-Test

- The analysis of the Knowledge and Competence domains identified three persistent learning gaps related to the importance of confirming the diagnosis of asthma for patients with apparent uncontrolled asthma, classification of interleukin cytokines, and treatment selection for asthma patients unmanaged by current therapies
  - Pre- and Post-Test scores were low on a Competence item asking learners to identify which the appropriate next step for a patient with a long history of diagnosed asthma and daily symptoms
  - Scores were also low on a Knowledge item asking learners to identify key Type 2 cytokines
  - A knowledge and a competence question both asked learners to select specific therapies for frequent asthma symptoms in spite of current treatments; scores were low for both
Appendix
Knowledge Items

All of the following are key Type 2 cytokines except:

- IL-4: 13.75% (Pre-Test), 5.38% (Post-Test)
- IL-5: 21.25% (Pre-Test), 2.31% (Post-Test)
- IL-8: 33.75% (Pre-Test), +105.13% (Post-Test)
- IL-13: 31.25% (Pre-Test), 23.08% (Post-Test)

N = 80 – 130

Which of the following add-on therapies would be most appropriate for a patient who has severe uncontrolled asthma despite GINA step 4 therapy and low levels of Type 2 inflammation?

- Maintenance oral corticosteroid: 11.83% (Pre-Test), 21.23% (Post-Test)
- Bronchial thermoplasty: √ (13.98% Pre-Test, 28.77% Post-Test)
- Omalizumab: √ (11.83% Pre-Test, 39.73% Post-Test)

N = 93 – 146
All of the following are associated with increased future risk for poor asthma outcomes, EXCEPT:

- Frequent use of rescue inhaler: 14.29% (Pre) vs 5.10% (Post)
- Severe exacerbation in the last year: 7.84% (Pre) vs 7.19% (Post)
- Frequent need for oral corticosteroids: 20.41% (Pre) vs 11.76% (Post)
- Use of targeted therapy: +21.59% (Post) vs 60.20% (Pre)

N = 98 – 153
A 59-year-old obese woman with 20-year history of physician diagnosed asthma presents with daily asthma symptoms, nighttime awakenings 2-3 nights per week, and frequent use of a rescue inhaler. She reports difficulty walking uphill or a flight of stairs. Current medications include high-dose ICS/LABA and LAMA. Which of the following would be the appropriate next step?

- Initiate targeted therapy
- Confirm diagnosis of asthma
- Consider bronchial thermoplasty
- Add theophylline

44-y/o man with history of asthma since childhood presents with frequent asthma symptoms despite treatment with high-dose ICS/LABA plus LAMA, and prednisone 10 mg/day. He has required two hospitalizations in the last one year for acute asthma. Comorbidities include atopic dermatitis, poorly controlled with topical agents. Spirometry reveals moderate airflow obstruction with bronchodilator reversibility. Patient demonstrates good inhaler technique and confirms regular use of medications. Serum IgE 20 kU/l. Negative allergen skin testing. Blood eosinophils 450 cells per mcL. Which of the following agents might be most appropriate at this time?

- Omalizumab
- Dupilumab
- Reslizumab
- Bronchial thermoplasty
Practice Strategy Item (given at 4 week follow-up)

Please rate your level of agreement with the following statement, since attending the Conversations program: I more often assess patients who have uncontrolled asthma for environmental triggers, inhaler technique, and comorbidities

- Never 2.59%
- Rarely 28.45%
- Sometimes 38.79%
- Often 8.62%
- Always 21.55%

N = 116
Confidence Items (given at 4 week follow-up)

Please rate your level of agreement with the following statement: I am much more confident in my ability to recognize patients who meet the diagnostic criteria for severe asthma

- **Strongly agree**: 21.55%
- **Agree**: 50.86%
- **Neutral**: 20.69%
- **Disagree**: 1.72%
- **Strongly disagree**: 5.17%

N = 116

Please rate your level of agreement with the following statement: I am much more confident in how to integrate biologic therapy into the care of patients with severe asthma

- **Strongly agree**: 18.10%
- **Agree**: 46.55%
- **Neutral**: 26.72%
- **Disagree**: 3.45%
- **Strongly disagree**: 5.17%

N = 116