THE GI PERSPECTIVE

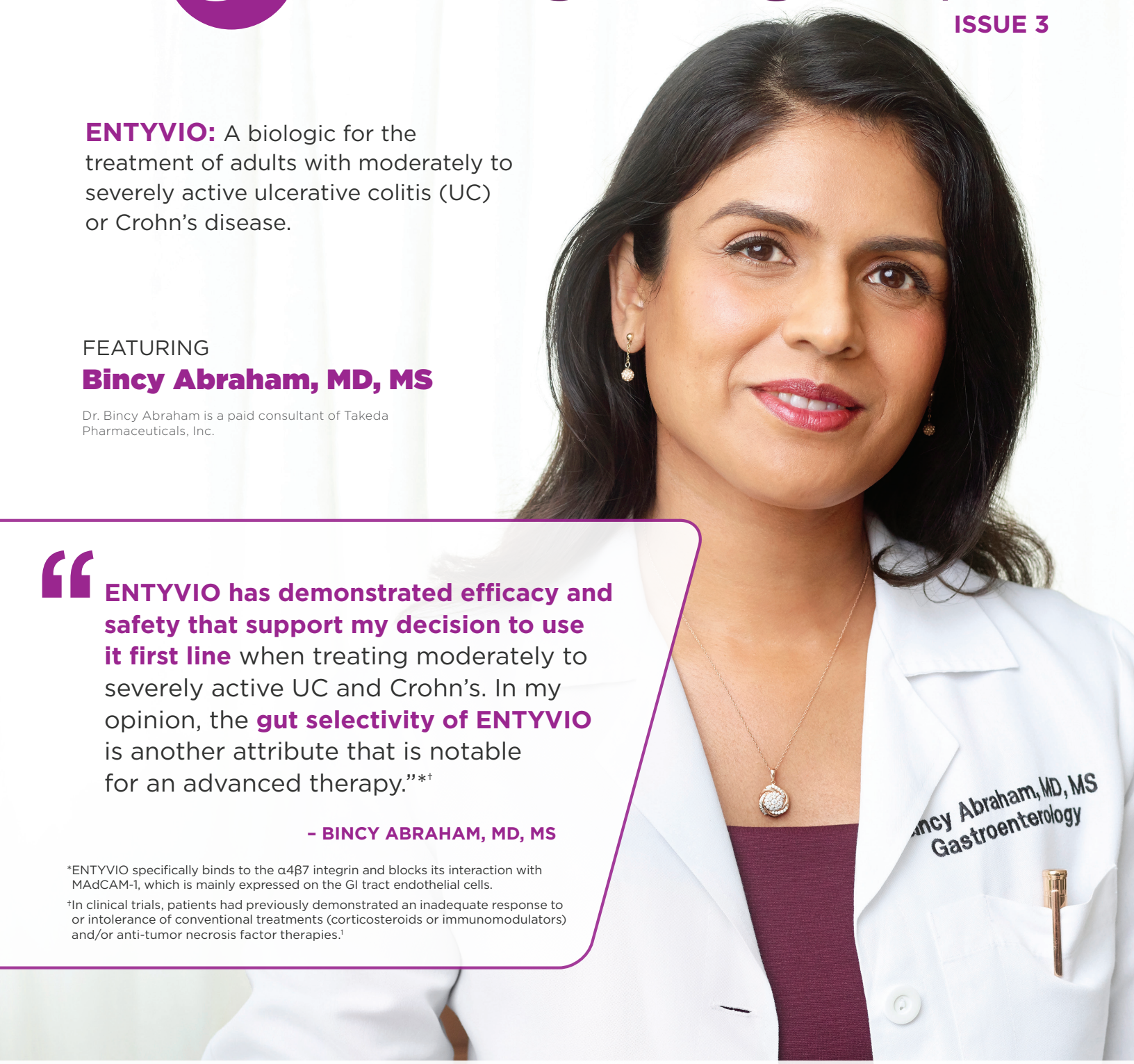
ISSUE 3

ENTYVIO: A biologic for the treatment of adults with moderately to severely active ulcerative colitis (UC) or Crohn's disease.

FEATURING

Bincy Abraham, MD, MS

Dr. Bincy Abraham is a paid consultant of Takeda Pharmaceuticals, Inc.



> **ENTYVIO has demonstrated efficacy and safety that support my decision to use it first line** when treating moderately to severely active UC and Crohn's. In my opinion, the **gut selectivity of ENTYVIO** is another attribute that is notable for an advanced therapy."*†
>
> **– BINCY ABRAHAM, MD, MS**

*ENTYVIO specifically binds to the α4β7 integrin and blocks its interaction with MAdCAM-1, which is mainly expressed on the GI tract endothelial cells.

†In clinical trials, patients had previously demonstrated an inadequate response to or intolerance of conventional treatments (corticosteroids or immunomodulators) and/or anti-tumor necrosis factor therapies.[1]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

Please click for additional Important Safety Information.

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> **Today we have many advanced therapies* to treat UC and Crohn's, but that makes it harder** to decide which to use first."

Scan to access the full interview

Dr. Bincy Abraham, MD, MS

- Associate Professor of Clinical Medicine in the Academic Division of Gastroenterology and Hepatology at Houston Methodist, Weill Cornell, Houston, Texas
- Chair of the Southern Texas Chapter of the Crohn's & Colitis Foundation Medical Advisory Committee
- Internationally recognized clinical trialist and expert in the treatment of inflammatory bowel disease

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EXAMINING CHALLENGES WHEN STARTING ADVANCED THERAPY IN UC AND CROHN'S AND HOW ENTYVIO MAY HELP with Dr. Bincy Abraham

What are your considerations when deciding on a first-line advanced therapy for moderately to severely active UC or Crohn's?

With so many options, it's complex to decide where to start. Key factors I consider include disease severity and location, presence of complications, and inflammatory or other comorbidities. Patient preferences like administration, lifestyle, and safety are important because I want a medication that the patients will stick with.

What information do you rely on when selecting a first-line advanced therapy in UC or Crohn's?

Clinical trial data, head-to-head study data, and long-term data from pivotal studies, registries, and real-world evidence. These data help me inform patients on risks versus benefits of treatment. There are treatment guidelines for UC and Crohn's from our national societies; however, we personalize our therapy to our patients.

How do you sequence ENTYVIO in your treatment paradigm for UC and Crohn's?

ENTYVIO is an appropriate first-line advanced therapy option for my patients with moderately to severely active UC or Crohn's because of its safety and efficacy data, especially in either TNF-naïve or failure patients.

What attributes of ENTYVIO do you find most attractive for the treatment of moderately to severely active UC or Crohn's?

The most informative data for ENTYVIO were remission rates at 1 year and long-term safety in both UC and Crohn's. The responses observed in the VARSITY trial in moderate-to-severe UC were also noteworthy. Lastly, ENTYVIO is a gut-selective therapy, which my patients like to learn about when I offer it as a treatment option.

*Advanced therapies are used after failure of conventional therapies.
UC=ulcerative colitis.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Infusion-Related and Hypersensitivity Reactions:** Infusion-related reactions and hypersensitivity reactions including anaphylaxis, dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have been reported. These reactions may occur with the first or subsequent infusions and may vary in their time of onset from during infusion or up to several hours post-infusion. If anaphylaxis or other serious infusion-related or hypersensitivity reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.

Please click for additional Important Safety Information.

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For adults with moderately to severely active ulcerative colitis or Crohn's disease.

PUT ENTYVIO FIRST FOR LONG-TERM RELIEF AND REMISSION*

*In clinical trials, patients had previously demonstrated an inadequate response to or intolerance of conventional treatments (corticosteroids or immunomodulators) and/or anti-tumor necrosis factor therapies.[1]

Treat Early

The moment your adult patients with moderate to severe Crohn's or UC are not well-controlled with conventional therapies, seek long-term relief and remission. Patients achieved remission at Week 52 vs placebo.[1]

Individual results may vary.

Treat Directly

ENTYVIO helps address inflammation where it occurs—in the gut.[1] ENTYVIO specifically binds to the α4β7 integrin and blocks its interaction with MAdCAM-1, which is mainly expressed on the GI tract endothelial cells.[1-7]

A WELL-STUDIED SAFETY PROFILE WITH UP TO

7 Years of Consistent Safety Results

Clinical trials evaluated safety in more than 3300 adults (UC, Crohn's, and healthy volunteers).[1] A separate open-label study of up to 7 years demonstrated **consistent results across safety parameters.[1,8,9†]**

†In a single-arm, open-label extension study, 2243 patients received ENTYVIO with a median exposure of 1072 days (range 1 to 3412 days).[8,9]

How would you describe the MOA of ENTYVIO to a colleague?

In inflammatory bowel disease, specific memory T lymphocytes use α4β7 integrins to squeeze through endothelial cells and get into the gut. ENTYVIO blocks these integrins, preventing these lymphocytes from getting into the gut and causing inflammation."

Scan to access MOA video

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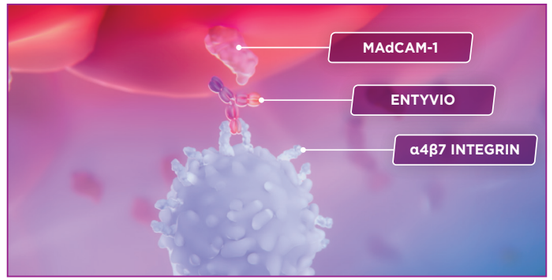
GI=gastrointestinal; MAdCAM-1=mucosal addressin cell adhesion molecule-1; MOA=mechanism of action; UC=ulcerative colitis.

MECHANISM OF ACTION

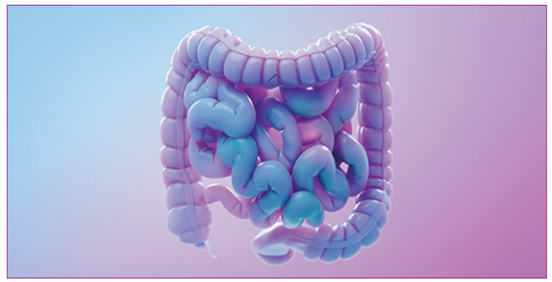
ENTYVIO is a gut-selective biologic[1-7]



Bind and Block

ENTYVIO is a monoclonal **antibody that was made to specifically bind to α4β7** and block its interaction with MAdCAM-1.[1]

As a result, certain **lymphocytes are blocked** from entering the GI tract.[4,5]



Reduce

ENTYVIO selectively reduces gut inflammation in ulcerative colitis and Crohn's disease.[1,4,5]

What do patients typically want to know about how ENTYVIO works?

Patients love to hear that ENTYVIO acts specifically in the GI tract to help control damaging inflammation. I find describing how the therapy works helps engage patients in their treatment."

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Infections:** Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections. Consider screening for tuberculosis (TB) according to the local practice.

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Scan for more GEMINI I data

ENTYVIO FOR UC

Rapid Response and Long-Term Remission

GEMINI I (UC Trials I and II) Study Design[1]

Two randomized, double-blind, placebo-controlled studies enrolled adult patients with moderately to severely active UC who had failed at least 1 conventional therapy, including corticosteroids or immunomodulators, and/or ≥1 anti-TNFα therapy. In UC Trial I, patients were randomized (3:2) to receive ENTYVIO 300 mg or placebo by intravenous infusion at Weeks 0 and 2. In UC Trial II, patients receiving ENTYVIO who demonstrated clinical response at Week 6 (from UC Trial I or an open-label cohort) were randomized (1:1:1) to receive either ENTYVIO 300 mg every 8 weeks, ENTYVIO 300 mg every 4 weeks, or placebo every 4 weeks. The ENTYVIO Q4W dosing regimen did not demonstrate additional clinical benefit over the Q8W dosing regimen. The Q4W dosing regimen is not the recommended dosing regimen.

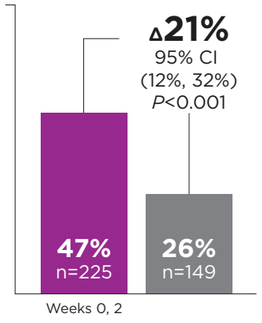
GEMINI I Primary End Points[1]

Overall population compared with placebo

ENTYVIO IV · Placebo

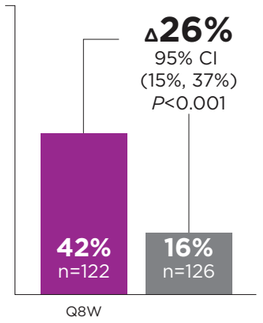
WEEK 6

Clinical response[1]*



WEEK 52

Clinical remission[1]†



> **What do you find most pertinent about the GEMINI I results?**
>
> The GEMINI I results demonstrated that ENTYVIO worked quickly. At Week 6, a significant number of patients achieved clinical response. Long-term remission and short- and long-term safety data were consistent with my experience in clinical practice."

*Clinical response=reduction in complete Mayo Score of ≥3 points and ≥30% from baseline with an accompanying decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of ≤1 point.
†Clinical remission=complete Mayo Score of ≤2 points and no individual subscore >1 point.
CD=Crohn's disease; CDAI=Crohn's Disease Activity Index; CI=confidence interval; NS=not significant; Q4W=every 4 weeks; Q8W=every 8 weeks; TNFα=tumor necrosis factor alpha; UC=ulcerative colitis.

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Scan for more GEMINI II data

ENTYVIO FOR CROHN'S

Long-Term Remission

GEMINI II (CD Trials I and III) and III (CD Trial II) Study Design[1]

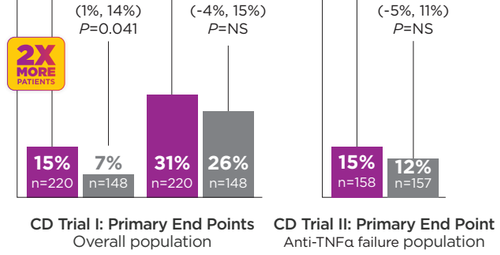
Three randomized, double-blind, placebo-controlled studies enrolled adult patients with moderately to severely active Crohn's who had failed at least 1 conventional therapy, including corticosteroids, immunomodulators, and/or ≥1 anti-TNFα therapy. Concomitant aminosalicylates, corticosteroids, and immunomodulators were permitted in all 3 trials. In Crohn's Trial I, patients were randomized (3:2) to receive ENTYVIO 300 mg or placebo by intravenous infusion at Weeks 0 and 2. In Crohn's Trial II, patients were randomized (1:1) to receive either ENTYVIO 300 mg or placebo at Weeks 0, 2, and 6. In Crohn's Trial III, patients receiving ENTYVIO who demonstrated clinical response (≥70-point decrease in CDAI score from baseline) at Week 6 (from Crohn's Trial I or an open-label cohort) were randomized (1:1:1) to receive either ENTYVIO 300 mg every 8 weeks, ENTYVIO 300 mg every 4 weeks, or placebo every 4 weeks. The ENTYVIO Q4W dosing regimen did not demonstrate additional clinical benefit over the Q8W dosing regimen. The Q4W dosing regimen is not the recommended dosing regimen.

GEMINI II and III Study End Points[1,8,10]

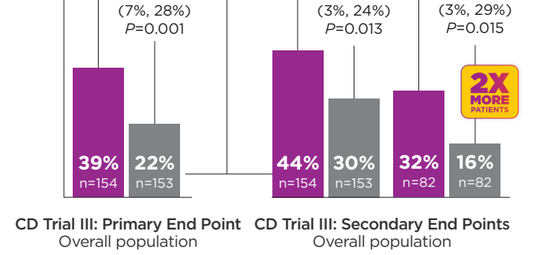
Overall population compared with placebo

ENTYVIO IV · Placebo

WEEK 6



WEEK 52



> **The significant clinical remission results at Week 52 in patients with moderate-to-severe Crohn's were notable from GEMINI II, as well as the safety profile observed in this study."**

*Clinical remission = CDAI score ≤150.
†Clinical response = ≥100-point decrease in CDAI from baseline.
‡Corticosteroid-free clinical remission: Assessed in the subgroup of patients who were receiving corticosteroids at baseline and who were in clinical response (defined as ≥70 decrease in CDAI from baseline) at Week 6 (n=82 for placebo and n=82 for ENTYVIO every 8 weeks). Corticosteroid-free clinical remission was defined as the proportion of patients in this subgroup that discontinued corticosteroids by Week 52 and were in clinical remission at Week 52.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Progressive Multifocal Leukoencephalopathy (PML):** PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML typically only occurs in patients who are immunocompromised. One case of PML in an ENTYVIO-treated patient with multiple contributory factors has been reported. Although unlikely, a risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms that may include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is suspected, withhold dosing with ENTYVIO and refer to neurologist; if confirmed, discontinue ENTYVIO dosing permanently.

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VARSITY

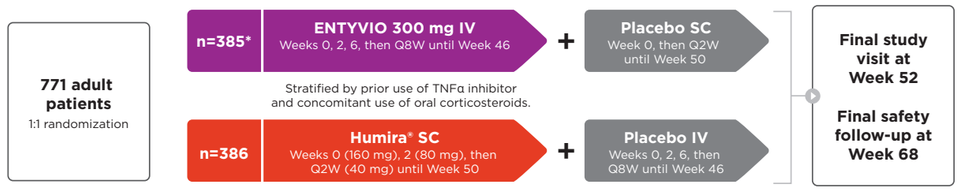
Scan for more VARSITY data

VARSITY:

The first head-to-head study of biologics in moderate to severe UC[11,12]

VARSITY Trial Study Design[8,11,13]

VARSITY was a double-blind, double-dummy, active-controlled trial that compared ENTYVIO with Humira® (adalimumab) in adults with moderately to severely active UC.[11]



- Eligible patients were adults (aged 18 to 85 years) with moderately to severely active ulcerative colitis, defined as a complete Mayo Score of 6 to 12 (range 0 to 12; higher scores represent more active disease), an endoscopic subscore of ≥2, colonic involvement of ≥15 cm, and a confirmed diagnosis of ulcerative colitis for ≥3 months. Anti-TNFα-naïve patients who had not responded or lost response to conventional treatments were eligible. Centrally read endoscopies were performed at Weeks 14 and 52
- Dosing was consistent with the US product label for both ENTYVIO and Humira®; no dose escalation was permitted for either treatment group. After induction, patients stayed in their treatment group throughout the maintenance phase (treat-through design)
- Enrollment of patients who discontinued treatment with an anti-TNFα (except adalimumab) due to documented reasons other than safety was capped at 25% (~21% was reached). Most of the trial population (97.3%) had moderately to severely active disease (Mayo Score 6-12). Patients with mild disease represented significant protocol deviations. Per-protocol sensitivity analyses indicated no change from overall population results
- Patients naïve to anti-TNFα therapy were enrolled if they were failing current treatment (eg, CS, 5-ASA, or immunomodulators). Per-protocol sensitivity analyses indicated no change from overall population results. Patients on a 5-ASA or immunomodulator at baseline maintained stable doses throughout the study

> **What is the value of head-to-head data when making treatment decisions in UC?**
>
> There is huge value in head-to-head data. These studies are the gold standard for comparative data."

Humira® (AbbVie Inc., North Chicago, IL). For information related to Humira, please see AbbVie.com.
*Includes 2 patients who were randomized but never received any study drug.
CS=corticosteroids; IV=intravenous; Q2W=every 2 weeks; Q8W=every 8 weeks; SC=subcutaneous; TNFα=tumor necrosis factor alpha; 5-ASA=5-aminosalicylate.

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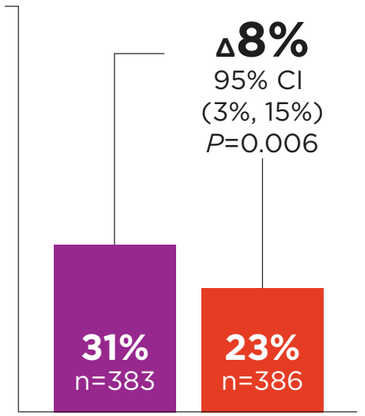
ENTYVIO DEMONSTRATED SUPERIORITY TO HUMIRA® IN CLINICAL REMISSION AT WEEK 52[11]

VARSITY Primary End Point

Overall population

WEEK 52 ENTYVIO IV Humira® (adalimumab)

Clinical remission[11]*



Safety Profile[8,11,13]

Study was not designed to assess safety differences

Adverse Events

- Adverse events† occurred in 62.7% of the patients (240 of 383) in the vedolizumab group and in 69.2% (267 of 386) in the adalimumab group. Serious adverse events‡ occurred in 11.0% of the patients (42 of 383) in the ENTYVIO group and in 13.7% (53 of 386) in the adalimumab group
- The most frequent AEs† for Humira® and ENTYVIO were as follows: ≥1 TEAE, 35.8% and 32.9%; ulcerative colitis, 16.3% and 11.5%; nasopharyngitis, 7.8% and 7.0%; headache, 5.4% and 7.0%; anemia, 6.7% and 5.2%; abdominal pain, 5.2% and 4.7%; upper respiratory tract infection, 4.4% and 5.2%

For full VARSITY safety data, visit ENTYVIOHCP.com by using the QR code to the left.

> **"VARSITY provided comparative information about ENTYVIO and Humira® on clinical remission, showing that ENTYVIO was superior."**

*Clinical remission was defined as a complete Mayo Score of ≤2 points and no subscore >1 point.
†Adverse events that occurred during the trial period. Trial period was the time from the first dose of a trial drug and up to 126 days after the last dose. Adverse events were classified according to the Medical Dictionary for Regulatory Activities System Organ Class categorization and preferred terms (version 21.0). The safety population was defined as all patients who received at least one dose of the study drug.
‡No cases of progressive multifocal leukoencephalopathy.
AE=adverse event; CI=confidence interval; TEAE=treatment-emergent adverse event.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Liver Injury:** There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.

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Scan for more GEMINI I data

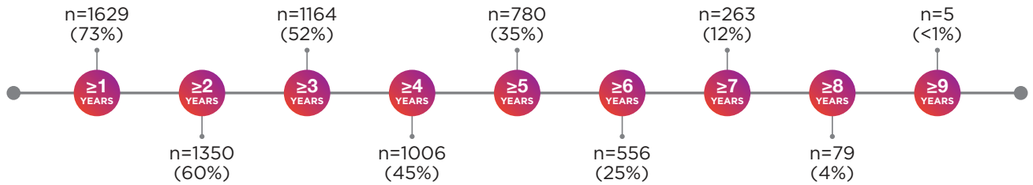
UP TO

7 YEARS OF CONSISTENT SAFETY DATA IN UC AND CROHN'S

GEMINI Long-Term Safety Study Design[1,8,9]

- GEMINI Long-Term Safety Study was a phase 3, single-arm, open-label, multinational study evaluating the long-term safety profile of ENTYVIO in patients with moderately to severely active UC or Crohn's
- Patients were enrolled from the phase 3 studies GEMINI I, GEMINI II, GEMINI III, a long-term phase 2 study, and included a cohort of ENTYVIO-naïve patients with UC and Crohn's. Data were collected from May 2009 to October 2017
- The study evaluated 2243 UC and Crohn's patients who received ENTYVIO with a median exposure of 42.4 months for UC (range 0.03 to 112.2 months) and 31.5 months for Crohn's (range 0.03 to 100.3 months)
- The safety population included all patients who received any dose of ENTYVIO

Length of Exposure to ENTYVIO



> UC and Crohn's are chronic diseases that patients will have for the rest of their lives. **It's critical that we choose a therapy that will not only work for them over the long term but also has a demonstrated safety profile."**

AE=adverse event; LTS=long-term safety; PY=patient-year; SAE=serious adverse event; UC=ulcerative colitis.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Live and Oral Vaccines:** Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

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No new safety signals up to 7 years in UC and Crohn's patients

NO NEW SIGNALS OF[8,9]:

Infections
Malignancies
Infusion-related reactions
Hepatic injury

- The most frequent AEs were disease exacerbations (35.9% UC, 35.3% Crohn's), nasopharyngitis (28.2% UC, 25.4% Crohn's) and arthralgia (17.3% UC, 24.4% Crohn's)
- 39.7% of AEs in UC and 46.2% of AEs in Crohn's were considered by the treating physician to be related to exposure to ENTYVIO

Exposure-adjusted incidence rates of selected AEs in the GEMINI Long-Term Safety Study*

	UC (n=894)		**Crohn's** (n=1349)	
	n (%)	**Incidence/ 1000 PYs**	n (%)	**Incidence/ 1000 PYs**
Any AE	829 (92.7)	**1220.5**	1295 (96.0)	**1799.2**
Any Serious AE	277 (31.0)	**90.9**	548 (40.6)	**146.5**
Total infections	591 (66.1)	**388.9**	937 (69.5)	**492.1**
Serious infections	61 (6.8)	**18.0**	146 (10.8)	**33.6**
Malignancies	58 (6.5)	**17.2**	92 (6.8)	**20.8**
Infusion reactions	36 (4.0)	**NA**	67 (5.0)	**NA**
Hepatic events	29 (3.2)	**8.4**	63 (4.7)	**14.1**
PML†	0 (0)	**0**	0 (0)	**0**

- GEMINI LTS identified no cases of PML with 7999 PYs of ENTYVIO exposure†

> **The ENTYVIO safety profile is consistent for up to 7 years. It hasn't changed over time. The side effects of GEMINI LTS align with those of previous studies."**

*Time-adjusted incidence rate per 1000 PYs=(number of patients experiencing an AE of interest/total person time in years) x 1000.
†Although unlikely, a risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms.

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GEMINI TRIALS I AND II

SAFETY PROFILE

ENTYVIO vs placebo:

A PROVEN SAFETY PROFILE

BASED ON 4 CLINICAL TRIALS[1]

> Although there is no drug without any potential for side effects, **ENTYVIO has shown consistent tolerability in my practice, which reassures my patients."**

ADVERSE REACTIONS OBSERVED IN THE GEMINI TRIALS[1]

Adverse reactions in ≥3% of ENTYVIO-treated patients and ≥1% higher than in placebo (UC Trials I and II* and CD Trials I and III*)

Adverse Reaction	ENTYVIO IV† (N=1434)	Placebo‡ (N=297)
Nasopharyngitis	13%	7%
Headache	12%	11%
Arthralgia	12%	10%
Nausea	9%	8%
Pyrexia	9%	7%
Upper respiratory tract infection	7%	6%
Fatigue	6%	3%
Cough	5%	3%
Bronchitis	4%	3%
Influenza	4%	2%
Back pain	4%	3%
Rash	3%	2%
Pruritus	3%	1%
Sinusitis	3%	1%
Oropharyngeal pain	3%	1%
Pain in extremities	3%	1%

*Data from patients receiving open-label ENTYVIO treatment at Weeks 0 and 2 (prior to entry into UC Trial II and Crohn's disease Trial III) and from Weeks 6 to 52 (nonresponders at Week 6 of UC Trial I and Crohn's disease Trial I) are included.
†Patients who received ENTYVIO for up to 52 weeks.
‡Patients who received placebo for up to 52 weeks.

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Adverse events observed in UC Trials I and II and CD Trials I and III[1]

INFECTIONS

Infection rates with ENTYVIO were 0.85 per patient-year vs 0.7 for placebo.

- Infections consisted primarily of nasopharyngitis, upper respiratory tract infection, sinusitis, and urinary tract infection
- 2% of patients discontinued ENTYVIO due to infections

SERIOUS INFECTIONS

Serious infection rates with ENTYVIO were 0.07 per patient-year vs 0.06 for placebo.

- Serious infections included anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis

IMMUNOGENICITY

The rate of detectable anti-vedolizumab antibodies at any time during the 52 weeks of continuous treatment with ENTYVIO was 6% (86 of 1427 patients).

- 20 of 86 patients were persistently positive (at 2 or more consecutive study visits) for anti-vedolizumab antibody, and 56 of 86 patients developed neutralizing antibodies to vedolizumab
- Among these 20 patients, 14 had undetectable or reduced vedolizumab serum concentrations. Five of the 20 patients with persistently positive anti-vedolizumab antibody achieved clinical remission at Week 52 in the controlled trials
- Overall, there was no apparent correlation of anti-vedolizumab antibody development to adverse reactions following intravenous administration of ENTYVIO

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Although unlikely, a risk of PML cannot be ruled out:

- PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML is caused by the John Cunningham (JC) virus and typically only occurs in patients who are immunocompromised
- 1 case of PML in an ENTYVIO-treated patient with multiple contributory factors has been reported in the postmarketing setting (eg, human immunodeficiency virus [HIV] infection with a CD4 count of 300 cells/mm^3 and prior and concomitant immunosuppression)

LIVER INJURY

ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.

3 patients reported serious adverse reactions of hepatitis with ENTYVIO; 1 additional case of serious hepatitis was seen in the open-label trial.

- These adverse reactions occurred following 2 to 5 ENTYVIO doses; however, it is unclear if the reactions indicated drug-induced or autoimmune etiology
- There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO
- All patients recovered following discontinuation of therapy with or without treatment with corticosteroids

MALIGNANCIES

Malignancies (excluding dysplasia and basal cell carcinoma) were reported in 0.4% (6 of 1434) of patients treated with ENTYVIO and in 0.3% (1 of 297) of patients treated with placebo.

- The number of malignancies in clinical trials was small; however, long-term exposure was limited

ADVERSE REACTIONS

Adverse reactions were reported in 52% of patients treated with ENTYVIO (N=1434) and 45% of patients treated with placebo (N=297).

- Over 52 weeks, 7% of patients treated with ENTYVIO experienced serious adverse reactions compared to 4% treated with placebo

INFUSION-RELATED REACTIONS (IRRs) AND HYPERSENSITIVITY REACTIONS

4% of patients treated with ENTYVIO (N=1434) experienced an IRR vs 3% of patients on placebo (N=297).

- 1 case of anaphylaxis (1 of 1434 patients treated with ENTYVIO) was reported by a Crohn's disease patient during the second infusion (symptoms reported were dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate) and was managed with discontinuation of infusion and treatment with antihistamine and IV hydrocortisone
- **Most frequently observed IRRs** in patients treated with ENTYVIO were nausea, headache, pruritus, dizziness, fatigue, infusion-related reaction, pyrexia, urticaria, and vomiting. These reactions generally occurred within the first 2 hours after the infusion and resolved with no treatment or following antihistamine and/or IV hydrocortisone treatment

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How do you discuss ENTYVIO as a therapeutic option with your patients?

Dr. Bincy Abraham: I explain the importance of not waiting to treat their UC or Crohn's. We discuss ENTYVIO's efficacy and safety data, and I emphasize the 7 years of safety data. Sharing my own clinical experience with using the medication encourages my patients.

How did VARSITY shift your perception of ENTYVIO for UC?

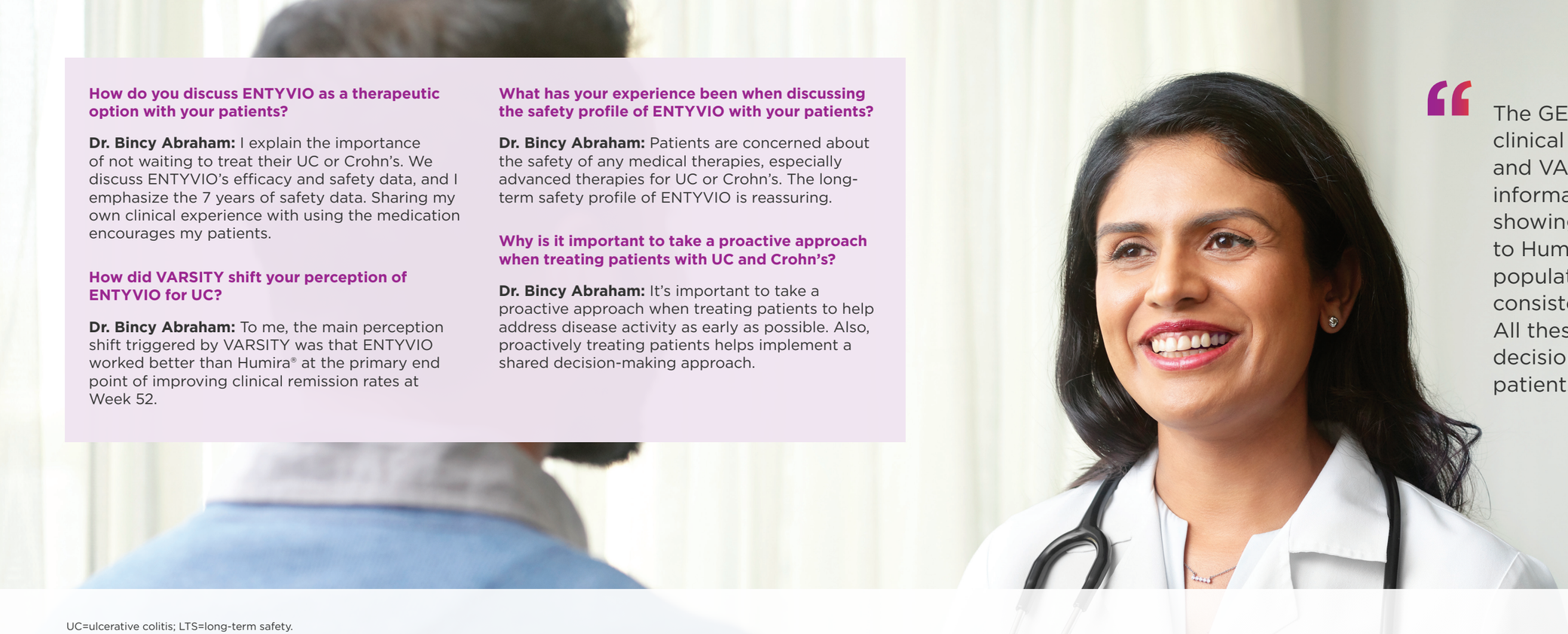
Dr. Bincy Abraham: To me, the main perception shift triggered by VARSITY was that ENTYVIO worked better than Humira® at the primary end point of improving clinical remission rates at Week 52.

What has your experience been when discussing the safety profile of ENTYVIO with your patients?

Dr. Bincy Abraham: Patients are concerned about the safety of any medical therapies, especially advanced therapies for UC or Crohn's. The long-term safety profile of ENTYVIO is reassuring.

Why is it important to take a proactive approach when treating patients with UC and Crohn's?

Dr. Bincy Abraham: It's important to take a proactive approach when treating patients to help address disease activity as early as possible. Also, proactively treating patients helps implement a shared decision-making approach.



"The GEMINI trials demonstrated clinical remission through Week 52, and VARSITY provided comparative information on clinical remission, showing that ENTYVIO was superior to Humira® at Week 52 in the overall population. GEMINI LTS showed consistent safety for up to 7 years. All these trials further support my decision to use ENTYVIO for my patients."

– BINCY ABRAHAM, MD, MS

UC=ulcerative colitis; LTS=long-term safety.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

WARNINGS AND PRECAUTIONS

- **Infusion-Related and Hypersensitivity Reactions:** Infusion-related reactions and hypersensitivity reactions including anaphylaxis, dyspnea, bronchospasm, urticaria, flushing, rash, and increased blood pressure and heart rate have been reported. These reactions may occur with the first or subsequent infusions and may vary in their time of onset from during infusion or up to several hours post-infusion. If anaphylaxis or other serious infusion-related or hypersensitivity reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.
- **Infections:** Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO, including anal abscess, sepsis (some fatal), tuberculosis, salmonella sepsis, Listeria meningitis, giardiasis, and cytomegaloviral colitis. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections. Consider screening for tuberculosis (TB) according to the local practice.
- **Progressive Multifocal Leukoencephalopathy (PML):** PML, a rare and often fatal opportunistic infection of the central nervous system (CNS), has been reported with systemic immunosuppressants, including another integrin receptor antagonist. PML typically only occurs in patients who are immunocompromised. One case of PML in an ENTYVIO-treated patient with multiple contributory factors has been reported. Although unlikely, a risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms that may include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is suspected, withhold dosing with ENTYVIO and refer to neurologist; if confirmed, discontinue ENTYVIO dosing permanently.

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WARNINGS AND PRECAUTIONS (cont'd)

- **Liver Injury:** There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.
- **Live and Oral Vaccines:** Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥3% and ≥1% higher than placebo) were: nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, pain in extremities, and injection site reactions with subcutaneous administration.

DRUG INTERACTIONS

Because of the potential for increased risk of PML and other infections, avoid the concomitant use of ENTYVIO with natalizumab products and with TNF blockers. Upon initiation or discontinuation of ENTYVIO in patients treated with CYP450 substrates, monitor drug concentrations or other therapeutic parameters, and adjust the dosage of the CYP substrate as needed.

INDICATIONS

Adult Ulcerative Colitis (UC):
ENTYVIO is indicated in adults for the treatment of moderately to severely active UC.

Adult Crohn's Disease (CD):
ENTYVIO is indicated in adults for the treatment of moderately to severely active CD.

DOSAGE FORMS & STRENGTHS:

- ENTYVIO Intravenous (IV) Infusion: 300 mg vedolizumab
- ENTYVIO Subcutaneous (SC) Injection: 108 mg vedolizumab

Please click for Full Prescribing Information.

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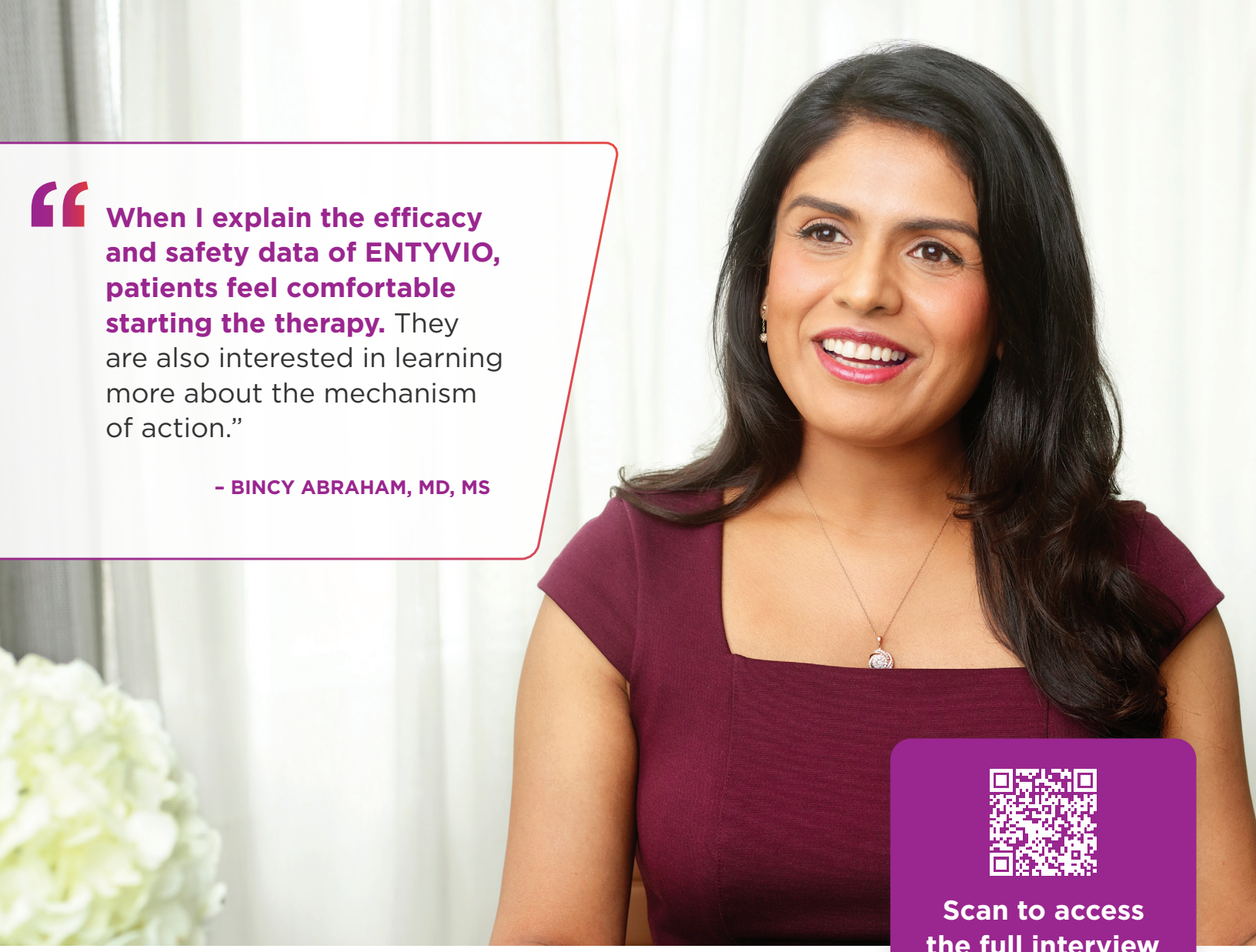

> **When I explain the efficacy and safety data of ENTYVIO, patients feel comfortable starting the therapy.** They are also interested in learning more about the mechanism of action."
>
> **– BINCY ABRAHAM, MD, MS**

Scan to access the full interview

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENTYVIO is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.

Please click for additional Important Safety Information.

References: 1. ENTYVIO (vedolizumab) prescribing information. Takeda Pharmaceuticals. **2.** Briskin M, Winsor-Hines D, Shyjan A, et al. Human mucosal addressin cell adhesion molecule-1 is preferentially expressed in intestinal tract and associated lymphoid tissue. *Am J Pathol*. 1997;151(1):97-110. **3.** Fedyk ER, Wyant T, Yang LL, et al. Exclusive antagonism of the α4β7 integrin by vedolizumab confirms the gut-selectivity of this pathway in primates. *Inflamm Bowel Dis*. 2012;18(11):2107-2119. **4.** Soler D, Chapman T, Yang LL, Wyant T, Egan R, Fedyk ER. The binding specificity and selective antagonism of vedolizumab, an anti-α4β7 integrin therapeutic antibody in development for inflammatory bowel diseases. *J Pharmacol Exp Ther.* 2009;330(3):864-875. **5.** Wyant T, Fedyk E, Abhyankar B. An overview of the mechanism of action of the monoclonal antibody vedolizumab. *J Crohns Colitis*. 2016;10(12):1437-1444. **6.** Wyant T, Leach T, Sankoh S, et al. Vedolizumab affects antibody responses to immunisation selectively in the gastrointestinal tract: randomised controlled trial results. *Gut*. 2015;64(1):77-83. **7.** Milch C, Wyant T, Xu J, et al. Vedolizumab, a monoclonal antibody to the gut homing α4β7 integrin, does not affect cerebrospinal fluid T-lymphocyte immunophenotype. *J Neuroimmunol*. 2013;264:123-126. **8.** Data on file. Takeda Pharmaceuticals. **9.** Loftus EV Jr, Feagan BG, Panaccione R, et al; for the GEMINI LTS study team. Long-term safety of vedolizumab for inflammatory bowel disease. *Aliment Pharmacol Ther*. 2020;52(8):1353-1365. **10.** Sandborn WJ, Feagan BG, Rutgeerts P, et al; for the GEMINI 2 Study Group. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2013;369(8):711-721. **11.** Sands BE, Peyrin-Biroulet L, Loftus EV Jr, et al. Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis. *N Engl J Med*. 2019;381(13):1215-1226. **12.** Macaluso FS, Maida M, Grova M, et al. Head-to-head comparison of biological drugs for inflammatory bowel disease: from randomized controlled trials to real-world experience. *Therap Adv Gastroenterol*. 2021;14:1-11. **13.** Sands BE, Peyrin-Biroulet L, Loftus EV Jr, et al. Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis. *N Engl J Med*. 2019;381(13):1215-1226 (supplemental appendix).

If you are a Colorado prescriber, please see the Colorado WAC **disclosure form**. If you are a Connecticut prescriber, please see the Connecticut WAC **disclosure form**.

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