
ICER Public Meeting: Biologic Therapies for the Treatment of Moderate-Severe Uncontrolled Asthma

November 29, 2018



**INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW**

WIFI Code: Hilton1118

Welcome and Introduction

Why are we here this morning?

“I often say my severe asthma is like a firecracker. When the fuse is lit, will it explode? Or will it fizzle out? You can never predict how an asthma exacerbation will end...

...Learning to control my symptoms and living with the risk of experiencing a debilitating flare-up are intricate parts of my journey with severe asthma.”

-Donna Matlach, Asthma Activist

Welcome and Introduction

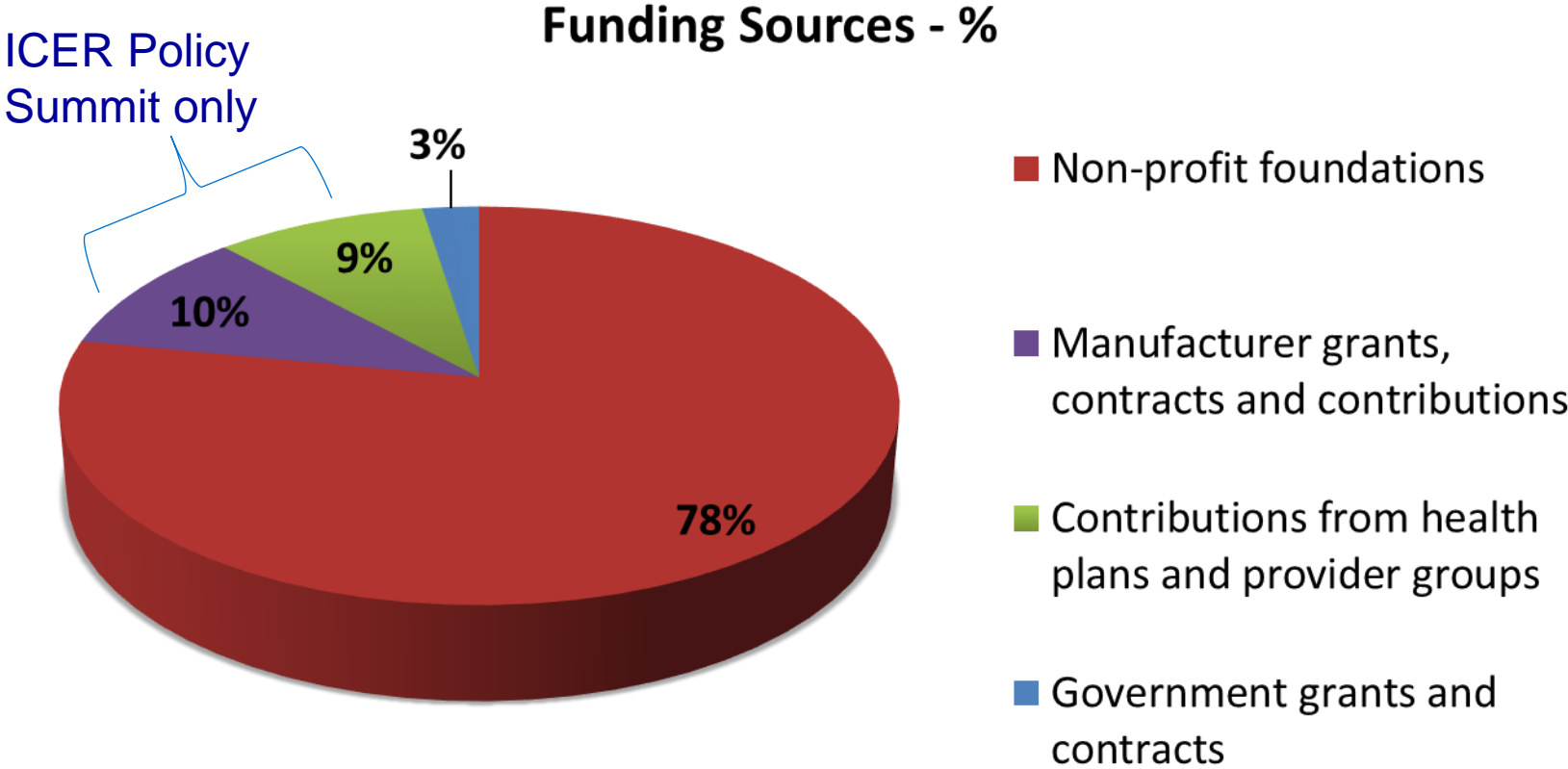
Why are we here this morning?

- New treatment options often raise questions about appropriate use, cost
- Patients get better access to affordable care when prices are aligned with clinical benefits and insurers reciprocate with fewer coverage restrictions
- Need for objective evaluation and public discussion of the evidence on effectiveness and value

Welcome and Introduction

- Midwest Comparative Effectiveness Public Advisory Council (CEPAC)
- The Institute for Clinical and Economic Review (ICER)

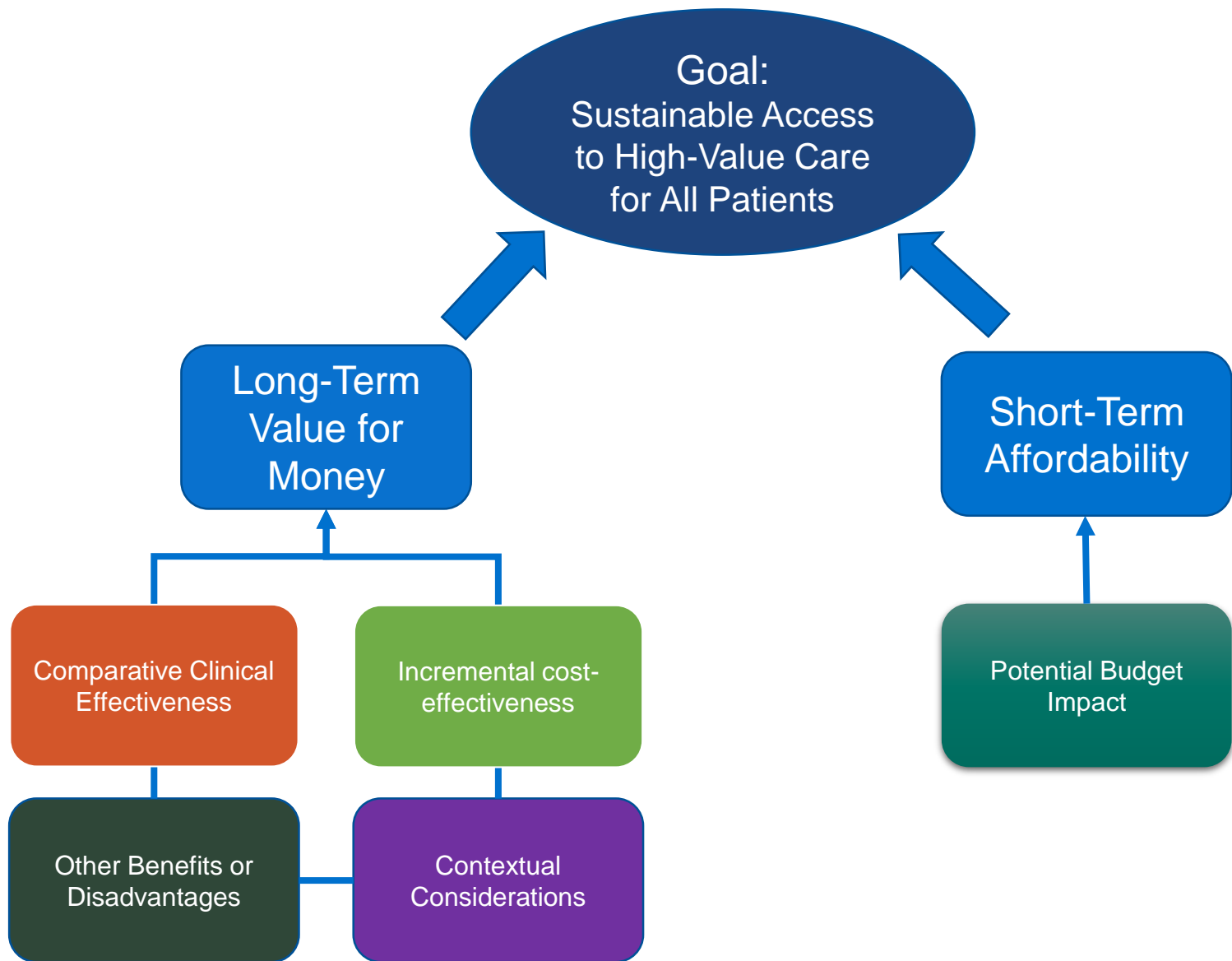
Sources of Funding, 2018



Welcome and Introduction

How was the ICER report on biologic therapies for asthma developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Colorado cost-effectiveness modeling
- Public comment and revision
- Expert report reviewers
 - David Stukus, MD
 - Kenny Mendez
 - Matt Stevenson, PhD
- How is the evidence report structured to support CEPAC voting and policy discussion?



Clinical and Patient Experts

Mario Castro, MD, MPH, Professor of Medicine, Pediatrics, and Radiology, Washington University School of Medicine

- **Disclosures:** Receives grant funding from AstraZeneca, GSK, and Sanofi-Aventis. Consultant for Genentech, Teva, and Sanofi-Aventis. Speaker for Astra-Zeneca, Genentech, Regeneron, Sanofi, and Teva.

Kaharu Sumino, MD, MPH, Pulmonary Physician, St. Louis VA Healthcare Center, Associate Professor of Medicine

- **Disclosures:** None declared.

Kenny Mendez, President and CEO, Asthma and Allergy Foundation of America

- **Disclosures:** AAFA receives funding from AstraZeneca, Genentech, GSK, Sanofi/Regeneron, and Teva.

Morning Agenda

Time	Activity
10:00 am – 10:15 am	Meeting Convened and Opening Remarks <ul style="list-style-type: none">• Steve Pearson, MD, MSc, President, ICER
10:15 am – 11:15 am	Presentation of the Evidence and Economic Modeling <ul style="list-style-type: none">• Jeffrey A. Tice, MD, University of California, San Francisco• Jonathan D. Campbell, PhD, University of Colorado Skaggs
11:15 am – 11:50 am	Manufacturer Public Comments and Discussion
11:50 am – 12:15 pm	Public Comments and Discussion
12:15 pm – 1:00 pm	Lunch
1:00 pm – 2:15 pm	Midwest CEPAC Panel Vote on Clinical Effectiveness and Value
2:15 pm – 2:25 pm	Break
2:25 pm – 3:40 pm	Policy Roundtable Discussion
3:40 pm – 4:00 pm	Reflections from Midwest CEPAC Panel
4:00 pm	Meeting Adjourned

Evidence Review

Jeffrey A. Tice, MD

Professor of Medicine

University of California San Francisco



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Key Review Team Members

- **Jeffrey A. Tice, MD,**
Professor of Medicine, UCSF
- **Judith Walsh, MD, MPH,**
Professor of Medicine, UCSF
- **Patricia Synnott, MALD, MPH,**
Senior Research Lead, ICER

Disclosures:

We have no conflicts of interest relevant to the report.

Background: Severe Asthma

- Asthma that requires treatment with high-dose inhaled corticosteroids, plus a second controller and/or systemic glucocorticoids
 - 5%-10% of individuals with asthma
 - 50% of asthma costs
- Standard of care
 - High-dose inhaled corticosteroid and second controller agent (long acting beta agonists)
- Biologic therapies are add-on therapies to standard of care
 - Target Type 2 inflammation: 50% of severe asthma phenotype

Biologic Therapies

Drug	Mechanism	FDA Approval
Omalizumab (Xolair)	Anti IgE	2007
Mepolizumab (Nucala)	Anti IL-5	2015
Reslizumab (Cinqair)	Anti IL-5	2016
Benralizumab (Fasenra)	Anti IL-5R α	2017
Dupilumab (Dupixent)	Anti IL-4R α	2018

Biologic Therapies: Differences in Administration

Drug	Route	Frequency	Location
Omalizumab (Xolair)	SC	Q 2-4 weeks	MD Office
Mepolizumab (Nucala)	SC	Q 4 weeks	MD Office
Reslizumab (Cinqair)	IV	Q 4 weeks	MD Office
Benralizumab (Fasenra)	SC	Q 8 weeks	MD Office
Dupilumab (Dupixent)	SC	Q 2 weeks	Home

Methods

- Systematic review following PRISMA guidelines
- Target population (FDA indications)
 - Adults and children ages 6 years and older with moderate to severe, uncontrolled asthma and evidence of eosinophilic inflammation or allergic asthma
- Interventions
 - 5 Biologic Therapies (prior slide)
- Comparator
 - Standard of care (Daily ICS and at least one other controller therapy)
 - Ideally other biologics

Key theme: Heterogeneity

- Age
- Asthma severity
- Number of exacerbations in the prior year
- Use of OCS
- Definition of an exacerbation
- Length of follow-up

Results:

Asthma exacerbations and FEV1

Treatment	Asthma Exacerbations Rate Ratio (95% CI)	FEV1 (L) Difference (95% CI)
Omalizumab ¹	0.52 (0.37-0.73)	0.06 (0.02-0.10)
Mepolizumab ²	0.45 (0.36-0.55)	0.10 (0.01-0.18)
Reslizumab ²	0.43 (0.33-0.55)	0.12 (0.08-0.16)
Benralizumab ²	0.59 (0.51-0.68)	0.13 (0.08-0.19)
Dupilumab 200mg ³	0.52 (0.41-0.66)	0.14 (0.08-0.19)
Dupilumab 300mg ³	0.54 (0.43-0.68)	0.13 (0.08-0.18)

¹ Cochrane 2014

² Cochrane 2017

³ Castro NEJM 2018

Results:

Symptoms and Quality of Life

Treatment	ACQ	SGRQ	AQLQ
Omalizumab ¹	NR	NR	0.26 (0.05-0.47)
Mepolizumab ²	-0.42 (-0.56 to -0.28)	-7.4 (-9.5 to -5.3)	NR
Reslizumab ²	-0.27 (-0.36 to -0.19)	NR	0.28 (0.17-0.39)
Benralizumab ²	-0.23 (-0.34 to -0.12)	NR	0.23 (0.11-0.35)
Dupilumab 200mg ³	-0.39 (-0.53 to -0.25)	NR	0.29 (0.15-0.44)
Dupilumab 300mg ³	-0.22 (-0.36 to -0.08)	NR	0.26 (0.12-0.40)

ACQ: Asthma Control Questionnaire, MCD \geq 0.5

SGRQ: St. George's Respiratory Questionnaire, MCD \geq 4

AQLQ: Asthma Quality of Life Questionnaire, MCD \geq 0.5

¹ Cochrane 2014

² Cochrane 2017

³ Castro NEJM 2018

Results:

Reduction in OCS dose versus placebo

Treatment	Dose reduction (%)	Off OCS (%)
Omalizumab	-45% vs +18%	32% vs 13%
Mepolizumab	-50% vs 0%*	14% vs 8%
Reslizumab	NR	NR
Benralizumab	-75% vs -25%*	52% vs 19%
Dupilumab 200mg	NR	NR
Dupilumab 300mg	-70% vs -42%	52% vs 29%

*Median

Subgroup results: NMA: Eos \geq 300, \geq 2 exacerbations, ACQ \geq 1.5

Treatment	Overall trials (RR)	Subgroup NMA (RR)
Omalizumab	0.52 (0.37-0.73)	0.33 (0.10-1.14)
Mepolizumab	0.45 (0.36-0.55)	0.36 (0.16-0.81)
Reslizumab	0.43 (0.33-0.55)	0.34 (0.11-1.03)
Benralizumab	0.59 (0.51-0.68)	0.59 (0.26-1.29)
Dupilumab 200mg	0.52 (0.41-0.66)	0.26 (0.08-0.79)
Dupilumab 300mg	0.54 (0.43-0.68)	0.26 (0.08-0.80)

Adverse Events

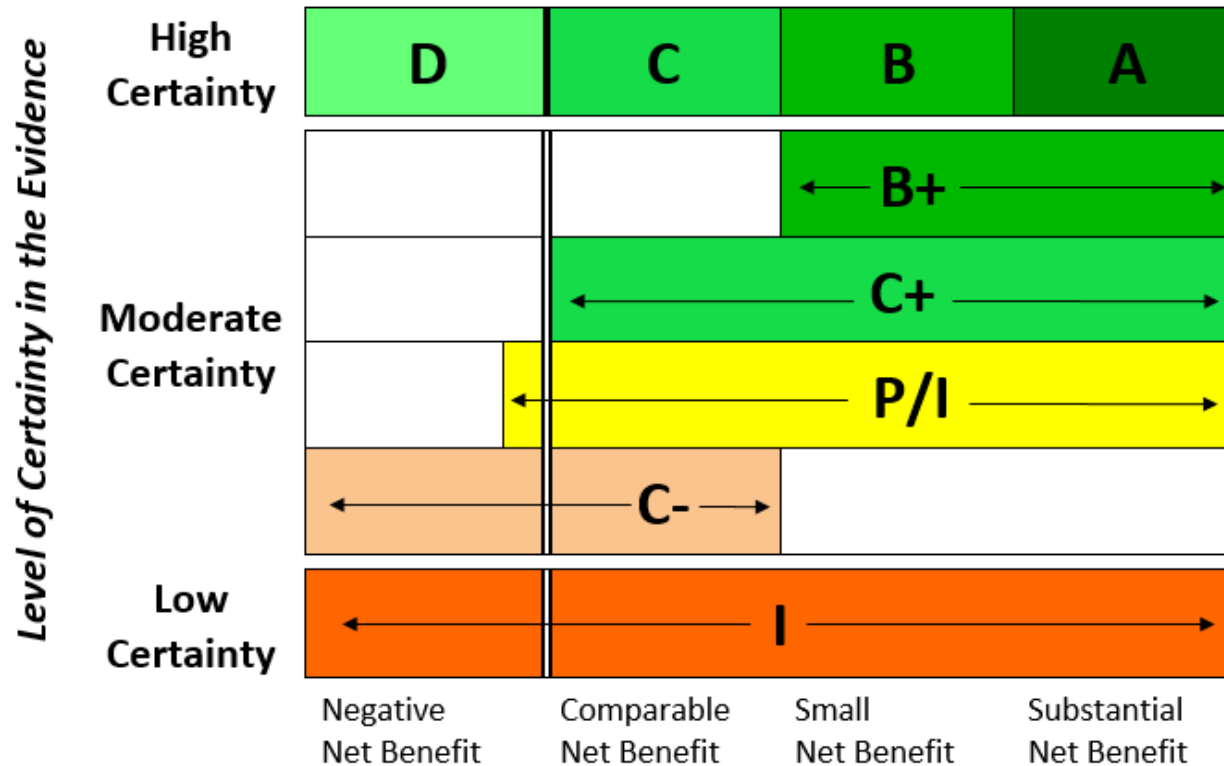
- No difference in SAEs
- No difference in hypersensitivity reactions
- More injection site reactions – mostly minor.
- Only dupilumab 300 mg had significantly more withdrawals due to adverse events (7.0% vs 3.1%)

Controversies and Uncertainties

- Heterogeneity of study populations / lack of head to head studies.
 - Editorial: the 5 therapies should be viewed “as essentially equivalently effective treatments.”
- Quality of life measures essential, but not consistently measured across trials (instrument, timing)
- Little long term and real world evidence for the more recently approved drugs (reslizumab, benralizumab, dupilumab)
- No clear definition of response to therapy – thus no guidance for continuing / stopping therapy

Evidence Matrix

Comparative Clinical Effectiveness



Effectiveness: Summary

- High certainty of small net benefit for **omalizumab** and **mepolizumab** as add-on maintenance treatment compared with standard of care (**B**)
- Moderate certainty of comparable or better net benefit for **reslizumab**, **benralizumab**, and **dupilumab** compared with standard of care (**C+**)
- There is low certainty in the comparative clinical effectiveness of the five biologic therapies (**I**)

Public comments

- Heterogeneity
- Some drugs have other benefits / indications
- NMA issues
 - Not transparent
 - Published NMAs – see appendix B
 - Specific data provided
- 48 to 56 weeks FU is “long-term”
- Focus on mechanism rather than outcomes

Questions?

Cost Effectiveness

Jonathan D. Campbell, PhD

University of Colorado Anschutz Medical Campus



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Rick Chapman, PhD, Institute for Clinical and Economic Review

Disclosures:

Financial support was provided to the University of Colorado from the Institute for Clinical and Economic Review.

University of Colorado researchers have no conflicts to disclose defined as more than \$10,000 in healthcare company stock or more than \$5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers.

Objective

- The primary aim of this analysis was to estimate the cost-effectiveness of each of the five biologic agents for the treatment of moderate to severe uncontrolled asthma with evidence of type 2 inflammation.
 - Captures broad population

Methods in Brief

Base-Case Population

Characteristic	Across All Biologic Agents*
Mean (SD) age in years	46 (42-50)
Mean (SD) weight (kg)	85 (75-95)
Percent female	62% (60%-64%)
Percent Chronic OCS Users†	17% (13%-28%)

*Values displayed are derived from the clinical review and averaged over trials; plausible ranges include the minimum and maximum values from an individual trial's evidence, where available.

†Chronic oral steroid (OCS) definitions differ by evidence source, but can be interpreted as the proportion of the biologic eligible cohort that use > 5 mg per day of prednisone or equivalent with high levels of adherence.

Interventions and Comparator

Interventions:

Omalizumab	75-375mg subcutaneous injection (1 every 2 or 4 weeks)
Mepolizumab	100mg subcutaneous injection (1 every 4 weeks)
Reslizumab	3mg/kg intravenous infusion (1 every 4 weeks)
Benralizumab	30mg subcutaneous injection (1 every 4 weeks * 3 then 1 every 8 weeks)
Dupilumab	200mg or 300mg subcutaneous injection (1 every 2 weeks)

Comparator:

- Standard of care (SoC) - daily inhaled corticosteroids plus at least one additional controller therapy.

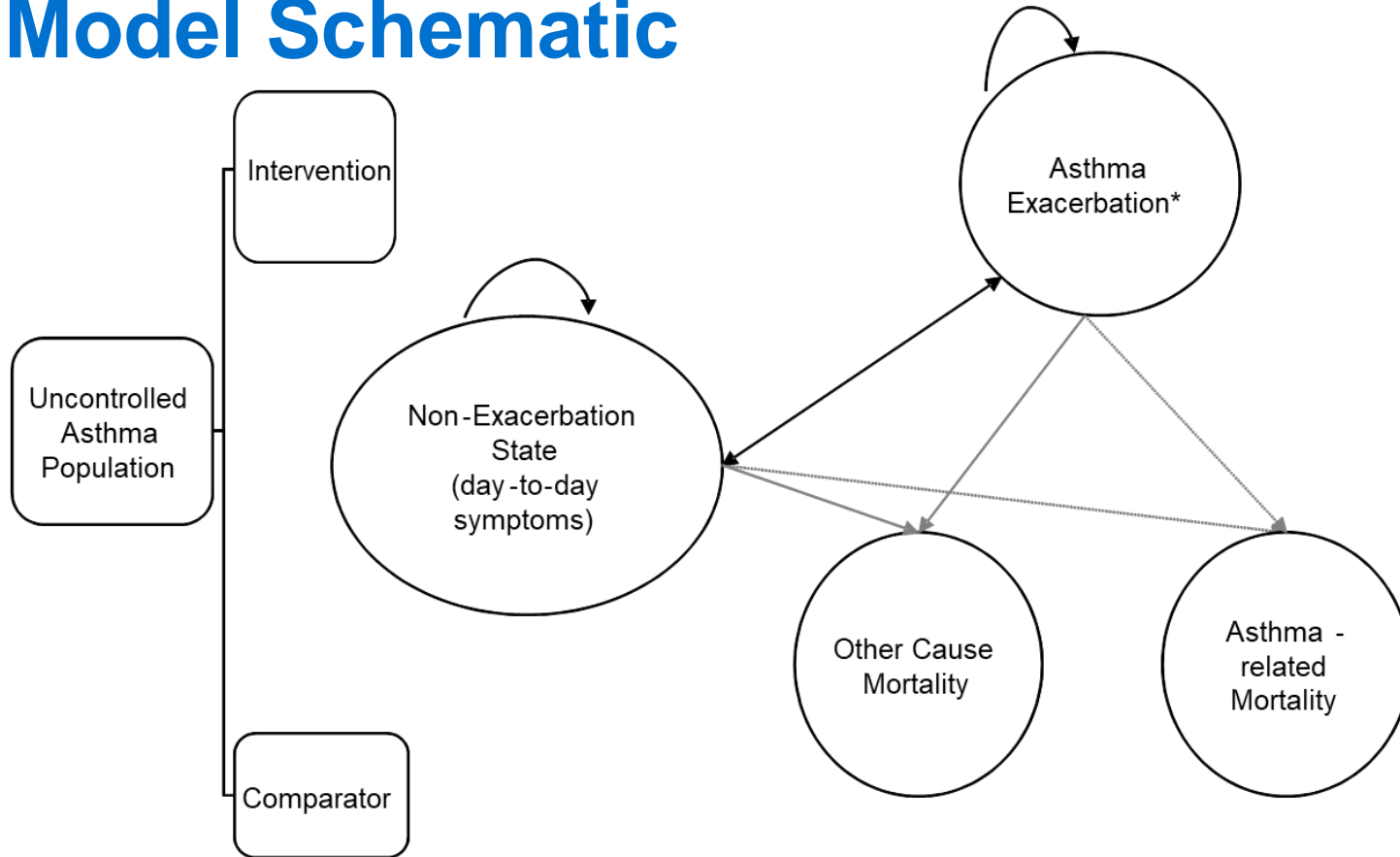
Methods Overview

- **Model:** Markov
- **Setting:** United States
- **Perspective:** Health care sector (direct medical care and drug costs)
- **Time Horizon:** Lifetime
- **Discount Rate:** 3% per year (costs and outcomes)
- **Cycle Length:** 2 weeks
- **Primary Outcome:** Cost per quality-adjusted life year (QALY) gained

Methods Highlights

- QALY Gains:
 - Day-to-day quality of life improvements
 - Asthma exacerbation reductions
 - Reductions in chronic oral steroid use
- Health Sector Costs:
 - Manufacturer-submitted net price
 - Cost offsets from reduced severe exacerbations and reduced chronic oral steroid use

Model Schematic



*Exacerbation could be defined into different subcategories:

1. Asthma related event that requires an oral steroid burst (but not emergency room or hospitalization)
2. Asthma related event that requires admittance to the emergency department (but not a hospitalization)
3. Asthma related event that requires a hospitalization

Key Assumptions

- Same SoC for all comparisons
- Utility for the non-exacerbation health state
- Exacerbations requiring an ED or hospitalization
~ increased mortality
- Chronic OCS ~ costs and disutility

Exacerbation-Related Inputs: Intervention

Characteristic	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab†
Rate Ratio for Exacerbations Resulting in Steroid Burst (w/o ED visit or hospitalization)	0.52 (0.37-0.73)	0.45 (0.36- 0.55)	0.43 (0.33-0.55)	0.59 (0.51- 0.68)	Not reported; assumed 0.52 (0.41- 0.66)
Rate Ratio for Exacerbations Resulting in ED visit (w/o hospitalization)	0.40 (0.19-0.82)*	0.36 (0.20- 0.66)	0.67 (0.39- 1.17)	0.68 (0.47- 0.98)	Not reported; assumed 0.52 (0.41- 0.66)
Rate Ratio for Exacerbations Resulting in Hospitalization	0.16 (0.06- 0.42)	0.31 (0.13- 0.73)	0.67 (0.39- 1.17)	0.68 (0.47- 0.98)	Not reported; assumed 0.52 (0.41- 0.66)

*Evidence source was not reported within the clinical review but was included in a prior meta-analysis

†Rate ratio for dupilumab for each subcategory of exacerbation was assumed the same as the overall exacerbation rate ratio.

Exacerbation-Related Inputs: SoC

Characteristic	Standard of Care Across All Biologics
Annualized Exacerbation Rate Per Person Year, End of Study (95% CI)*	1.30 PPY (plausible range: 0.9- 2.3)
Proportion of Exacerbations Resulting in Steroid Burst (without ED visit or hospitalization)†	90%
Proportion of Exacerbations Resulting in ED visit (without hospitalization) †	5%
Proportion of Exacerbations Resulting in Hospitalization†	5%

PPY: Per Person Year;

*Values displayed are derived from the clinical review unless otherwise specified, averaged over trials; plausible ranges include the minimum and maximum values from an individual trial evidence, where available.

†Assumed based off of values from Ortega et al. 2014, Bousquet et al. 2005, and Castro et al. 2015.

Utilities

- Direct elicitation not available
- Mapping options: ACQ, AQLQ, or SGRQ
- Non-exacerbation utility was 0.062 greater for biologic vs. SoC using SGRQ mapping
- Exacerbation disutility applied for two weeks
- Chronic OCS disutility applied for lifetime

Manufacturers Submitted Net Price

Characteristic	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab
Unit	150 mg vial	100 mg	100 mg/ml vial	30 mg	2 x 200mg or 2 x 300mg
Wholesale Acquisition Cost (WAC)	\$1,084.66	\$2,868.67	\$878.80	\$4,752.11	\$2,931.54
Manufacturer Net Price (% of WAC)	\$802.64* (74% of WAC)	\$2,272† (79% of WAC)	\$804.10‡ (91% of WAC)	\$4,265¥ (90% of WAC)	\$2,384.62^ (81% of WAC)

*Per manufacturer: "Net price per 150mg vial was calculated using the manufacturer-provided annual net cost. Omalizumab's average annual net cost per adult patient is \$28,895. Average annual net cost of treatment for adults with allergic asthma only (as of July 2018) assuming three 150 mg vials per month. Net cost assumption is an average cost reflecting all price concessions given to customers, and inclusive of all statutory discounts and rebates. This calculation is an estimate for the purposes of financial modeling. Cost of treatment per patient varies as dosing depends on age, weight and IgE level and pricing differs by provider and payer (commercial insurance or government program)."

†Per manufacturer: "Average net sales price is inclusive of WAC rebates, allowances, and returns."

‡Per manufacturer: "This net price reflects a weighted average after applying statutory discounts."

¥Per manufacturer: "The net price for each 30mg/ml pre-filled syringe of Benralizumab is \$4265. This price includes government statutory rebates, allowances, and returns." Benralizumab will have an additional cost of \$6,302.30 for the first year of treatment due to the higher frequency of administration for the first three doses.

^Per the manufacturer: "The net price of \$31,000 should be considered as inclusive of all discounts applied to dupilumab throughout the value chain and not just reflective of rebates alone." Dupilumab will have an additional cost of \$1,192.31 for the first year of treatment due to the loading dose.

Results

Base-Case Discounted Costs and Outcomes

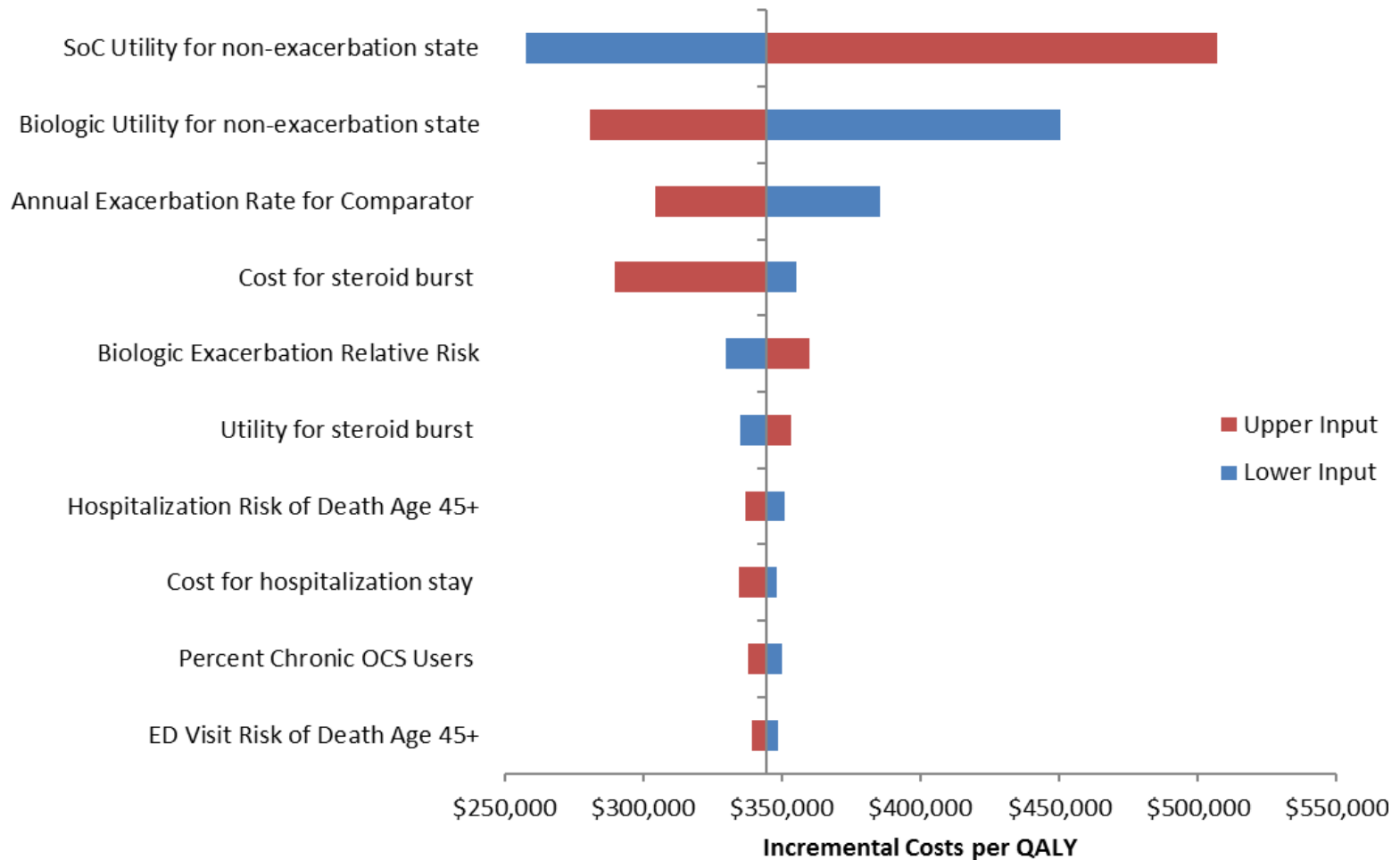
- Total lifetime discounted QALY:
 - Biologic therapies: 16.00-16.32 QALYs
 - SoC: 14.59 QALYs
- Total lifetime discounted costs:
 - Biologic therapies: \$715,000 to \$771,000
 - SoC: \$193,000

Base-Case Discounted Incremental Results

	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab
Cost per QALY Gained (vs. SoC)	\$325,000/ QALY	\$344,000/ QALY	\$391,000/ QALY	\$371,000/ QALY	\$374,000/ QALY

QALY: Quality-adjusted life year, SoC: Standard of care

One-Way Sensitivity Analysis: Mepolizumab



Probabilistic Sensitivity Analysis

	Cost-Effective at \$50,000 per QALY	Cost-Effective at \$100,000 per QALY	Cost-Effective at \$150,000 per QALY
Omalizumab	0%	0%	0%
Mepolizumab	0%	0%	0%
Reslizumab	0%	0%	0%
Benralizumab	0%	0%	0%
Dupilumab	0%	0%	0%

QALY: Quality-adjusted life year

Scenario Analyses

- Modified societal perspective
 - Incremental \$/QALY reduced by 5% to 10%
- NMA subgroup
 - Incremental \$/QALY reduced by 0% to 12%
- Responder scenario
 - Identify and treat only responders for long-term
 - All benefits go to responder subset
 - Incremental \$/QALY ranged from \$199,000/QALY to \$222,000/QALY

Collective Best-Case Scenarios

Incremental CE Ratio

	#1 (favorable inputs)	#2 (#1 and assume 100% chronic OCS users)	#3 (#1 and responder scenario)
Cost per QALY gained (vs. SoC)	\$226,000/ QALY	\$174,000/ QALY	\$156,000/ QALY

QALY: quality-adjusted life year, SoC: standard of care

1. Used most favorable exacerbation and chronic oral steroid inputs and the lowest annualized price;
2. #1 and assumed a subpopulation of only those on chronic oral corticosteroids as a part of SoC and;
3. #1 and assumed the responder scenario.

Limitations

- Lack of evidence for responders and discontinuation
- Assumed constant treatment benefits, lifetime duration
- Indirect mortality impact through reduced asthma-related hospitalizations and ED visits
- Health utility for the day-to-day non-exacerbation health state was identified as the most influential input.

Public Comments Summary

- Concerns over using an average SoC across assessed biologics
- Suggestion to consider treatment responders within the base-case finding
- Including the patient's voice in value metrics

Conclusions

- Biologic agents provide gains in quality-adjusted survival
- Biologic agents seem to be priced higher than the modeled benefits
- Higher value care through:
 - careful patient selection
 - continued biologic therapy for only treatment responders

Questions?

Extra Slides

Treatment Regimen

Characteristic	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab
Treatment dose	75-375 mg every 2 to 4 weeks (assumed 36 vials per year with wastage)	100 mg every 4 weeks	3.0 mg/kg every 4 weeks (assumed 2 to 3 single-use 100mg/ml vials per administration or 36 per year with wastage)	30 mg every 4 weeks (first 3 doses) then every 8 weeks	200mg or 300 mg every 2 weeks
Route of administration	Subcutaneous injection	Subcutaneous injection	Intravenous infusion	Subcutaneous injection	Subcutaneous injection
Relative Reduction in chronic oral corticosteroid use post trial (% biologic vs. % SoC with chronic use > 5mg per day)	0.78 (67.8% vs. 87.0%)	0.68 (46% vs. 68%)	1.0 (No comparative evidence reported)*	0.61 (41% vs. 67%)	0.46 (31% vs. 67%)

*For evidence “Not reported,” no difference was assumed (i.e., relative reduction of 1.0) between biologic plus SoC versus SoC alone.

Productivity Costs

Input	Variable	Source
Average Hourly Wage	\$24.68 per hour	Bureau of Labor Statistics, 2018
Hours missed per week (Asthma Biologic)	1.46	Data on File (Genentech)
Hours missed per week (Standard of Care)	3.09	Data on File (Genentech)

One-Way Sensitivity Analyses

Mepolizumab vs. SoC

Input Name	Lower ICER	Upper ICER	Lower Input*	Upper Input*
SoC Utility for Non-Exacerbation State	\$258,000	\$507,000	0.74	0.80
Biologic Utility for Non-Exacerbation State	\$451,000	\$281,000	0.81	0.85
Annual Exacerbation Rate for Comparator	\$385,000	\$304,000	0.78	1.95
Cost for Exacerbation-Related Steroid Burst	\$355,000	\$290,000	\$0	\$9,172
Biologic Overall Exacerbation Relative Risk	\$330,000	\$360,000	0.34	0.54
Utility for Exacerbation-Related Steroid Burst	\$335,000	\$353,000	0.57	0.76
Hospitalization Risk of Death Age 45+ Years	\$351,000	\$337,000	0.021	0.029
Cost for Hospitalization Stay	\$348,000	\$335,000	\$702	\$27,798
SoC Percent Chronic OCS Users	\$350,000	\$338,000	10.9%	24.2%
ED Visit Risk of Death Age 45+	\$349,000	\$339,000	0.015	0.021

ED: Emergency department, ICER: Incremental cost-effectiveness ratio, SoC: Standard of care

*Note lower input may reflect either upper or lower ICER value depending on the direction that the input has on the ICER output.

Manufacturer Public Comment and Discussion

Speakers

Name	Title	Company
Mark S. Forshag, MD, MHA	US Medical Expert – Respiratory	GlaxoSmithKline
Margaret Garin, MD, MSCR	Director, Clinical Development, Global Research and Development	Teva
Benjamin Kramer, MD	Vice President, Immunology and Ophthalmology, US Medical Affairs	Genentech
Andreas Kuznik, PhD	Senior Director, Health Economics and Outcomes Research	Regeneron
Frank Trudo, MD, MBA	Vice President, US Medical Affairs, Respiratory	AstraZeneca

Public Comment and Discussion

Bradley Becker, MD

St. Louis University School of Medicine

Professor, Allergy and Immunology, Departments of Pediatrics and Internal Medicine

Conflicts of interest:

- None disclosed.

Sarah Franz, RN

St. Louis Children's Hospital

Registered Nurse, Pediatric Intensive Care Unit

Conflicts of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies.

Richard K. Murray, MD
AAFA, Harvard University
Board Member, ALI Fellow

Conflicts of interest:

- None declared.

Teresa Quarles, MSW

Patient Advocate

Conflicts of interest:

- None declared.

Tonya Winders

Allergy & Asthma Network

President and CEO

Conflicts of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies.

Allergy & Asthma Network has received funding for unbranded disease education & awareness in excess of \$5,000 from AstraZeneca, Genentech, GSK, Sanofi Genzyme, and Teva.

Lunch

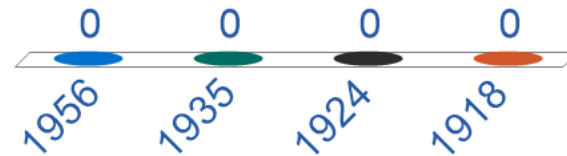
Meeting will resume at 1:00 pm

Voting Questions

WIFI Code: Hilton1118

In what year did the Macy's Day Parade begin?

- A. 1956
- B. 1935
- C. 1924
- D. 1918



1. For patients ≥ 12 years with uncontrolled, moderate to severe asthma, and eosinophilic phenotype:

Is the evidence adequate to demonstrate that the net health benefit of dupilumab is superior to that provided by standard of care (ICS plus at least one additional controller medication)?

- A. Yes
- B. No



2. For patients ≥ 12 years with uncontrolled, severe asthma, and eosinophilic phenotype:

Is the evidence adequate to distinguish the net health benefit among **mepolizumab**, **reslizumab**, and **benralizumab**?

A. Yes

B. No



3. For patients ≥ 12 years with uncontrolled, severe asthma, and eosinophilic phenotype:

(If no on question 2) Is the evidence adequate to distinguish the net health benefit *between dupilumab* and these three treatments (**mepolizumab**, **reslizumab**, and **benralizumab**)?

A. Yes

B. No

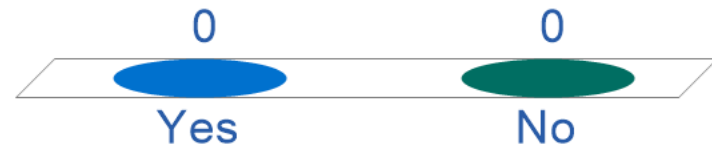


4. For patients ≥ 12 years with uncontrolled, severe asthma, and eosinophilic phenotype:

Is the evidence adequate to distinguish the net health benefit *between* **omalizumab** and these three treatments (**mepolizumab**, **reslizumab**, and **benralizumab**)?

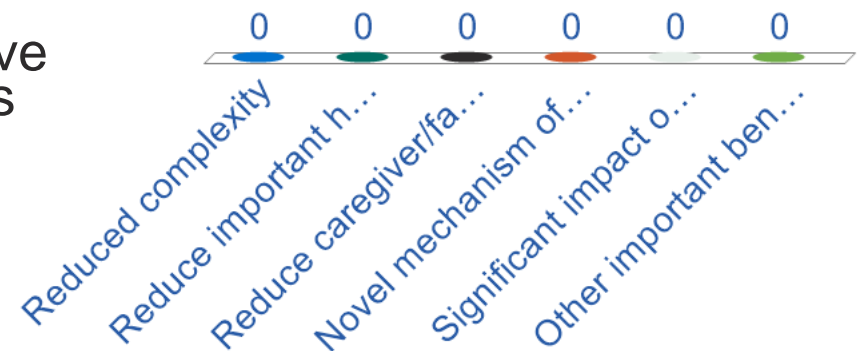
A. Yes

B. No



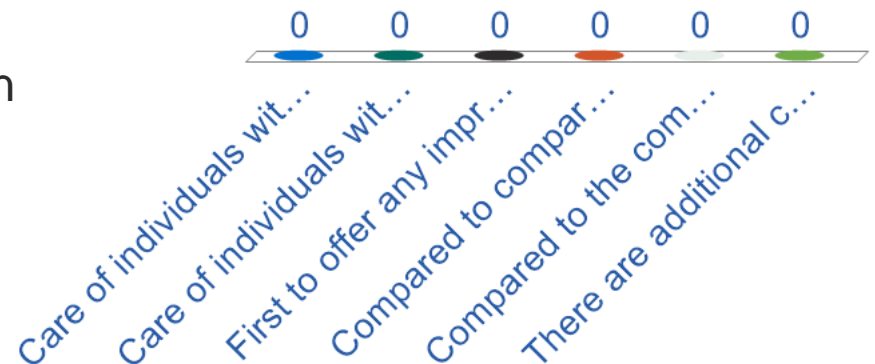
5. In the treatment of patients ≥ 12 years with moderate to severe asthma, does dupilumab offer one or more of the following potential other benefits or disadvantages compared to best usual care without biologic treatment? (select all that apply)

- A. Reduced complexity
- B. Reduce important health disparities
- C. Reduce caregiver/family burden
- D. Novel mechanism of action or approach
- E. Significant impact on improving return to work/overall productivity
- F. Other important benefits or disadvantages that should have an important role in judgments of the value



6. Are any of the following contextual considerations important in assessing the long-term value for money of **dupilumab** versus best usual care without biologics? (select all that apply)

- A. Care of individuals with condition of high severity
- B. Care of individuals with condition with high lifetime burden of illness
- C. First to offer any improvement
- D. Compared to comparator, there is significant uncertainty about long-term risk of serious side effects
- E. Compared to the comparator, significant uncertainty about magnitude or durability of the long term benefits of this intervention
- F. There are additional contextual considerations that should have an important role in judgments of the value of this intervention



Break

Meeting will resume at 2:25 pm

Policy Roundtable

Policy Roundtable Participants

Name	Title	COI Declaration
Mario Castro, MD, MPH	Washington University School of Medicine	Receives grant funding from AstraZeneca, GSK, and Sanofi-Aventis. Consultant for Genentech, Teva, and Sanofi-Aventis. Speaker for Astra-Zeneca, Genentech, Regeneron, Sanofi, and Teva.
David Evan, BA	Teva	Full-time employee of Teva.
Marsha Fisher, MD, FACOG	Anthem BCBS of Missouri	Full-time employee of Anthem BCBS of Missouri.
Mark S. Forshag, MD, MHA	GlaxoSmithKline	Full-time employee of GlaxoSmithKline.
Jeremy Fredell, PharmD, BCPS	Express Scripts	Full-time employee of Express Scripts.
Benjamin Kramer, MD	Genentech	Full-time employee of Genentech.
Andreas Kuznik, PhD	Regeneron	Full-time employee of Regeneron.
Donna J. Matlach, DMin, MM, CDA	Allergy and Asthma Network	AAN has received funding from AstraZeneca, Genentech, GSK, Sanofi Genzyme, and Teva.
Kenny Mendez, MBA	Asthma and Allergy Foundation of America	AAFA receives funding from AstraZeneca, Genentech, GSK, Sanofi/Regeneron, and Teva.
Kaharu Sumino, MD, MPH	Saint Louis VA Medical Center, Washington University School of Medicine	None declared.
Frank Trudo, MD, MBA	AstraZeneca	Full-time employee of AstraZeneca.

CEPAC Panel Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on/about December 20
 - Includes description of CEPAC votes, deliberation; policy roundtable discussion
- Materials available at <https://icer-review.org/topic/asthma/>

Adjourn