Getting to the Gut of the Matter:

Closing the Gaps in Diagnosis, Effective Treatment, and Comprehensive Care in IBS and CIC



Supported by an educational grant from Allergan and Ironwood Pharmaceuticals.

**#IBSCIC** 

Provided by: CME Outfitters



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Disclosures

- Speakers Bureau: Allergan, Salix
   Pharmaceuticals; Synergy Pharmaceuticals Inc.
- Consultant: Allergan; IM HealthScience; Shire; Synergy Pharmaceuticals Inc.

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- Grants: Biomerica, Inc.; Ironwood
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  Pharmaceuticals; Salix Pharmaceuticals; Valeant



## Kareen Turner, MPH, RD

Disclosures





# **Learning Objectives**

- Improve the diagnostic accuracy of IBS and CIC through patient queries, patient-centered communication, and use of diagnostic tools.
- Apply evidence-based treatment strategies for relief of IBS and CIC in patients with persistent symptoms despite initial dietary and OTC approaches.
- Promote collaborative care strategies that facilitate comprehensive management of IBS and CIC, including early initiation of care and optimal long-term management.

# Meet Mr. Stanley

46 year old referred from primary care physician with symptoms of diarrhea and abdominal pain over the past 6-8 months

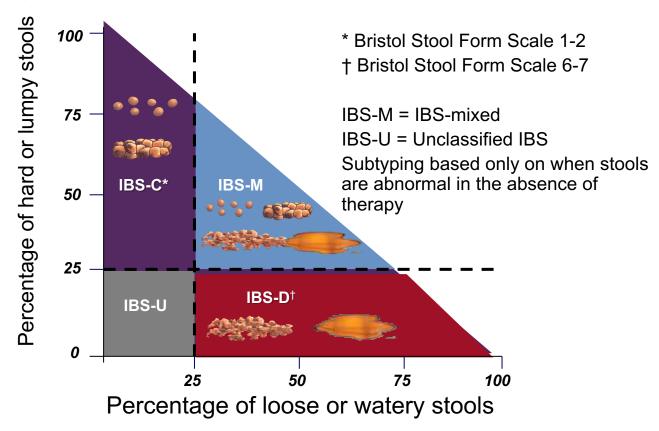




### **IBS: Rome IV Criteria\***

- Recurrent abdominal pain 1 day per week associated with two or more of the following:
  - Related to defecation
  - Onset associated with a change in the frequency of stool
  - Onset associated with a change in the form of stool

#### **IBS Subtypes Are Still Based on Stool Consistency**



Lacy BE, et al. *Gastroenterology*. 2016;150(6):1257-1492.

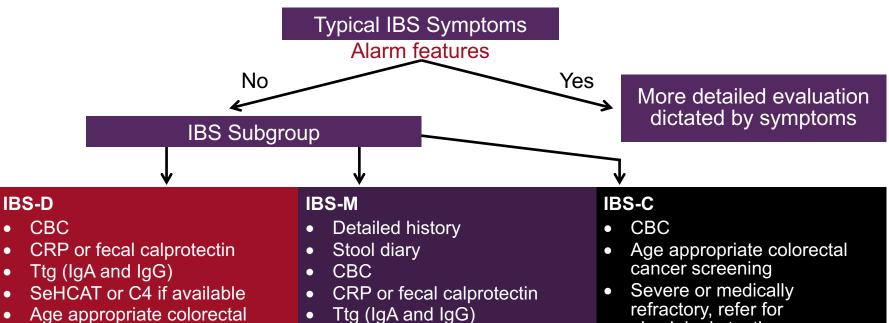
# Alarm Features in Patients With Suspected IBS

- Onset of symptoms after age 50
- GI bleeding or iron-deficiency anemia
- Nocturnal diarrhea
- Weight loss
- Family history of organic GI disease (colorectal cancer, IBD, celiac disease)



Patients with alarm features should be referred for further investigation

#### Work-Up of Patients with Suspected IBS



- cancer screening When colonoscopy or sigmoidoscopy performed, obtain random biopsies
- Ttg (IgA and IgG) Age appropriate colorectal cancer screening
- Consider abdominal x-ray

refractory, refer for physiologic testing

Chey WD, et al. JAMA 2015;313:949.

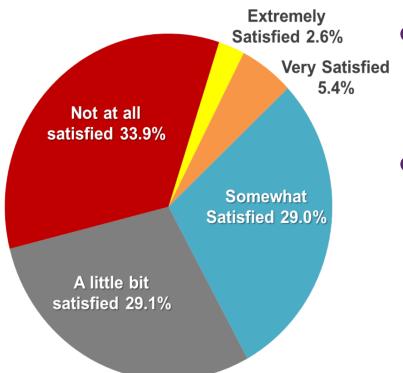
# Diagnostic Testing for Patients with Suspected IBS-D

- Colonoscopy to rule out inflammatory bowel disease (IBD)
  - Prospective study of 900 non-constipated patients undergoing colonoscopy found IBD in <1% of IBS patients and none of the healthy controls
  - When colonoscopy or sigmoidoscopy is performed, obtain biopsies to exclude microscopic colitis
- Noninvasive biomarkers may be more cost effective means of screening for IBD in patients with IBS symptoms
  - Fecal calprotectin: < 40 μg/g</li>
  - C-reactive protein (CRP): < 0.5 mg/dl</li>
  - Biomarkers conferred < 1% risk of IBD in patients with IBS symptoms

**IBS-D Treatment Strategies** 

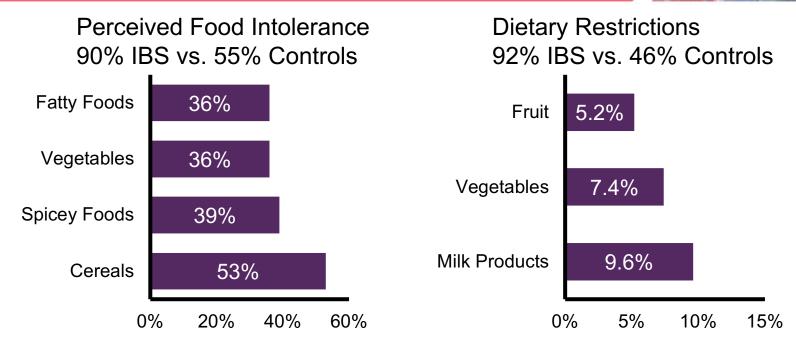


# IBS Patients are Dissatisfied with Non-Specific Treatment Options



- Treatments included:
  - Analgesics, antidepressants, anti-diarrheals, antispasmodics, narcotics (18%)
- Would give up 25% of remaining life (avg 15 years) and 14% would risk 1/1000 chance of death for treatment that would eliminate symptoms

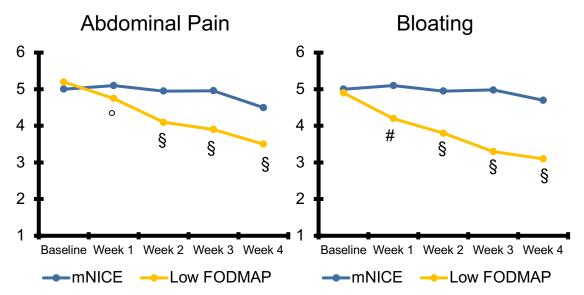
## **Survey on Diet and IBS**



- 135 patients with IBS, 111 healthy controls
- Only a small proportion sought healthcare advice on dietary restrictions

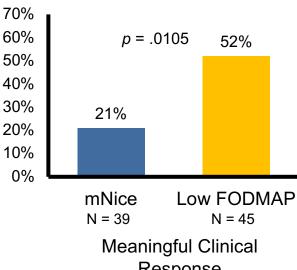
Hayes P, et al. J Hum Nutr Diet. 2014;27(Suppl 2): 36-47.

## Low FODMAP Diet vs. mNICE Diet: **IBS-QOL Scores**



P values refer to the change within group compared to baseline score  $\circ = p \le .01$ ;  $\# = p \le .001$ ;  $\S = p \le .0001$ 

Proportion with Improvement from Baseline ≥ 14 (IBS-QOL)



Response

Eswaran SL, Chey WD, et al. Am J Gastroenterol. 2016;111(12):1824-1832. Eswaran SL, Chey WD, et al. Clin Gastroenterol Hepatol 2017;15(12):1890-1899.

# Systematic Review and Meta-Analysis of Peppermint Oil in IBS

	Illustrative Co (95				
	Assessed Risk	Corresponding Risk			
Outcomes	Control	Peppermint Oil vs PBO	Relative Effect (95% CI)	Participants (Studies)	Quality of the Evidence (GRADE)
Global improvement in IBS symptoms	308 per 1,000	687 per 1,000 (548 to 866)	RR 2.23 (1.78-2.81)	392 (5 studies)	Moderate
Improvement in abdominal pain	268 per 1,000	547 per 1,000 (440 to 748)	RR 2.14 (1.64-2.79)	357 (5 studies)	Moderate
Adverse events	126 per 1,000	218 per 1,000 (160 to 297)	RR 1.73 (1.27-2.36)	474 (7 studies)	Moderate

- AEs mild and transient in nature
  - Heartburn, dry mouth, belching, peppermint taste, peri-anal cold sensation, HA

Khanna R, et al. J Clin Gastroenterol. 2014;48:505-512.

# Synthetic Opiate Preparations

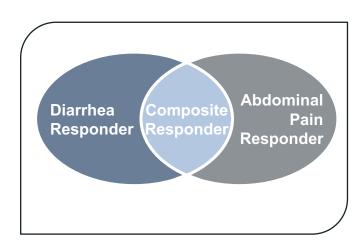
- Loperamide: low potency mu agonist; poor absorption, limited ability to cross blood-brain barrier<sup>1</sup>; available OTC, inexpensive
  - Labeled for acute diarrhea
  - Chronic diarrhea: best used expectantly; 2-4 mg before meals and qhs if needed
    - May also be helpful for patients with fecal incontinence (tightens anal sphincter)
  - No evidence loperamide slows recovery from infectious diarrhea
- Diphenoxylate/Difenoxin: Meperidine derivatives combined with lowdose atropine to discourage abuse<sup>2</sup>
  - Similar potency to loperamide but less well tolerated
  - Schedule V medications
- Common AEs: constipation, crampy abdominal pain, nausea
- Not well studied in IBS

<sup>1.</sup> Baker DE. Rev Gastroenterol Disord. 2007;7 Suppl 3:S11-18.

<sup>2.</sup> http://www.pdr.net/drug-summary/Motofen-atropine-sulfate-difenoxin-hydrochloride-2988

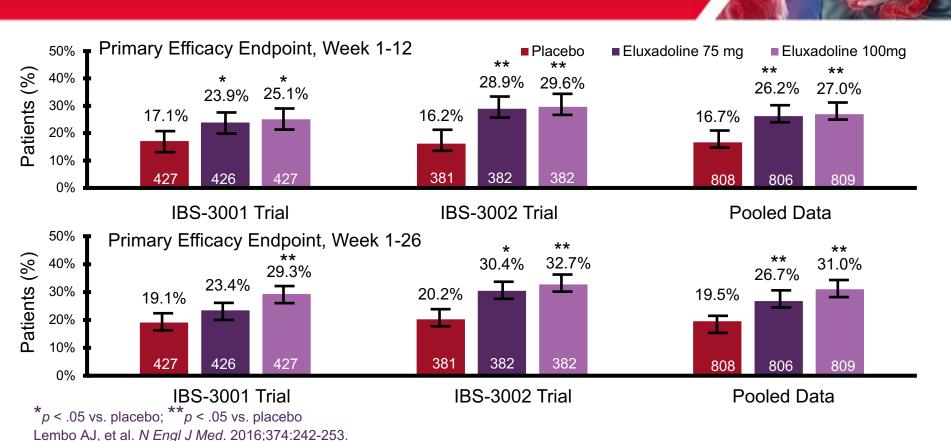
#### Eluxadoline

- Mixed opioid receptor modulator approved for IBS-D
  - Mu (μ) opioid receptor agonist and kappa (κ) opioid receptor agonist; delta (δ) opioid receptor antagonist<sup>1,2</sup>
  - Proportion of composite responders<sup>3</sup>
    - ≥ 30% reduction in worst abdominal pain score AND improvement in stool consistency of < 5 on the BSFS</li>
    - Daily improvement in BOTH symptoms on at least 50% of days in the trial



<sup>1.</sup> Fujita W et al. *Biochemical Pharmacology*. 2014. http://dx.doi.org/10.1016/j.bcp.2014.09.015.; 2. Wade PR, et al. *British Journal of Pharmacology*. 2012;167:1111-1125.; 3. Lembo AJ, et al. *N Engl J Med*. 2016;374:242-253.

## Eluxadoline



## **Eluxadoline Safety**

Most Common Adverse Events in Phase 3 Trials (> 4% in Either Treatment Arm and > Placebo)

	Placebo (n = 808)	Eluxadoline 75 mg (n = 859)	Eluxadoline 100 mg (n = 807)
Adverse Events		n (%)	
Constipation*	20 (2.5)	60 (7.4)	74 (8.6)
Nausea	41 (5.1)	65 (8.1)	64 (7.5)
Abdominal pain <sup>†</sup>	33 (4.0)	47 (5.9)	62 (7.2)
Vomiting	11 (1.4)	32 (4.0)	36 (4.2)
Gastroenteritis‡	27 (3.4)	36 (4.4)	19 (2.2)
URI	32 (4.0)	27 (3.3)	47 (5.5)
Nasopharyngitis	27 (3.3)	33 (4.1)	23 (2.7)

	Eluxadoline 75 mg (n = 807)* 2 (0.2%)	Eluxadoline 100 mg (n = 1,032)† 8 (0.8%)			
Sphincter of Oddi spasm (SOS) <sup>‡</sup> All events resolved upon treatment discontinuation, typically improving by the following day; 80% of cases occurred within 1 week of treatment, and the rest within 1 month.	1 patient had abdominal pain and elevated hepatic enzymes     1 patient had abdominal pain and lipase elevation <3x ULN	<ul> <li>7 patients had abdominal pain and elevated hepatic enzymes</li> <li>1 patient had pancreatitis, occurring within minutes of taking treatment</li> </ul>			
Pancreatitis	2 (0.2%)	3 (0.3%)			
All pancreatic events resolved with lipase normalization upon treatment discontinuation; 80% resolved within 1 week.	<ul> <li>3 patients had excessive alcohol intake</li> <li>1 patient had biliary sludge</li> <li>1 patient discontinued treatment prior to symptom onset</li> </ul>				

<sup>\*</sup>All constipation events were non-serious – 1.4% of patients receiving eluxadoline and 0.2% receiving placebo discontinued due to non-serious constipation; 
†Abdominal pain = abdominal pain, abdominal pain upper, abdominal pain lower; 
†Gastroenteritis = gastroenteritis and viral gastroenteritis

Cash B, et al. *Am J Gastroenterol*. 2017;112:365-74.

#### **Alosetron**

- 5-HT3 antagonist: attenuates motor and secretory activity and transmission of sensory signals to the brain
- Indicated for severe, refractory IBS-D in women
- 8 RCTs, 4341 patients (predominantly women)
  - RR of IBS not improving 0.79 (CI: 0.69-0.90); NNT=7.5
  - More AEs with alosetron; NNH= 10; constipation; colon ischemia: 1/1000 patient-years
  - Remains 3rd line pharmacotherapy

Study	Treatment n/N	Control n/N	RR (Random) 95% CI	RR (Random) 95% CI
Camilleri (1999)	179/290	54/80	+	0.91(0.77, 1.09)
Bardhan (2000)	166/345	57/117	+	0.99 (0.80, 1.23)
Camilleri (2000)	191/324	229/323	-	0.83 (0.74, 0.93)
Camilleri (2001)	182/309	235/317	•	0.79 (0.71, 0.89)
Lembo (2001)	144/532	156/269	+	0.47 (0.39, 0.55)
Chey (2004)	167/351	197/363	-	0.88 (0.76, 1.01)
Chang (2005)	268/534	77/128	-	0.83 (0.71, 0.98)
Krause (2007)	279/529	122/176	4	0.76 (0.67, 0.86)
Subtotal (95% CI)	3,214	1,773	<b>~</b>	0.79 (0.69, 0.90)
		Fa	0.1 0.2 0.5 1 2 5 vors Treatment Favors	10 Control

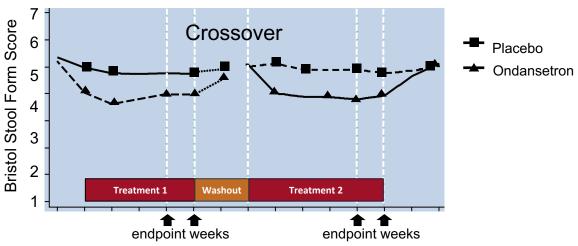
## **Alosetron Safety**

- Dosage and indication
  - 0.5 mg BID, for female patients with chronic, severe IBS-D who have not responded adequately to conventional therapy<sup>1</sup>
- Risk and Mitigation Strategy (REMS) program modified in January 2016 to eliminate requirements for patient attestation form and affixing prescribing program stickers to prescriptions for alosetron<sup>2</sup>
- Adverse events<sup>3</sup>
  - Ischemic colitis: 0.95 cases per 1,000 patient-years
  - Serious complications of constipation: 0.36 cases per 1,000 patientyears

<sup>1.</sup> FDA Package Insert. Available at https://www.accessdata.fda.gov/drugsatfda\_docs/label/2002/21107s5lbl.pdf. Accessed May 18, 2018. 2. FDA. Alosetron tablets and authorized generic tablets. Risk evaluation and mitigation strategy (REMS). Available at http://www.accessdata.fda.gov/drugsatfda\_docs/rems/Lotronex\_2016-01-07\_REMS\_Document%20.pdf. Accessed May 18, 2018.; 3. Chang L et al. *Am J Gastroenterol*. 2010;105:866-875.

#### **Ondansetron**

Effect of Ondansetron 4-8 mg TID for 5 Weeks in Patients with Rome III IBS-D (N = 120)\*

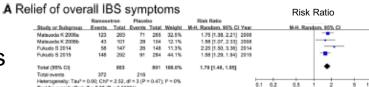


- Improvement also noted in stool frequency and urgency
- No effect on abdominal pain or bloating

Garsed K, et al. Gut. 2014;63:1617-1625.

<sup>\*</sup>Randomized, double-blind, dose-titration study. Primary endpoint was average stool consistency in last 2 weeks of treatment. Improvements in urgency, frequency, bloating but NOT pain.

- Ramosetron
  - High 5-HT3 binding affinity: potent and prolonged receptor blockade and antiemetic effects compared with older 5-HT3 antagonists
  - Meta-analysis of 4 IBS RCTs with 1623 patients (ramosetron vs. placebo)
    - Effective in men and women.
    - Overall IBS relief OR 1.70 (95% CI: 1.48 to 1.95)
    - Relief of abdominal pain/discomfort OR 1.41 (95% CI: 1.24 to 1.59)
    - Improvement in diarrhea OR 1.71 (95% CI: 1.40 to 2.08)
    - Higher rates of constipation; no colon ischemia



#### B Relief of abdominal discomfort/pain

								NISK Natio
	Ramose	tron	Place	bo		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% Cl	Year	w M-H. Random, 95% CI
Metsueda K 2008a	120	263	88	265	33.2%	1.37 [1.11, 1.70]	2008	18
Metsueda K 2008b	38	101	27	104	9.2%	1.45 [0.96, 2.18]	2008	8
Fulludo 8 2014	60	147	37	148	13.3%	1.63 [1.16, 2.29]	2014	4
Fukudo 8 2015	150	292	107	284	44.3%	1.36 [1.13, 1.64]	2015	6
Total (95% CI)		803		801	100.0%	1.41 [1.24, 1.50]		
Total events	366		259					
Heterogeneity: Tau <sup>c</sup> =	0.00; CNP	= 0.91,	of = 3 (P	= 0.820	( IF = Q%			0.1 0.2 0.5 1 2 5 10
Test for overall effect:	Z = 5.40 (F	< 0.00	001)					Favours placebo Favours remosetron

Dick Datio

Dick Datio

Dick Datio

#### C Improvement in abnormal bowel habits

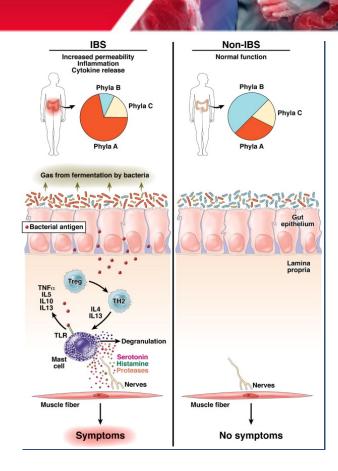
			INSK INGUU				
	Ramose	rtrom	Place	bo		Rink Ratio	
Study or Subgroup	Dvents	Total	<b>Events</b>	Total	Weight	H-H, Random, 95% Cl Year	M-H. Random, 95% CI
Matsueda K 2006a	115	263	63	266	29.9%	1.84 [1.42, 2.37] 2008	-
Matsueda K 2008s	44	101	31	104	14.3%	1.46 [1.01, 2.11] 2008	-
Fekudo 8 2014	62	147	23	148	10.4%	2.28 [1.47, 3.52] 2014	
Fukudo 8 2015	147	292	88	284	45.4%	1.62 [1.32, 2.00] 2016	-
Total (95% CI)		803		801	100.0%	1.72 [1.50, 1.98]	•
Total events	358		205				
Heterogeneity: Tau* = 0	0.00; Chiř	= 2.92,	df = 3 (P	= 0.40)	1" = 0%		0.1 0.2 0.5 1 2 5 10
Test for overall effect: 2	Z = 7.60 (F	< 0.00	001)				Favours placebo Favours remosetron

#### D Improvement in stool consistency

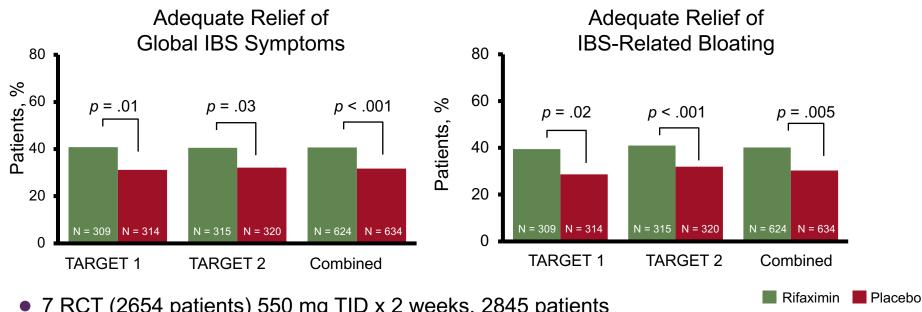
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	Remove	tron	Place	bo		Rink Ratio	
Study or Subgroup	Dyenta	Total	Events	Total	Weight	M-H. Random, 95% Cl Year	M-H, Random, 95% CI
Fukudo 8 2014	65	147	37	148	36.6%	1,77 [1,27, 2,47] 2014	-
Fulludo 8 2015	119	292	99	294	64,4%	1.68 [1.31, 2.15] 2015	-
Total (95% CI)		439		432	100.0%	1.71 [1.40, 2.08]	•
Total events	184		106				
Heterogeneity: Tau <sup>2</sup> =	0.00; ChiP	= 0.06.	df = 1 (P	= 0.80)	10 = 01%		D1 02 D5 1 2 5 10
Test for overall effect:	Z = 6.29 (F	< 0.00	001)				Favours placebo Favours remosetron

#### **Probiotics**

- 53 RCT in IBS (mostly IBS-D), 26 trials at low risk for bias, 5545 patients
- Probiotics superior to placebo
  - RR of IBS not improving 0.81 (CI: 0.74-0.88); NNT = 7
    - Combination probiotics: RR = 0.79 (0.68-0.91)
  - Symptoms most likely to improve: pain, bloating, flatulence
  - Significant heterogeneity and evidence of publication bias
  - Low rate of adverse events vs. placebo



### Rifaximin\* for IBS-D

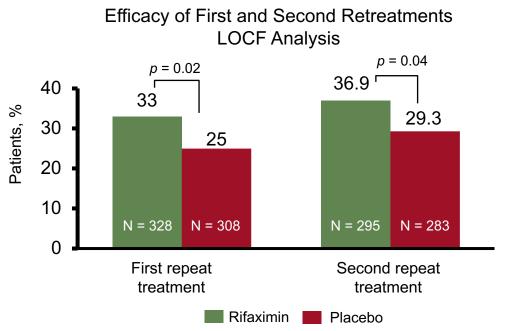


- 7 RCT (2654 patients) 550 mg TID x 2 weeks, 2845 patients
- Rifaximin superior to placebo: RR of IBS not improving 0.82 (CI: 0.72-0.95); NNT = 8
  - Adverse events equal to placebo; 2/3 responders need repeat treatment

Ford A, et al. Am J Gastroenterol. 2018. In press.; Pimentel M, et al. N Engl J Med. 2011;364:22-32.

<sup>\*</sup>Rifaximin is not FDA approved for IBS-D.

# Rifaximin\* for IBS-D: Effects of Repeat Treatment for Loss of Response



Urgency and bloating improved significantly with both repeat treatments

Abdominal pain and stool consistency improved significantly with first retreatment

LOCF, last observation carried forward. Responder defined as subjects responding to IBS-related Abdominal Pain and Stool Consistency for ≥2 of 4 weeks. Recurrence defined as a loss of response for ≥3 of 4 weeks. Lembo A, et al. *Gastroenterology* 2016;151(6):1113-1121.

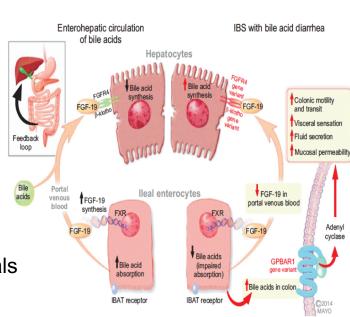
<sup>\*</sup>Rifaximin is not FDA approved for IBS-D.

# Bile Acid Sequestrants

- Bile acid malabsorption: prevalence estimates
   1% in the general population; 25-50% in
- Excess bile acids in colon

IBS-D

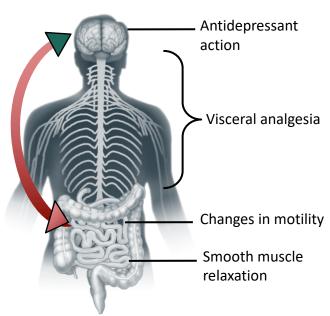
- increase visceral sensation and fluid secretion via intracellular cAMP, mucosal permeability and/or CI- secretion
- Value in diarrhea due to ileal disease/ resection.
  - Diabetic diarrhea, post-vagotomy diarrhea, postcholecystectomy diarrhea; small, uncontrolled trials of bile acid sequestrants suggest benefit in IBS; 4-16 gm/day
  - Availability of 7C4 serum test may identify likely responders; needs study



## **Antidepressants in IBS\***

- Meta-analysis of 16 RCTs demonstrated that TCAs and SSRIs reduce global IBS symptoms and abdominal pain in IBS patients<sup>1</sup>
- TCAs best studied antidepressants<sup>1</sup>
  - SSRIs likely to increase small bowel and colonic transit and may be preferred in IBS-C<sup>2-4</sup>
  - SNRIs not yet studied in large RCTs<sup>2</sup>

#### Potential Antidepressant Actions in IBS<sup>3</sup>



<sup>\*</sup>Not FDA approved for IBS

<sup>1.</sup> Ford AC, et al. Am J Gastroenterol. 2014;109:1350-1365; 2. Grover M, Drossman DA. Gastroenterol Clin N Am. 2011;40:183-206. 3. Chey WD, et al. Gut Liver. 2011;5:253-266. 4. Gorard DA, et al. Aliment Pharmacol Ther. 1994;8:159-166.

### Meet Ms. Tran

34 years old referred from primary care physician for hard stools with straining with defecation over past 3-4 years. Colonoscopy 3 years ago was normal.

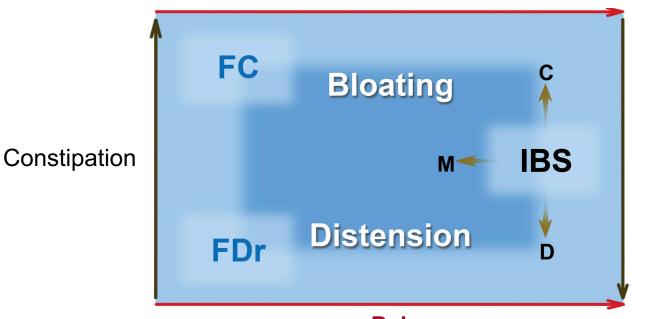




# Differentiating Functional Constipation from IBS-C







Diarrhea

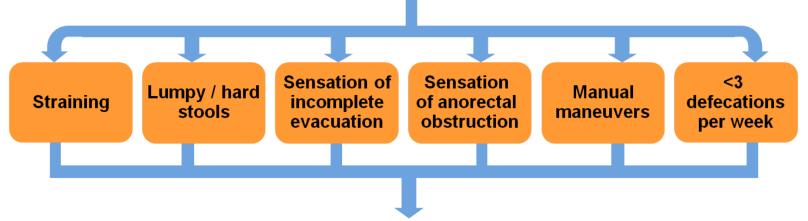
**Pain** 

FC = Functional constipation; FDr = Functional diarrhea Lacy BE, et al. *Gastroenterology*. 2016;150(6):1257-1492.

## Rome IV Criteria for Functional Constipation



Must include ≥2 of the following (>25% of defecations):



## Loose stools rarely present without laxative use insufficient criteria for IBS

\*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

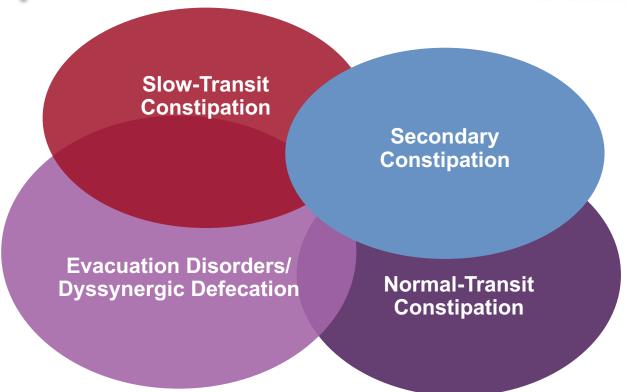
Mearin F, et al. *Gastroenterology*. 2016;150(6):1257-1492.

#### **Ms.Tran: Clinical Course**

- Although Ms. Tran reported that she had experimented with laxatives, in your examination, you determine that she was taking a low dose of a bulk laxative because she was hesitant to push the dosing limits.
- You decide to recommend an osmotic laxative and schedule an appointment for her to return to the office for follow-up in 4 weeks
- At her next visit, she reports little change

# Potential Etiologies of Constipation





Mertz H, et al. Am J Gastroenterol.1999;94:609-615.; Rao SS, et al. Am J Gastroenterol. 2005;100:1605-1615.

## Performance of DRE for Dyssynergia in Chronic Constipation

		95% CI	
Chronic Constipation by Rome III, N = 209	Estimated value	Lower limit	Upper limit
Sensitivity	0.75	0.68	0.81
Specificity	0.87	0.68	0.96
Positive Predictive Value	0.97	0.92	0.90
Negative Predictive Value	0.37		

Take Home Points: DRE reliably identifies patients with dyssynergic defecation and facilitates selection of patients for further physiologic testing

DRE = digital rectal examination

Tantiphlachiva K, et al. Clin Gastroenterol Hepatol 2010;8:955.

#### Other Tests for Chronic Constipation

- For patients with alarm features; lack of response to laxative therapies consider additional alternatives/overlap:
  - GI transit (Sitz markers or wireless pH-motility capsule testing): Identify slow colon transit
  - Balloon expulsion/Anorectal manometry/Defecography: Suspected pelvic floor dysfunction; dyssynergia; Hirschsprung's disease

Colon transit time Slow colonic transit with Normal transit with abnormal Slow colonic transit normal abnormal balloon balloon expulsion/anorectal balloon expulsion expulsion/anorectal manometry manometry Slow transit and defecation Defecation disorder Slow transit disorder

Lacy BE, Brunton SA. *MedGenMed* 2005;7(2):19. Cash BD, et al. *Rev Gastroenterol Disord* 2007;7:116–33.

Approaches to Symptom Management in IBS-C and CIC

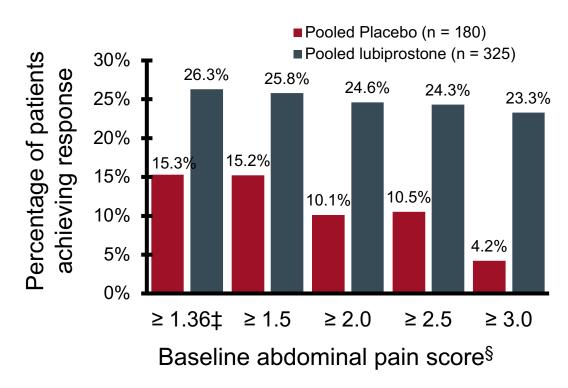


### Lubiprostone

- Non-absorbable gastrointestinal-targeted bicyclic functional fatty acid
- Selectively activates CIC-2 chloride channels, enhancing intestinal fluid secretion
  - Restoration of tight junction integrity (animal models)
- Dosing/indications:
  - 8 mcg BID: IBS-C in adult women
  - 24 mcg BID: CIC and OIC

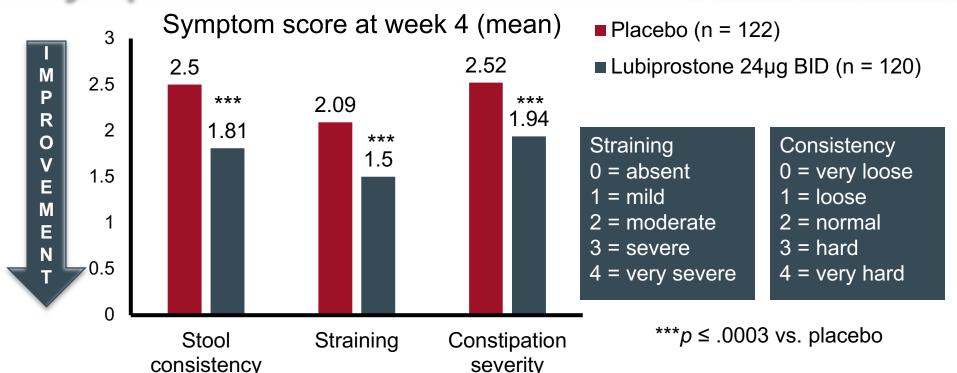
#### **Lubiprostone in IBS-C**

 Composite treatment response defined as ≥30% improvement in abdominal pain and ≥1 increase in spontaneous bowel movements per week vs. baseline for ≥6 of 12 treatment weeks by baseline abdominal pain score



<sup>\*</sup>p < .01. † p < .05. ‡ Equivalent to 3 on a scale of 0–10. § Scale from 0 (absent) to 4 (very severe). Chang L, Chey WD, et al. *Aliment Pharmacol Ther*. 2016;44(10):1114-1122.

# **Lubiprostone Improves Multiple Symptoms of CIC**



Johanson JF, et al, Am J Gastroenterol 2008;103:170-177.

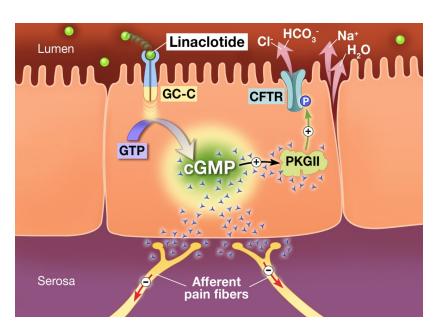
## **Lubiprostone Tolerability**

Lubiprostone Adverse Events Reported in ≥ 2% of Patients with IBS-C and CIC				
	IBS-C (8 mcg BD)	CIC (24 mcg QD, 24 mcg BID)	Placebo	
Gastrointestinal Nausea Diarrhea Abdominal pain Flatulence Abdominal distension Abdominal discomfort Vomiting	8% 7% 5% 3%	17%-29% 7%-12% 3%-8% 3%-6% 6% 2%-3% 3%	4%-3% 4%-<1% 5%-2% 2%	
<b>Respiratory</b> Dyspnea		2%-3%	1%	
Nervous System Disorders Headache Dizziness		3%-11% 3%	5%	

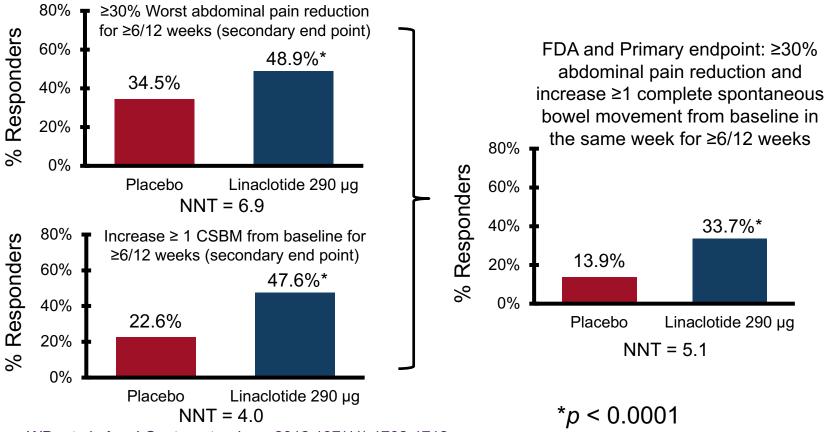
https://www.accessdata.fda.gov/drugsatfda\_docs/label/2012/021908s010lbl.pdf.

#### Linaclotide

- Guanylate cyclase-C (GC-C) agonist
- Non-absorbed peptide binds to GC-C receptor, increases cGMP
  - cGMP activates CFTR to secrete anions and fluid; may mediate visceral sensation
- Dosing/indications:
  - 290 mcg/day: IBS-C in adults
  - 145 mcg/day: CIC in adults



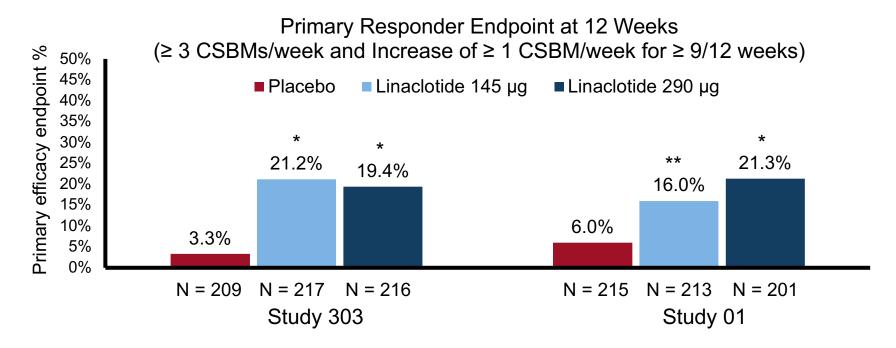
#### **Linaclotide in IBS-C**



Chey WD, et al. Am J Gastroenterology. 2012;107(11):1702-1712.

# Linaclotide Improves CSBM Frequency in CIC





\*p < .001 vs placebo; \*\* p ≤ .01 vs placebo CSBM = Complete spontaneous bowel movement Lembo AJ, et al. *N Engl J Med*. 2011;365:527-536.

### Linaclotide Tolerability



#### Linaclotide Adverse Events Reported in ≥ 2% of Patients with IBS-C and CIC

	IBS-C, 290 mcg	CIC, 145 mcg	Placebo
Gastrointestinal Diarrhea Abdominal pain Flatulence Abdominal Distension	20% 7% 4% 2%	16% 7% 6% 3%	3%-5% 5%-6% 2%-5% 1%-2%
Infections and Infestations Viral gastroenteritis Upper respiratory tract infection Sinusitis	3%	5% 3%	1% 4% 2%
Nervous System Disorders Headache	4%		3%

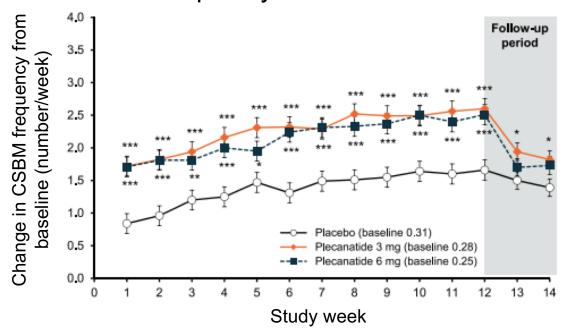
https://www.accessdata.fda.gov/drugsatfda\_docs/label/2012/202811s000lbl.pdf.

#### **Plecanatide**

- Uroguanylin analogue (GC-C agonist) with pH selective receptor activity
  - Maximum binding efficiency at lower pH; minimal binding at high pH
- Dosing/indications
  - 3 mg daily: IBS-C and CIC in adults

#### Plecanatide in CIC

Change in weekly complete spontaneous bowel movement frequency from baseline.



<sup>\*\*\*</sup>p < .001, \*\*p < .05 versus placebo. Error bars indicated standard error. Plecanatide 6 mg dose not FDA approved for CIC. DeMicco M, et al. *Therap Adv Gastroenterol.* 2017;10(11):837-851.

### **Plecanatide Tolerability**

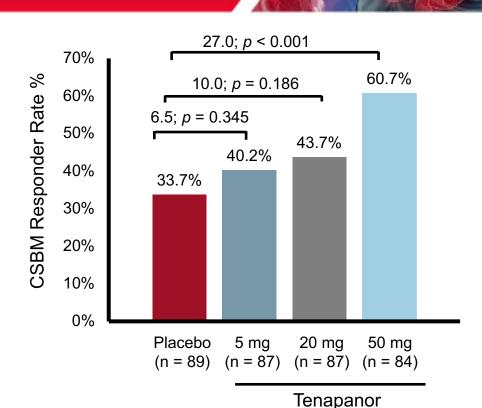


## Plecanatide Adverse Events Reported in ≥ 2% of Patients with IBS-C and CIC

	IBS-C, 3 mg	CIC 3 mg	Placebo
<b>Gastrointestinal</b> Diarrhea	4.3%	5%	1%

#### Tenapanor\* in CIC

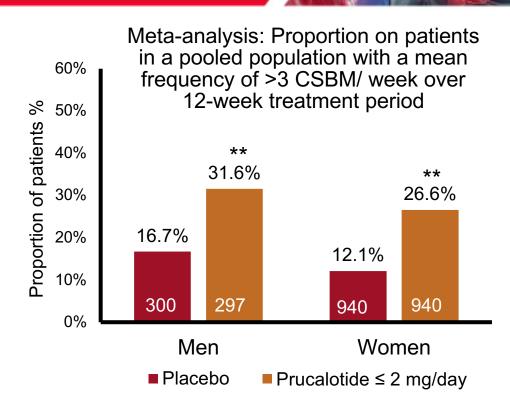
- NHE3 inhibitor
- 50 mg bid resulted in a significantly higher CSBM responder rate than placebo
  - Primary endpoint: increase ≥ 1 CSBM per week from baseline for ≥ 6/12 treatment weeks (ITT analysis)
- Most frequent adverse events were diarrhea, headache, urinary tract infection, abdominal pain



<sup>\*</sup>Not FDA approved for IBS Chey WD, et al. *Am J Gastroenterol.* 2017;112(5):763-774.

#### Prucalopride\* in CIC

- 5-HT4 receptor agonist<sup>1</sup>
  - Highly selective affinity; no known cardiac effects
- Approved in EU/Canada
- Majority of adverse events were mild: nausea, diarrhea, abdominal pain, headache

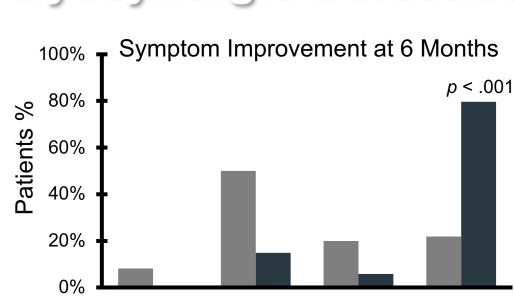


<sup>\*</sup>Not approved by the FDA for CIC

<sup>\*\*</sup>*p* < .001 vs. placebo

<sup>1.</sup> Wong BS, et al. Clin Exp Gastroenterol. 2010;3:49-56.; 2. Camilleri M, et al. Dig Dis Sci. 2016;61(8):2357-2372.

### Biofeedback Therapy for Dyssynergic Defecation



No

Change

■ PEG (n = 55) ■ Biofeedback (n = 54)

Fair

Major

PEG = Polyethylene glycol laxative Chiaroni G, et al *Gastroenterology.* 2006;130(3):657–664.

Worse

- Patients randomized to receive 5 weekly biofeedback sessions or PEG 14.6–29.2 g/day plus 5 weekly counselling sessions in preventing constipation
- Symptom improvement measured by patients' response to question, "How would you grade your symptom improvement?"
- Improvement in biofeedback group maintained at 12 and 24 months

## Role of Microbiome in Targeted Strategies

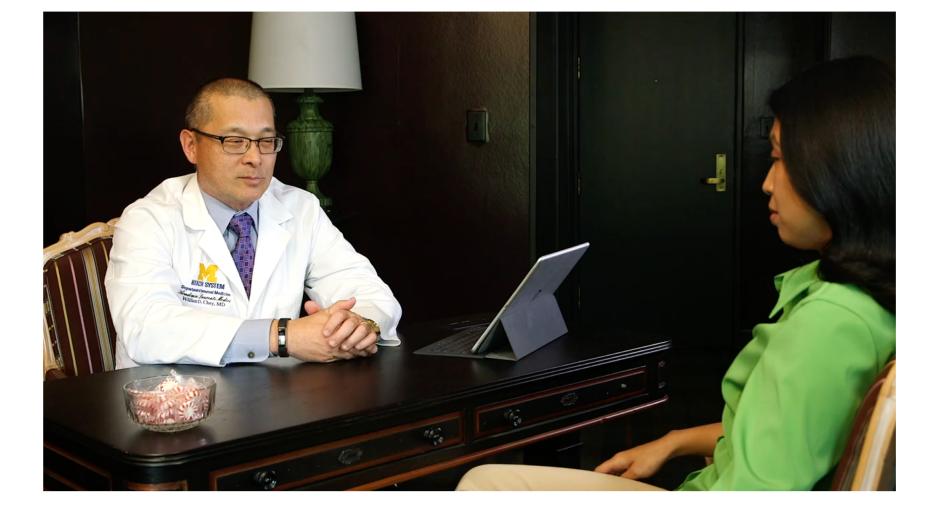




Team-based **Collaborative Care** Approaches to the Comprehensive Management of IBS and CIC

Ms. Tran Follow-up Visit





# Three Components of Shared Decision-Making

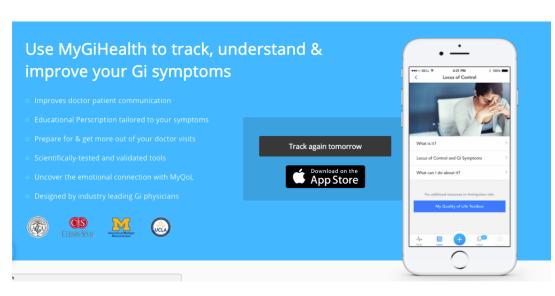
- Clear, accurate and unbiased medical evidence about reasonable alternatives—including non medical interventions—and the risks/benefits
- Clinician expertise in communicating and tailoring information for individual patients
- Incorporate patient values, goals, informed preferences, and concerns, which may include treatment burdens

# Interdisciplinary Treatment of IBS and CIC

- Team-based strategies
  - MDs: GI/PCP/APPs
    - Key consultants: Urogynecology, colorectal surgery
  - Nutrition: Registered dietician
  - Behavioral therapies: GI psychologist
  - Physical therapist
- Ongoing care when symptoms persist
- Communication
- Best practices

# Decision Aids and Digital Health

- Assessment tools
- Learning center/patient education
- Quality of life
- Doctor visit prep
- Find a specialist, treatment center



#### **SMART Goals**

Specific, Measurable, Attainable, Relevant, Timely



- Make a confident diagnosis of IBS or CIC through using patient interviews, application of Rome IV criteria, and appropriate diagnostic testing
- Once the diagnosis is made, initiate evidence-based treatment for relief of IBS and CIC to address persistent symptoms despite initial dietary and OTC approaches
- Promote interdisciplinary, collaborative care strategies that facilitate comprehensive management of IBS and CIC
- Engage patients in shared decision-making, considering their preferences and treatment goals

Questions & Answers



# 3 Things to Do to Claim ABIM MOC Credit



- 1. Actively participate in the meeting by responding to ARS and/or asking the faculty questions

  (It's ok if you miss answering a question or get them wrong, you can still claim MOC)
- 2. Complete the evaluation form found on your tables (For live stream participants, follow the credit claim link)
- 3. Be sure to fill in your **ABIM ID number** and **DOB** (MM/DD) on the evaluation, so we can submit your credit to ABIM.



#### **Quality Payment Program (QPP)**

How to Claim this Activity as a QPP Improvement Activity

- Actively participate by responding to ARS and/or asking the faculty questions
- Complete the 2 forms found on your table:
  - Evaluation form found on your table
  - The Quality Payment Program Improvement Activity form
- Over the next 90 days, actively work to incorporate improvements in your clinical practice from this presentation
- Complete the follow-up survey from CME Outfitters in approximately 3 months

CME Outfitters will send you confirmation of your participation to submit to CMS attesting to your completion of a QPP Improvement Activity.

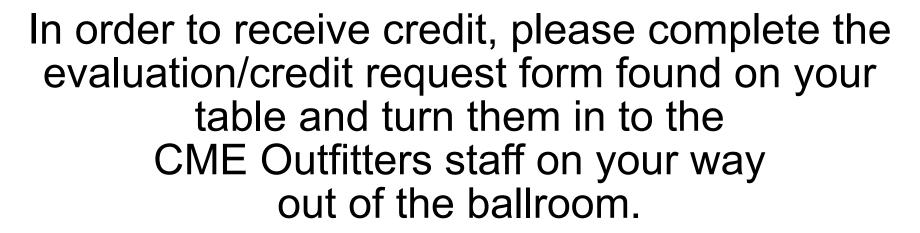
#### **Downloadable Resources**



Presentation slides, the course guide booklet, credit request/evaluation form, and the Quality Payment Program Improvement Activity form will be available for download at:

www.CMEOutfitters.com/IBSCICresources

### **Obtaining CME/CE Credit**



Don't forget: If claiming ABIM MOC credit, please write ABIM # on your form.

Thank you!

# **Come Back for Breakfast Tomorrow!**





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Combining the Latest Evidence
and Engaging Teaching Tools
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Sunday, June 3, 2018

Breakfast starts at 6:00 am ET Presentation starts at 6:30 am ET Marriott Marquis Liberty Ballroom

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## **Thank You!**

Don't forget to turn in your forms so you can collect your credit.

