

**Table S1: The search strategy to identify the top 100 highest-cited original articles from WOSCC database.**

Type	Search Query	Results
Search #1	TOPIC: (biologic therapy) OR TOPIC: (biological therapy) OR TOPIC: (biologic treatment) OR TOPIC: (biological treatment) OR TOPIC: (biologic agent) OR TOPIC: (biological agent) OR TOPIC: (biologic drugs) OR TOPIC: (biological drugs) OR TOPIC: (anti-tumor necrosis factor) OR TOPIC: (anti-TNF) OR TOPIC: (infliximab) OR TOPIC: (IFX) OR TOPIC: (adalimumab) OR TOPIC: (ADA) OR TOPIC: (certolizumab) OR TOPIC: (CZP) OR TOPIC: (anti-integrin) OR TOPIC: (vedolizumab) OR TOPIC: (VEDO) OR TOPIC: (natalizumab) OR TOPIC: (NAT) OR TOPIC: (anti-IL-12/23) OR TOPIC: (ustekinumab) OR TOPIC: (UST)	403,580
Search #2	TOPIC: (Crohn disease) OR TOPIC: (Crohn's disease)	49,706
Search #3	#1 AND #2 AND Document Types: (Articles)	5,489

Note:

Indexes= SCI-EXPANDED, CCR-EXPANDED.

Timespan= From January, 1991 to December, 2020.

WOSCC: Web of Science Core Collection.

**Table S2: The top 100 highest-cited original articles in the biologic therapy of CD.**

Rank	Article	TC
1	Hanauer SB, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. <i>Lancet</i> . 2002;359:1541-1549.	2,978
2	Keane J, et al. Tuberculosis associated with infliximab, a tumor necrosis factor (alpha)-neutralizing agent. <i>New Engl J Med</i> . 2001;345:1098-1104.	2,649
3	Rutgeerts P, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. <i>New Engl J Med</i> . 2005;353:2462-2476.	2,461
4	Present DH, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. <i>New Engl J Med</i> . 1999;340:1398-1405.	1,931
5	Colombel JF, et al. Infliximab, Azathioprine, or Combination Therapy for Crohn's Disease. <i>New Engl J Med</i> . 2010;362:1383-1395.	1,923
6	Baert F, et al. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. <i>New Engl J Med</i> . 2003;348:601-608.	1,517
7	Colombel JF, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: The CHARM trial. <i>Gastroenterology</i> . 2007;132:52-65.	1,460
8	Sands BE, et al. Infliximab maintenance therapy for fistulizing Crohn's disease. <i>New Engl J Med</i> . 2004;350:876-885.	1,436
9	Hanauer SB, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial. <i>Gastroenterology</i> . 2006;130:323-332.	1,114
10	Sandborn WJ, et al. Vedolizumab as Induction and Maintenance Therapy for Crohn's Disease. <i>New Engl J Med</i> . 2013;369:711-721.	1,054
11	Dignass A, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Current management. <i>J Crohns Colitis</i> . 2010;4:28-62.	1,045
12	Vandullemen HM, et al. Treatment of Crohn's disease with antitumor necrosis factor chimeric monoclonal-antibody (CA2). <i>Gastroenterology</i> . 1995;109:129-135.	926
13	Rutgeerts P, et al. Efficacy and safety of retreatment with anti-tumor necrosis factor antibody (infliximab) to maintain remission in Crohn's disease. <i>Gastroenterology</i> . 1999;117:761-769.	873
14	Hueber W, et al. Secukinumab, a human anti-IL-17A monoclonal antibody, for moderate to severe Crohn's disease: unexpected results of a randomised, double-blind placebo-controlled trial. <i>Gut</i> . 2012;61:1693-1700.	872
15	D'Haens G, et al. Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn's disease: an open	863

randomised trial. *Lancet*. 2008;371:660-667.

16 Gomollon F, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. *J Crohns Colitis*. 2017;11:3-25. 835

17 Sandborn WJ, et al. Certolizumab pegol for the treatment of Crohn's disease. *New Engl J Med*. 2007;357:228-1238. 791

18 Schreiber S, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. *New Engl J Med*. 2007;357:239-250. 762

19 Van Assche G, et al. Brief report - Progressive multifocal leukoencephalopathy after natalizumab therapy for Crohn's disease. *New Engl J Med*. 2005;353:362-368. 759

20 Froslic KF, et al. Mucosal healing in inflammatory bowel disease: Results from a Norwegian population-based cohort. *Gastroenterology*. 2007;133:412-422. 750

21 Colombel JF, et al. The safety profile of infliximab in patients with Crohn's disease: The Mayo Clinic experience in 500 patients. *Gastroenterology*. 2004;126:19-31. 690

22 Beaugerie L, et al. Lymphoproliferative disorders in patients receiving thiopurines for inflammatory bowel disease: a prospective observational cohort study. *Lancet*. 2009;374:1617-1625. 686

23 Rutgeerts P, et al. Comparison of scheduled and episodic treatment strategies of infliximab in Crohn's disease. *Gastroenterology*. 2004;126:402-413. 685

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25 Sandborn WJ, et al. Adalimumab induction therapy for Crohn disease previously treated with infliximab - A randomized trial. *Ann Intern Med*. 2007;146:829-838. 668

26 Sandborn WJ, et al. Etanercept for active Crohn's disease: A randomized, double-blind, placebo-controlled trial. *Gastroenterology*. 2001;121:1088-1094. 663

27 Sandborn WJ, et al. Ustekinumab induction and maintenance therapy in refractory Crohn's disease. *New Engl J Med*. 2012;367:1519-1528. 656

28 Lichtenstein GR, et al. Serious infections and mortality in association with therapies for Crohn's disease: TREAT registry. *Clin Gastroenterol Hepatol*. 2006;4:621-630. 655

29 Sandborn WJ, et al. Natalizumab induction and maintenance therapy for Crohn's disease. *New Engl J Med*. 2005;353:1912-1925. 651

30	Suhre K, et al. Human metabolic individuality in biomedical and pharmaceutical research. <i>Nature</i> . 2011;477:54-60.	632
31	Feagan BG, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. <i>New Engl J Med</i> . 2016;375:1946-1960.	623
32	Parameswaran N, et al. Tumor necrosis factor- $\alpha$ signaling in macrophages. <i>Crit Rev Eukaryot Gene Expr</i> . 2010.20:87-103.	618
33	Ghosh S, et al. Natalizumab for active Crohn's disease. <i>New Engl J Med</i> . 2003;348:24-32.	616
34	Van Den Brande JMH, et al. Infliximab but not etanercept induces apoptosis in lamina propria T-lymphocytes from patients with Crohn's disease. <i>Gastroenterology</i> . 2003;124:1774-1785.	575
35	Beaugerie L, et al. Predictors of Crohn's disease. <i>Gastroenterology</i> . 2006;130:650-656.	572
36	D'Haens G, et al. Endoscopic and histological healing with infliximab anti-tumor necrosis factor antibodies in Crohn's disease: A European multicenter trial. <i>Gastroenterology</i> . 1999;116:1029-1034.	569
37	Baert F, et al. Mucosal healing predicts sustained clinical remission in patients with early-stage Crohn's disease. <i>Gastroenterology</i> . 2010;138:463-468.	563
38	Hyams J, et al. Induction and maintenance infliximab therapy for the treatment of moderate-to-severe Crohn's disease in children. <i>Gastroenterology</i> . 2007;132:863-873.	554
39	Yousry TA, et al. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. <i>New Engl J Med</i> . 2006;354:924-933.	550
40	Sandborn WJ, et al. A randomized trial of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with moderate-to-severe Crohn's disease. <i>Gastroenterology</i> . 2008;135:1130-1141.	532
41	Ruemmele FM, et al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. <i>J Crohns Colitis</i> . 2014;8:1179-1207.	517
42	Scallon B, et al. Binding and functional comparisons of two types of tumor necrosis factor antagonists. <i>J Pharmacol Exp Ther</i> . 2002;301:418-426.	514
43	Garcia-Olmo D, et al. Expanded adipose-derived stem cells for the treatment of complex perianal fistula: a Phase II clinical trial. <i>Dis Colon Rectum</i> . 2009;52:79-86.	498
44	Cosnes J, et al. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. <i>Gut</i> . 2005;54:237-241.	490
45	Hanauer SB, et al. Incidence and importance of antibody responses to infliximab after maintenance or episodic treatment in Crohn's disease. <i>Clin</i>	489

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60 Rutgeerts P, et al. Scheduled maintenance treatment with infliximab is superior to episodic treatment for the healing of mucosal ulceration associated with Crohn's disease. *Gastrointest Endosc.* 2006;63:433-442. 424

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77	Ciccocioppo R, et al. Autologous bone marrow-derived mesenchymal stromal cells in the treatment of fistulising Crohn's disease. <i>Gut</i> . 2011;60:788-798.	358
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CD: Crohn disease; TC: Total citation.