JAK Inhibitors and Monoclonal Antibodies for the Treatment of Atopic Dermatitis: Effectiveness and Value

Public Meeting — July 23, 2021

Meeting materials available at: https://icer.org/assessment/atopic-dermatitis-2021/#timeline

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Patient and Clinical Experts

- **Samantha Bittner**, Patient Expert
  - *No financial conflicts to disclose.*

- **Wendy Smith Begolka,** MBS, Vice President of Scientific and Clinical Affairs, National Eczema Foundation
  - The National Eczema Association has received grants and sponsorship awards from a variety of industry partners, including Pfizer, AbbVie, Sanofi, Regeneron, Incyte, and LEO Pharma.

- **Dr. Elaine Siegfried,** MD, Professor of Pediatrics and Dermatology, Saint Louis University School of Medicine
  - Dr. Elaine Siegfried has received consulting fees and honoraria from industry partners, including Incyte, Regeneron, Sanofi, LEO Pharma, Pfizer, and AbbVie for participation in clinical trials as a PI. She also received funding from Pfizer to support a two-year fellowship position at Saint Louis University.

- **Dr. Jonathan Silverberg,** MD, PhD, MPH, Associate Professor, George Washington University School of Medicine and Health Sciences
  - Dr. Jonathan Silverberg has received funding from industry partners, including AbbVie, Eli Lilly, Incyte, LEO Pharma, Regeneron, and Sanofi.

Why are we here today?

I think it's difficult for people to understand how living with eczema can vary greatly from person to person. Everyone's experience with eczema is unique and fluctuating. Eczema can simply be a mild annoyance to some; to others, it can be a debilitating condition that significantly reduces quality of life. The severity of one's eczema can wax and wane over time. Additionally, not only are there many different types of eczema, but there are also many different ways to manage and treat this condition. What works for one person's eczema might not work for someone else's.

Justin, Atopic Dermatitis Patient

Why Are We Here Today?

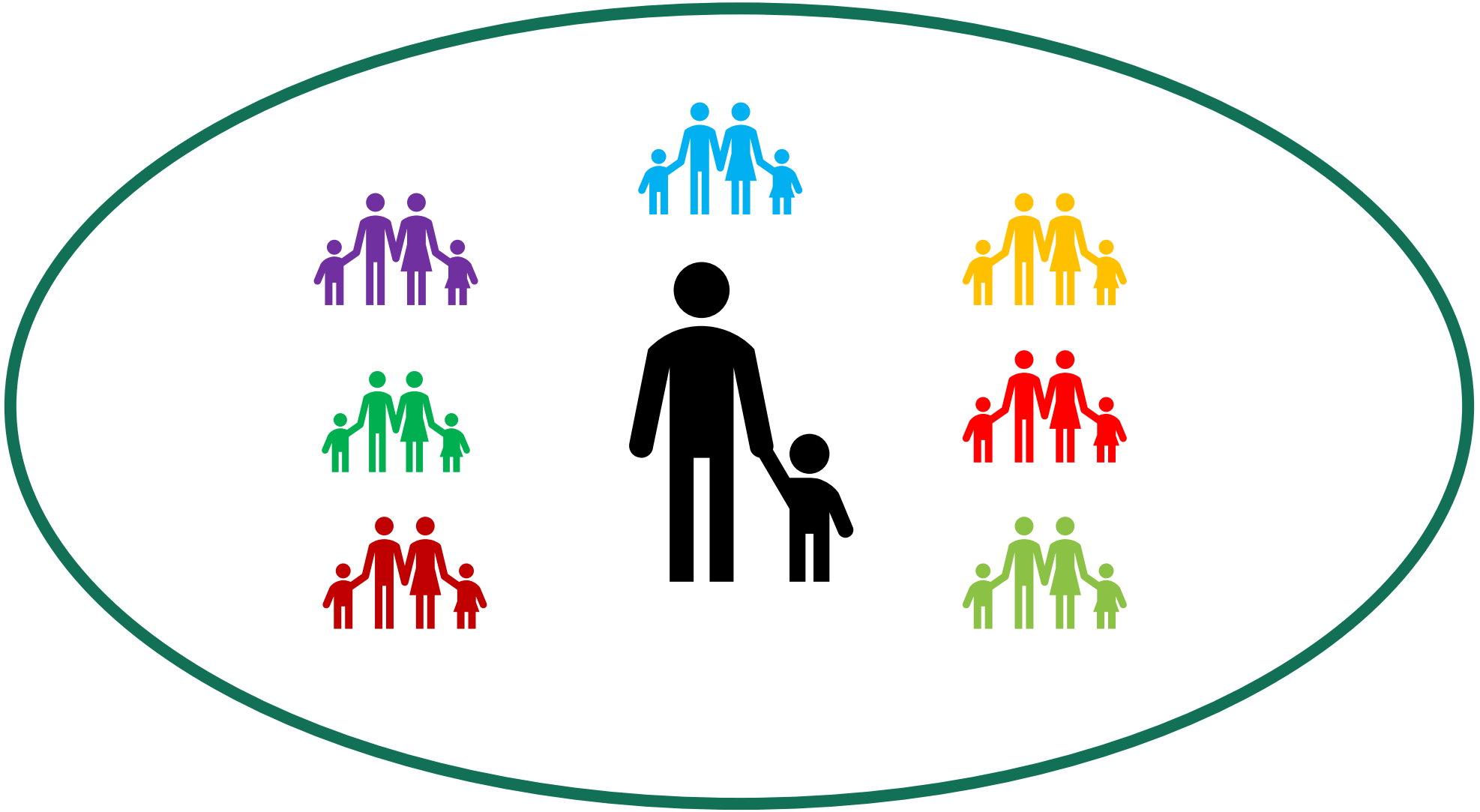
- What happens the day these treatments are approved by the FDA?
- Patients can have difficulty accessing drugs
  - Coverage eligibility
  - Costs (out-of-pocket and insurance premiums)
- What happens to others in the health care “system”?

The Impact of Rising Health Care Costs

Leonard Edloe
Richmond, Virginia

The Whitman family
Bird City, Alaska

The Maccoux family
Brooklyn Park, Minnesota

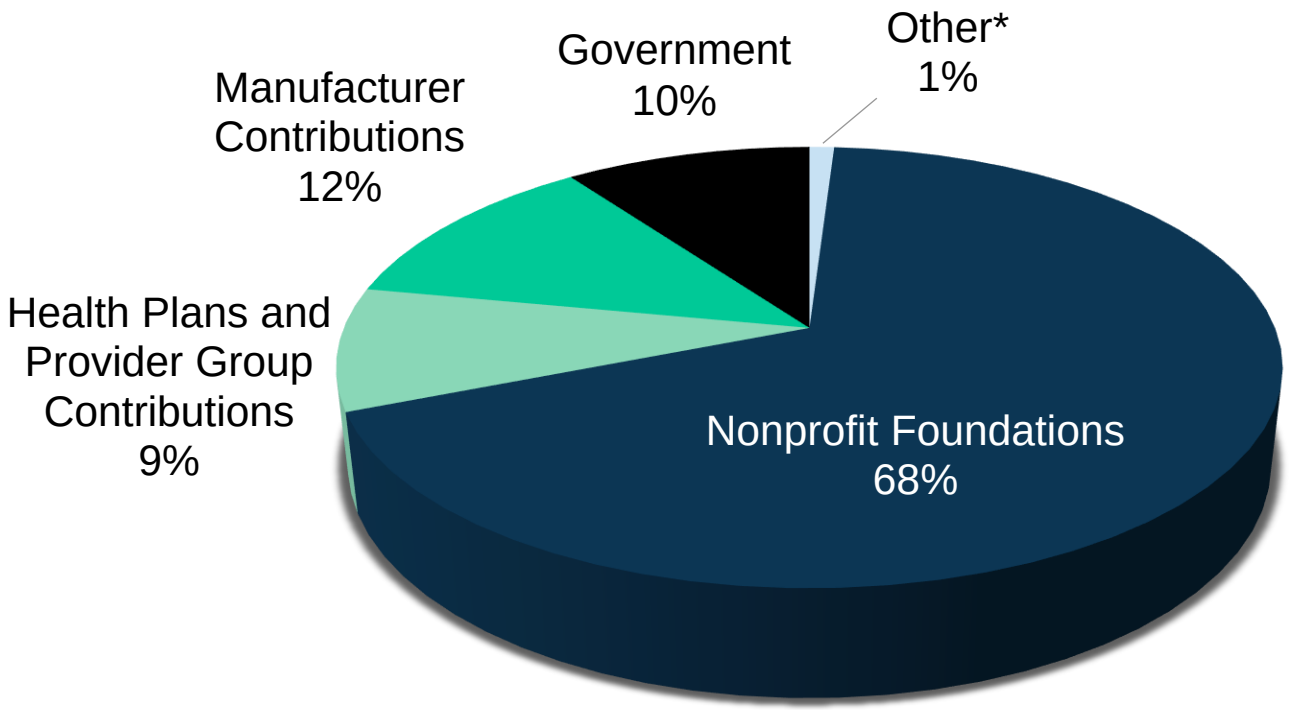


Organizational Overview

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

Sources of Funding, 2021

https://icer.org/who-we-are/independent-funding/



*Individual / matching contributions and speech stipends

How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Washington cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Wendy Smith Begolka**, MBS, Vice President, Scientific and Clinical Affairs, National Eczema Association
  - **Jonathan Silverberg**, MD, PhD, MPH, Associate Professor of Dermatology, The George Washington University School of Medicine and Health Sciences
  - **Eric Simpson**, MD, MCR, Professor of Dermatology, Oregon Health & Science University, School of Medicine
- How is the evidence report structured to support CEPAC voting and policy discussion?

Value Assessment Framework: Long-Term Value for Money

Agenda

9:00am – 9:20am	Meeting Convened and Opening Remarks
9:20am - 9:50am	Presentation of the Clinical Evidence
9:50am – 10:20am	Presentation of the Economic Model
10:20am - 10:50am	Manufacturer Comments and Discussion
10:50am – 11:10am	Public Comments and Discussion
11:10am – 11:25am	Break
11:25am – 12:55pm	New England CEPAC Vote on Clinical Effectiveness and Value
12:55pm – 1:40pm	Lunch Break
1:40pm – 2:50pm	Policy Roundtable
2:50pm – 3:20pm	Reflections from New England CEPAC
3:20pm	Meeting Adjourned

Presentation of the Clinical Evidence

Steven J. Atlas, MD, MPH

Physician / Associate Professor of Medicine

Massachusetts General Hospital / Harvard Medical School

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Key Collaborators

- **Foluso Agboola, MBBS, MPH,** Vice President of Research, ICER
- **Grace Fox, PhD,** (Former) Research Lead, Evidence Synthesis, ICER
- **Serina Herron-Smith, BA,** Research Assistant, ICER
- **Emily Nhan, BA,** Research Assistant, ICER

Disclosures:

Financial support provided to Dr. Atlas from ICER through Massachusetts General Hospital

Dr. Atlas has 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 insurer

Background: Atopic Dermatitis

Burden of disease

- Atopic dermatitis is a common, chronic skin condition affecting 11-15% of children and 7-10% of adult in the United States (US)
- Annual costs ~$5.3 billion dollars in the US, including over $1 billion in health care costs

Presentation and Symptoms

- Initially, red papules and vesicles with weeping, oozing and crusting skin. Over time, lesions dry, scaly, or excoriated with skin thickening, erosions, cracking and bleeding
- Primary symptom is itching that varies in severity
- Severity is based upon the amount and location of skin involved, its appearance, and the subjective impact of symptoms

Impact on Patients

- For patients with moderate to severe disease, atopic dermatitis can have a profound impact on quality of life
- Itch can lead to a host of additional problems including skin pain and infections as well as disrupting sleep
- Sleep disturbance and daytime fatigue can affect performance including that in school and work
- Lead to psychological stress including loss of self-esteem, anxiety, depression, and suicidal thoughts
- Not only can impact the patient, but also families, caregivers, friends, and relationships

Standard of Care and Management

- For all patients, skin care includes use of moisturizers and emollients and avoiding triggers such as heat/cold, low humidity, and known allergens
- Topical steroid creams for short-term, intermittent use, and maintenance with topical calcineurin inhibitors or a phosphodiesterase 4 (PDE-4) inhibitor
- For those not controlled with topical therapies, phototherapy or systemic therapies affecting the body's immune response are used
- Short-term use of systemic oral steroids, often overused, or cyclosporine with long-term use of oral methotrexate, azathioprine or mycophenolate mofetil
- Dupilumab, an IL-4 receptor antagonist administered by injection, now commonly used for those with moderate to severe disease

Scope of Review

- **Moderate to Severe Atopic Dermatitis Population**: compare the clinical effectiveness of abrocitinib, baricitinib, upadacitinib, and tralokinumab
  - Comparators:
    - Topical therapies (including emollients with or without a topical steroid or calcineurin inhibitor)
    - Dupilumab
- **Mild to Moderate Atopic Dermatitis Population**: compare the clinical effectiveness of topical ruxolitinib cream
  - Comparators: topical vehicle (placebo) or topical therapies (including topical steroids or calcineurin inhibitors)

New Treatments for Atopic Dermatitis

Intervention Generic Name (Brand Name)	Mechanism of Action	Delivery Route	Prescribing Information
Moderate to Severe Population			
Abrocitinib	JAK inhibitor	Oral	100-200mg once daily
Baricitinib (Olumiant)	JAK inhibitor	Oral	1-2mg once daily
Upadacitinib (Rinvoq)	JAK inhibitor	Oral	15-30mg once daily
Tralokinumab	IL-13 monoclonal antibody	Subcutaneous injection	600mg initial dose then 300mg every 2 weeks*
Mild to Moderate Population			
Ruxolitinib Cream	JAK inhibitor	Topical	0.75-1.5% twice daily

JAK: Janus kinase, IL: interleukin

* There may be an option for dosing tralokinumab every four weeks in some patient

Key Clinical Outcomes

- For eligible population at 16 weeks
  - 12 weeks for abrocitinib
  - 8 weeks for ruxolitinib cream
- Primary outcomes from clinical trials
  - Eczema Area Severity Index (EASI) - EASI response is the percentage improvement in score from baseline (ex. EASI-75 is the percent improvement from baseline that is ≥75%)
  - Investigator's Global Assessment (IGA) - IGA response is a score of 0 or 1 (clear or almost clear skin) and can also include an improvement from baseline of ≥2 points
- Secondary outcomes from clinical trials
  - Peak Pruritus Numerical Rating Scale (PP-NRS) - ≥4 point improvement from baseline
  - Other patient reported outcomes - sleep, anxiety, quality of life
  - Harms - side effects, discontinuation, infections (ex. herpetic)

Insights from Discussions with Patients and Caregivers

- Though most with atopic dermatitis have a milder course, this may lead to an underappreciation of its profound effect on all aspects of a patient's life
- Many deficiencies with current therapies support need for new ones that work quickly, provide sustained relief and are safe for long-term use
- Concerns about high cost of care including multiple over-the-counter treatments, provider visits, prescription creams and systemic medications

Clinical Evidence

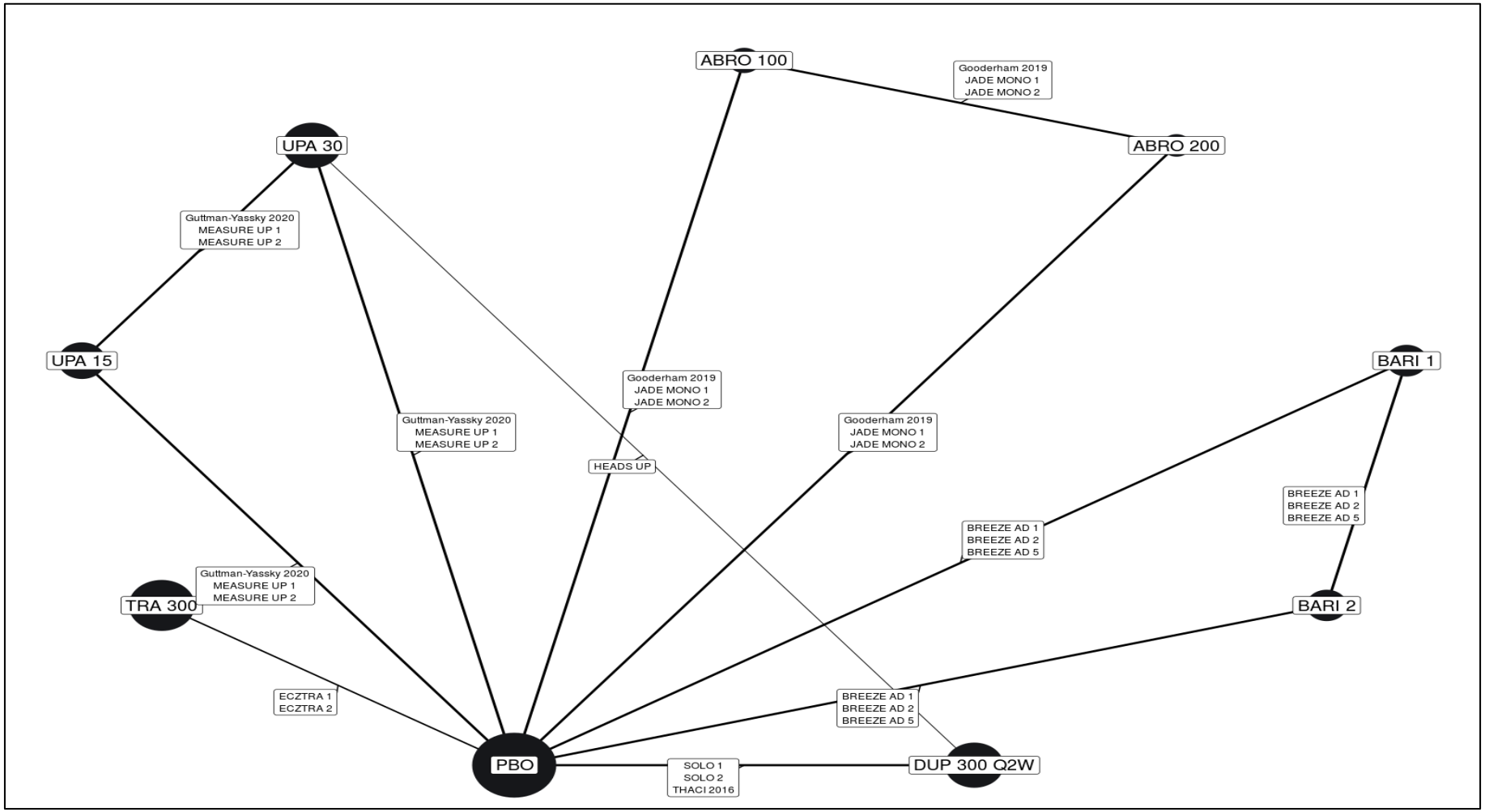
Key Clinical Trials – Moderate to Severe Population

- We conducted systematic review based on the PICOT criteria
- We identified 21 trials to include in network meta-analysis (NMA)
  - Includes 15 monotherapy (placebo only) and 6 combination trials

Interventions	N of Trials	Patients (n)	Patients 12-17 yr (n)
Abrocitinib	4*	1,782	124**
Baricitinib	5	2,112	0
Tralokinumab	3	1,976	0
Upadacitinib	5*	3,443	344
Dupilumab	4	2,498	0**

*Includes 1 direct comparison trial with dupilumab; all other trials were placebo controlled
**Additionally had an adolescent only trial; those data are not presented here

Network Diagram: Monotherapy (placebo only) Trials

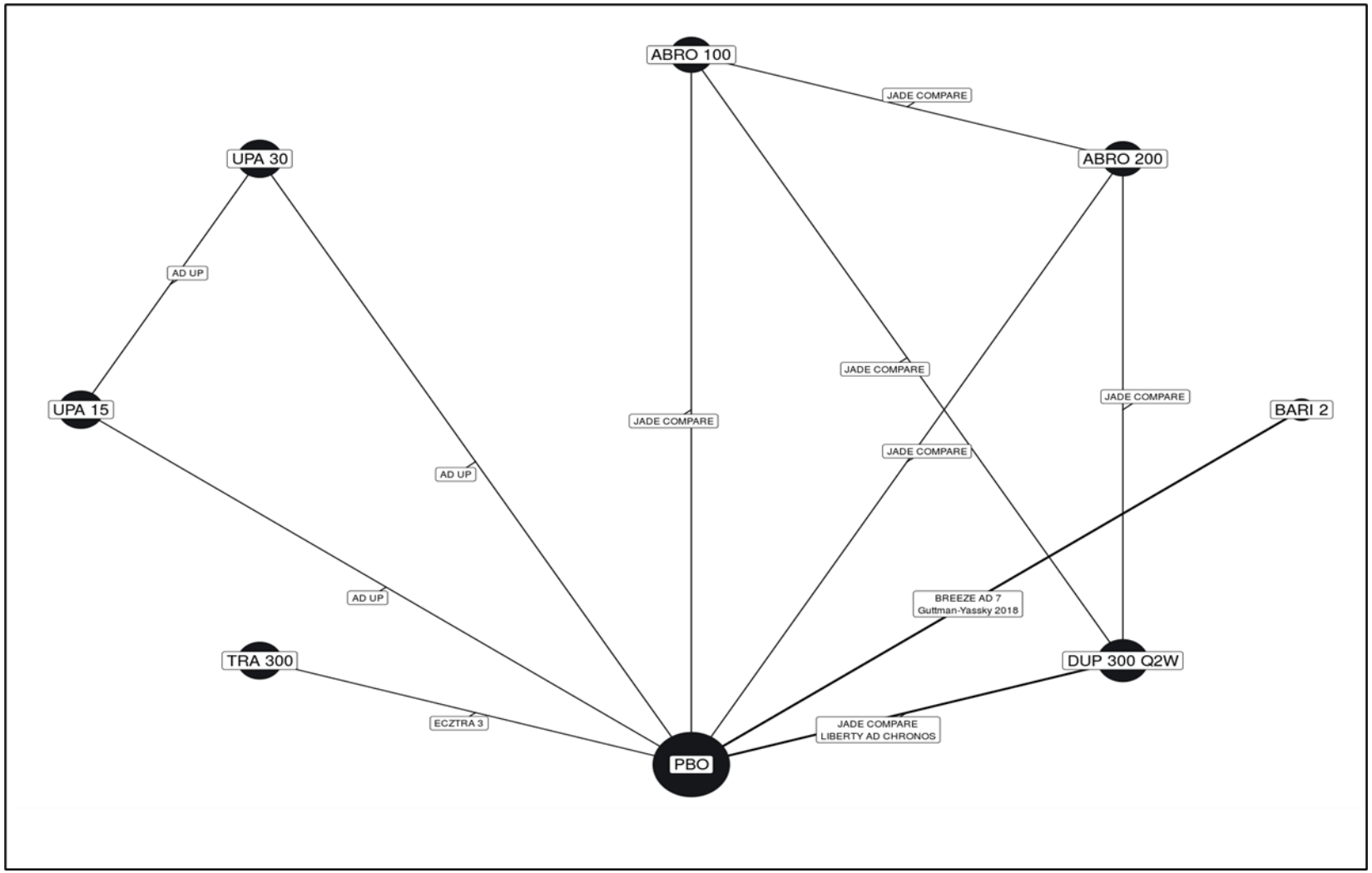


Results – Percentage of Patients Achieving EASI-75*

Treatment	EASI-75 (median %)	95% credible interval
Placebo	12	1-13
Baricitinib (1 mg)	19	14-25
Baricitinib (2 mg)	29	23-37
Tralokinumab	31	24-38
Abrocitinib (100 mg)	40	30-50
Abrocitinib (200 mg)	58	49-68
Upadacitinib (15 mg)	55	48-61
Upadacitinib (30 mg)	67	61-73
Dupilumab	49	42-55

* NMA results only include patients ≥18 years old

Network Diagram: Combination (placebo + topical therapy) Trials



NMA Results: Monotherapy and Combination Trials

- All interventions had higher odds of achieving EASI-75, IGA Response and patient reported itch response (PP-NRS≥4) compared to placebo
- Interventions in the monotherapy trials had higher odds of achieving these outcomes than interventions in the combination therapy trials
- Interventions in the monotherapy and combination trials had higher odds of achieving investigator reported outcome (IGA Response) than the patient reported itch outcome

Treatment	Monotherapy Trials	Combination Trials*
	Odds Ratio (range for interventions)	
EASI-75	1.62 - 5.71	1.69 - 3.62
IGA Response	2.16 - 8.77	1.63 - 4.61
Itch (PP-NRS ≥4)	1.69 - 4.99	1.42 - 3.36

*Baricitinib trials do not include 1mg dose

Other Important Outcomes

- NMA Results: Interventions vs. Dupilumab
  - Outcomes favor higher doses of upadacitinib and abrocitinib (direct comparisons)
  - Outcomes generally superior compared to baricitinib and tralokinumab
- Patient outcomes including sleep, quality of life, anxiety, depression show similar benefits favoring for the interventions vs. placebo
- Adolescents: outcomes similar to those of adults for abrocitinib and upadacitinib
- Limited long-term outcomes – suggest continuing benefit of the interventions and no new safety signals

Key Clinical Trials – Mild to Moderate Population

- Systematic review based on the PICOT criteria identified 3 trials

Trials	Intervention	Comparator	Patients (n)	Patients 12-17 yr (n)
TRuE AD 1	Ruxolitinib cream (0.75, 1.5%)	Vehicle (placebo)	631	245
TRuE AD 2			618	
Phase 2 trial (Kim 2020)	Ruxolitinib cream 1.5%	Vehicle or 0.1% triamcinolone cream	307	0

Outcomes – mild to moderate population

Trial	Treatment	EASI 75	IGA	Itch (PP-NRS)
		Percentage Achieving (range)		
TRuE AD 1 & 2	Vehicle (placebo)	14.4 - 24.6	7.6 - 15.1	15.4 -16.3
	Ruxolitinib cream (0.75%)	51.5 - 56.0	39.0 - 50.0	40.4 -42.7
	Ruxolitinib cream (1.5%)	61.8 - 62.1	51.3 - 53.8	50.7 - 52.2

- Other patient reported outcomes showed similar favorable results compared to vehicle (placebo)
- Adolescents: outcomes similar to those of adults
- Limited data comparing ruxolitinib 1.5% to medium potency steroid cream suggests similar or better outcomes
- Limited long-term outcomes – suggest continuing benefit of the interventions

Harms

- Trials in patients with moderate to severe atopic dermatitis
  - Serious adverse events and discontinuations were uncommon and comparable for active therapies and placebo
  - Conjunctivitis, herpetic infections and other adverse events were also similar among treatment arms
  - For patients in long-term combination trials, harms leading to discontinuation were uncommon and similar or slightly higher for patients receiving placebo
- Oral JAK inhibitors approved for other indications include warnings for adverse events including serious infections, cancer and blood clots
- Trials in patients with mild to moderate atopic dermatitis
  - Adverse events were uncommon and similar or less frequent for ruxolitinib compared to vehicle (placebo)

Controversies and Uncertainties

- No direct comparison of new agents - use of indirect quantitative methods (NMAs) more uncertain than if there were head-to-head studies
- Although side effects of oral JAK inhibitors were uncommon, worrisome side effects led FDA warnings on this class of agents for other indications
  - FDA delayed review for all JAK inhibitors, including topical ruxolitinib cream
- Tralokinumab works through a mechanism more similar to dupilumab than the JAK inhibitors, but lacks the long-term safety profile of dupilumab
- Patients with atopic dermatitis often have other allergic conditions such as rhinitis and asthma, but it is unknown how the new agents affect these other conditions

Potential Other Benefits and Contextual Considerations

- Abrocitinib, baricitinib, ruxolitinib, tralokinumab and upadacitinib are new therapies that reflect improved understanding of disease mechanisms
- New therapies may improve quality of life including social interactions with family and friends, educational achievement, and work performance
- Oral JAK therapies for moderate to severe atopic dermatitis may reduce patient and caregiver/family burden over existing therapies

Public Comments Received

- Outcomes from the clinical trials do not capture the full range of potentially beneficial consequences of new therapies for atopic dermatitis on life activities including school and work
- Sanofi/Regeneron disagreed with a statement in the draft report that given a similar mechanism of action, the long-term safety of tralokinumab may be similar to that seen for dupilumab

Summary for Patients with Atopic Dermatitis

- For moderate to severe population: abrocitinib, baricitinib, tralokinumab and upadacitinib
  - Improved outcomes compared to placebo
  - Compared to dupilumab: abrocitinib and upadacitinib similar or slightly better, and baricitinib and tralokinumab similar or slightly worse
  - Few serious harms reported with low discontinuation rates, but ongoing concerns about potentially serious harms for oral JAK inhibitors
- For mild to moderate population: ruxolitinib cream
  - Improved outcomes compared to vehicle (placebo)
  - Few serious harms reported with low discontinuation rates

ICER Evidence Ratings for Atopic Dermatitis

Treatment	Comparator	Evidence Rating
Moderate to Severe Population		
Abrocitinib, Baricitinib, Tralokinumab, Upadacitinib	Topical therapies alone	Promising but inconclusive (P/I)
	To each other	Insufficient (I)
Abrocitinib, Upadacitinib	Dupilumab	Insufficient (I)
Baricitinib, Tralokinumab	Dupilumab	Comparable or inferior (C-)
Mild to Moderate Population		
Ruxolitinib	Vehicle (placebo)	Comparable or better (C++)
	Topical therapies	Insufficient (I)

Questions?

JAK Inhibitors and Monoclonal Antibodies for the Treatment of Atopic Dermatitis: Effectiveness and Value

Elizabeth Brouwer, PhD, MPH

Research Scientist

The CHOICE Institute, Department of Pharmacy, University of Washington

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Key Review Team Members

- **Josh J. Carlson**, PhD, MPH, Associate Professor
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Disclosures:

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

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

Objective

Estimate the cost-effectiveness of abrocitinib, baricitinib (Olumiant™), tralokinumab, and upadacitinib (Rinvoq™) compared to topical emollients and dupilumab (Dupixent®)

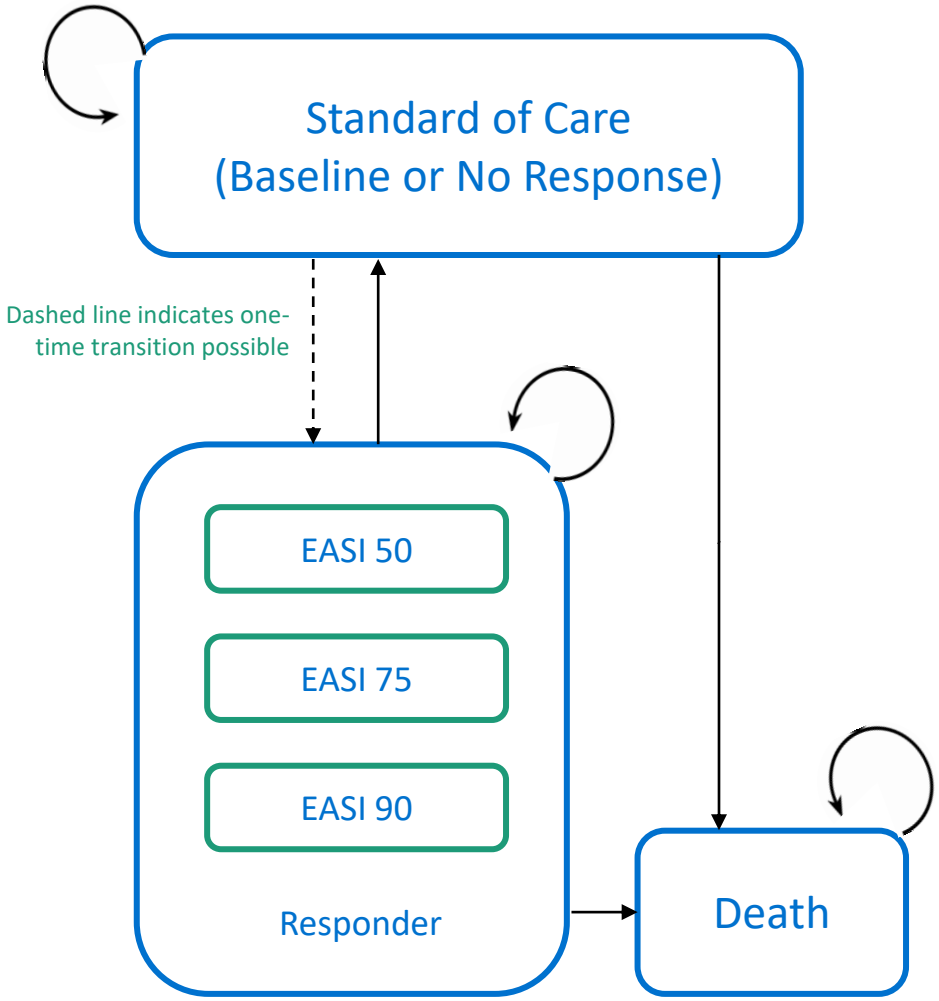
Methods in Brief

Methods Overview

- **Model**: Markov
- **Target Population**: Adults with moderate to severe atopic dermatitis
- **Setting**: United States
- **Perspective**: Health Care Sector Perspective
- **Time Horizon**: 5 years
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 16-weeks
- **Primary Outcomes**: Cost per quality-adjusted life year (QALY) gained; cost per equal value life year (evLY) gained; cost-consequence of PROs for itch, sleep, and anxiety/depression

Model Schematic and Key Assumptions

- Transitions to the response state occur after one cycle. Patients do not change response levels after the initial response while on treatment.
- After transitioning off treatment, quality of life and costs are assumed to be equivalent to a patient who was eligible for treatment but never treated.
- Among responders, discontinuation rates do not vary by responder level.
- Patients on only topical treatment (placebo arm) who achieve ≥EASI 50 after the first cycle transition to non-response state at a rate equivalent to discontinuation rates for placebo patients in the relevant clinical trials.
- Atopic dermatitis disease and treatments do not affect mortality.



Key Model Inputs: Initial Health State Transition Probabilities

	EASI 50-74	EASI 75-89	EASI 90+	Total Responders
Abrocitinib				73%
Baricitinib				44%
Tralokinumab				46%
Upadacitinib				80%
Dupilumab				64%
Standard of Care	9.6%	6.5%	5.3%	21.4%

Source: Network Meta-Analysis
Abbreviations: EASI- Eczema Area Severity Index

Key Model Inputs: Discontinuation Rates

	Year 1	Year 2+	Source
Abrocitinib	[redacted]	[redacted]	JADE COMPARE
Baricitinib	[redacted]	[redacted]	BREEZE-AD3
Tralokinumab	5.04%	5.04%	ECZTRA 2
Upadacitinib	(assumed equivalent to highest in class)		BREEZE-AD3 (proxy)
Dupilumab	3.77%	4.87%	LIBERTY AD-SOLO CONTINUE; LIBERTY AD OLE
Standard of Care	25.40%	25.40%	ECZTRA 1 & 2

All extension trial discontinuation rates standardized to a 16-week cycle

Key Model Inputs: Therapy Costs

	WAC per Dose	Discount from WAC*	Net Price per Dose	Net Price per Year
Abrocitinib (200 mg qd)†	$128	17%	$113	$41,397
Baricitinib (Olumiant™, 2 mg qd)	$79	33%	$53	$19,402
Tralokinumab (300 mg q2w)†	$1,602	26%	$1,193	$31,132
Upadacitinib (Rinvoq™, 30 mg qd)	$176	1%	$174	$63,393
Dupilumab (Dupixent®, 300 mg 2qw)	$1,602	26%	$1,193	$31,132

*SSR Health, LLC, was used for estimating discounts from wholesale acquisition cost
†Using placeholder prices

Key Model Inputs: Non-Therapy Health Care Costs

	Value	Source
Annual Health State Costs		
Non-responder	$18,588.62	Data provided by manufacturer
EASI 50-74	$10,100.58	
EASI 75-89	$8,910.17	
EASI 90+	$8,595.68	
One-time Injection Training and Monitoring Costs		
Office visit/self-injection training	$23.00	CPT 99211
General practitioner visit	$57.00	CPT 99212
Blood panel	$7.77	CPT 85025

Abbreviations – EASI: Eczema Area Severity Index
All costs in 2021 USD

Key Model Inputs: Patient Reported Outcomes (PRO)

	PP-NRS (Itch)	PP-NRS (Itch)	POEM (Sleep)	SCORAD (Sleep)	ADerm-IS (Sleep)	HADS (Anxiety/ Depression)
Drug	**Tralokinumab**	**Upadacitinib**	**Tralokinumab**	**Tralokinumab**	**Upadacitinib**	**Tralokinumab**
Pooled Baseline*						
EASI 50-74						
EASI 75-89						
EASI 90-100						
Source for pooled baseline*	ECZTRA 1, 2, MEASURE UP 1, 2, AD UP, BREEZE AD5, MONO1-2, COMPARE	ECZTRA 1, 2, MEASURE UP 1, 2, AD UP, BREEZE AD5, MONO1-2, COMPARE	ECZTRA 1, 2	ECZTRA 1, 2	Measure Up1, 2, and AD Up	LP0162-1326/1339/1325
Source for drug-specific scores	ECZTRA 1, 2,	MEASURE UP 1, 2, and AD UP	ECZTRA 1, 2	ECZTRA 1, 2	Measure Up1, 2, and AD Up	LP0162-1326/1339/1325

Abbreviations – EASI: eczema area severity index; PP-NRS: peak pruritus numeric rating scale; POEM: patient-oriented eczema measure; SCORAD: scoring atopic dermatitis; Aderm-IS: atopic dermatitis impact scale; HADS: hospital anxiety and depression scale;

Key Model Inputs: Health State Utilities

Health State	Value	Source
Non-responder	[redacted]	ECZTRA 1 & 2, MEASURE UP 1 & 2, AD UP, SOLO 1 & 2
EASI 0-49	[redacted]	
EASI 50-74	[redacted]	
EASI 75-89	[redacted]	
EASI 90-100	[redacted]	

Abbreviations: EASI - eczema area severity index

Results

Base-Case Results

Treatment	Drug Cost	Total Cost	QALYs (and evLYs)
Abrocitinib*	$113,200	$178,400	3.59
Baricitinib	$26,900	$105,300	3.23
Tralokinumab*	$51,700	$127,700	3.29
Upadacitinib	$151,300	$219,700	3.51
Dupilumab	$72,400	$141,900	3.47
Standard of Care (Topicals)	$-	$87,800	2.98

*Using a placeholder price
Abbreviations: QALYs – quality-adjusted life years; evLYs – equal value life-years

Base-Case Incremental Results

Drug	Comparator	Incremental Cost	Incremental QALYs	Incremental cost per QALY gained
Abrocitinib*	SoC	$90,600	0.61	$148,300*
Baricitinib	SoC	$17,500	0.26	$71,600
Tralokinumab*	SoC	$39,900	0.32	$129,400*
Upadacitinib	SoC	$131,800	0.53	$248,400
Dupilumab	SoC	$54,000	0.50	$110,300
Abrocitinib*	Dupilumab	$36,500	0.12	$303,400*
Baricitinib	Dupilumab	Less Costly	Less Effective	Less Costly, Less Effective
Tralokinumab*	Dupilumab	Less Costly	Less Effective	Less Costly, Less Effective*
Upadacitinib	Dupilumab	$77,800	0.03	$1,912,200

Abbreviations –QALY: quality-adjusted life-year, SoC: Standard of Care

*Using a placeholder price

Base-Case PRO Results

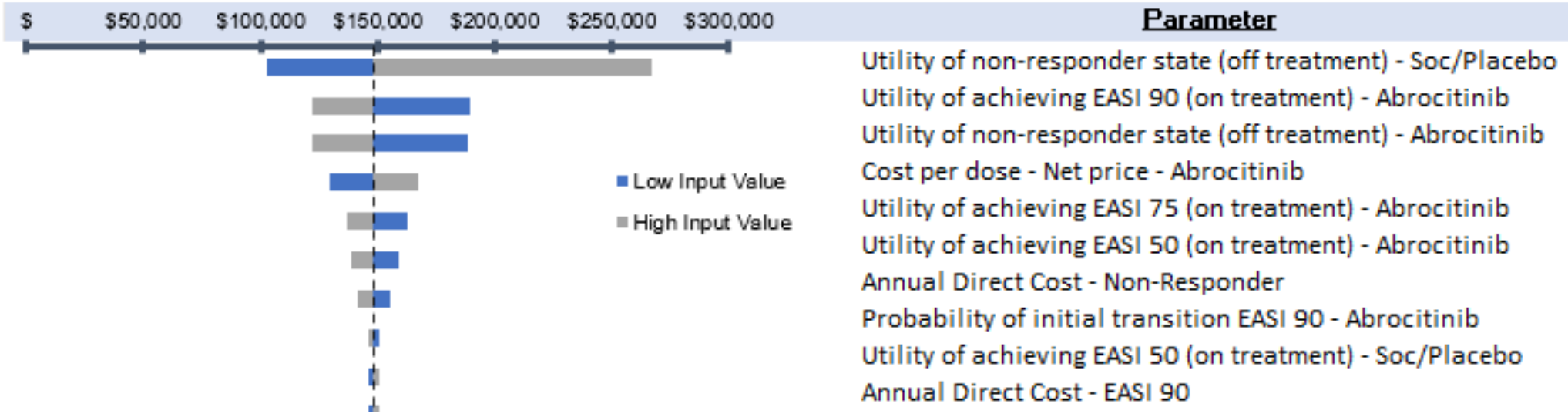
Treatment	Total Cost	PP-NRS (itch)†	POEM (sleep)†	SCORAD (sleep)†	ADerm-IS (sleep)†	HADS (depression and anxiety)†
Tralokinumab*	$127,700	-1.11	-0.52	-1.23	NA	-1.23
Upadacitinib	$219,700	-1.65	NA	NA	-5.75	NA
Standard of Care (Topicals)	$87,800	-0.15	-0.08	-0.19	-0.55	-0.19

*Using a placeholder price
Abbreviations –NA: not available; PP-NRS: peak pruritus numeric rating scale; POEM: patient-oriented eczema measure; SCORAD: scoring atopic dermatitis; Aderm-IS: atopic dermatitis impact scale; HADS: hospital anxiety and depression scale;

One Way Sensitivity Analyses

- Across all modeled comparisons, the health state utility values were identified as the most influential model parameters on the incremental cost-effectiveness ratios, followed by the drug cost, initial transition probabilities, non-responder direct costs, and discontinuation rates.

- Example tornado diagram for abrocitinib versus Standard of Care:



Probabilistic Sensitivity Analysis vs SOC

% Cost-Effective at	$50,000 per QALY	$100,000 per QALY	$150,000 per QALY	$200,000 per QALY
Abrocitinib*	0%	3%	49%	82%
Baricitinib	45%	74%	85%	90%
Tralokinumab*	12%	43%	65%	75%
Upadacitinib	0%	0%	3%	25%
Dupilumab	0%	38%	76%	92%

*Using placeholder prices
Abbreviations - QALY: quality-adjusted life year; SOC: standard of care

Scenario Analysis: Modified Societal Perspective

Description: We included productivity loss due to moderate-to-severe AD as indirect costs by health state (derived from WPAI questionnaire in Upadacitinib clinical trials).

Treatment	Comparator	Cost per QALY Gained in Base Case Analysis	Cost per QALY Gained in Scenario Analysis	% Change
Abrocitinib*	SoC	$148,300	$132,000	-11%
Baricitinib	SoC	$71,600	$56,100	-22%
Tralokinumab*	SoC	$129,400	$113,900	-12%
Upadacitinib	SoC	$248,400	$231,800	-7%
Dupilumab	SoC	$110,300	$94,200	-15%
Abrocitinib*	Dupilumab	$303,400	$285,800	-6%
Baricitinib	Dupilumab	Less Costly, Less Effective	Less Costly, Less Effective	NA
Tralokinumab*	Dupilumab	Less Costly, Less Effective	Less Costly, Less Effective	NA
Upadacitinib	Dupilumab	$1,912,200	$1,888,800	-1%

*Using a placeholder price

Abbreviations – QALYs: quality-adjusted life-years; NA – not applicable

Other Scenario Analyses

- **Lifetime Time Horizon:**
  - Extended the model time horizon from 5-years to lifetime
  - ICERs vs SoC decreased by 4% to 13% across therapies
  - Upadacitinib became dominated vs dupilumab

- **Concurrent Topical Corticosteroids (TCS):**
  - Updated initial transition probabilities based on a new NMA with TCS and added the cost of TCS
  - Costs of therapies increased 6% to 36%; QALYs increased 2% to 4%
  - ICERS vs SoC increased 9% to 14%
  - Upadacitinib became dominated vs dupilumab

Limitations

- Differential effects of the treatments modeled on conditions such as itch and sleep may not be completely captured by generic quality of life instruments.
- Potential incremental effects of some of these treatments on quality of life in sub-populations of people with atopic dermatitis (i.e. co-occurring asthma or chronic rhinosinusitis) were not explicitly captured in the current model.
- SAEs that occurred in less than 5% of the trial population were excluded, however, we note that some rare SAEs have occurred with JAK inhibitor in other indications that may impact both costs and patient health-related quality of life in atopic dermatitis patients. Additionally, we assume a population not at increased CVD risk.

Comments Received

- LEO Pharma and Sanofi/Regeneron criticized the implied equivalence of long-term safety between the JAK inhibitor and monoclonal antibody drug classes in the model due to the exclusion of SAEs, a noted limitation of the model.

- Pfizer thought the assumed exclusion of patients over 50 with increased cardiovascular risk was inappropriate speculation on the treatment population. We chose to exclude that population as our model does not include a scenario where the drug increases risk of mortality.

- Requests from Pfizer and LEO Pharma led to the inclusion of two additional scenario analyses that can be found in the report's supplemental appendix: 1) abrocitinib patients evaluated after the initial 12 weeks on therapy rather than at 16 weeks led to very small decrease in ICERs, and 2) a proportion of tralokinumab patients decreasing dosing frequency after 16 weeks led to decrease in drug costs and ICERs.

- Abbvie criticized the 1% discount rate applied to upadacitinib based on SSR Health information. ICER reviewed the calculation and confirmed that we accurately reflected the available pricing and discounting data and did not use any quarters of data where the net pricing in SSR Health was above that of the WAC pricing in estimating the net price and corresponding discount rates. ICER would welcome manufacturer-provided net price data.

- Abbvie pointed out that the source of cost data in the draft report did not capture differential economic savings by health state (EASI 50 vs 75 vs 90). They provided an internal claims-based analysis of health costs for atopic dermatitis patients by severity level, which was reviewed by ICER and incorporated into the model.

Conclusions

- We found abrocitinib to produce the most QALYs (3.59) of therapies considered, followed closely by upadacitinib (3.51) and dupilumab (3.47) over the 5-year time horizon. Baricitinib produced the fewest (3.23).
- Compared to the standard of care with emollients only:
  - Baricitinib was cost-effective at a $100,000/QALY threshold
  - Dupilumab was cost-effective at a $150,000/QALY threshold
  - For upadacitinib, a discount of ~36% off WAC would be needed to achieve a $150,000/QALY threshold
    - The estimated net price is $174 per dose, which is a 1% discount from the WAC
  - Abrocitinib and tralokinumab's cost-effectiveness will be finalized when prices are available

Questions?

Manufacturer Public Comment and Discussion

Manufacturer Public Commenters

Speaker	Title	Affiliation
Andrew J. Thorpe, PhD	Senior Medical Director, US Dermatology Team Leader	Pfizer
Meghan Feely, MD, FAAD	Senior Medical Advisor, U.S. Medical Affairs, Bio-Medicines	Eli Lilly
Kyle Hvidsten, MPH	Vice President, Head of Global Health Economics and Value Assessment, Sanofi	Sanofi
Ahmad Naim, MD	Vice President, Medical Affairs	Incyte

Andrew J. Thorpe, PhD
Senior Medical Director, US Dermatology Team Leader, North America Medical Affairs, Inflammation and Immunology, Pfizer

Conflicts of Interest:

- *Dr. Thorpe is a full-time employee of Pfizer.*

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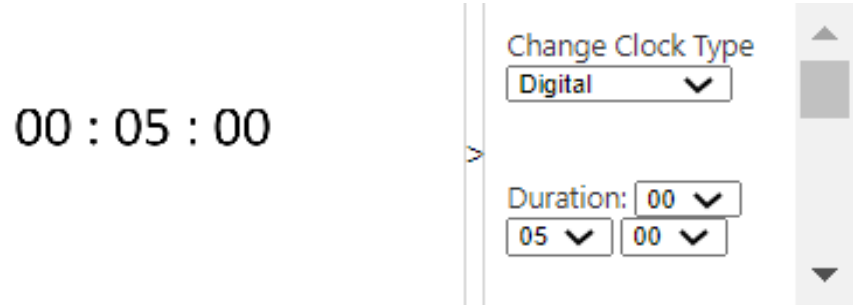
Meghan Feely, MD, FAAD
Senior Medical Advisor, U.S. Medical Affairs, Bio-Medicines

Conflicts of Interest:

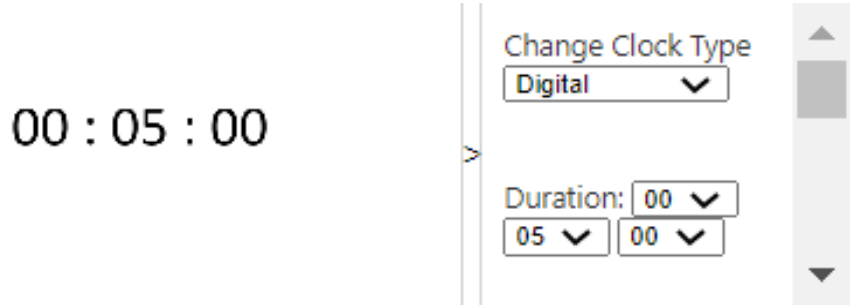
- *Dr. Feely is a full-time employee of Eli Lilly.*



Kyle Hvidsten, MPH
Vice President, Head of Global Health Economics and Value Assessment, Sanofi

Conflicts of Interest:

- *Kyle is a full-time employee of Sanofi.*



Ahmad Naim, MD
Vice President, Medical Affairs, Incyte

Conflicts of Interest:

- *Dr. Naim is a full-time employee of Incyte.*

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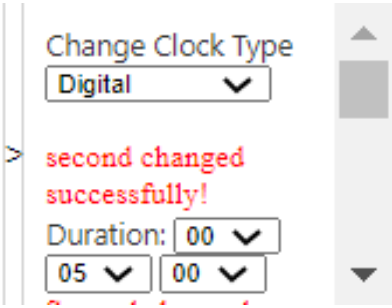

Public Comment and Discussion

Samantha Bittner
Patient Ambassador, National Eczema Association

Conflicts of Interest:

- *No financial conflicts of interest to disclose.*

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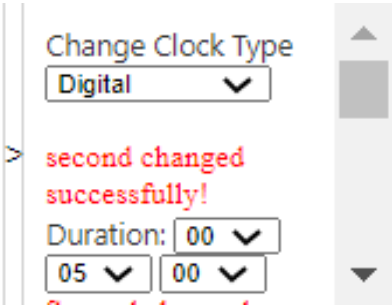

Break

Meeting will resume at 11:15am ET

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Voting Questions

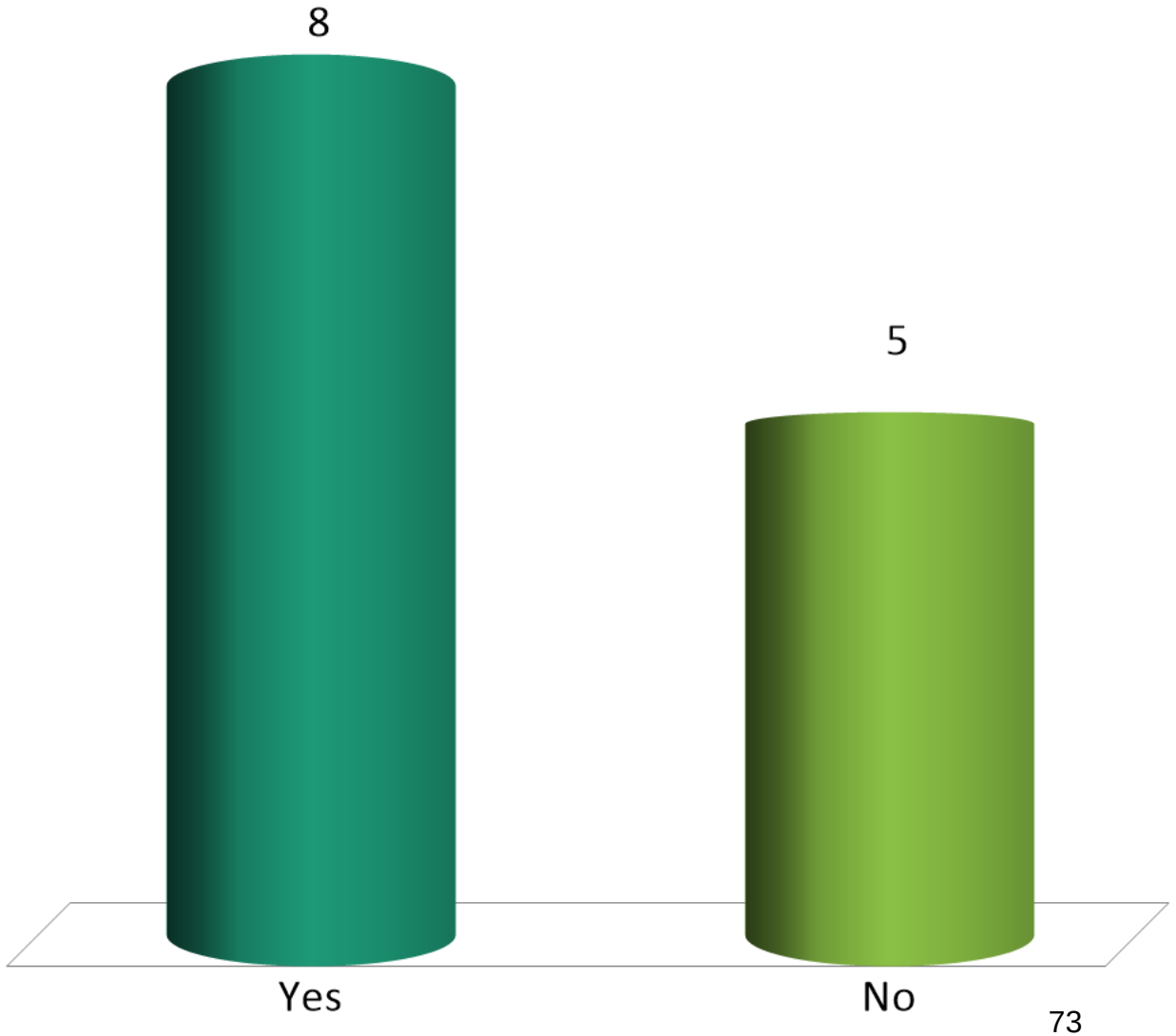
Clinical Evidence

Patient Population for questions 1-4:
Adults with moderate-to-severe atopic dermatitis whose disease has either not responded adequately to topical therapies, or for whom topical therapies have not been tolerated, or are medically inadvisable. Usual care in such patients is defined as use of topical emollients and avoidance of exacerbating factors.

1. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of **abrocitinib** added to usual care is superior to that provided by usual care alone?

A. Yes

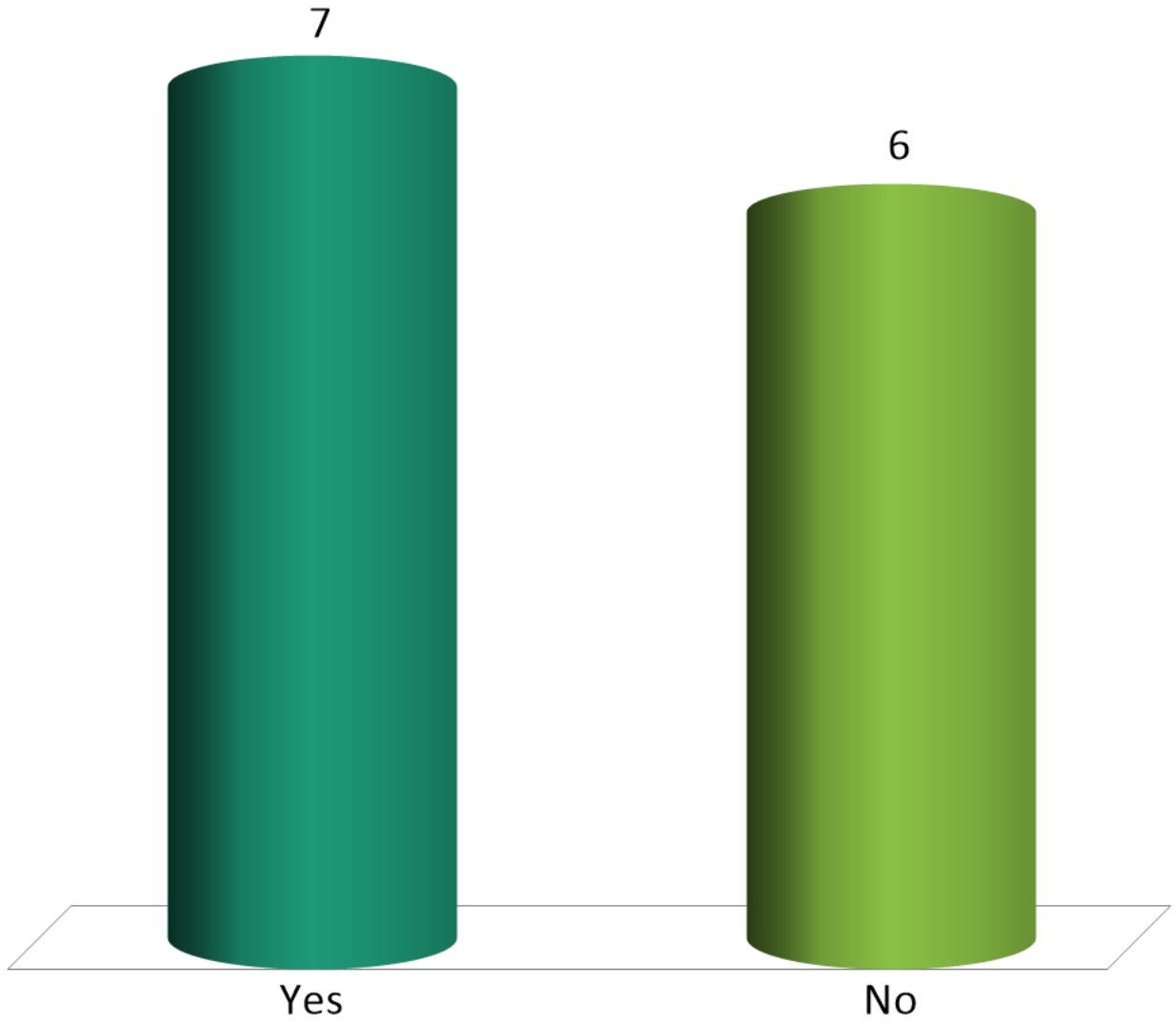
B. No



2. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of **baricitinib** added to usual care is superior to that provided by usual care alone?

A. Yes

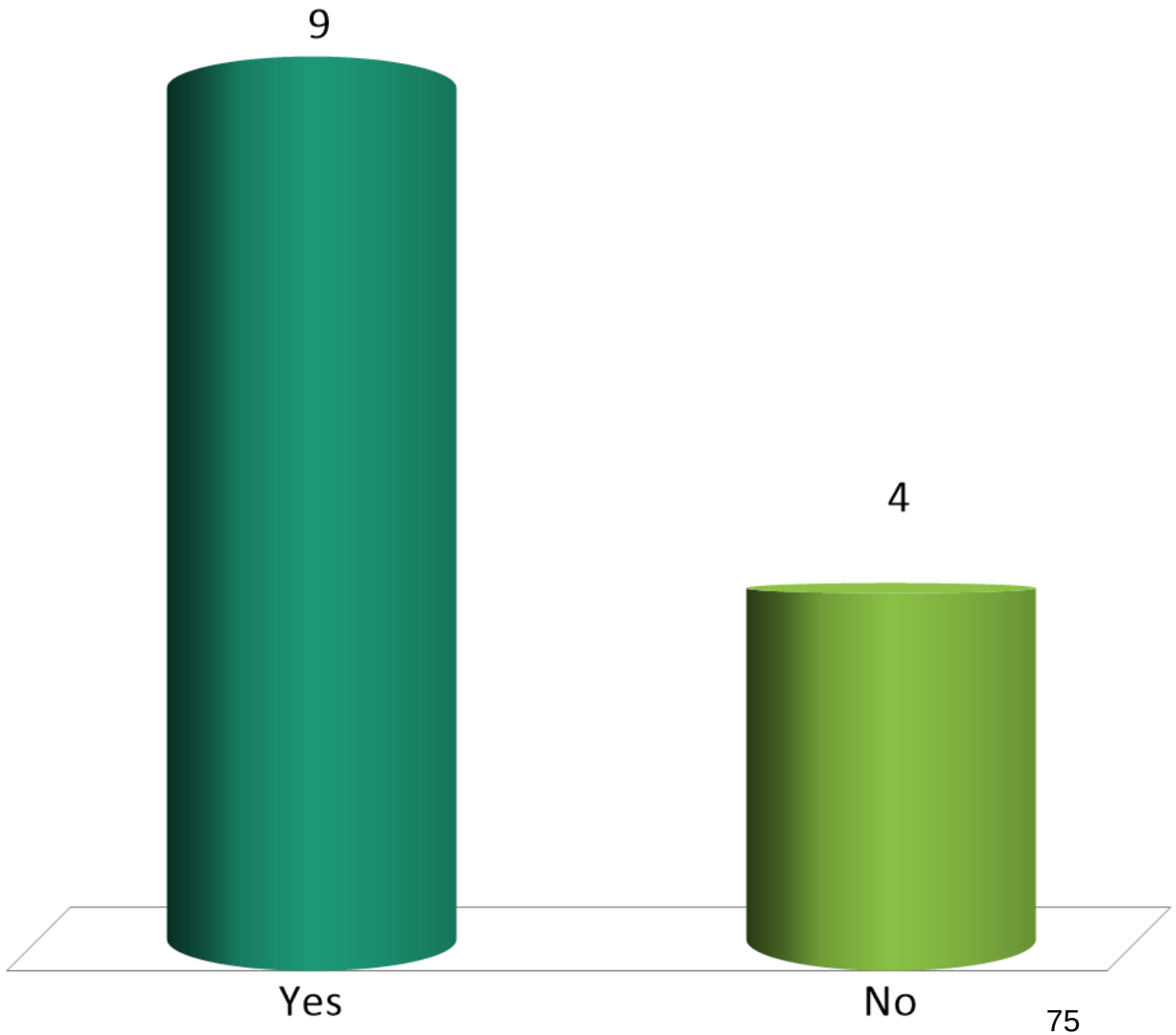
B. No



3. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of **upadacitinib** added to usual care is superior to that provided by usual care alone?

A. Yes

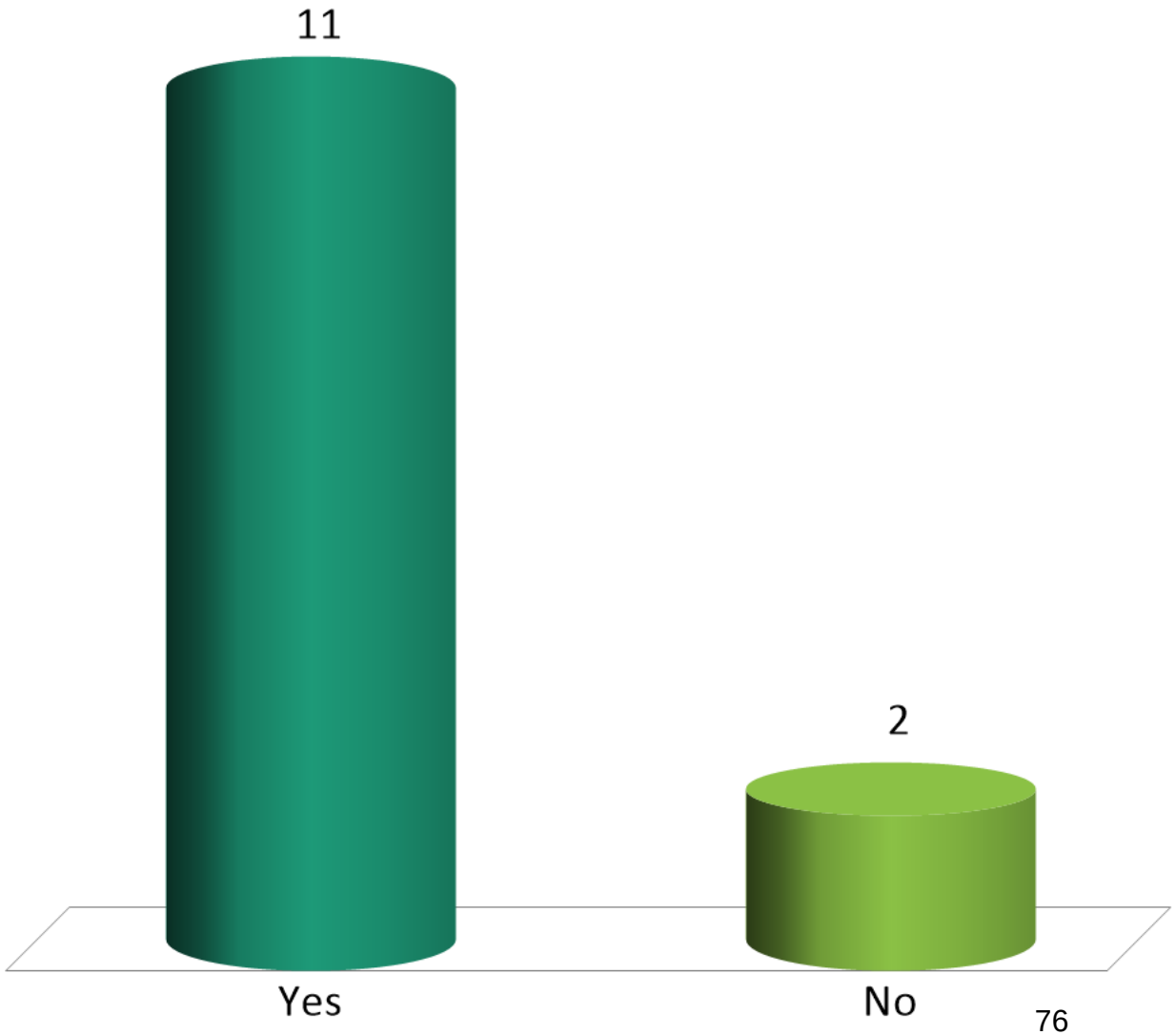
B. No



4. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of **tralokinumab** added to usual care is superior to that provided by usual care alone?

A. Yes

B. No

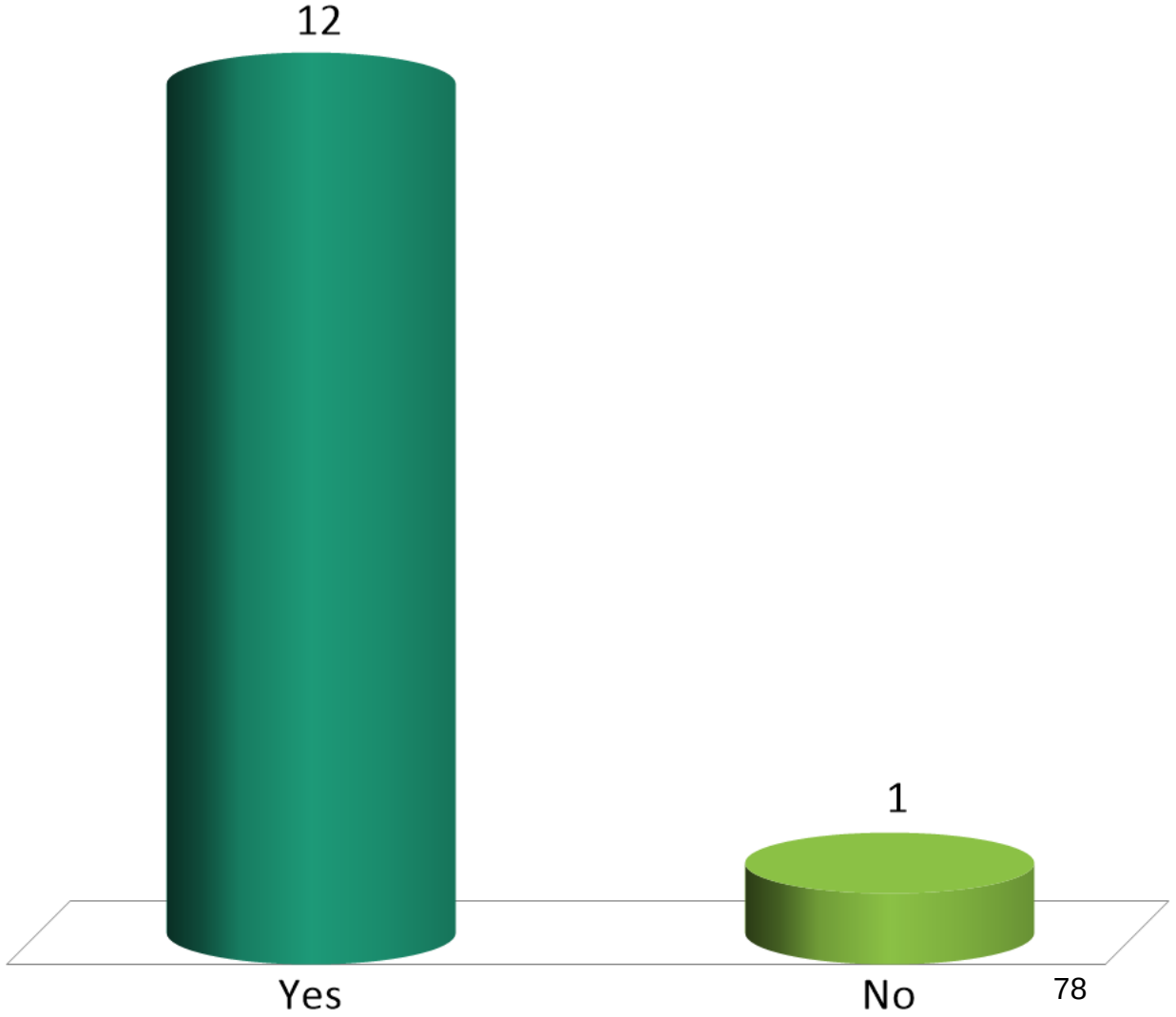


***Patient Population for Questions 5**:*
Adolescents and Adults with mild-to-moderate atopic dermatitis.

5. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of **ruxolitinib** is superior to that provided by topical emollients alone?

A. Yes

B. No



Contextual Considerations and Potential Other Benefits or Disadvantages

6. When making judgments of overall long-term value for money, what is the relative priority that should be given to *any* effective treatment for Atopic Dermatitis, on the basis of the following contextual considerations:

Acuity of need for treatment of individual patients based on the severity of the condition being treated

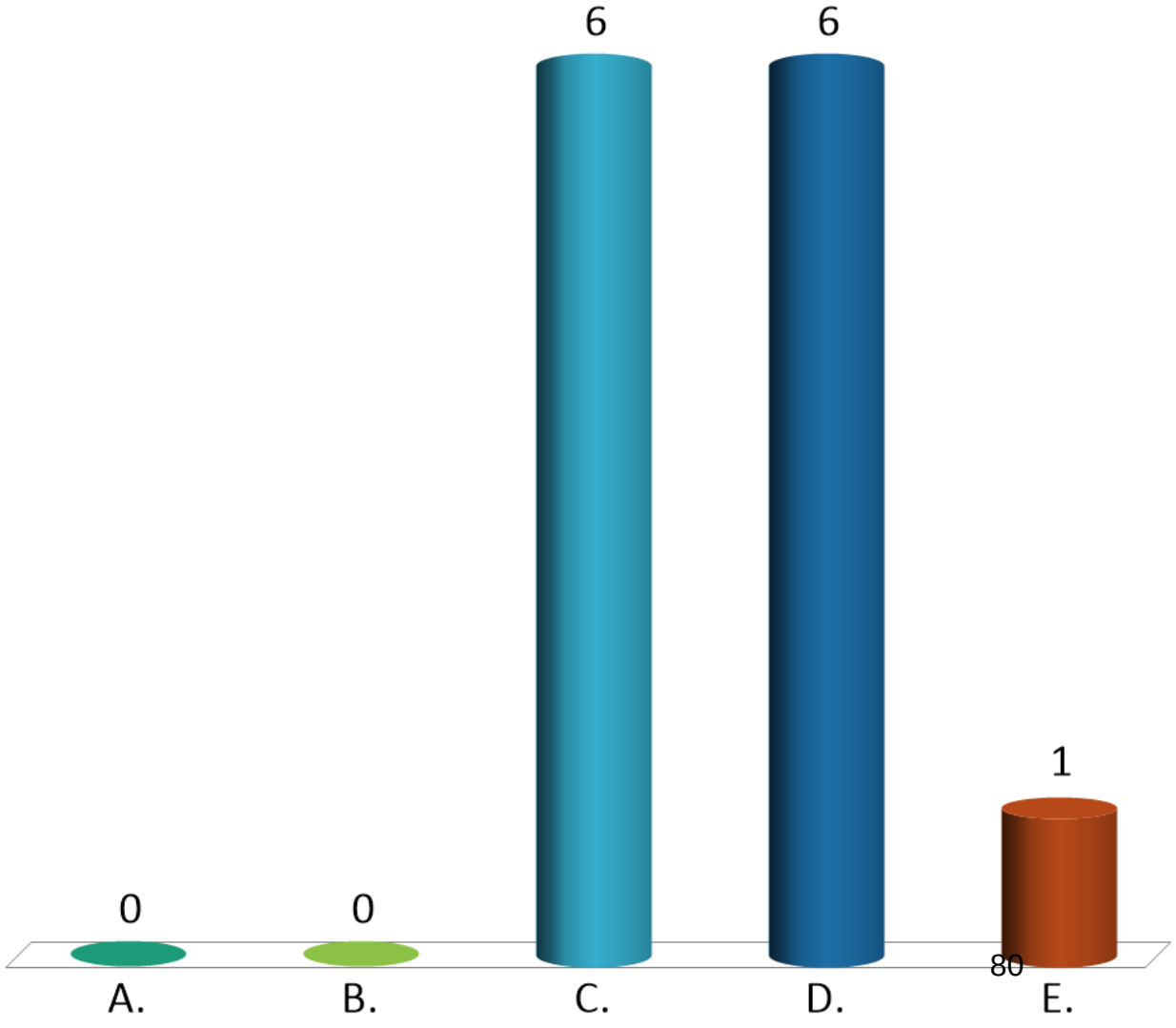
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



7. When making judgments of overall long-term value for money, what is the relative priority that should be given to *any* effective treatment for Atopic Dermatitis, on the basis of the following contextual considerations:

Magnitude of the lifetime impact on individual patients of the condition being treated

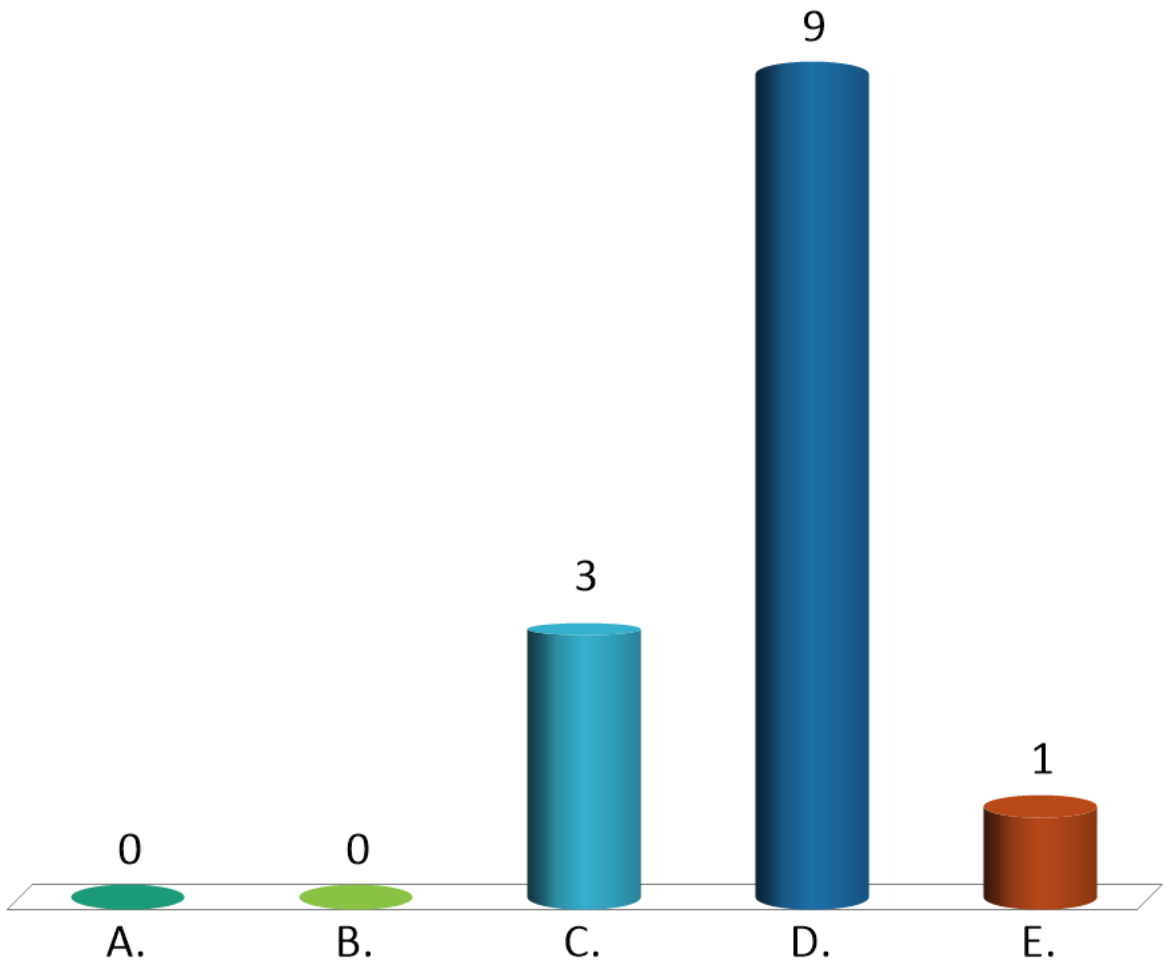
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



For questions 8-12, considering the average effects of the new systemic therapies as a group, what are the relative effects of the new therapies versus usual care (use of topical emollients and avoidance of exacerbating factors) on the following outcomes that inform judgment of the overall long-term value for money.

8. Patients' ability to achieve major life goals related to education, work, or family life

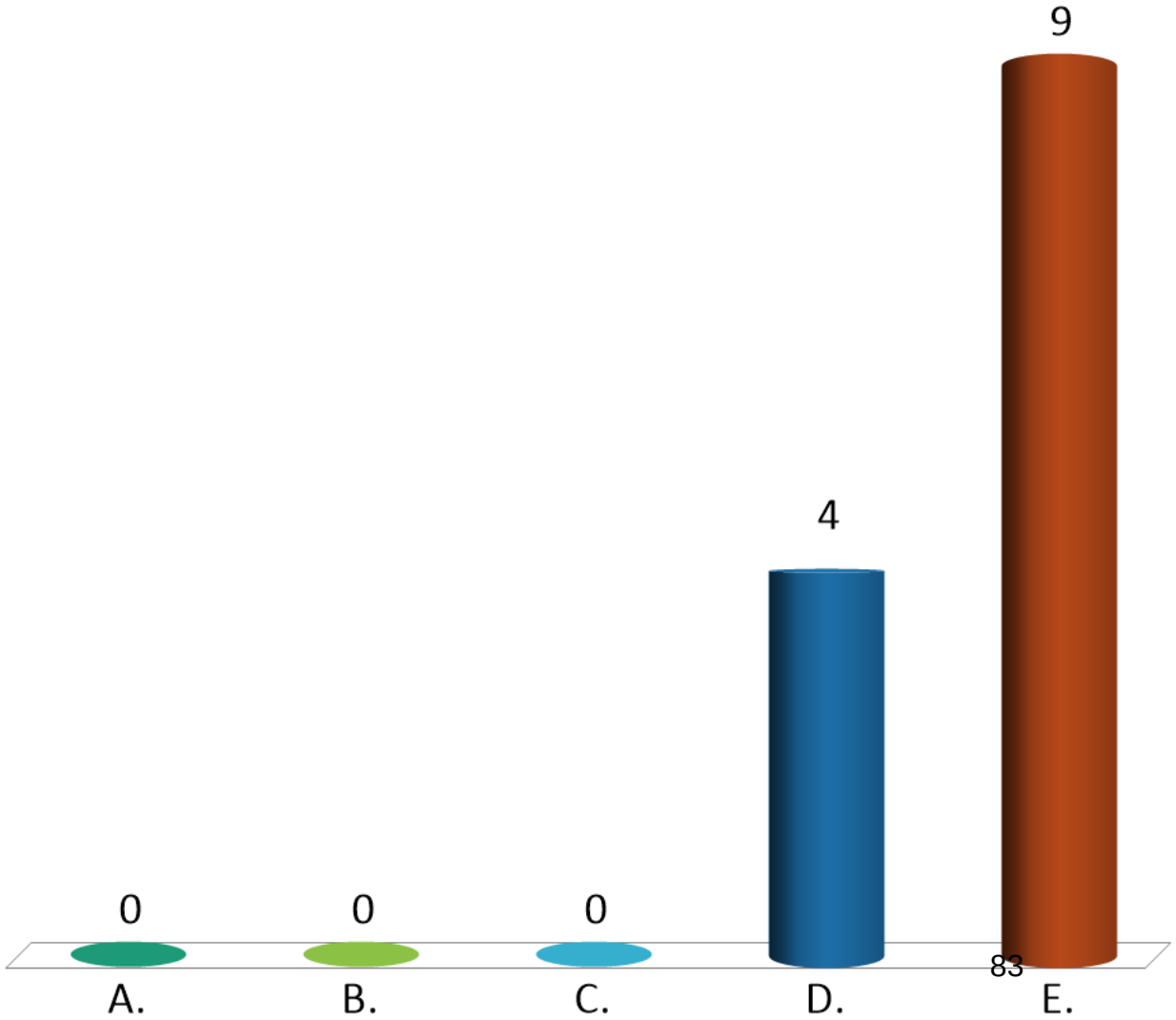
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



9. Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

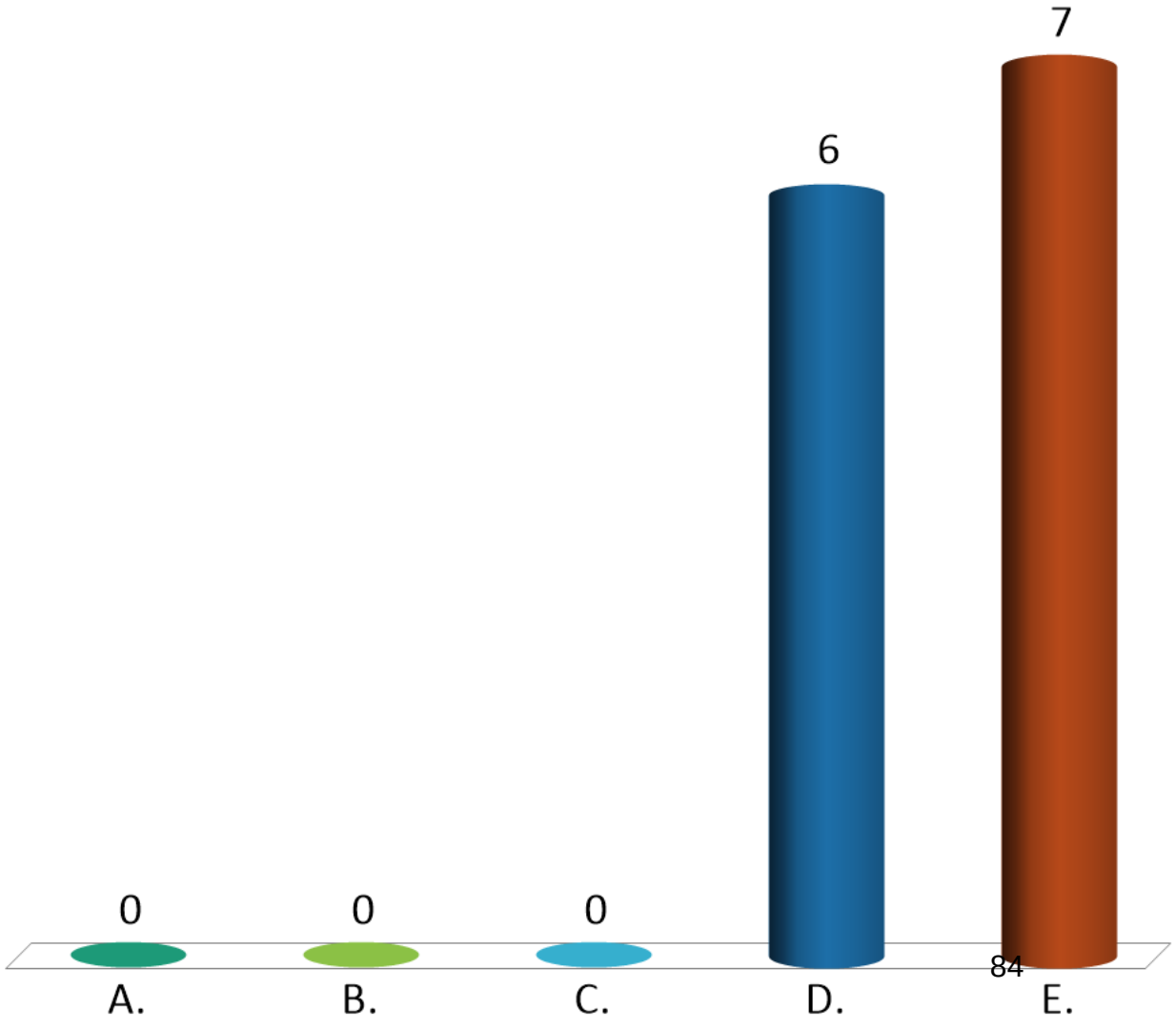
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



10. Society's goal of reducing health inequities

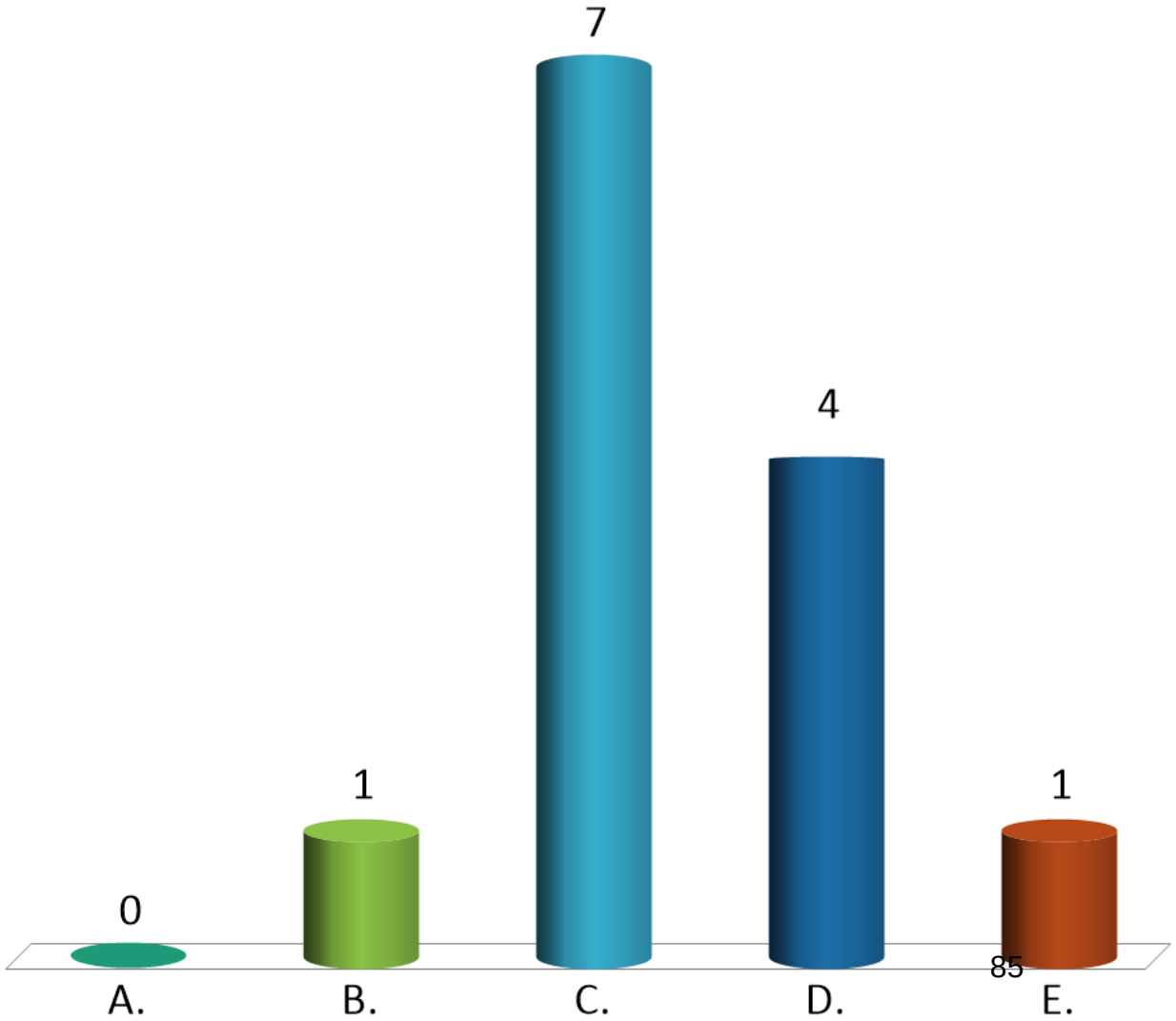
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



11. What are the relative effects of the JAK inhibitors as a class versus dupilumab on patients' ability to manage and sustain treatment given the complexities of the regimens?

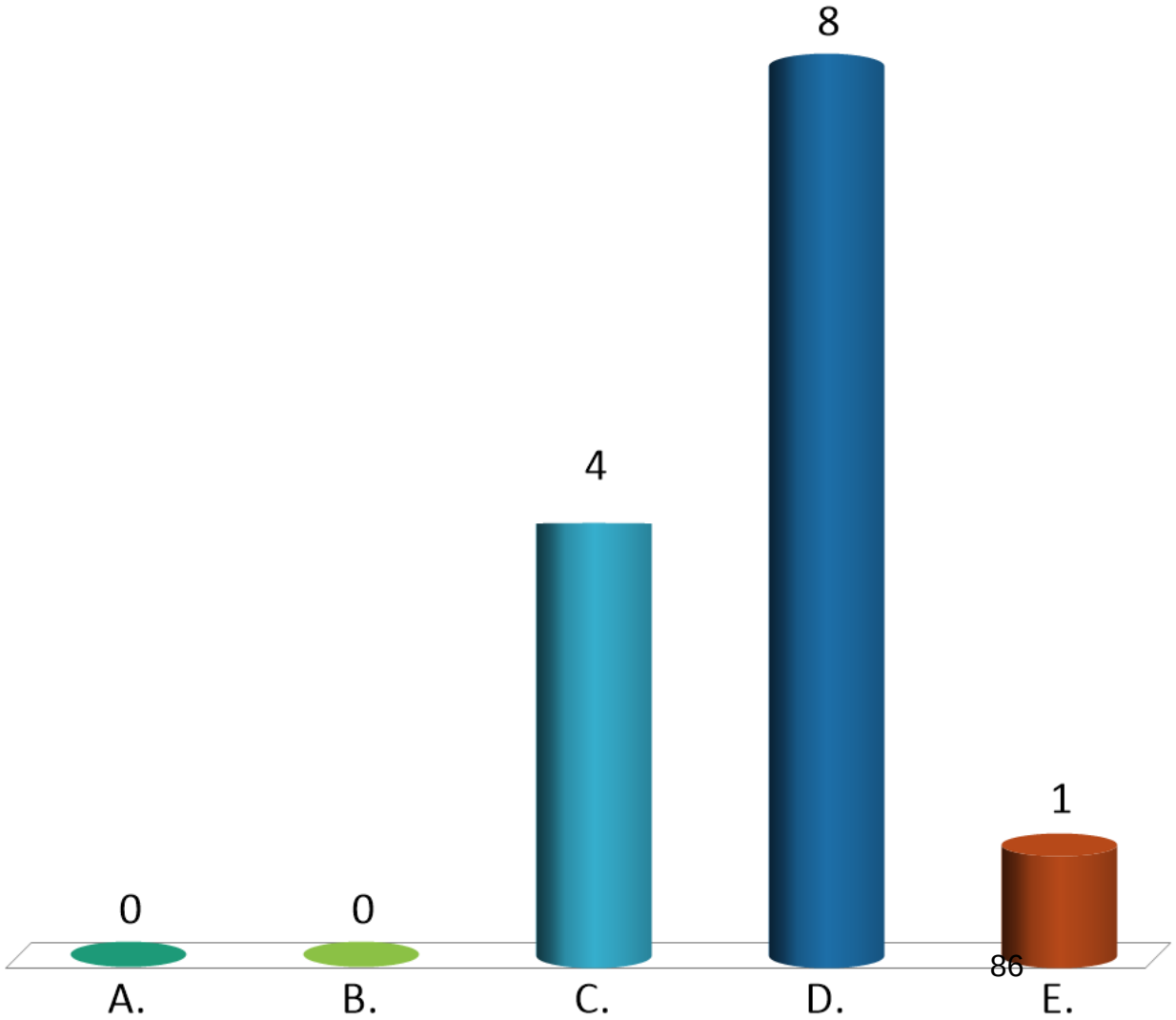
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



12. What are the relative effects of tralokinumab versus dupilumab on patients' ability to manage and sustain treatment given the complexities of the regimens?

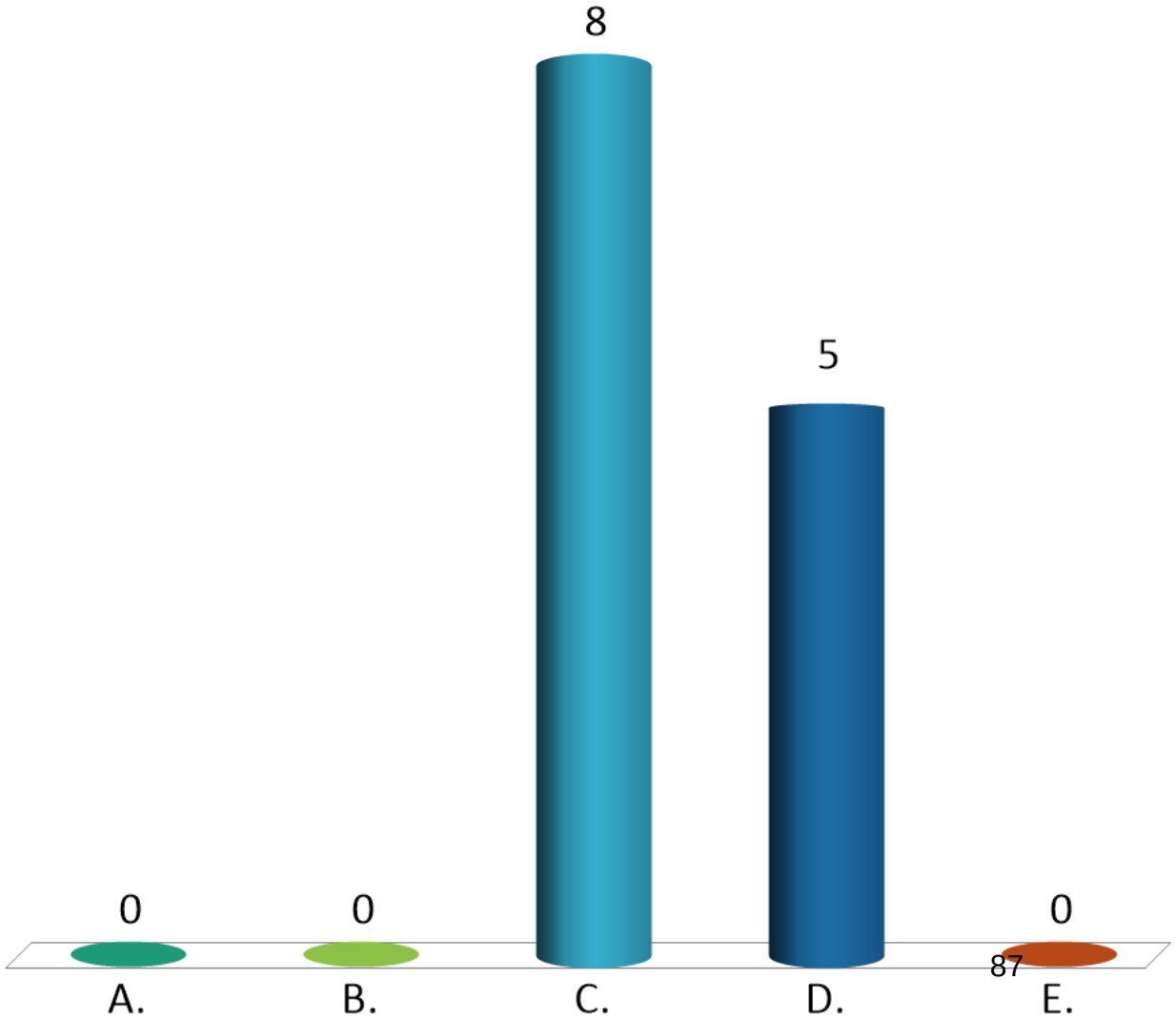
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



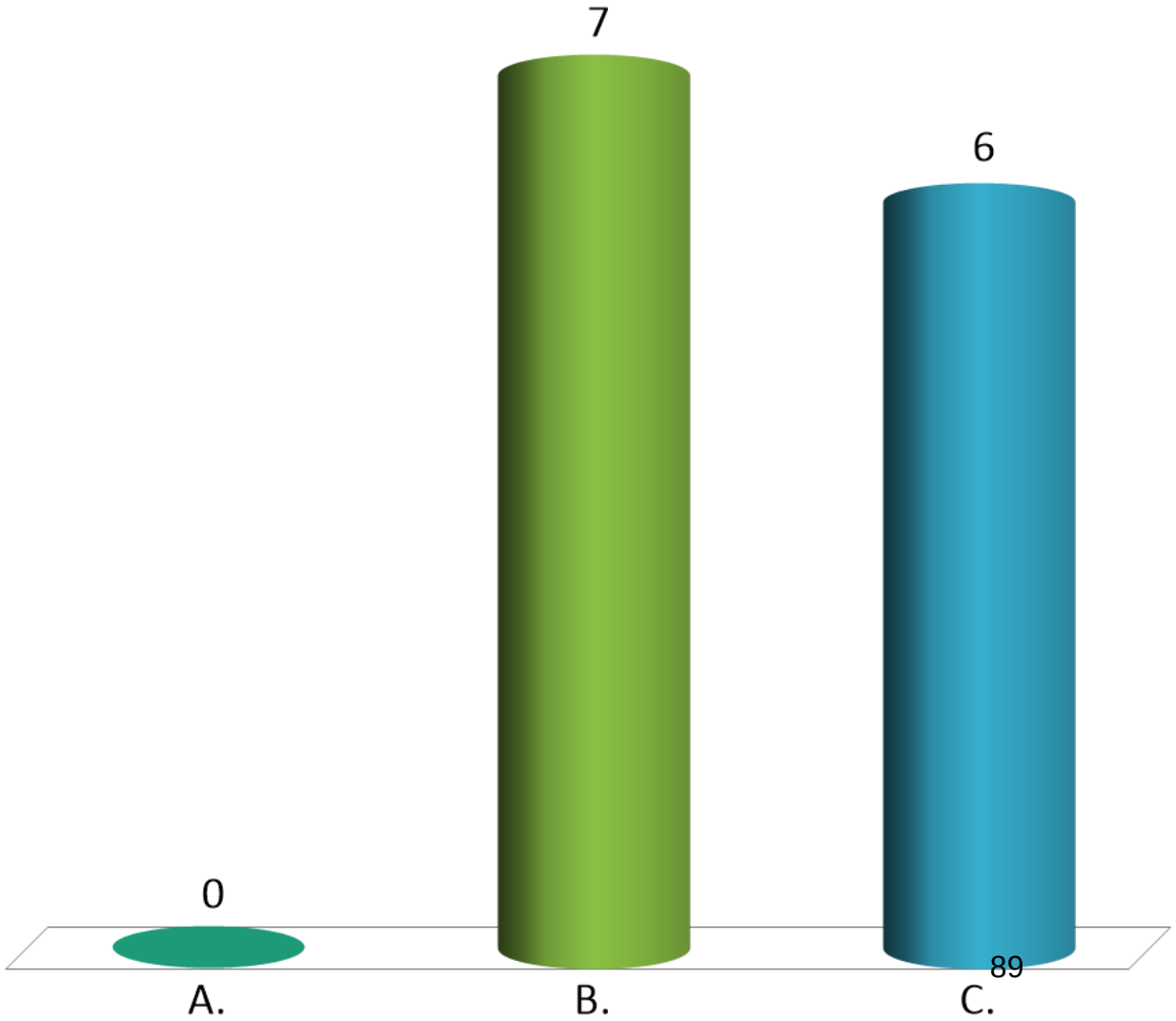
Long-term Value for Money

13. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with **baricitinib** versus usual care?

A. Low long-term value for money at current prices

B. Intermediate long-term value for money at current prices

C. High long-term value for money at current prices

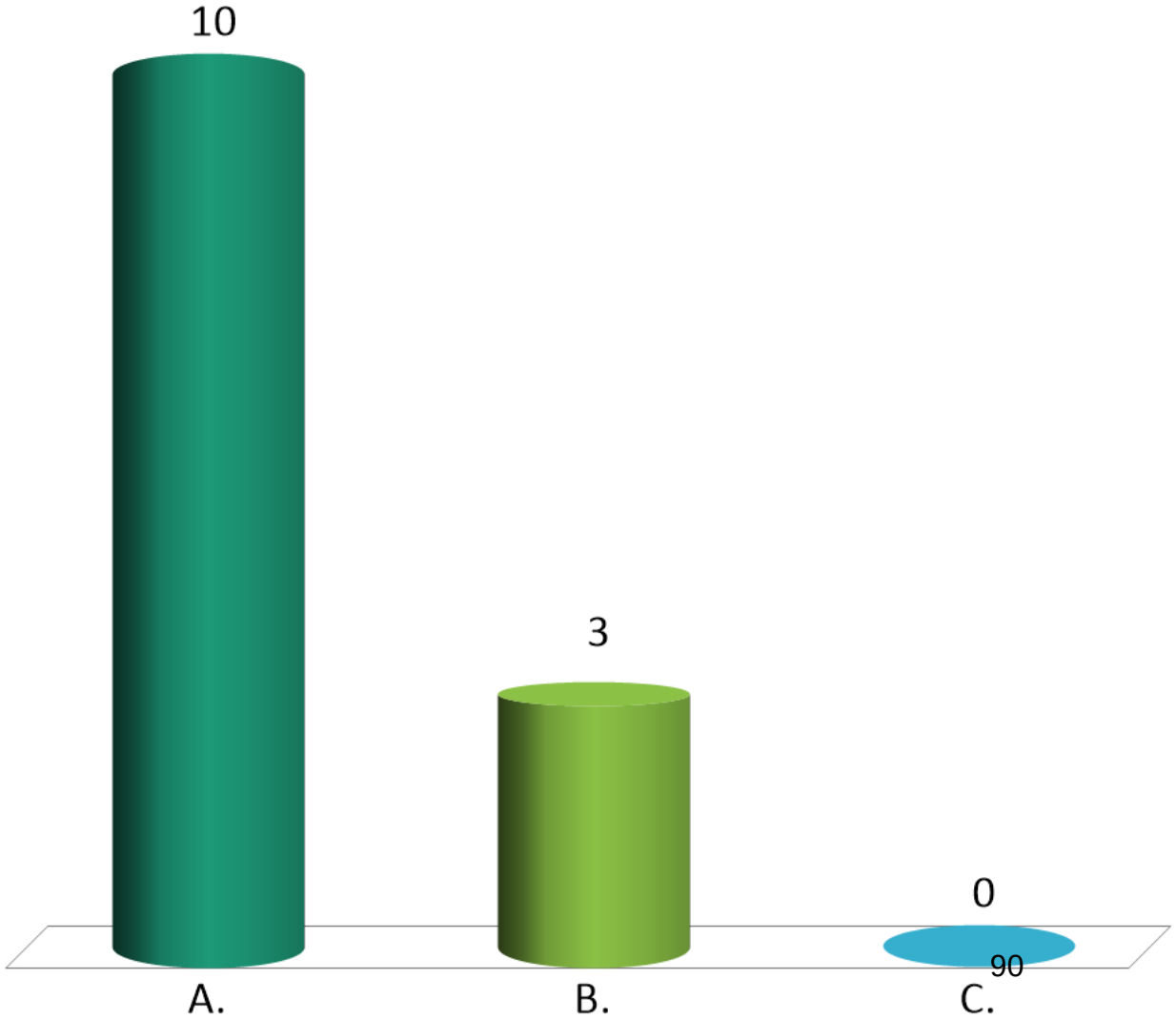


14. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with **upadacitinib** versus usual care?

A. Low long-term value for money at current prices

B. Intermediate long-term value for money at current prices

C. High long-term value for money at current prices



Lunch

Meeting will resume at 1:40pm ET

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Samantha Bittner, Patient Ambassador, National Eczema Association	No financial conflicts to disclose.
Thomas Brownlie, MS, Senior Director, Pfizer Inc.	Thomas is a full-time employee of Pfizer Inc.
Jeffrey Casberg, MS, RPh, Vice President of Pharmacy, IPD Analytics	Jeffrey is a full-time employee of IPD Analytics.
Michele Guadalupe, MPH, Associate Director of Advocacy and Access, National Eczema Association	The National Eczema Association has received grants and sponsorship awards from a variety of industry partners, including Pfizer, AbbVie, Sanofi, Regeneron, Incyte, and LEO Pharma.
Catherine Herren, PharmD, MS, Advisor, Value Development, Eli Lilly, and Company	Dr. Catherine Herren is a full-time employee of Eli Lilly and Company.
Kyle Hvidsten, MPH, Vice President, Head of Global Health Economics and Value Assessment, Sanofi	Kyle is a full-time employee of Sanofi.
Erik Schindler, PharmD, Director, Emerging Therapeutics and Outcome-Based Contracting, UnitedHealthcare Pharmacy	Dr. Erik Schindler is a full-time employee of UnitedHealthcare Pharmacy.
Elaine Siegfried, MD, Professor of Pediatrics and Dermatology, Saint Louis University School of Medicine	Dr. Elaine Siegfried has received consulting fees and honoraria from industry partners, including Incyte, Regeneron, Sanofi, LEO Pharma, Pfizer, and AbbVie for participation in clinical trials as a PI. She also received funding from Pfizer to support a two-year fellowship position at Saint Louis University.
Jonathan Silverberg, MD, PhD, MPH, Associate Professor, George Washington University School of Medicine and Health Sciences	Dr. Jonathan Silverberg has received funding from industry partners, including AbbVie, Eli Lilly, Incyte, LEO Pharma, Regeneron, and Sanofi.
Wendy Smith Begolka, MBS, Vice President of Scientific and Clinical Affairs, National Eczema Association	The National Eczema Association has received grants and sponsorship awards from a variety of industry partners, including Pfizer, AbbVie, Sanofi, Regeneron, Incyte, and LEO Pharma.

New England CEPAC Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around August 17th
  - Includes description of New England CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/atopic-dermatitis-2021/#timeline

Adjourn

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