



The JAK/STAT Signaling Pathway and its Role in Immune-mediated Inflammatory Disease: Impact on the Treatment of IBD

Final Outcomes Report

Gilead Sciences Grant ID: #02668

Series Overview

The educational intervention is comprised of two learning paths focusing on updates in treatment of immune-mediated inflammatory disease and application of emerging JAK/STAT therapies. The education was delivered via a series of regional meetings.

Learning Paths:

- Gastroenterology
- Rheumatology

Outcomes within this report are reflective of the **Gastroenterology** meetings.

Of the 30 regional meetings that occurred for this educational series, 16 were focused on the Gastroenterology learning path.

Overview

Activity Description: One-hour live educational visiting professorship programs (VPPs) implemented in community hospitals throughout the country that offer an update on the latest developments in emerging treatments for IBD. These meetings incorporate case presentations, didactic lectures, and/or clinical topic discussions.

Activities occurred: April 12, 2018 through December 20, 2018

Credit: 1.0 *AMA PRA Category 1 Credit™*

Sponsored by: The Academy for Continued Healthcare Learning (ACHL)

Supported by: An educational grant from Gilead Sciences, Inc.

Intended Audience: This activity is intended for gastroenterologists, and other clinicians interested in learning more about the JAK/STAT signaling pathway.

Outcomes Methodology: Activity-related changes in clinician knowledge and competence were evaluated by using evaluation assessments, and pre/post to compare baseline to post intervention/education. Self-attested changes to clinician performance was measured with a 30-day follow-up survey.

Program Information

INSTITUTION NAME	LOCATION	PROGRAM DATE	TOTAL LEARNERS	FACULTY
Norwegian American Hospital	Chicago, IL	5/31/18	43	Joel Pekow, MD
Community Hospital	Grand Junction, CO	6/15/18	6	Themistocles Dassopoulos, MD
Citizens Medical Center	Victoria, TX	7/26/18	20	Bincy Abraham, MD, MS
Shawnee Mission Medical Center	Shawnee Mission, KS	8/7/118	9	Bincy Abraham, MD, MS
Delaware County Memorial Hospital	Drexel Hill, PA	9/22/18	14	Thomas Ullman, MD
Florida Hospital DeLand	DeLand, FL	9/27/18	15	Joel Pekow, MD
St. Mary's Medical	San Francisco, CA	9/27/18	35	Sarah Streett, MD

Program Information (cont.)

INSTITUTION NAME	LOCATION	PROGRAM DATE	TOTAL LEARNERS	FACULTY
East Jefferson General Hospital	Metairie, LA	10/30/18	28	Thomas Ullman, MD
O'Connor Hospital	San Jose, CA	10/30/18	11	Sarah Streett, MD
Interfaith Medical Center	Brooklyn, NY	11/1/18	62	Bruce Sands, MD, MS
Mount Sinai Hospital	Chicago, IL	11/9/18	40	Joel Pekow, MD
New York Presbyterian Hospital Weill Cornell Medicine	New York, NY	11/12/18	14	Thomas Ullman, MD
St. Vincent's East	Birmingham, AL	11/20/18	44	Joel Pekow, MD
Our Lady of Lourdes Memorial Hospital	Binghamton, NY	12/6/18	35	Thomas Ullman, MD
Holy Cross Hospital	Chicago, IL	12/19/18	21	Joel Pekow, MD
Boston Medical Center	Boston, MA	12/20/18	13	Bruce Sands, MD, MS

Faculty Information



Russell Cohen, MD, FACG, AGAF (Chair)

Professor of Medicine, Pritzker School of Medicine
Director, Inflammatory Bowel Disease Center
Co-Director, Advanced IBD Fellowship Program
The University of Chicago Medical Center
Chicago, IL

**Content and faculty advisor, no speaking engagements*



Bincy Abraham, MD, MS

Associate Professor of Clinical Medicine
Weill Cornell Medical College
Director, Gastroenterology Fellowship Program, Houston
Methodist
Director & Distinguished Professor - Fondren Inflammatory
Bowel Disease Program Houston Methodist
Houston, TX

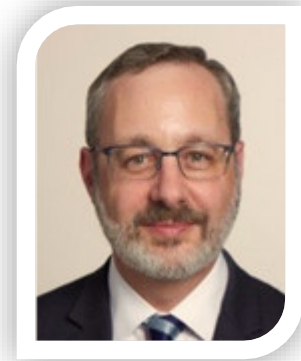
Faculty Information (cont.)



Themistocles Dassopoulos, MD
Director Baylor Scott and White Center
for Inflammatory Bowel Diseases
Adjunct Professor of Medicine, Texas
A&M University
Dallas, TX



Joel Pekow, MD
Assistant Professor of Medicine,
Section of Gastroenterology,
Hepatology, and Nutrition
University of Chicago Medicine and
Biological Sciences
Chicago, IL



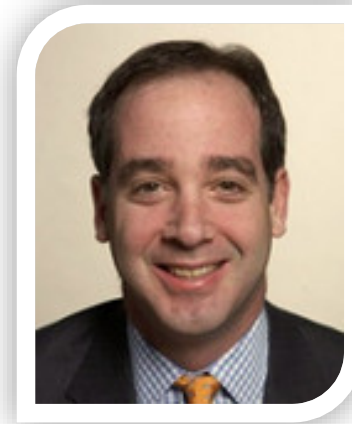
Bruce Sands, MD, MS
Chief of the Dr. Henry D. Janowitz
Division of Gastroenterology
Dr. Burrill B. Crohn Professor of
Medicine
Icahn School of Medicine at Mount
Sinai
Mount Sinai Health System
New York, NY

Faculty Information (cont.)



Sarah Streett, MD

Clinical Associate Professor
Division of Gastroenterology and Hepatology
Clinical Director of Inflammatory Bowel Disease
Stanford University
Stanford, CA



Thomas Ullman, MD

Chief, Division of Gastroenterology
Montefiore Medical Center/Albert Einstein College
of Medicine
New York, NY



Executive Summary



Participation*

410 Clinical Participants; 175 Certificates Issued

Practicing Type

88% Physicians, 1% Physicians Assistants, 3% Pharmacists, 5% NP/RNs, 3% Others

Objectivity & Balance

Objectivity and balance rated as good/excellent by 100% of learners

Learning Objectives

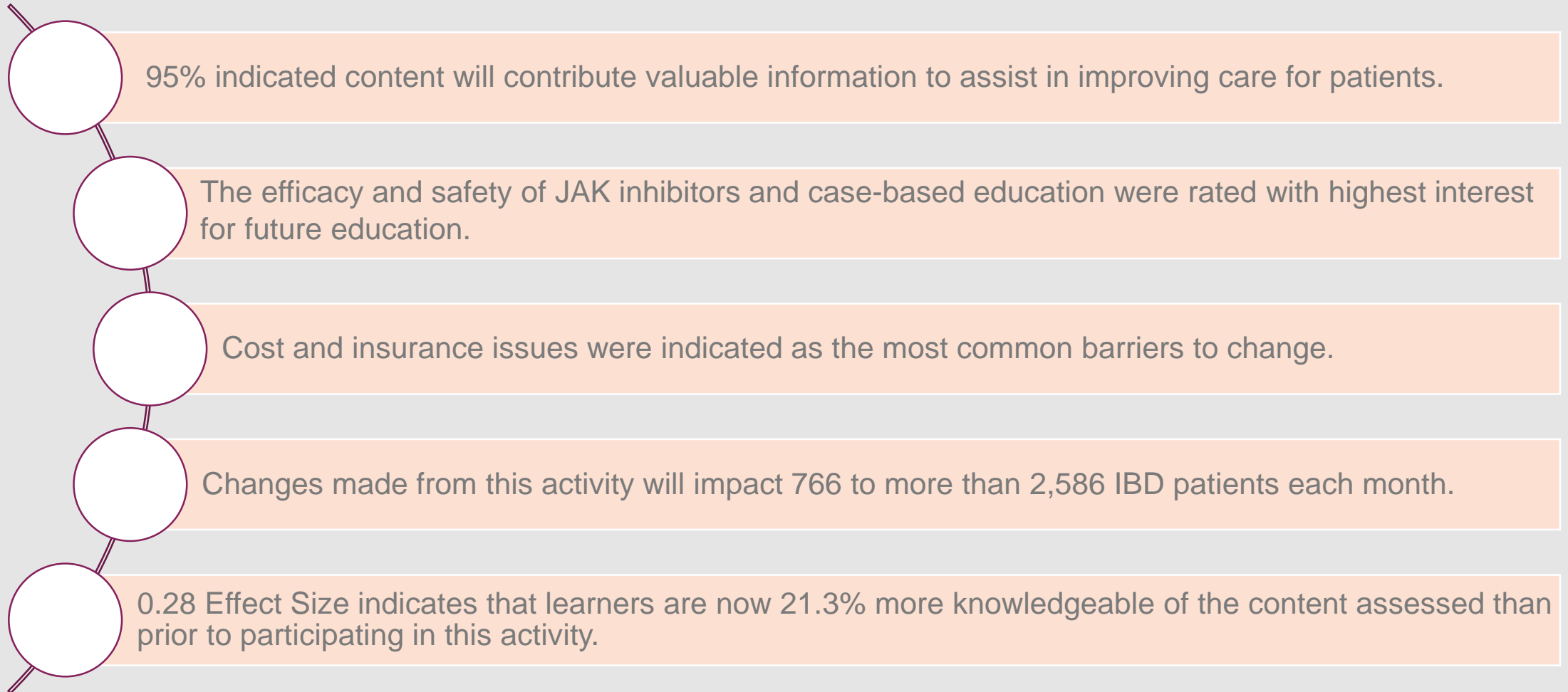
100% of learners strongly agree or agree that all learning objectives were met, with an average rating of 3.72/4.0

Faculty

Drs. Abraham, Dassopoulos, Pekow, Streett, Sands, and Ullman were highly rated 3.93/4.0

**917 total learners and 360 certificates across both learning paths*

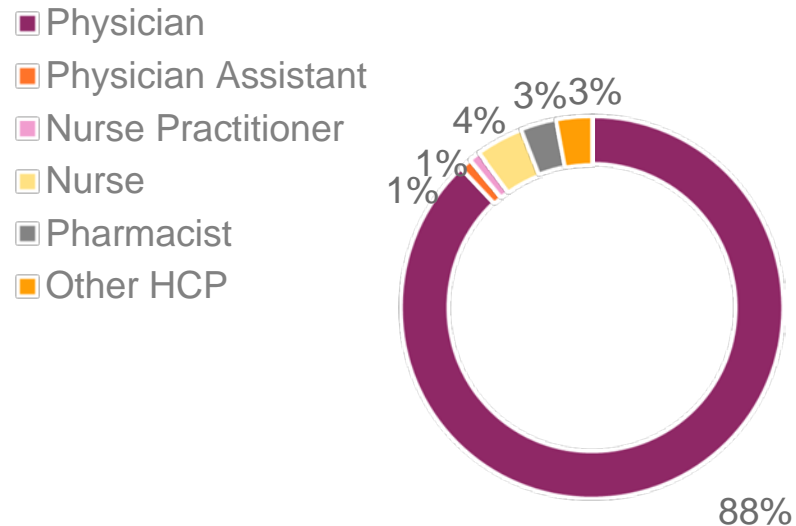
Executive Summary (cont.)



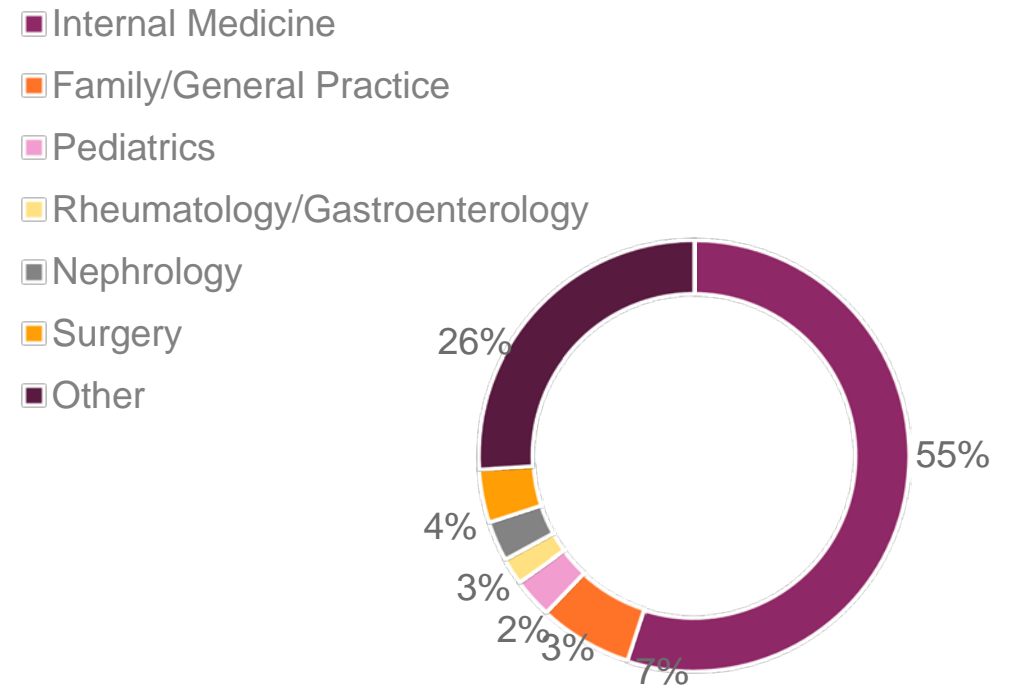
Level 1: Participation

Participants	Certificates
410	175

Participation by Clinician Type



Participation by Specialty



Level 2: Learning Objectives

Please rate the following objectives to indicate if you are better able to:	Analysis of Respondents Rating scale: 4=Strongly Agree; 1=Strongly Disagree
Outline the role of the JAK/STAT signaling pathway in the inflammation and disease progression of immune-mediated inflammatory diseases such as IBD	3.74
Discuss unmet clinical needs and the need for novel targets in IBD	3.70
Interpret clinical trial efficacy and safety data of JAK inhibitors under investigation for UC and Crohn's disease	3.73

100% of learners strongly agree or agree that all learning objectives were met, with an average rating of 3.72/4.0.

100% of learners would recommend this activity to a colleague!

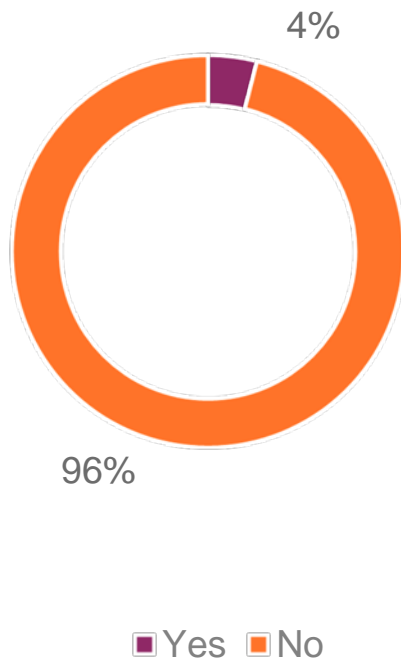
Level 2: Faculty Evaluation

Please rate the faculty on the criteria listed Rating scale: 4=Excellent; 1=Poor	Ability to effectively convey the subject matter	Expertise on the subject matter
Bincy Abraham, MD, MS	3.78	3.83
Themistocles Dassopoulos, MD	3.80	4.0
Joel Pekow, MD	3.95	3.95
Sarah Streett, MD	4.0	4.0
Thomas Ullman, MD	3.89	3.88
Bruce Sands, MD	3.86	3.91

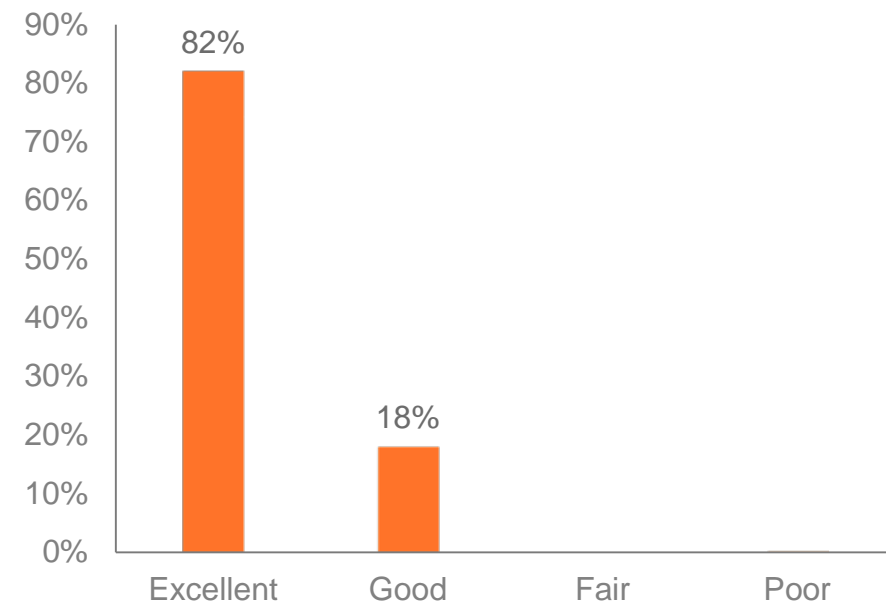
The faculty were rated good or excellent across all areas by 100% of learners, with an average rating of 3.93/4.0.

Objectivity & Balance

Did you perceive any bias?



Rating of objectivity & balance

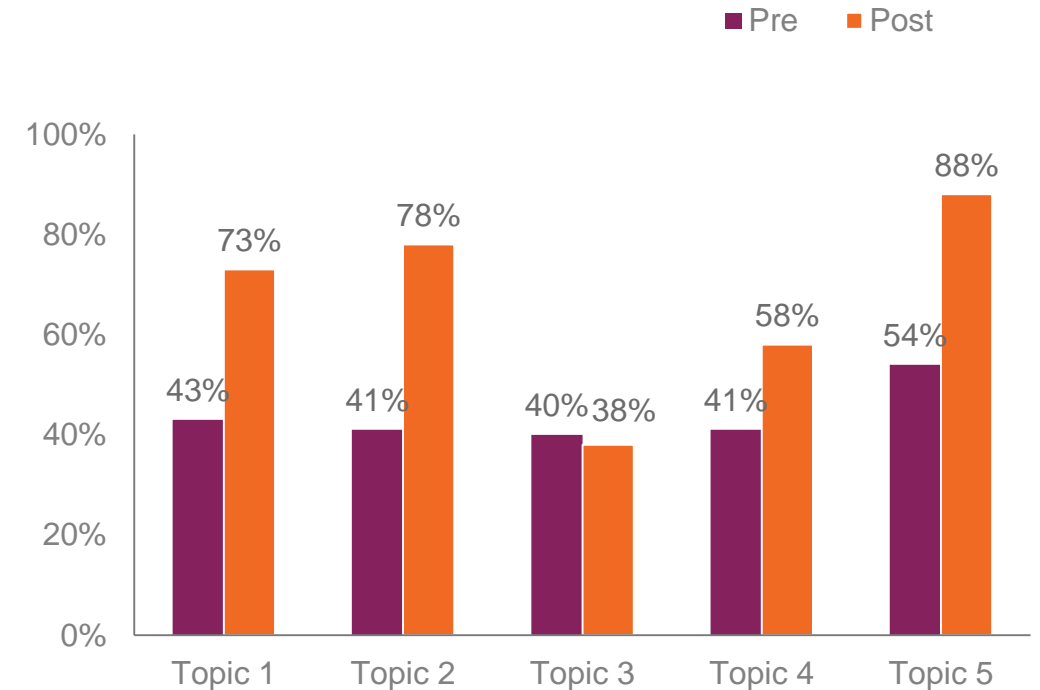


Activity was perceived as objective, balanced and non-biased.

N=175

Levels 3-4: Pretest vs. Posttest

Overview of Correct Responses	
Topic	% Change
Signaling pathways	↑ 70%
Available and emerging JAK inhibitors	↑ 90%
Selection of therapy	↓ - 5%
Filgotinib clinical trial data	↑ 41%
Safety of JAK inhibitors	↑ 63%



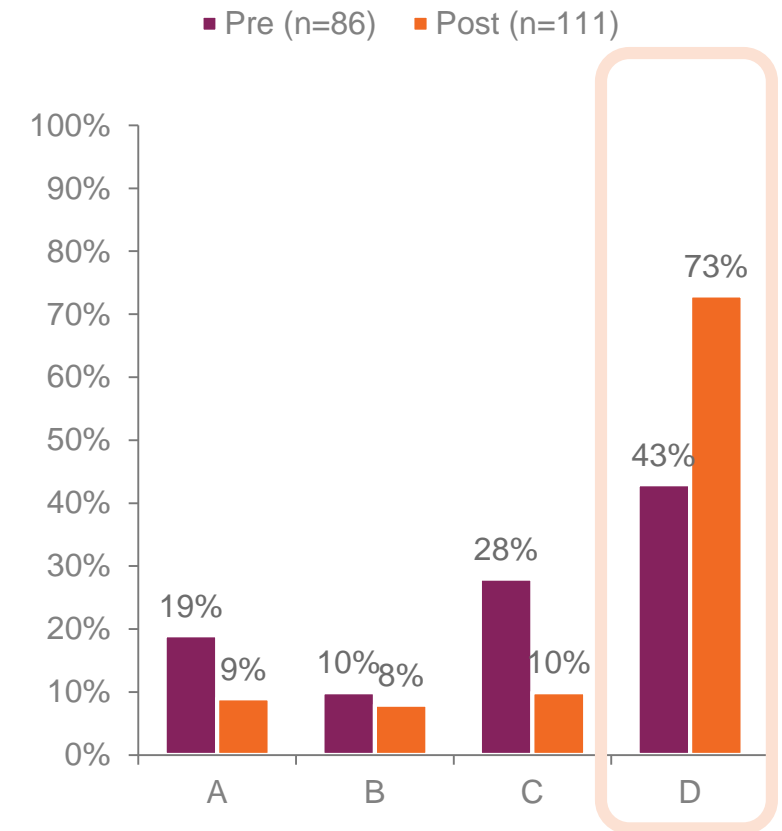
Participants demonstrated improved knowledge and competence on four of five pre/posttest questions.

Levels 3-4: Pretest vs. Posttest

Signaling pathways

- Which of the following describes the relationship between TNF-alpha and the JAK/STAT signaling pathway?
 - TNF-alpha is a negative inhibitor of the JAK/STAT pathway
 - TNF-alpha signals via JAK1 homodimers
 - TNF-alpha signals via JAK1/JAK2 heterodimers
 - TNF-alpha has a different signal transduction pathway**

The percentage of learners correctly answering this question increased from 43% to 73%, suggesting that learners gained familiarity with the JAK/STAT pathway and how it differs from other targets in the management of IBD.



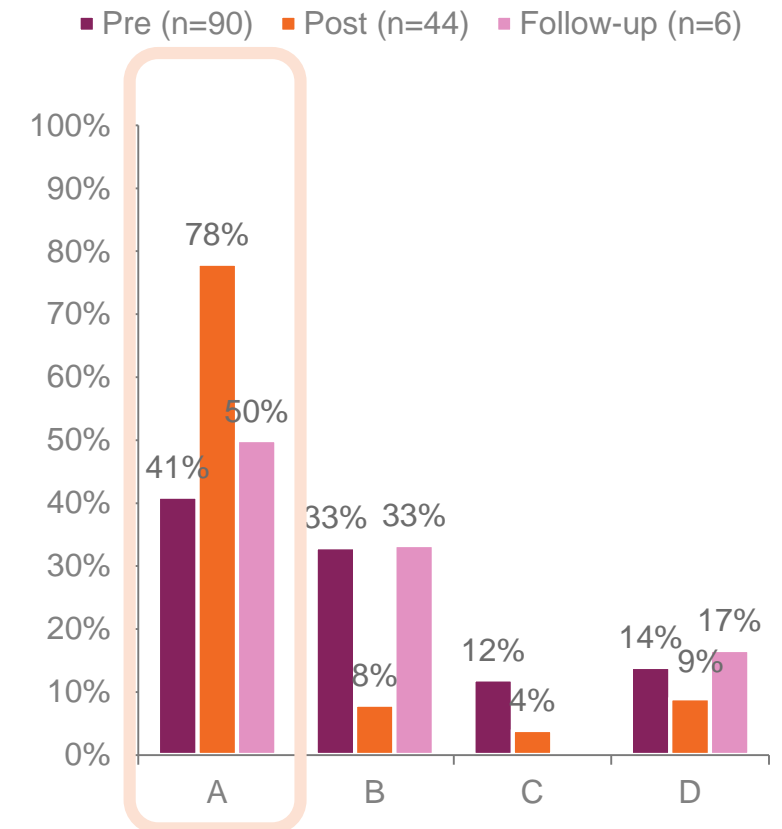
Levels 3-4: Pretest vs. Posttest

Available and emerging JAK inhibitors

2. The available and emerging JAK inhibitors inhibit different members of the JAK family. The investigational agent filgotinib works by inhibiting which of the following?

- A. JAK1
- B. JAK1/2
- C. JAK1/3
- D. JAK1/2/3 and Tyk2

The proportion of learners accurately identifying the MOA of filgotinib increased 90% after participation in the activity. This increased knowledge may assist learners in differentiating across the JAK inhibitors as they become available for managing IBD, however slippage (-36%) was observed in a 30-day follow-up survey.

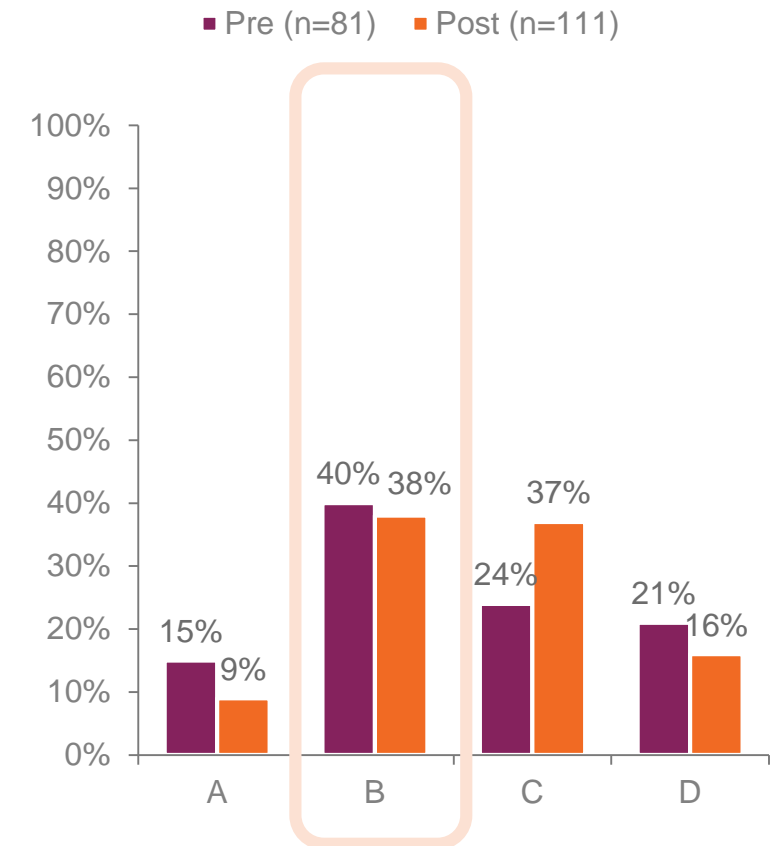


Levels 3-4: Pretest vs. Posttest

Selection of therapy

3. Based on available clinical trial data, which of the following IBD patients might be expected to elicit the highest response rate to a JAK inhibitor?
- A. A patient who demonstrated a clinical response to induction therapy with certolizumab pegol, but experienced a loss of response after 9 months of therapy
 - B. A patient who underwent a course of infliximab, but did not demonstrate an adequate response after 6 weeks**
 - C. A patient receiving oral steroid therapy who continues to experience symptoms
 - D. A patient who initiated infliximab therapy, but experienced a loss of response due to anti-drug antibodies

More learners correctly answered this question before their participation in the activity. This shift may reflect faculty speculation that the JAK inhibitors may become first-line therapies for IBD. Nevertheless, continued education should focus on evidence-based selection of therapy and the role of the JAK inhibitors in current treatment paradigms.

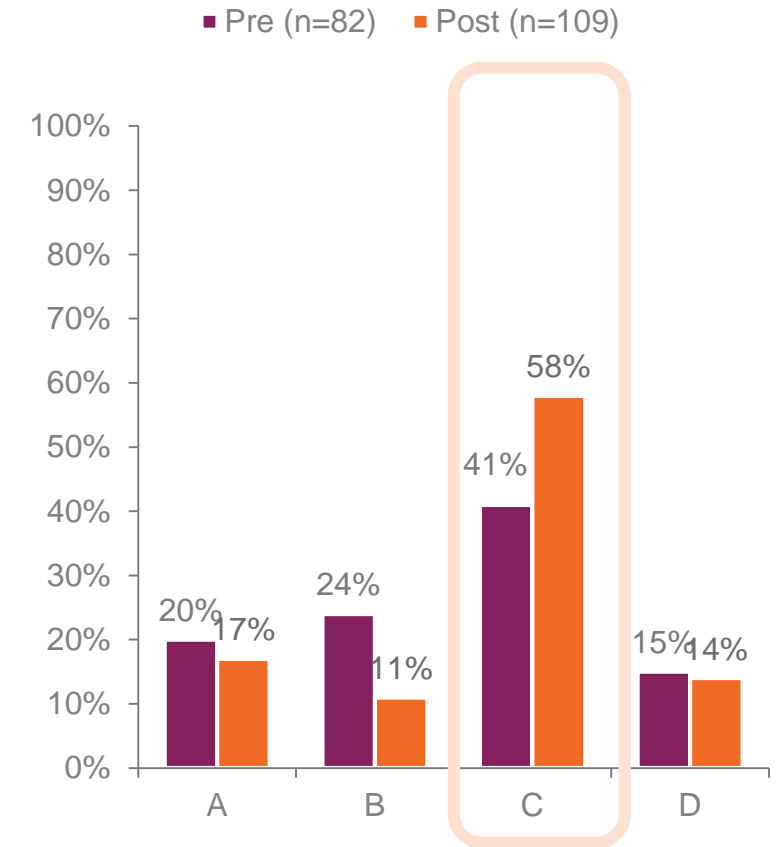


Levels 3-4: Pretest vs. Posttest

Filgotinib clinical trial data

4. Which of the following statements on available clinical trial data with filgotinib in IBD is correct?
- A. One-third of ulcerative colitis receiving filgotinib achieved clinical remission, but benefits have not been demonstrated in Crohn's disease
 - B. Filgotinib was effective as induction therapy for IBD, but not as maintenance therapy
 - C. Approximately one-half of Crohn's disease patients achieved clinical remission in a clinical trial**
 - D. Filgotinib failed to demonstrate benefits in a clinical trial of Crohn's disease patients due to a high placebo response

Results from this question on available filgotinib clinical trial data demonstrate an increase in knowledge and underscore the importance of continuing to review relevant clinical trial aspects (ie, patient populations and endpoints) in future educational endeavors.

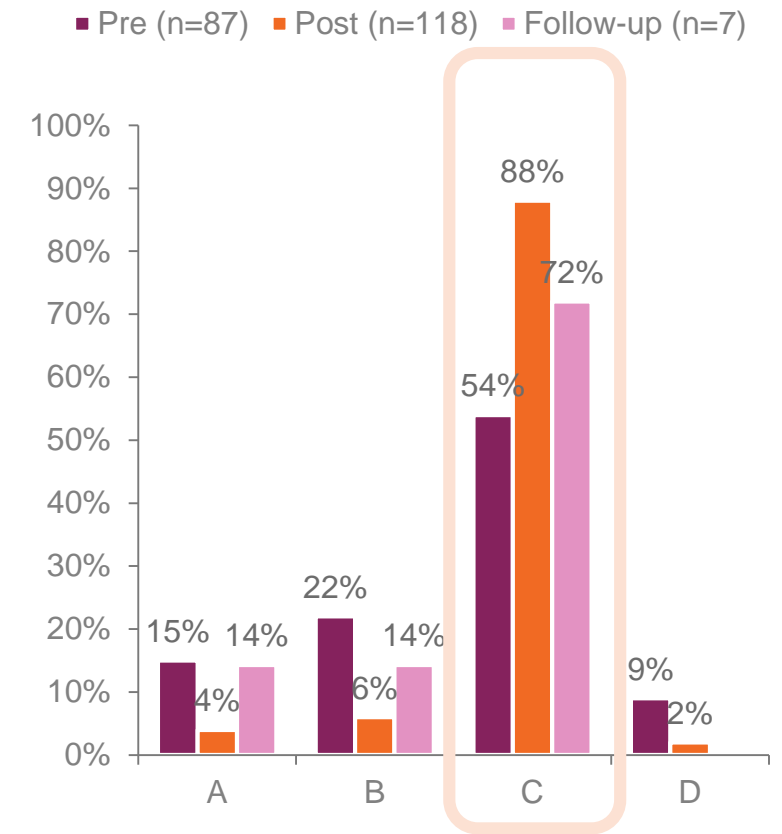


Levels 3-4: Pretest vs. Posttest

[Clinical Case Question] Safety of JAK inhibitors

5. AM, a 45-year old woman who is considering initiation of a JAK inhibitor asks about the potential risk of developing cancer given her knowledge of the biologic therapies. Based on a long-term analysis of the safety of tofacitinib for the treatment of RA, which of the following would you highlight as having the highest incidence rate during your discussion with AM?
- A. Malignancies
 - B. Serious infections
 - C. Herpes zoster infection**
 - D. GI perforations

The proportion of learners correctly answering this question increased 63%, suggesting increased knowledge of the accumulating safety data with the JAK inhibitors and how they differ from the biologics. 30-days following the activity, 72% demonstrated recall of the same topic.



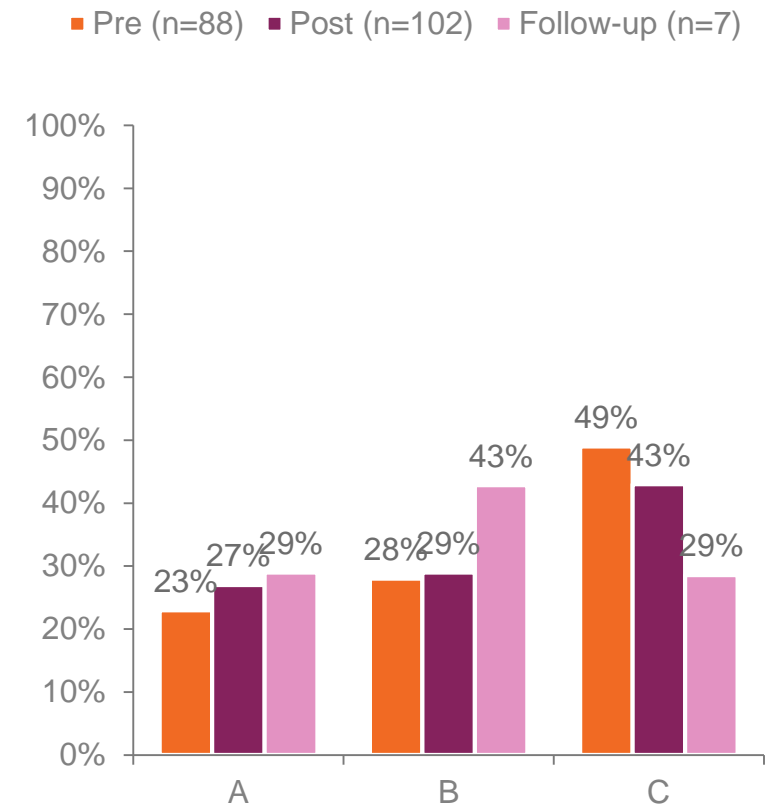
Practice Behavior

Availability of JAK inhibitors and application in clinical practice

As new JAK inhibitors become available, how will you apply them in clinical practice?

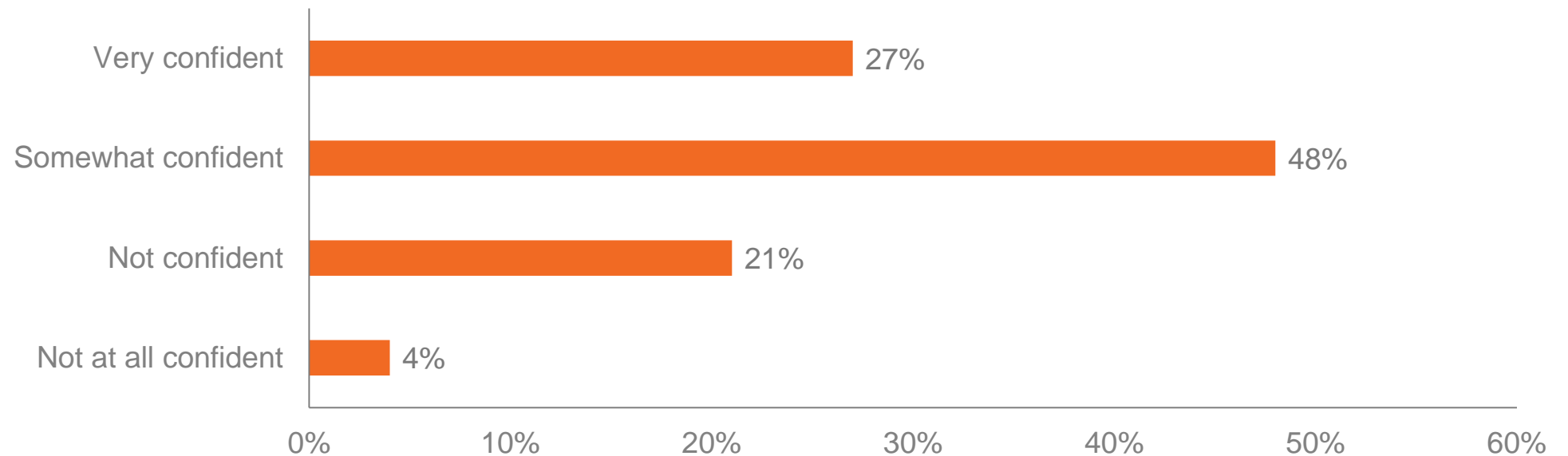
- A. I will offer them to patients as soon as they are available
- B. I will wait to hear of experiences from my colleagues
- C. I will wait until additional safety data are available

Approximately one-quarter of learners indicate an intent to use new JAK inhibitors as they become available. However, these data indicate a hesitation to apply new therapies. Ongoing education should address efficacy and safety as a means to reduce this hesitation, particularly since this is a new class of agents for IBD.



Prescribing Behavior Confidence

How confident are you prescribing the available JAK inhibitor for your patients with IBD in the future?

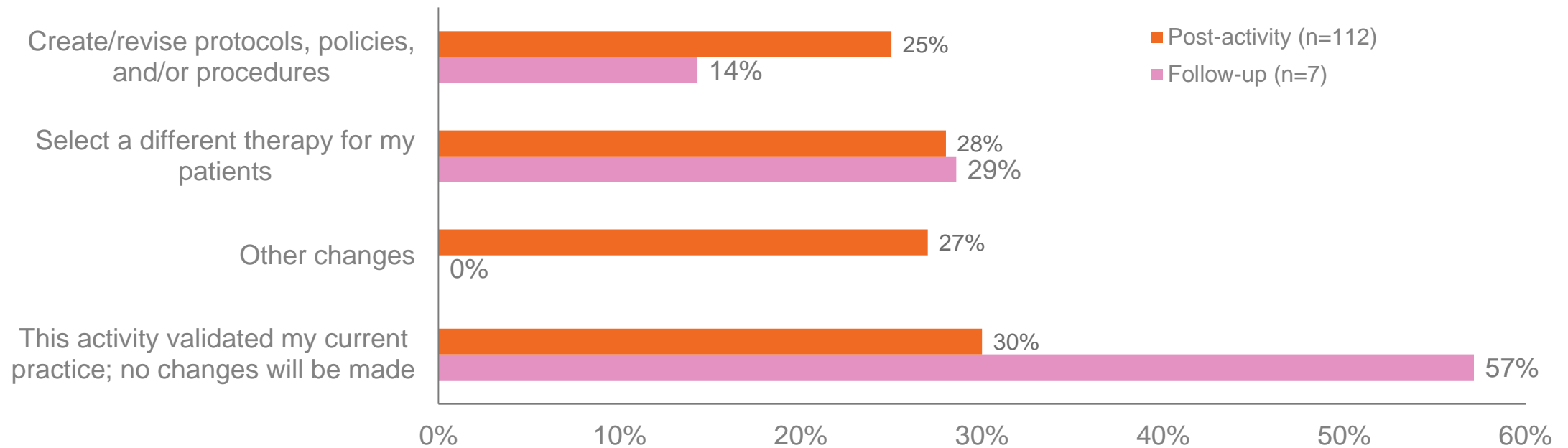


75% of learners are somewhat or very confident prescribing the available JAK inhibitors for patients with IBD.

N=138; multiple responses allowed

Level 4-5: Practice Change

How do you plan/did you make changes to your practice to improve patient care based on what you learned in this activity?

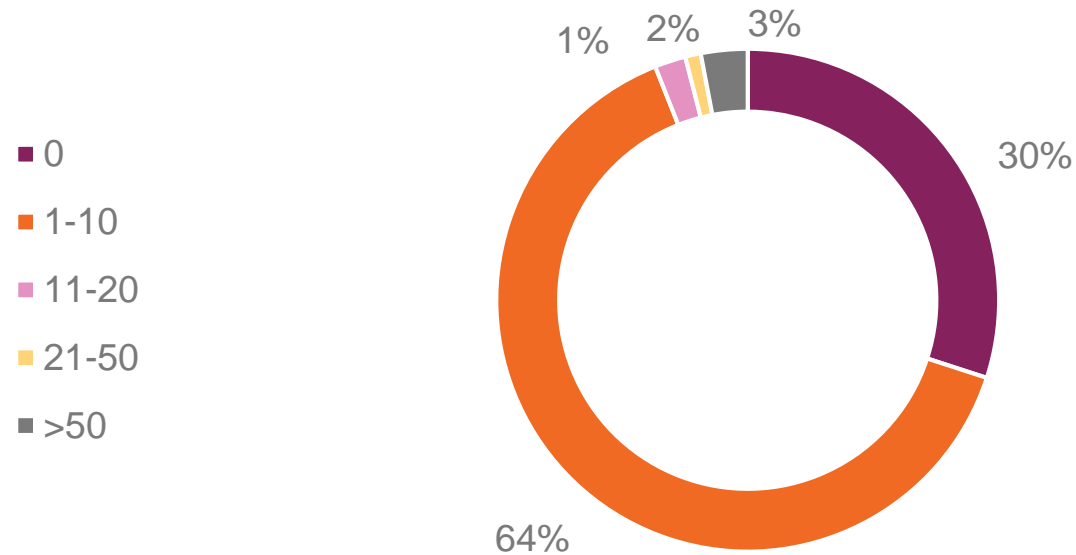


70% of learners plan to change their practice! Of the learners who completed a 30-day follow-up survey, 43% self-attest to making changes in their practice.

Multiple responses allowed

Patient Care Impact

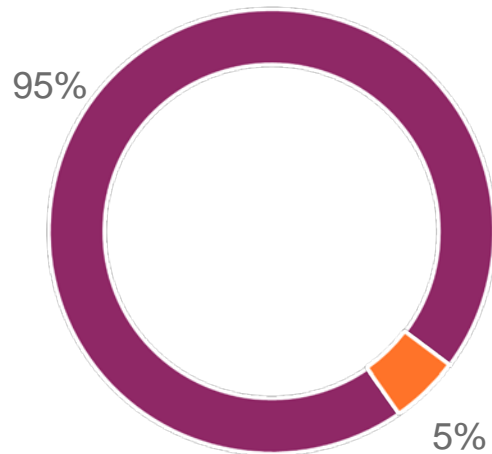
Number of patients with IBD seen per month:



Changes will impact 766 to more than 2,586 IBD patients each month. This assumes data in chart above is representative of all healthcare professionals in attendance (410), who indicated they would change their practice as a result of their participation in this activity (70%).

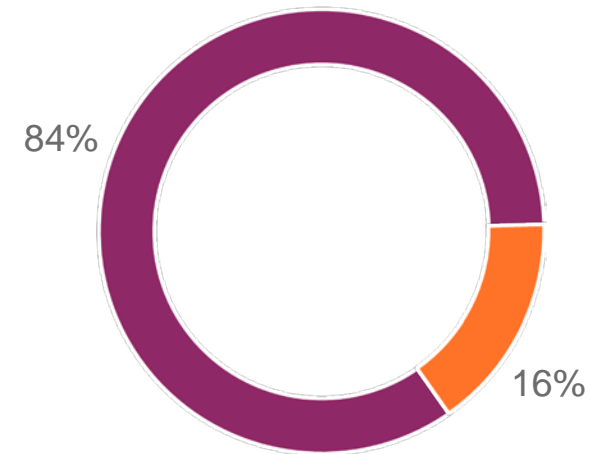
Improving Quality of Care

Does the content contribute valuable information that will assist in improving quality of care for patients?



■ Yes ■ No

Was the content relevant to your practice?



■ Yes ■ No

95% of participants indicated that the activity content is essential to improving care quality of IBD patients who would benefit from a JAK inhibitor, indicating highly effective educational content that stressed the critical importance of quality care for this at-risk patient cohort.

N=120

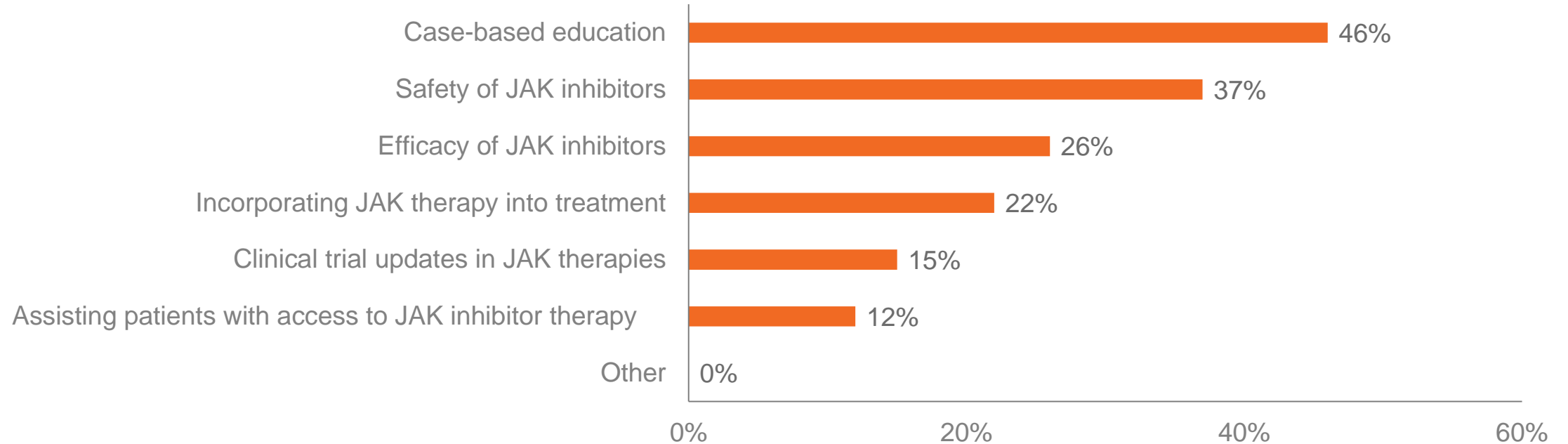
Barriers to Planned Change

The following barriers were noted by learners as impeding their ability to make changes to their practice:

- Cost (6)
- Patient resistance
- Limited time, will refer to GI and cooperative work closely
- Insurance coverage barriers (3)
- Formulary restriction
- The importance of a JAK inhibitor that is effective inducing clinical remission
- Availability of IBD specialists

Participants indicated cost as most common barrier to implementing changes in their practice, followed by insurance coverage.

Topics of Interest



The efficacy and safety of JAK inhibitors and case-based education had the highest interest for future education.

N=101; multiple responses allowed

Level 4: Activity Impact

Take-away pearls as a result of attending:

- Time for insurance for patients' education
- Updating patients on this inhibitor, their primary care
- Patients need PAP, new therapy options
- Hope to decrease use of corticosteroids, Increase dose of JAK if needed
- Differential Dx. between ulcerative colitis and Crohn's disease
- Induce remission and maintain remission
- I have additional mode of therapy available for treatment of IBD
- Side effect info for patients' recommendation for herpes zoster vaccine JAK inhibitors
- Keep an open mind
- Improve quality of life, Remission maintenance
- Define disease severity and extent, Induce clinical remission, Maintenance of clinical remission
- Immunology of JAK Inhibitor
- Concerns about cost, safety and preference of oral therapy
- Timely patient selection for JAK Therapy
- New knowledge of role in IMID
- New treatment for UC that is oral and consider JAK inhibitors for UC patients
- Control JAK/STAT inhibitors in IBD
- Treat fighters
- Advise/educate friends and family with IBD, also PT's seen in wound healing center
- Induction of remission, maintenance of remission
- Updating patients on this inhibitors , their primary care
- Healing and symptomatic improvement and survival
- Use of JAK-STAT inhibitors for UC/CP

Faculty Insights

I remember the senior faculty, Dr. Raybin at St. Mary's Medical in San Francisco saying that they had not had a GI/IBD talk of this caliber in many years, and how exciting to learn of the advances in the field.

- Sarah Streett, MD

From my interaction from other physicians they [discussed how they] were completely new to this type of treatment [and] its mechanism of action and were happy to learn of its potential for treatment in IBD.

-Bincy Abraham, MD, MS



Contact Information

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