A Free, 60-Minute Live and On-Demand Activity for Patients with UC

Premiere Date: Thursday, November 7, 2019

7:00 PM - 8:00 PM ET (live)

On the Web: http://bit.ly/TV-106

FACULTY: David T. Rubin, MD, FACG, AGAF, FACP, FASGE

Take advantage of our LIVE Q&A segment during this webcast!

During the webcast type a question in the box under the presentation

Email your question or comment: questions@cmeoutfitters.com

All other questions: Call CME Outfitters at 877.CME.PROS

This continuing education activity is provided by



INFORMATION FOR PARTICIPANTS

Statement of Need

We don't have to tell you that managing your ulcerative colitis (UC) is challenging. At times it seems like you need to be a physician yourself in order to understand the data and the decisions that are best for you. Practice guidelines are designed for gastroenterologists and their care teams; however, knowledge about how the guidelines are developed and how they apply to the individual are important for understanding your doctor's decisions in managing your UC.

Dr. Rubin has you covered! In this live and on-demand webcast, Dr. Rubin will share his insights and take your LIVE questions to help you manage your disease and take back control of your UC.

What you will learn:

At the end of this activity, participants should be able to:

- Recognize the importance of practice guidelines and how they apply to UC.
- · Establish long-term treatment goals to heal the inflamed bowels instead of masking the symptoms.
- · Identify key markers of inflammation in inflammatory bowel disease and how they are used in practice.
- Evaluate the risk of colorectal cancer and colostomy in UC.
- Engage with your UC doctor to discuss your disease and strategies to establish and maintain clinical remission.

Target Audience

Individuals with ulcerative colitis

Financial Support

Supported by an educational grant from Takeda Pharmaceuticals U.S.A., Inc.

FACULTY BIO & DISCLOSURES

David T. Rubin, MD, FACG, AGAF, FACP, FASGE

Dr. Rubin is Chief of the Section of Gastroenterology, Hepatology & Nutrition and the Co-Director of the Digestive Diseases Center at The University of Chicago Medicine. Dr. Rubin earned a medical degree with honors at The University of Chicago Pritzker School of Medicine. He completed his residency in internal medicine and fellowships in gastroenterology and clinical medical ethics at the University of Chicago, where he served as Chief Resident and Chief Fellow. Prior to his current appointments, Dr. Rubin served for 11 years as Director of the Gastroenterology, Hepatology and Nutrition fellowship program. He also currently serves as an associate faculty member at the MacLean Center for Clinical Medical Ethics and as an associate investigator at the University of Chicago Comprehensive Cancer Center.

Dr. Rubin is a Fellow of the American Gastroenterological Association (AGA), the American College of Gastroenterology (ACG), the American Society for Gastrointestinal Endoscopy (ASGE), and the American College of Physicians (ACP) as well as an active national member of the Crohn's & Colitis Foundation (CCF) and is on the Board of Trustees for the ACG. Among numerous awards and honors, Dr. Rubin was chosen by his peers as a member of Best Doctors (recognized for superior clinical ability) and America's Top Physicians (gastroenterology). Additionally, he twice received the ACG's Governor's Award of Excellence in Clinical Research (2003 and 2013), the Cancer Research Foundation Young Investigator's Award (2004), and the UC Postgraduate Teaching Award in recognition of significant contributions for fellowship education (2006). In 2012, he received the CCF Rosenthal Award, a national leadership award bestowed upon a volunteer who has contributed in an indisputable way to the quality of life of patients and families. He is currently the Chair-Elect of the National Scientific Advisory Committee of the CCF. He is an Associate Editor of the journal Gastroenterology and Co-Editor of the ACG On-Line Educational Universe.

Dr. Rubin is the editor of a best-selling book on inflammatory bowel disease (IBD), now in its 3rd edition, and an author or coauthor of many peer-reviewed articles on treatment and management of IBD as well as cancer in IBD and novel paradigms. He is also first author of the in-progress ACG Guidelines for ulcerative colitis. His current research is in the area of progressive complications from uncontrolled inflammation, the doctor-patient relationship in IBD, and a variety of collaborative studies related to the microbiome and intestinal disease. He is also a featured media contact for issues related to IBD (satellite radio, television, and print media) and maintains a popular twitter feed @IBDMD (> 6,000 followers). His principal research interests include novel IBD therapies and outcomes, colon cancer prevention, and clinical medical ethics.

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Dr. Rubin reports that he receives grants from AbbVie Inc.; Genentech, Inc./Roche; Janssen Pharmaceuticals, Inc.; Prometheus Laboratories Inc.; Shire; and Takeda Pharmaceuticals U.S.A., Inc. He is a consultant for AbbVie Inc.; AbGenomics; Allergan; Arena Pharmaceuticals, Inc.; Biomica; Bristol-Myers Squibb Company; Dizal Pharmaceutical; Eli Lilly and Company; Ferring Pharmaceuticals Inc.; Genentech, Inc./Roche; Janssen Pharmaceuticals, Inc.; Medtronic; Merck & Co., Inc.; Napo Pharmaceuticals, Inc.; Pfizer Inc.; Shire; Takeda Pharmaceuticals U.S.A., Inc.; and TARGET PharmaSolutions, Inc. He receives other financial or material support as a member of the Board of Trustees for the American College of Gastroenterology; as Co-Founder, CFO of Cornerstones Health, Inc. (non-profit); and as Co-Founder of GoDuRn, LLC.

Olga Askinazi, PhD (planning committee) has no disclosures to report.

Jan Perez (planning committee) has no disclosures to report.

Sharon Tordoff (planning committee) has no disclosures to report.

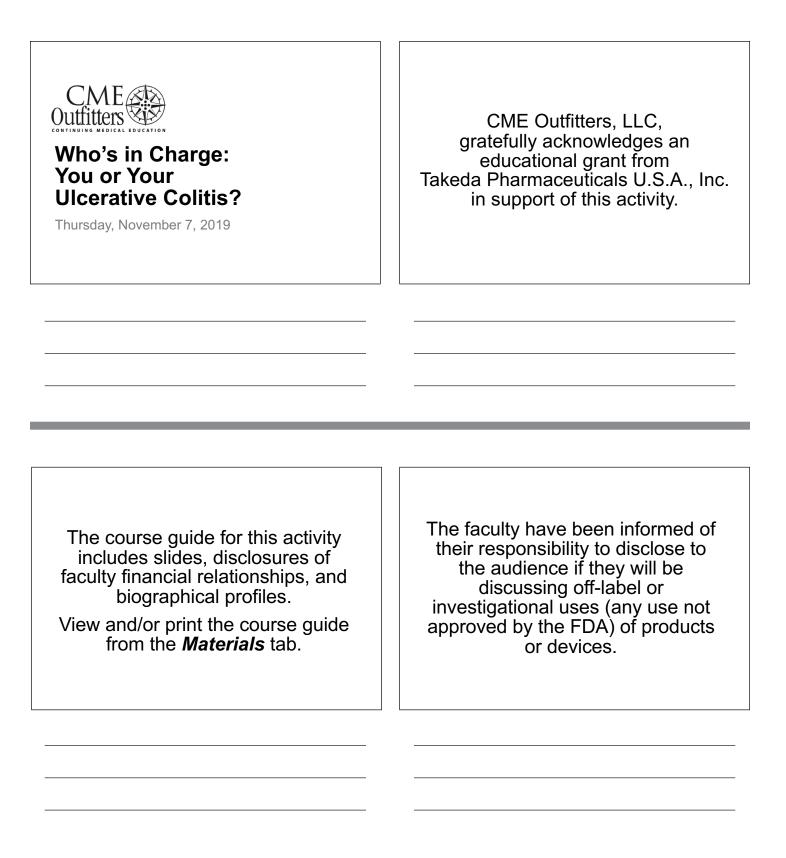
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Activity Slides

The slides that are presented in this activity will be available to download and print out at the CME Outfitters website: **www.cmeoutfitters.com**. Activity slides may also be obtained via fax or email by calling **877.CME.PROS**.





David T. Rubin, MD, FACG, AGAF, FACP, FASGE

Joseph B. Kirsner Professor of Medicine Section Chief, Gastroenterology, Hepatology and Nutrition Co-Director, Digestive Diseases Center University of Chicago Medicine Chicago, IL

David T. Rubin, MD, FACG, AGAF, FACP, FASGE

Disclosures

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New Guidelines in Ulcerative Colitis:

Why Should I Care?

What Is Ulcerative Colitis?

- Chronic inflammation of large intestine
- Cause unknown
- Relapsing + remitting
- Treatable! New treatments and treatment goals



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Why Are Clinical Practice Guidelines What Do Patients with Inflammatory Bowel Disease (IBD) Say? Important? Are you aware of clinical • Guidelines are written by experts in the field • They contain recommendations for clinicians about patient care A lot of IBD patients are very confused and there's a lot of misinformation on guidelines for • These recommendations are based on the most recent clinical research and are usually updated every few years the care of Clinicians should refer to the guidelines to ensure that their patients with the Internet. treatment decisions are in line with the current standards **İBD?** Remember! You have a right to confirm that your doctor is aware of and considering guideline recommendations Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413; Ko CW, et al. Gastroenterology. 2019;156(3):748-764. Levels of Evidence **Limitations of Guidelines** Can become out-of-date quickly Opinion of experts without research Increasing Don't apply to ALL patients quality Cases reported Sometimes ignored by payers strength of evidence Randomized trials that are blinded Multiple randomized trials

U.S. Ulcerative Colitis (UC) Guidelines In 2019, two U.S. societies updated their UC guidelines: American College of Gastroenterology (for mild, moderate, and severe UC) American Gastroenterological Association (for mild and

ACG Clinical Guideline: Ulcerative Colitis in Adults

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moderate UC)

CLINICAL PRACTICE GUIDELINES

AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis

Cynthia W. Ko. Skadnen Sngal, "Joseph D, Ferestein," Corinna Falck-Yiter," And Repimod K. Cross, "on behalf of the American Gastroenter Association Institute Cinicial Guidelines Committee

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Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413; Ko CW, et al. Gastroenterology. 2019;156(3):748-764

| What's | New | in | the | 2019 | UC |
|---------|------|----|-----|------|----|
| Guideli | nes? | | | | |

- Shift from reactive management of flares to proactive monitoring and prevention of flares
- Treatment choice based on both <u>inflammatory activity</u> and <u>prognosis</u>
- Healing of the bowel is a target of treatment
- New therapies: budesonide, golimumab, vedolizumab, tofacitinib, and ustekinumab
- Infection with bacterium *C. difficile* should be ruled out in all patients
- Stool test (calprotectin) instead of colonoscopy

Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413; Ko CW, et al. Gastroenterology. 2019;156(3):748-764.

Goals of Management of UC

- Clarify disease activity and severity
 - How much bowel is involved?
 - What is the risk for surgery?
- Induction of remission (fast!)
 - Clinical remission
 - Healing the bowel
- Prevention of relapse (maintenance)
 No steroids
- Prevention of disease + drug related complications (infections, hospitalization, surgery, cancer)

What Do Patients with IBD Say?

What would remission look like to you?

Remission looks like being able to live my life fully without suffering from IBD, without putting things aside. I have activities that I can't participate in just from the symptoms and the pain from IBD. I have had to sit out from things. I've had to leave work early because of my symptoms. So remission to me is not having to do things like that where my life is impacted in a negative way.



The Different Levels of UC Activity

American College of Gastroenterology Index

| | Remission | Mild | Moderate-Severe | Fulminant |
|---------------------------|---------------|------------------|-----------------|----------------------|
| Stools (#/day) | Formed stools | < 4 | > 6 | > 10 |
| Blood in stools | None | Intermittent | Frequent | Continuous |
| Urgency | None | Mild, occasional | Often | Continuous |
| Hemoglobin | Normal | Normal | < 75% of normal | Transfusion required |
| ESR | < 30 | < 30 | > 30 | > 30 |
| CRP (mg/L) | Normal | Elevated | Elevated | Elevated |
| FCP (μg/g) | < 150-200 | > 150-200 | > 150-200 | > 150-200 |
| Endoscopy (Mayo subscore) | 0-1 | 1 | 2-3 | 3 |
| UCEIS | 0-1 | 2-4 | 5-8 | 7-8 |

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; FCP = fecal calprotectin; UCEIS = UC Endoscopic Index of Severity. Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413.

Prognosis (Severity) of UC

Being diagnosed younger than age 40 Extensive colitis (involvement of more of the large intestine) Severe inflammation seen on scope Needing hospitalization for the colitis Elevated CRP (blood test of inflammation)

Low serum albumin (blood test of nutrition and health)

Rubin DT, et al. Am J Gastroenterol, 2019:114(3):384-413.

Questions for Dr. Rubin?

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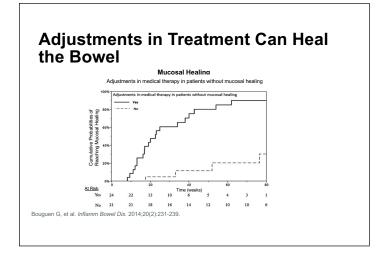
Tweet Questions: #TakeChargeofUC

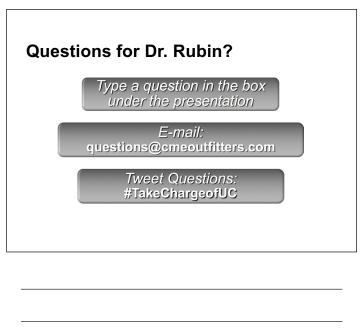


Controlling Symptoms and Inflammation:

Why Do Both Matter?

What Is Clinical Remission of UC? What Do Patients with IBD Say? Has your clinician discussed Formed stool with you the difference No, I have never actually had No blood between symptom control that compared by a doctor. and healing of the bowel? He's actually never discussed No urgency healing. It's pretty much Sleeping through the night without bowel movement always the discussion on how to keep it at bay; how to keep Able to pass gas without fear of leaking it under control. Clinical Remission = Improved Quality of Life Why Is Clinical Remission Not Enough? Clinical remission is • Up to 50% of patients in clinical remission have persistent inflammation **NECESSARY** • Inflammation that persists increase risk of relapse UC causes ulcerations in the lining of the bowel called the mucosa but • Mucosal healing means healing of the ulcers in the bowel lining • Studies show that mucosal healing lowers the risk for relapse, **NOT SUFFICIENT** colectomy, and colon cancer for control of UC 4 We suggest treating patients with UC to achieve mucosal healing defined as resolution of inflammatory changes (Mayo endoscopic subscore 0 or 1)) to increase the likelihood of sustained steroid-free remission and prevent hospitalizations and surgery (conditional recommendation, low quality of evidence) Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413; Magro F, et al. J Crohns Colitis. 2017;11(6):649-670







Treatments for UC

Available Therapies for UC

- Aminosalicylates (5-ASA)
- Biologics and small-molecule therapies
 - Anti-TNF therapies: Remicade® (infliximab), Humira® (adalimumab), Simponi® (golimumab)
 - Anti-integrin therapy: Entyvio® (vedolizumab)
 - JAK inhibitor: Xeljanz® (tofacitinib)
 - Anti-interleukin 12/23 therapy: Stelara® (ustekinumab)
- Surgery

Rutgeerts P, et al. N Engl J Med. 2005;353(23):2462-2476. Sandborn WJ, et al. Gastroenterology. 2012;142(2):257-265. Sandborn WJ, et al. Gastroenterology. 2014;14(1):95-109. Feágan BG, et al. N Engl J Med. 2013;369(8):699-710. Sandborn WJ, et al. N Engl J Med. 2017;376:1723-1736. Sands BE, et al. N Engl J Med. 2019;34(1):1723-1736. Sands Be, et al. N Engl J Med. 2019;34(1):1723-1736. Sands Be, et al.

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Historical Treatment Strategies for IBD: Symptom-Based, Short-Term Goals Disease activity at presentation? Overlosporine/ Tofaciting Anti-The Tofaciting Anti-The Tofaciting Anti-The Ustekinumab Ustekinumab Ustekinumab Ustekinumab Ustekinumab Induction Immediately Immediate

Why Immune Therapy for UC?

- UC is a state of increased and apparently uncontrolled immune activity of the colon
- The goal of immune therapy is NOT to immune suppress a patient
- The goal of immune therapy is to modify or turn down the active immune system long enough for the body to "reset" itself and to heal

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- 1. Start with symptom resolution
- 2. Get to a healed bowel and normal labs
 - Objective evidence of disease control
- 3. Developing customized treatment plans
 - Do you know where your disease is located?
 - What is your individual prognosis?
 - Does your IBD flare seasonally?
 - What is your plan at the earliest sign of relapse?

| General | Principles | of | Treatme | nts : | for | IBD |
|---------|-------------------|----|---------|-------|-----|-----|
| (cont.) | • | | | | | |

- 4. Choose induction therapy based on activity (how sick now) and severity (prognosis)
 - Use non-immune therapies first for milder disease
 - Use organ selective therapies before systemic therapies when possible
 - Optimize first therapy
- Don't use steroids too long!
- 5. Choose maintenance therapy based on severity of disease and induction therapy
- 6. Monitor for stable disease control over time!

General Principles of Treatments for IBD (cont.)

7. Prevention is key to good health!

- Vaccination for preventable illnesses
- Cancer prevention
 - · Colon cancer prevention with scheduled colonoscopies
 - · Skin cancer monitoring with annual dermatology visits
 - · Annual Pap smears
- Regular visits to your IBD doctor

Mild or Moderate UC: ACG and AGA Recommendations 2019

| Condition | ACG and AGA Recommendations | | | |
|---|--|----------------------|--|--|
| Extensive mild-moderate UC | 5-ASA therapy | | | |
| Left-sided mild-moderate UC | Rectal 5-ASA (enema or suppository) + oral 5-ASA | | | |
| Mild-moderate UC w/suboptimal response to 5-ASA | Budesonide MMX Oral prednisone budesonide MMX | | | |
| Mild-moderate proctitis | Rectal 5-ASA (e | nema or suppository) | | |
| Opinion on systemic steroids | Recommendation against systemic steroids | Not addressed | | |

Rubin DT, et al. Am J Gastroenterol. 2019;114(3):384-413. Ko CW, et al. Gastroenterology. 2019;156(3):748-764

Induction of Remission: Moderate or Severe UC

- $\bullet~$ UC failing to respond to 5-ASA therapy \to oral systemic corticosteroids $^{1\text{-}4}$
- Moderate UC → oral budesonide MMX¹
- Moderate-severe UC of any extent → oral systemic corticosteroids^{1,3,4}
- Biological therapies:
 - Anti-TNF therapy using adalimumab, golimumab or infliximab¹⁻⁵
 - Vedolizumab^{1,4}
 - Ustekinumab
- Infliximab in combination with a thiopurine1-4
- Tofacitinib¹
- ullet If failed anti-TNF o vedolizumab¹⁻⁴ or tofacitinib¹ or ustekinumab

Rubin DT, et al. Am J Gastroenterol. 2019;114:384-413. 2. Hardbord M, et al. J Crohns Colitis. 2017;11(7):769-784
 Bressler B, et al. Gastroenterology. 2015;148(5):1035-1058.e3. 4. Coi CH, et al. Intest Res. 2017;15(1):7-37.

Maintenance of Remission: Moderate or Severe UC

- Recommend against systemic steroids^{1,3,5}
- Thiopurines¹⁻⁵
- Recommend against using methotrexate 1-3
- Biological therapies:
 - Anti-TNF therapy using adalimumab, golimumab or infliximab¹⁻⁵
 - Vedolizumab^{1,4}
 - Ustekinumab
- Tofacitinib¹

Rubin DT, et al. Am J Gastroenterol. 2019;114:384-413. 2. Hardbord M, et al. J Crohns Colitis. 2017;11(7):769-784.
 Bressler B, et al. Gastroenterology. 2015;148(5):1035-1058.e3. 4. Col CH, et al. Intest Res. 2017;15(1):7-37.
 Wei CS, et al. Intest Res. 2017;15(2):266-257.

Phew. I'm in Remission, Now What?

- Monitoring
- Stool tests for calprotectin and lactoferrin are efficient ways to monitor remission
- Long-term, sustained healing is maintained through regular monitoring and testing

| `````` | Remember! |
|------------------|---|
| -()- | Remember! If you stop your medications, you risk returning to inflammation and IBD symptoms |
| ₩ | IBD symptoms |

Rubin DT, et al. Am. J. Gastroenterol. 2019:114(3):384-413:

What Do Patients with IBD Say?

Has your clinician discussed with you markers of disease activity, why they are important, and how often they need to be evaluated?

When I am having any type of symptoms, my doctor will order labs and I know that she is looking for specific markers. I never have discussions with her about what the markers are specifically that she is looking for. I wish that I did have a better idea of what it is in the labs that she is trying to net



Why Do Therapies Stop Working?

- •Reasons for loss of response:
 - Body finds a new pathway of inflammation
 - Infection on top of the UC
 - For biological therapies, your body can develop immunity to the therapy (like a reaction to a vaccination)
 - You stop taking the medicine

What to Do if Your Medicine Stops Working

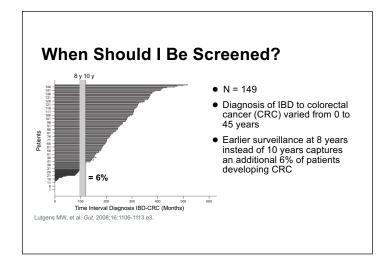
- Confirm inflammation
- Rule out infection
- Check on the drug level
- Consider dose changes
- Consider short-term fix (steroids?...)
- Cycle to another therapy in the same class
- Swap to a new mechanism

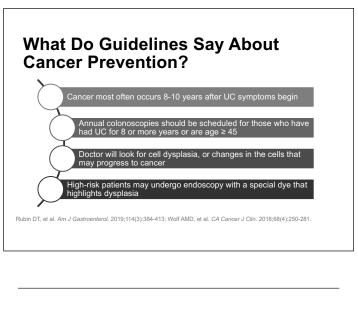
Questions for Dr. Rubin? Type a question in the box under the presentation E-mail: questions@cmeoutfitters.com Tweet Questions: #TakeChargeofUC Cancer in UC: Am I at Risk?

What Do Patients with IBD Say? How worried are you about colorectal cancer? Very concerned and not sure of my risk A little worried, but I believe my risk is low 1 think about it all the time Not at all

Individuals with UC are at increased risk for developing colorectal cancer However, only 5% of people with severe UC develop cancer Your doctor should schedule regular cancer screenings Did you know? Colorectal cancer is one of the most preventable and treatable cancers when identified early

Am I at Risk for Colorectal Cancer?



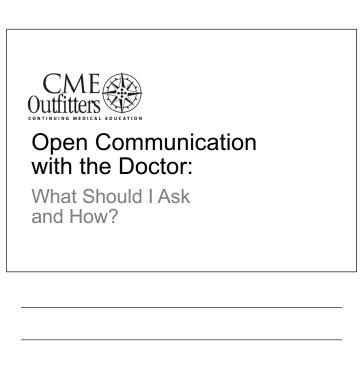


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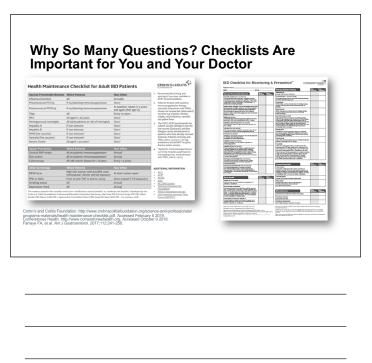
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Tweet Questions: #TakeChargeofUC



What Is Shared Decision-Making? BOTTOM LINE: You, as a patient, have a right to participate in decisions about your treatment. Do not hesitate to ask questions, request clarifications, and do your own research! explains benefits and risks of each atient asks



Tips for Communicating with Your Doctor

- Prepare for your appointments ahead of time by keeping track of your symptoms
- Make a list of your questions from the most important to the least important; start the appointment by bringing up your list; go through your list and make notes or bring a voice recorder
- Consider bringing a close family member who can ask questions from their perspective
- Set treatment goals with your doctor and ensure you're checking them at each appointment

What Questions Should I Ask?

- How active is my disease?
- How much of my bowel is involved?
- What is my risk of needing surgery?
- What is the goal of my treatment?
- Am I on target to achieve mucosal healing?
- How do my medications work?
- What are the side effects of these medications?
- What will my insurance cover?
- How long might it take before I see an improvement?
- How is my disease activity being monitored?
- Am I at risk for cancer? How is it being monitored?

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