CHANCE OF IMPROVEMENT IN SYMPTOMS

Biologics are among the most effective type of medicines used to treat IBD. One year after starting a biologic, 30 to 55% of individuals can expect to be in clinical remission (i.e. a significant decrease in symptoms related to IBD).

Research studies have found that all the biologic medicines are effective at treating IBD when compared to placebo (i.e. inactive substance that looks like the study drug, but contains no medication). However, there have been very few research trials directly comparing one biologic to another biologic. Therefore, it is important to talk with your doctor on which medicine may be the most effective at leading to remission for you.

RISK OF LYMPHOMA

Table 1 shows the chances of getting lymphoma for each of the commonly used biologics. The risk of lymphoma depends on the way that the biologic works in reducing inflammation in the intestinal tract. It also likely depends on whether you are also taking an immunomodulator medicine, such as azathioprine or 6-mercaptopurine, at the same time. If you want to revisit the "What is the risk of lymphoma?" page in the IBD&me "Learn More" section, please click here. In Table 2, we also list the U.S. Food and Drug Administration (FDA) "Black Box" cancer-related warnings for each biologic. For some medicines, the U.S. FDA will put a "Black Box" warning on the prescription drug's label that is designed to call attention to serious or life-threatening risks.

Table 1. Chances of Getting Lymphoma

Biologic	Type of IBD	Way Biologic Works	Chances of Getting Lymphoma Each Year
Cimzia® (certolizumab pegol)	CD	Blocks tumor necrosis factors	6 out of 10,000 [1]
Entyvio® (vedolizumab)	CD and UC	Blocks integrins	2 out of 10,000 (i.e. same as baseline risk without biologic)
Humira® (adalimumab)	CD and UC	Blocks tumor necrosis factors	6 out of 10,000 [1]
Remicade® (infliximab)	CD and UC	Blocks tumor necrosis factors	6 out of 10,000 [1]
Simponi® (golimumab)	UC	Blocks tumor necrosis factors	6 out of 10,000 [1]
Stelara® (ustekinumab)	CD	Blocks interleukins	2 out of 10,000 (i.e. same as baseline risk without biologic)

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

Table 2. U.S. FDA “Black Box” Cancer-Related Warnings

Biologic	U.S. FDA “Black Box” Cancer-Related Warning [2]
Cimzia® (certolizumab pegol)	• Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Cimzia is a member.
Entyvio® (vedolizumab)	• No “Black Box” warning.
Humira® (adalimumab)	• Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Humira is a member. • Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescent and young adults with inflammatory bowel disease treated with TNF blockers including Humira.
Remicade® (infliximab)	• Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Remicade. • Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including Remicade. All cases were reported in patients with Crohn’s disease and ulcerative colitis, the majority of whom were adolescent or young adult males. This rare, aggressive T-cell lymphoma is fatal. All of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with Remicade at or prior to diagnosis.
Simponi® (golimumab)	• Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Simponi is a member.
Stelara® (ustekinumab)	• No “Black Box” warning.

Abbreviations: FDA, Food and Drug Administration; TNF, tumor necrosis factor.

References:

1. Siegel CA. Risk of lymphoma in inflammatory bowel disease. Gastroenterology & Hepatology. 2009;5(11):784.

2. U.S. Food & Drug Administration. FDA Online Label Repository. 2017; Available from: https://labels.fda.gov/.

RISK OF SCALY SKIN RASH

The table shows the chances of getting a scaly skin rash (psoriasis) while taking each of the commonly used biologics. Depending on the medicine the chances can be as low as 1% or as high as 12%.

Biologic	Type of IBD	Chances of Scaly Skin Rash [1]
Cimzia® (certolizumab pegol)	CD	9%
Entyvio® (vedolizumab)	CD and UC	3%
Humira® (adalimumab)	CD and UC	6 to 12%
Remicade® (infliximab)	CD and UC	1 to 10%
Simponi® (golimumab)	UC	3%
Stelara® (ustekinumab)	CD	Less than 1%

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

References:

1. UpToDate. 2017; Available from: https://www.uptodate.com/.

RISK OF SERIOUS INFECTION

Table 1 shows the chances of getting a serious infection for each of the commonly used biologics. As you can see, the risk of getting a severe infection is pretty low. In Table 2, we also list the U.S. Food and Drug Administration (FDA) "Black Box" infection-related warnings for each biologic. For some medicines, the U.S. FDA will put a "Black Box" warning on the prescription drug's label that is designed to call attention to serious or life-threatening risks.

Table 1. Chances of Getting a Serious Infection

Biologic	Type of IBD	Chances of Getting a Serious Infection
Cimzia® (certolizumab pegol)	CD	3% [1]
Entyvio® (vedolizumab)	CD and UC	2 to 6% [2,3]
Humira® (adalimumab)	CD and UC	2 to 3% [4,5]
Remicade® (infliximab)	CD and UC	3 to 4% [6,7]
Simponi® (golimumab)	UC	3% [8]
Stelara® (ustekinumab)	CD	2% [9,10]

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

Table 2. U.S. FDA “Black Box” Infection-Related Warnings

Biologic	U.S. FDA “Black Box” Infection-Related Warning [11]
Cimzia® (certolizumab pegol)	• Increased risk of serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. • Cimzia should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Cimzia. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative.
Entyvio® (vedolizumab)	• No “Black Box” warning.
Humira® (adalimumab)	• Increased risk of serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. • Humira should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Humira. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative.
Remicade® (infliximab)	• Increased risk of serious infections leading to hospitalization or death, including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens. • Remicade should be discontinued if a patient develops a serious infection or sepsis during treatment. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Remicade. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative.

Simponi® (golimumab)	• Serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal (such as histoplasmosis), and other opportunistic infections have occurred in patients receiving Simponi. • Simponi should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Simponi. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative.
Stelara® (ustekinumab)	• No “Black Box” warning.

Abbreviations: FDA, Food and Drug Administration; TNF, tumor necrosis factor.

References:

1. Schreiber S, Khaliq-Kareemi M, Lawrance IC, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. N Engl J Med. 2007;357(3):239-50.

2. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710.

3. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711-21.

4. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007;132(1):52-65.

5. Sandborn WJ, van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2012;142(2):257-65.e1-3. Epub 2011/11/09.

6. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005;353(23):2462-76.

7. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002;359(9317):1541-9.

8. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014;146(1):96-109.e1.

9. Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med. 2016;375(20):1946-60.

10. Sandborn WJ, Gasink C, Gao LL, et al. Ustekinumab induction and maintenance therapy in refractory Crohn's disease. N Engl J Med. 2012;367(16):1519-28.

11. U.S. Food & Drug Administration. FDA Online Label Repository. 2017; Available from: https://labels.fda.gov/.

TIME IN BETWEEN DOSES

When taking a biologic, there are two phases – the induction (i.e. starting) period followed by the maintenance period. During induction, you will generally receive higher and more frequent doses to help improve your chances of responding to the medicine. The Table lists the induction dosing schedule for each medicine.

If your IBD symptoms improve during the induction period, then you will enter the maintenance phase and the doses will be more spaced out. The Table shows how often the maintenance doses for the currently available biologics are generally given. Depending on the medicine, it can be as often as every 2 weeks or spaced out every 8 weeks.

Biologic	Type of IBD	Induction Dosing Schedule	Maintenance Dosing Schedule	Route for Maintenance Doses
Cimzia® (certolizumab pegol)	CD	Weeks 0, 2, 4	Every 4 weeks	Injected under the skin
Entyvio® (vedolizumab)	CD and UC	Weeks 0, 2, 6	Every 8 weeks	Given through an IV into the vein
Humira® (adalimumab)	CD and UC	Weeks 0, 2	Every 2 weeks	Injected under the skin
Remicade® (infliximab)	CD and UC	Weeks 0, 2, 6	Every 8 weeks	Given through an IV into the vein
Simponi® (golimumab)	UC	Weeks 0, 2	Every 4 weeks	Injected under the skin
Stelara® (ustekinumab)	CD	Single dose *	Every 8 weeks	Injected under the skin

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; IV, intravenous; UC, ulcerative colitis.

* The induction dose of Stelara is given through an IV into the vein.

TOLERABILITY OF UNWANTED SIDE EFFECTS

Table 1 shows the chances of stopping a biologic because of side effects. Depending on the medicine, the chances can be as low as 4% or as high as 15%. In Table 2, we also list the U.S. Food and Drug Administration (FDA) "Black Box" warnings for each biologic. For some medicines, the U.S. FDA will put a "Black Box" warning on the prescription drug's label that is designed to call attention to serious or life-threatening risks.

Table 1. Chances of Stopping Medicine Because of Side Effects

Biologic	Type of IBD	Chances of Stopping Medicine Because of Side Effects
Cimzia® (certolizumab pegol)	CD	8% [1]
Entyvio® (vedolizumab)	CD and UC	6 to 8% [2,3]
Humira® (adalimumab)	CD and UC	7 to 9% [4,5]
Remicade® (infliximab)	CD and UC	8 to 15% [6,7]
Simponi® (golimumab)	UC	9% [8]
Stelara® (ustekinumab)	CD	4% [9,10]

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

Table 2. U.S. FDA “Black Box” Warnings

Biologic	U.S. FDA “Black Box” Warning [11]
Cimzia® (certolizumab pegol)	• Increased risk of serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. • Cimzia should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Cimzia. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative. • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Cimzia is a member.
Entyvio® (vedolizumab)	• No “Black Box” warning.
Humira® (adalimumab)	• Increased risk of serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. • Humira should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Humira. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative. • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Humira is a member. • Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescent and young adults with inflammatory bowel disease treated with TNF blockers including Humira.

Remicade® (infliximab)	• Increased risk of serious infections leading to hospitalization or death, including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens. • Remicade should be discontinued if a patient develops a serious infection or sepsis during treatment. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Remicade. • Monitor all patients for active tuberculosis during treatment, even if initial latent tuberculosis test is negative. • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Remicade.
	• Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including Remicade. All cases were reported in patients with Crohn's disease and ulcerative colitis, the majority of whom were adolescent or young adult males. This rare, aggressive T-cell lymphoma is fatal. All of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with Remicade at or prior to diagnosis.
Simponi® (golimumab)	• Serious infections leading to hospitalization or death including tuberculosis, bacterial sepsis, invasive fungal (such as histoplasmosis), and other opportunistic infections have occurred in patients receiving Simponi. • Simponi should be discontinued if a patient develops a serious infection or sepsis. • Perform test for latent tuberculosis; if positive, start treatment for tuberculosis prior to starting Simponi. • Monitor all patients for active tuberculosis during treatment, even if initial latent TB test is negative. • Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Simponi is a member.
Stelara® (ustekinumab)	• No "Black Box" warning.

Abbreviations: FDA, Food and Drug Administration; TNF, tumor necrosis factor.

References:

1. Schreiber S, Khaliq-Kareemi M, Lawrance IC, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. N Engl J Med. 2007;357(3):239-50.

2. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med. 2013;369(8):711-21.

3. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710.

4. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007;132(1):52-65.

5. Sandborn WJ, van Assche G, Reinisch W, et al. Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2012;142(2):257-65.e1-3.

6. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002;359(9317):1541-9.

7. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005;353(23):2462-76.

8. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. Gastroenterology. 2014;146(1):96-109.e1.

9. Sandborn WJ, Feagan BG, Fedorak RN, et al. A randomized trial of Ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with moderate-to-severe Crohn's disease. Gastroenterology. 2008;135(4):1130-41.

10. Sandborn WJ, Gasink C, Gao LL, et al. Ustekinumab induction and maintenance therapy in refractory Crohn's disease. N Engl J Med. 2012;367(16):1519-28.

11. U.S. Food & Drug Administration. FDA Online Label Repository. 2017. Available from: https://labels.fda.gov/.

WAY YOU RECEIVE THE MEDICINE

The Table shows how the currently available biologics are given. One option is to give it through an IV into the vein either in a clinic or at home. Another option is to inject the medicine yourself under the skin at home.

Give through an IV into the vein	Injected under the skin
Entyvio® (vedolizumab)	Cimzia® (certolizumab pegol)
Remicade® (infliximab)	Humira® (adalimumab)
Stelara® (ustekinumab) - starting dose *	Simponi® (golimumab)
	Stelara® (ustekinumab) - maintenance doses *

* When taking a biologic, there are two phases – the induction (i.e. starting) period followed by the maintenance period. During induction, higher and more frequent doses are generally given to improve your chances of responding to the medicine. If your IBD symptoms improve during induction, then you later receive maintenance doses that are more spaced out.