

Biologics – Matching Drugs to Patients

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Where discoveries are delivered.sm

Outline

Treatment sequencing
 New agents

 IBD pipeline
 Local delivery of drugs to the GI tract
 Combination therapy

 Individual therapies (precision medicine)

Treatment Sequencing

First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis

Study name				Even	ts / Total	Odds ratio and 95% CI
	Odds ratio	Lower limit	Upper limit	Group-A	Group-B	
ULTRA 1 2013	2.19	1.14	4.19	32 / 150	16/145	
ULTRA 2 2012	2.23	1.06	4.67	24 / 130	12/130	
Suzuki 2014	0.86	0.34	2.18	9/90	11/96	
Adalimumab vs. Placebo	1.80	1.17	2.77	65/370	39/371	
PURSUIT Phase 2 2014	1.99	0.74	5.32	13/71	7/69	
PURSUIT Phase 3 2014	3.18	1.74	5.79	45/253	16/251	
Golimumab vs. Placebo	2.80	1.68	4.67	58 / 324	23/320	
ACT 1 2005	3.15	1.69	5.89	43 / 121	18/121	
ACT 2 2005	8.49	3.63	19.88	41/121	7/123	
Jiang 2015	4.12	1.57	10.76	22/41	9/41	
Xian 2015	2.48	0.79	7.77	11/50	5/49	
Infliximab vs. Placebo	4.07	2.68	6.16	117 / 333	39/334	
OCTAVE 1 2016	1.76	0.81	3.82	56 / 222	9/56	
OCTAVE 2 2016	3.04	1.03	8.95	43 / 195	4/47	
Tofactinib vs. Placebo	2.12	1.13	3.98	99 / 417	13 / 103	
UNIFI 2019	2.04	1.04	4.02	27 / 147	15/151	
Ustekinumab vs. Placebo	2.04	1.04	4.02	27 / 147	15/151	
VARSITY 2019	1.24	0.86	1.78	84 / 304	72/305	
edolizumab vs. Adalimumab	1.24	0.86	1.78	84 / 304	72/305	
GEMINI 1 2014	4.26	1.58	11.52	30 / 130	5/76	
Motoya 2019	2.25	0.83	6.10	22/79	6/41	
Vedolizumab vs. Placebo	3.10	1.53	6.26	52 / 209	11/117	
Efficacy of The	rapies	for In	duction	n of Endos	copic Im	0.1 0.2 0.5 1 2 5 Favors intervention Favors co provement – First-line
Efficacy of The	rapies	for In	duction	n of Endos	copic Im	0.1 0.2 0.5 1 2 5 Favors intervention Favors co provement – First-line
Efficacy of The Sudy name	rapies	for In		n of Endos	copic Im	0.1 0.2 0.5 1 2 5 Favors intervention Favors co pprovement – First-line Odds ratio and 95% Cl
Efficacy of The Study name	rapies Odds ratio	for In	Upper limit	of Endos Evente Group-A	copic Im s / Total Group-B	0.1 0.2 0.5 1 2 5 Favors intervention Favors co aprovement — First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013	Odds ratio 1.79	for In Lower limit 1.12	Upper limit 2.86	Frendos Events Group-A 74 / 150	Group-B	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement - First-line Odds ratio and 95% CI
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012	Odds ratio 1.79 1.24	for In Lower limit 1.12 0.76	Upper limit 2.86 2.03	Group - A 74 / 150 61 / 130	Copic Im 5 / Total Group-B 51 / 145 54 / 130	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014	Odds ratio 1.79 1.24 1.85	for In Lower limit 1.12 0.76 1.01	Upper limit 2.86 2.03 3.38	Group-A 74 / 150 61 / 130 40 / 90	copic Im s / Total Group-B 51 / 145 54 / 130 29 / 96	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimuma bys. Placebo	Odds ratio 1.79 1.24 1.85 1.58	for In Lower limit 1.12 0.76 1.01 1.18	Upper limit 2.86 2.03 3.38 2.13	Group-A 74 / 150 61 / 130 40 / 90 175 / 370	Copic Im Group-B 51 / 145 54 / 130 29 / 96 134 / 371	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 2 2014	Odds ratio 1.79 1.24 1.85 1.58 1.48	for In Lower limit 1.12 0.76 1.01 1.18 0.74	Upper limit 2.86 2.03 3.38 2.13 2.95	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71	Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% CI
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014	Codds ratio 1.79 1.24 1.85 1.58 1.88 1.82	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.26	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71 107 / 253	Copic Im Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69 72 / 251	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% CI
Efficacy of The Sudy name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adailmumab vs. Piacobo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Gellinumab vs. Piacoba	Codds ratio 1.79 1.24 1.85 1.58 1.48 1.48 1.82 1.74	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.26 1.25	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71 107 / 253 136 / 324	copic Im s / Total Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69 72 / 251 94 / 320	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Sudy name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005	Odds ratio 1.79 1.24 1.85 1.58 1.48 1.82 1.74 3.18	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.26 1.25 1.88	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71 107 / 253 136 / 324 75 / 121	copic lm Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69 72 / 251 94 / 320 41 / 121	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Oddsratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimumab vs. Placebo Act 1 2005	Codds ratio 1.79 1.24 1.58 1.48 1.48 1.48 1.82 1.74 3.18 3.40	for In Lowert limit 1.12 0.06 1.01 1.18 0.74 1.26 1.25 1.88 2.01	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71 107 / 253 136 / 324 75 / 121	copic Im s / Total Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69 72 / 251 94 / 320 41 / 121 38 / 123	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jiano 2015	Odds ratio 1.79 1.24 1.85 1.48 1.48 1.48 1.82 1.74 3.18 3.40 4.38	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.25 1.88 2.01 1.70	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 73/121 24/41	copic Im 5 / Total Group-B 51 / 145 54 / 130 29 / 96 134 / 371 22 / 69 72 / 251 94 / 320 41 / 121 38 / 123 10 / 41	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jang 2015 Xiao 2015	Odds ratio 1.79 1.24 1.85 1.58 1.48 1.48 1.74 3.18 3.40 4.38 2.64	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.25 1.88 2.01 1.70 1.01	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88	Group-A 74 / 150 61 / 130 61 / 130 29 / 71 107 / 253 136 / 324 75 / 121 73 / 121 24 / 41 17 / 50	Copic Im s/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 41/121 38/123 10/41 8/49	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% CI
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adaliumab vs. Placebo PURSUIT Phase 3 2014 POIRSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jang 2015 Xian 2015 Infliximab vs. Placebo	Oddss ratio 1.79 1.24 1.85 1.48 1.48 1.48 1.48 1.48 1.48 3.40 4.38 2.64	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.26 1.25 1.88 2.01 1.70 1.01 2.39	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 24/41 17/50 188/333	copic Im 6/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 41/121 38/123 10/41 8/49 97/334	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jiang 2015 Xian 2015 Xian 2015 Infliximab vs. Placebo OCTURE 1 2016	Odds ratio 1.79 1.24 1.85 1.58 1.85 1.85 1.85 1.82 1.74 3.18 3.40 4.33 2.64 3.32 1.80	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.25 1.88 2.01 1.70 1.01 2.39 0.04	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88 4.60 3.44	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 73/121 73/121 17/50 189/333 88/232	copic lm s/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 10/41 8/49 97/334 15/65	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 2 2014 PURSUIT Phase 2 2014 Golimumab vs. Placebo ACT 1 2005 Jang 2015 Xian 2015 Infiliximab vs. Placebo OCTAVE 1 2016	Codds ratio 1.79 1.24 1.58 1.58 1.48 1.48 1.82 1.74 3.18 3.40 4.38 2.64 4.332 1.80 2.42	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.25 1.88 2.01 1.70 1.01 1.70 1.01 1.239 0.94	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88 5.77 11.27 6.83 4.60 3.44 5.20	Group-A 74 / 150 61 / 130 61 / 130 01 75 / 370 29 / 71 107 / 253 136 / 324 75 / 121 73 / 121 24 / 41 17 / 50 188 / 333 88 / 222 71 / 105	copic lm s/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 41/121 38/123 10/41 8/49 97/334 15/56	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimuma vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimuma vs. Placebo ACT 1 2005 Jang 2015 Xian 2015 Infliximab vs. Placebo OCTAVE 1 2016 OCTAVE 1 2016	Codds ratio 1.79 1.24 1.85 1.58 1.88 1.82 1.74 3.40 4.38 2.64 3.320 2.82 1.80 2.42	for In Lower limit 1.12 0.76 1.01 1.18 0.74 1.25 1.88 2.01 1.70 1.01 2.39 0.94 1.101	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 5.37 11.27 6.88 4.60 3.44 5.29 3.44 5.29	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 24/41 17/50 189/333 88/222 71/195	Copic Im 6/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 41/121 38/123 10/41 8/49 97/334 9/736 9/47 9/47	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jiang 2015 Xian 2015 Infliximab vs. Placebo OCTAVE 2 2016 OCTAVE 2 2016	Codds ratio 1.79 1.24 1.85 1.58 1.74 3.18 3.40 4.38 2.64 3.32 1.80 2.42 2.03 1.60	for In Lower limit 1.12 0.76 1.01 1.28 1.25 1.88 2.01 1.70 1.01 2.39 0.94 1.10 1.23	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88 5.77 11.27 6.83 4.60 3.34 2.9 3.34	Group-A 74 / 150 61 / 130 61 / 130 02 / 71 107 / 253 136 / 324 75 / 121 73 / 121 24 / 41 17 / 50 189 / 333 88 / 222 71 / 195 159 / 417	Copic Im 5/ Total Group-B 51/ 145 54/ 130 22/ 69 72/ 251 94/ 320 41/ 121 10/ 41 86/ 123 10/ 41 15/ 56 9/ 47 9/ 47 22/ 103 20/ 165 156 156 156 156 157 107 107 107 107 107 107 107 10	0.1 0.2 0.5 1 2 5 Favors intervention Favors comprovement – First-line Odds ratio and 95% CI
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2012 Suzuki 2014 PURSUIT Phase 2 2014 PURSUIT Phase 2 2014 PURSUIT Phase 3 2014 ACT 1 2005 ACT 2 2005 Jiang 2015 Xian 2015 Infliximab vs. Placebo OCTAVE 1 2016 OCTAVE 1 2016 OCTAVE 1 2016	Codds ratio 1.79 1.24 1.85 1.48 1.48 1.82 1.74 3.18 3.40 4.38 2.64 3.32 1.80 2.42 2.03 1.80 2.42 4.64	for In Lower limit 1.12 0.76 1.07 1.18 8 2.01 1.170 0.04 1.10 1.239 0.04 1.10 1.239 0.04 1.12 1.239 1.12 1.239 1.2	Upper Upper 2.86 2.03 3.38 2.95 2.64 2.41 5.38 5.77 11.27 6.88 4.60 3.44 5.29 3.34 3.34 3.34 3.13 2.13	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 24/41 17/50 188/333 88/222 71/195 159/417 49/147	Copic Im 6/Total Group-B 51/145 54/130 29/96 134/371 22/69 72/251 38/123 38/123 38/123 38/123 38/123 38/123 38/123 38/123 38/123 38/123 38/121 10/41 8/49 9/47 32/151 5/56 9/47 32/151 5/56 9/47 32/151 5/57	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adailmumab vs. Placebo PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jang 2015 Xian 2015 Infiliximab vs. Placebo OCTAVE 1 2016 OCTAVE 1 2016 OCTAVE 2 2016 Tofactinib vs. Placebo UNIFI 2019 Ustekinumab vs. Placebo	Codds ratio 1.79 1.24 1.85 1.58 1.48 1.48 1.48 1.48 1.74 3.18 3.40 4.38 2.64 3.32 1.80 2.42 2.03 1.86 1.86 1.86 0.2.42 2.03 1.86 0.2.42 2.03 1.86 0.2.42 0.2.42 0.2.42 0.2.42 0.2.42 0.2.42 0.2.42 0.2.42 0.2.440000000000	for In Lower limit 1.12 0.76 1.01 1.18 1.25 1.88 2.01 1.01 1.01 1.01 1.01 1.01 1.01 1.01	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 5.38 5.77 11.27 6.88 4.60 3.44 5.29 3.34 3.13 3.13 3.13	Group-A 74/150 61/130 40/90 175/370 29/71 107/253 136/324 75/121 73/121 24/41 17/50 189/333 88/222 71/195 159/417 49/147 49/147	copic Im group-B 51/145 54/130 29/96 134/371 22/69 72/251 94/320 41/121 38/123 10/41 8/49 97/334 15/56 9/47 24/103 32/151 32/151	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% Cl
Efficacy of The Study name ULTRA 1 2013 ULTRA 2 2012 Suzuki 2014 Adalimumab vs. Placebo PURSUIT Phase 3 2014 PURSUIT Phase 3 2014 Golimumab vs. Placebo ACT 1 2005 ACT 2 2005 Jiang 2015 Xian 2015 Infliximab vs. Placebo OCTAVE 1 2016 OCTAVE 1 2016 Tofactinib vs. Placebo UNIFI 2019 Ustekinumab vs. Placebo GEMINI 1 2014	Odds ratio 1.79 1.24 1.85 1.58 1.82 1.74 4.88 1.82 1.74 4.33 2.64 2.32 2.03 1.86 6.86 8.86 2.91	for In Lower limit 1.12 0.76 1.01 1.25 1.88 2.01 1.170 0.94 1.10 1.239 0.94 1.10 1.239 0.94 1.10 1.239 0.94 1.11 1.12 1.53 1.11 1.53 1.54 1.54 1.54 1.55 1.54 1.55 1.55 1.55	Upper limit 2.86 2.03 3.38 2.13 2.95 2.64 2.41 5.38 5.77 11.27 6.88 5.77 11.27 6.88 5.77 3.34 3.13 3.13 3.13 5.42	Group-A 74 / 150 61 / 130 40 / 90 175 / 370 29 / 71 107 / 253 136 / 324 75 / 121 24 / 41 17 / 50 188 / 333 88 / 222 71 / 195 159 / 417 49 / 147 64 / 130 0 / 90	Copic Im 5/ Total Group-B 51 / 145 54 / 130 22 / 96 134 / 371 22 / 69 72 / 251 94 / 320 41 / 121 38 / 123 10 / 41 8 / 49 9 / 7 32 / 151 32 / 151 32 / 151 19 / 76 19 / 76	0.1 0.2 0.5 1 2 5 Favors intervention Favors co approvement – First-line Odds ratio and 95% CI



Singh S, Sandborn WJ. Clinical Gastroenterology and Hepatology 2020 182179-2191.

First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis

A	Efficacy of Therapies for Induction of Clinical Remission – Second-line									
	Study name		Events / Total			s / Total	Odds ratio and 95% Cl			
		Odds ratio	Lower limit	Upper limit	Group-A	Group-B				
	ULTRA 2 2012	1.36	0.49	3.80	9/98	7/101				
	Adalimumab vs. Placebo	1.36	0.49	3.80	9/98	7 / 101				
	OCTAVE 1 2016	9.23	1.24	68.83	32 / 254	1/65				
	OCTAVE 2 2016	19.46	1.17	322.92	28 / 234	0/70				
	Tofacitinib vs. Placebo	11.88	2.32	60.89	60 / 488	1/135				
	UNIFI 2019	11.51	2.65	49.96	21 / 166	2/161				
	Ustekinumab vs. Placebo	11.51	2.65	49.96	21 / 166	2/161				
	VARSITY 2019	2.10	0.90	4.88	18 / 79	10/81				
	Vedolizumab vs. Adalimumab	2.10	0.90	4.88	18 / 79	10/81				
	GEMINI 1 2014	3.30	0.68	16.11	8/82	2/63				
	Motoya 2019	0.96	0.27	3.40	8/85	4/41				
	Vedolizumab vs. Placebo	1.55	0.58	4.16	16 / 167	6 / 104				
							0.01 0.1 1 10 100			
							Eavors Intervention Eavors Control			
в	Efficacy of The	rapies	s for lı	nduct	ion of End	doscop	Dic Improvement — Second-line			
	C	odds L atio	limit	Upper limit	Group-A	Group-B				
	ULTRA 2 2012	1.10	0.59	2.04	28 / 98	27 / 101				
	Adalimumab vs. Placebo	1.10	0.59	2.04	28 / 98	27 / 101				
	OCTAVE 1 2016	4.82	1.68	13.80	61 / 254	4/65				
	OCTAVE 2 2016	4.60	1.60	13.22	51/234	4/70				
	Tofacitinib vs. Placebo	4.71	2.23	9.92	112 / 488	8/135				
	UNIFI 2019	3.64	1.78	7.46	35 / 166	11 / 161				
	Ustekinumab vs. Placebo	3.64	1.78	7.46	35 / 166	11 / 161				
	GEMINI 1 2014	1.69	0.78	3.64	25 / 82	13 / 63				
	Motoya 2019	0.84	0.37	1.93	22 / 85	12/41				
	Vedolizumab vs. Placebo	1.22	0.70	2.15	47 / 167	25 / 104				
							0.1 0.2 0.5 1 2 5 10			
							Favors Intervention Favors Control			



Singh S, Sandborn WJ. Clinical Gastroenterology and Hepatology 2020 182179-2191.

Vedolizumab Versus Adalimumab for Active Ulcerative Colitis





Systematic review with network meta-analysis: first-line induction pharmacotherapy for moderate-severe Crohn's disease

	Experime	intal	Conti	lor		Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI			
1.1.1 Infliximab vs. Placebo										
Lemann 2006	43	57	22	58	90.1%	5.03 [2.25, 11.22]				
Targan 1997	12	27	1	24	9.9%	18.40 [2.16, 156.58]				
Subtotal (95% CI)		84		82	100.0%	6.35 [3.04, 13.28]				
Total events	55		23							
Heterogeneity: Chi ² =	1.27, df =	1 (P =	0.26); P	= 229	í					
Test for overall effect:	Z = 4.91	(P < 0.0)	00001)							
1.1.2 Adalimumah vs	Placebo									
CLASSIC 1 2006	57	76	à	74	91 EV	2 08 11 72 0 221				
Watanaha 2011	6	14	2	10	19.5%	2 00 10 46 19 591				
Subtotal (95% CI)	0	90	-	84	100.0%	3.80 [1.76, 8.18]				
Total events	22		11							
Heterogeneity Chi ² =	0.07. df =	1 (P =	0.791 8	- 0%						
Test for overall effect:	7 = 3.41	P = 0.0	00061							
		ų — 4.								
1.1.3 Certolizumab p	egol vs. P	lacebo								
Sandborn 2011	68	215	53	209	100.0%	1.36 (0.89, 2.08)	+			
Subtotal (95% CI)		215		209	100.0%	1.36 [0.89, 2.08]	★			
Total events	68		53							
Heterogeneity: Not app	plicable									
Test for overall effect:	Z = 1.43	(P = 0.)	15)							
1.1.4 Vedolizumah v	. Placebo									
CEMIN II 2013	21	115	7	78	62.1%	2 27 10 91 5 621				
CEMIN II 2014	16	51	é	50	17.08	2 35 11 10 0 471				
Subtotal (95% CI)	10	166		128	100.0%	2.68 [1.35, 5.31]				
Total events	37		13			,,				
Heterogeneity Chi ² =	0.31 m =	1 (P =	0.581 P	- 05						
Test for overall effect:	Z = 2.82	P = 0.0	0051							
There is a second second		0 - 0.1								
1.1.5 Ustekinumab vs. Placebo										
UNITI-2 2016	80	200	39	200	100.0%	2.75 [1.76, 4.32]				
Subtotal (95% CI)		200		200	100.0%	2.75 [1.76, 4.32]				
Total events	80		39							
Heterogeneity: Not app	plicable									
Test for overall effect: $Z = 4.41$ (P < 0.0001)										
							0.05 0 2 1 6 20			
Figure 3							Favours control Favours experimental			

Singh S, Sandborn WJ. Alimentary Pharmacology & Therapeutics 2018.

Systematic review with network meta-analysis: second-line induction pharmacotherapy for moderate-severe Crohn's disease



Figure 4

Singh S, Sandborn WJ. Alimentary Pharmacology & Therapeutics 2018.



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our <u>disclaimer</u> for details.

ClinicalTrials.gov Identifier: NCT03464136

Recruitment Status ① : Active, not recruiting First Posted ① : March 13, 2018 Last Update Posted ① : September 30, 2020

Guselkumab induction therapy in patients with moderate-tosevere Crohn's disease

Clinical Remission



Sandborn W. UEGW 2020 Abstract.

New Agents

The IBD Pipeline

- Anti-integrin therapy
 - Etrolizumab
 - **PTG-200**
 - ZP10000
 - **MORF-057**
- Janus kinase (JAK) inhibitor therapy Filgotinib – JAK1 Upadacitinib – JAK1 Izencitinib (TD-1473) – JAK 1,2,3 Abrocitinib (PF-06700841) – JAK1 Ritlecitinib (PF 06651600) – JAK3 Brepocitinib (PF-06700841) – Tyk2 Deucravacitinib (BMS-986165) – Tyk2
- S1P1 modulator therapy
 - Ozanimod
 - **Etrasimod**
 - Amiselmod
- Lymphocyte Activation Gene-3 GSK'781

- Anti-interleukin 12 (p19) therapy Geselkumab
 - Risankizumab
 - Mirikizumab Brazikumab
- Microbiome SER-287
- HIF-a Stabilizer GB004
- Anti-TL1A therapy PF-06480605 PRA023
- Cyclosporine ST-0529
- Cap binding complex/micro RNA 124 ABX464
- TLR-9 antisense Cobitolimod
- LANCL2 BT11

New Agents in Phase 3

JAK inhibitors Filgotinib Upadacitinib • Anti-p19 (interleukin 23) antibodies Risankizumab **Mirikizumab** Guselkumab **Brazikumab** S1P modulators Ozanimod **Etrasimod**

Ozanimod induction therapy in patients with moderate-to-severe ulcerative colitis: results at Week 10



^a3-component Mayo score results: rectal bleeding score (RBS) = 0, stool frequency score ≤ 1 and ≥ 1 -point reduction from baseline, and mucosal endoscopy score (MES) ≤ 1 without friability; ^bReduction in 3-component Mayo score of ≥ 2 points and $\geq 35\%$, and reduction in RBS of ≥ 1 point or absolute RBS of ≤ 1 point; ^cMES ≤ 1 without friability; ^dEndoscopic improvement plus histological remission (Geboes<2.0; no neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue) in the same patient.

Data based on all randomized patients who received ≥ 1 dose of study treatment (intent-to-treat population). Missing data handled using non-responder imputation. *P*-values refer to odds ratios (not shown) based on 2-sided Cochran-Mantel-Haenszel test.

Sandborn W. UEGW 2020 Abstract.

Ozanimod maintenance therapy in patients with moderate-to-severe ulcerative colitis who responded to ozanimod induction therapy: results at Week 52



 a Clinical remission at 52 weeks in the subset of patients who were in remission at Week 10; b Clinical remission at 52 weeks without corticosteroids for \geq 12 weeks; c Remission at Weeks 10 and 52 in all patients who entered the maintenance phase.

Data based on all randomized patients who received ≥ 1 dose of study treatment (intent-to-treat population). Missing data handled using non-responder imputation. *P*-values based on odds ratios (not shown) using a 2-sided Cochran-Mantel-Haenszel test.

Sandborn W. UEGW 2020 Abstract.

Local Delivery of Drugs to the GI Tract

Small molecules

 Mesalamine
 Budesonide
 Izencitinib (TD-1473)
 MORF-057
 GB004
 ST-0529

Antisense
 Cobitolimod

Combination Therapy

SONIC: Clinical Remission Without Corticosteroids at Week 26 in Crohn's Disease



IFX, infliximab AZA, azathioprine

Colombel JF, Sandborn WJ, et al. N Engl J Med. 2010 Apr 15;362(15):1383-1395.

Efficacy and safety of simultaneous treatment with two biologic medications in refractory Crohn's disease

Edward Yang¹ | Nicola Panaccione² | Natalie Whitmire¹ | Parambir S. Dulai¹ | Niels Vande Casteele¹ | Siddharth Singh¹ | Brigid S. Boland¹ | Angelina Collins¹ | William J. Sandborn¹ | Remo Panaccione³ | Robert Battat^{1,4}

	Baseline	Post treatment
PRO-2 score (median)	24.1	13.4
Clinical remission	0/22 (0%)	9/22 (41%)
Mild	2/22 (9%)	2/22 (9%)
Moderate	20/22 (91%)	9/22 (41%)
Severe	0/22 (0%)	2/22 (9%)
Clinical response	n/a	11/22 (50%)
Endoscopic		
Remission	0/23 (0%)	6/23 (26%)
Improvement	n/a	10/23 (43%)

Combination Biologics: Prospective Trials

- Vedolizumab, adalimumab, methotrexate
- Geselkumab, golimumab

Possible Combinations

	Anti-TNF	Selective anti- integrin	Anti-IL 12/23	Anti IL 23	Systemic JAK inhibitor	Local JAK inhibitor	S1P1 modulator
Anti-TNF	NA	Yes	? No	?	No	Yes	? No
Selective anti- integrin	Yes	NA	Yes	Yes	Yes	Yes	Yes
Anti IL 12/23	? No	Yes	NA	NA	? No	Yes	?
Anti IL 23	?	Yes	NA	NA	No	Yes	?
Systemic JAK inhibitor	No	Yes	No	No	NA	Yes	? Yes
Local JAK inhibitor	Yes	Yes	Yes	Yes	Yes	NA	Yes
S1P1 modulator	? No	Yes	Yes	Yes	No	Yes	NA

Individual Therapies (Precision Medicine)

- Clinical decision support tools
- Therapeutic drug monitoring
- Companion diagnostic tests

Prognostic Clinical Decision Support Tool (CDST) with stratified treatment outcomes in the VICTORY consortium in patients with ulcerative colitis



Dulai PS, Sandborn WJ. Clinical Gastroenterology and Hepatology 2020.

Prognostic Clinical Decision Support Tool (CDST) with stratified treatment outcomes in the VICTORY consortium in patients with Crohn's disease





Gastroenterology 2018 155, 687-695.e10DOI: (10.1053/j.gastro.2018.05.039) Copyright © 2018 AGA Institute<u>Terms and Conditions</u> Dulai P, Sandborn WJ. Gastroenterology 2018

Treatment algorithm in patients with clinical symptoms (infliximab and HACA concentrations)



¹Patients should have endoscopic or radiologic imaging ²This strategy may be preferable HACA, human anti-chimeric antibody; TNF, tumor necrosis factor

Afif W, Sandborn WJ. Am J Gastroenterol 2010

RBC Thiopurine Methyl Transferase (TPMT) Enzyme Activity in 283 Clinical Laboratory Samples



Otterness: Clin Pharmacol Ther, 1997

Percent change from baseline in serum IL22 levels in MEDI2070 and placebo groups (A) and percentage of patients with clinical response (B) and with clinical remission (C) over time, by baseline serum IL22 levels.







Sands BE. *Gastroenterology* 2017 153, 77-86.e6DOI: (10.1053/j.gastro.2017.03.049) Copyright © 2017 AGA Institute Terms and Conditions

What Does the Future Hold

- Combination therapy AND
- Local delivery of drugs to the GI tract AND
- Precision medicine

Conclusions

- Positioning of biologics can be informed by network metaanalyses and head to head trials
- There is a large pipeline of new agents for IBD. Late stage products are focused on JAK inhibitors, anti-p19 (interleukin 23) antibodies, and S1P modulators
- Multiple agents targeting gut delivery are in early stage development
- Precision medicine will play an increasing role in the care of IBD patients