| **Author, year** | **Study design** | **Start year of enrollment / Length of followup** | **Location / Multicenter** | **Adherence reported / Adherence >80% in each study arm** | **Inclusion criteria** |
| --- | --- | --- | --- | --- | --- |
| **Randomized controlled trials evaluating biologics** |
| Colombel, 200782 | RCT, parallel arms with a 4-week run-in period | Start year: 2003Duration of assigned treatment: 52 weeks | US, North America, Europe, Australia, AfricaMulticenter | No | Adults, CD only, CDAI (220-450), no use of adalimumab, moderate-severe disease, not pregnant, not nursing, using adequate contraception, no short bowel syndrome, no ostomy, no obstructive symptoms with strictures, no history of TB, no demyelinating disease, no cancer, other criteria |
| Feagan, 200781 | RCT, parallel arms | Start year: 2001Duration of assigned treatment: 48 weeks | US, North America, Europe, Australia, AfricaMulticenter | No | Adults, CD only, CDAI (<220), no short bowel syndrome, no ostomy, no abscess, no obstructive symptoms with strictures, other criteria |
| Feagan, 200890 | RCT, parallel arms with a 4-week run-in period | Start year: 2003Duration of assigned treatment: 52 weeks | US, North America, EuropeMulticenter | No | Adults, CD only, no previous surgery (bowel resection in past 6 months), CDAI (220-450), no use of adalimumab, moderate-severe disease, not pregnant, not nursing, using adequate contraception, no short bowel syndrome, no ostomy, no obstructive symptoms with strictures, no history of TB, no demyelinating disease, no cancer, other criteria |
| Hanauer, 200286 | RCT, parallel arms with a 2-week run-in period | Start year: 1999Duration of assigned treatment: 52 weeks | US, North America, Europe, IsraelMulticenter | No | Adults, CD only, CDAI (220-400), previous use of antibiotics, 5-aminosalicylate acids, corticosteroids, thiopurines, methotrexate, no use of TNF-alpha inhibitors, infliximab, other criteria |
| Mantzaris, 200988 | RCT, parallel arms with a 6-week run-in period | Start year: NRDuration of assigned treatment: 2 years | EuropeNumber of centers NR | YesYes | Adults, CD only, CDAI (>180), active disease, not pregnant, not nursing, no history of TB, other criteria |
| Rutgeerts, 199985 | RCT, parallel arms with a 16-week run-in period | Start year: 1995Duration of assigned treatment: 36 weeks | US, North America, EuropeMulticenter | YesYes | Adults, CD only, no previous surgery (proctocolectomy or total colectomy), CDAI (220-400), no ostomy, no obstructive symptoms with strictures, other criteria |
| Sandborn, 200783 | RCT, parallel arms with a 4-week run-in period | Start year: 2002Duration of assigned treatment: 52 weeks | US, North America, EuropeMulticenter | No | Adults, CD only, CDAI (<150), in remission for >4 weeks, inactive disease, using adequate contraception, other criteria |
| Sands, 200487 | RCT, parallel arms with a 14-week run-in period | Start year: 2000Duration of assigned treatment: 40 weeks | US, North America, Europe, IsraelMulticenter | No | Adults, CD only, no use of infliximab, no abscess, no obstructive symptoms with strictures, other criteria |
| Schreiber, 200784 | RCT, parallel arms with a 6-week run-in period | Start year: 2004Duration of assigned treatment: 18 weeks | WorldwideMulticenter | No | Adults, CD only, CDAI (220-450), no use of TNF-alpha inhibitors, infliximab, adalimumab, certolizumab pegol, no short bowel syndrome, no ostomy, no abscess, no obstructive symptoms with strictures, no history of TB, no demyelinating disease, no cancer, other criteria |
| Van Assche, 200889 | RCT, parallel arms | Start year: 2004Duration of assigned treatment: 2 years | EuropeMulticenter | No | Pediatrics, adults, CD only, previous use of methotrexate, infliximab, immunosuppressives (azathioprine/6-MP or methotrexate), perianal fistulizing, not pregnant, not nursing, other criteria |
| **Randomized controlled trials evaluating thiopurines** |
| Candy, 199553 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 12 weeks | AfricaSingle center | No | Pediatrics, adults, CD only, no previous surgery (extensive surgery for Crohn's disease), CDAI (>200), not pregnant, not nursing, other criteria |
| Lemann, 200598 | RCT, parallel arms | Start year: 1995Duration of assigned treatment: 18 months | EuropeMulticenter | No | Adults, CD only, no previous surgery (except limited perianal surgery in past 42 months), CDAI (<150), in remission for >42 months, previous use of azathioprine, no use of antibiotics, 5-aminosalicylate acids, corticosteroids, inactive disease, other criteria |
| Mantzaris, 2009102 | RCT, parallel arms | Start year: 1998Duration of assigned treatment: 1.5 years | EuropeNumber of centers NR | YesYes | Adults, CD only, no previous surgery (intestinal resection), CDAI (<150), previous use of corticosteroids, no use of infliximab, mesalamine-only maintenance therapy, effective prior treatment with azathioprine, perianal fistulizing, not pregnant, not nursing, no history of TB, other criteria |
| O'Donoghue, 1978100 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 6 months | EuropeSingle center | YesYes | Adults, CD only, in remission for >6 months, previous use of azathioprine, inactive disease |
| Rosenberg, 1975104 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 26 weeks | USSingle center | YesYes | Adults, CD only, previous use of corticosteroids, not pregnant, not nursing, other criteria |
| Summers, 197956 | RCT, parallel arms | Start year: 1971Duration of assigned treatment: 24 months | USMulticenter | No | Adults, CD only, CDAI (<150), inactive disease, not pregnant, no abscess, no obstructive symptoms with strictures, no history of TB, other criteria |
| Vilien, 2004101 | RCT, parallel arms | Start year: 2000Duration of assigned treatment: 1 year | Location: NRNumber of centers NR | No | CD only, no previous surgery (in past 3 months), previous use of thiopurines, azathioprine, no use of corticosteroids, inactive disease, other criteria |
| Willoughby JM, 197199 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 24 weeks | EuropeSingle center | No | CD only, previous use of corticosteroids, active and inactive disease |
| **Randomized controlled trials evaluating methotrexate** |
| Feagan, 2000105 | RCT, parallel arms | Start year: 1993Duration of assigned treatment: NR | US, North AmericaMulticenter | YesYes | Adults, CD only, previous use of methotrexate, inactive disease, not pregnant, no cancer, other criteria |
| **Randomized controlled trials evaluating corticosteroids** |
| Bergman, 1976223 | RCT, parallel arms | Start year: 1969Duration of assigned treatment: 33 weeks | EuropeMulticenter | YesYes | Adults, CD only, no use of corticosteroids, salazopyrine, azathioprine, other criteria |
| Brignola, 1988112 | RCT, parallel arms with a 4-week run-in period | Start year: 1983Duration of assigned treatment: 6 months | EuropeMulticenter | No | Adults, CD only, CDAI (<150), LI >100, other criteria |
| Cortot, 2001107 | RCT, parallel arms | Start year: 1996Duration of assigned treatment: 22 weeks | Europe, Asia, AfricaMulticenter | No | Adults, CD only, no previous surgery (resection of ileum of >100 cm or who require immediate surgery), CDAI (<201), previous use of corticosteroids, inactive disease, not pregnant, not nursing, no ostomy, no abscess, no history of TB, other criteria |
| de Franchis, 1997118 | RCT, parallel arms with a 4-8-week run-in period | Start year: 1991Duration of assigned treatment: 24 months | EuropeMulticenter | YesYes | Adults, CD only, CDAI (<150), previous use of corticosteroids, no use of immunomodulators in past 3 months, not pregnant, not nursing, no obstructive symptoms with strictures, other criteria |
| Ferguson, 1998108 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 12 months | Europe, AustraliaMulticenter | YesYes | Adults, CD only, no previous surgery (ileostomy or previous small bowel resection of >100 cm), CDAI (<150), inactive disease, not pregnant, not nursing, no ostomy, no abscess, other criteria |
| Greenberg, 199466 | RCT, parallel arms | Start year: 1991Duration of assigned treatment: 8 weeks | North AmericaMulticenter | YesYes | Adults, CD only, CDAI (>200), not pregnant, not nursing, no cancer, other criteria |
| Greenberg, 1996111 | RCT, parallel arms with a 8-week run-in period | Start year: 1992Duration of assigned treatment: 52 weeks | North AmericaMulticenter | YesNo | Adults, CD only, CDAI (<150), inactive disease, not pregnant, not nursing, no ostomy, no cancer, other criteria |
| Gross, 1998109 | RCT, parallel arms | Start year: NRDuration of assigned treatment: NR | EuropeMulticenter | YesYes | Adults, CD only, CDAI (<150), in remission for >8 weeks, previous use of prednisolone |
| Hanauer, 2005106 | RCT, parallel arms | Start year: 1995Duration of assigned treatment: 52 weeks | USMulticenter | YesYes | Adults, CD only, no previous surgery (ileostomy, colostomy, gastric surgery other than for closure of perforation or selective vagotomy or resection of ileum >100cm), CDAI (<150), in remission for >10 weeks, no use of immunomodulators in past 90 days, corticosteroids in past 14 days, mesalamine or NSAIDs for more than 3 consecutive days, inactive disease, not pregnant, not nursing, no history of TB, no cancer, other criteria |
| Issenman, 1993196 | Prospective cohort | Start year: NR Mean followup duration: 2 years | North AmericaSingle center | NA | Pediatrics, CD only, males, active disease |
| Lofberg, 1996110 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 12 months | EuropeMulticenter | YesYes | Adults, CD only, no previous surgery (ilestomy or prior small bowel resection >100 cm), CDAI (<150), no short bowel syndrome, no ostomy, other criteria |
| Malchow, 198464 | RCT, parallel arms | Start year: 1975Duration of assigned treatment: 6 weeks | EuropeMulticenter | YesYes | Adults, CD only, not pregnant, no abscess, no obstructive symptoms with strictures, other criteria |
| Mantzaris, 2003113 | RCT, parallel arms with a 1-month run-in period | Start year: 1994Duration of assigned treatment: 1 year | EuropeSingle center | No | Adults, CD only, no previous surgery (intestinal resection), CDAI (<150), no use of mesalamine maintenance therapy, azathioprine unless withdrawn at least 3 months before start of trial due to side effects, inactive disease, not pregnant, not nursing, other criteria |
| Singleton, 197975 | RCT, parallel arms with a 8-week run-in period | Start year: NRDuration of assigned treatment: 6 months | USMulticenter | YesYes | Adults, CD only, CDAI (<150), previous use of prednisone, sulfasalazine and prednisone, inactive disease, other criteria |
| Summers, 197956 | RCT, parallel arms | Start year: 1971Duration of assigned treatment: 24 months | USMulticenter | No | Adults, CD only, CDAI (<150), inactive disease, not pregnant, no abscess, no obstructive symptoms with strictures, no history of TB, other criteria |
| **Randomized controlled trials evaluating aminosalicylates** |
| Arber, 1995121 | RCT, parallel arms | Start year: 1991Duration of assigned treatment: 12 months | IsraelMulticenter | YesYes | CD only, HBI (<4), in remission for >6 months, other criteria |
| Bresci G, 1995125 | RCT, parallel arms with a 6-week run-in period | Start year: 1988Duration of assigned treatment: 4 years | EuropeSingle center | YesYes | Adults, CD only, no previous surgery , CDAI (<150), Laboratory Index (LI) <100, inactive disease, not pregnant, other criteria |
| Brignola, 1992124 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 4 months | Location: NRSingle center | YesYes | CD only, CDAI (<150), Laboratory activity (LA) >100, in remission for >4 weeks, no use of corticosteroids, corticosteroids in past 4 weeks, inactive disease |
| Cezard, 2009194 | RCT, parallel arms | Start year: 1991Duration of assigned treatment: 1 year | EuropeMulticenter | No | Pediatrics, CD only, HBI (>5), no use of 5-aminosalicylate acids, thiopurines, methotrexate, active disease, other criteria |
| Gendre, 1993122 | RCT, parallel arms | Start year: 1985Duration of assigned treatment: 2 years | EuropeMulticenter | YesYes | CD only, CDAI (<150), in remission for >24 months, no use of corticosteroids, corticosteroids and immunomodulators in past month, inactive disease, not pregnant, other criteria |
| Mahmud, 2001116 | RCT, parallel arms | Start year: 1992Duration of assigned treatment: 52 weeks | EuropeMulticenter | No | Adults, CD only, CDAI (<150), in remission for >1 months, no use of corticosteroids, thiopurines, immunomodulators (other than ASA) not pregnant, not nursing, no obstructive symptoms with strictures, other criteria |
| Malchow, 198464 | RCT, parallel arms | Start year: 1975Duration of assigned treatment: 6 weeks | EuropeMulticenter | YesYes | Adults, CD only, not pregnant, no abscess, no obstructive symptoms with strictures, other criteria |
| Prantera, 1992123 | RCT, parallel arms | Start year: 1988Duration of assigned treatment: 12 months | EuropeMulticenter | YesYes | Adults, CD only, CDAI (<150), perianal fistulizing, no obstructive symptoms with strictures, other criteria |
| Prantera, 2005115 | RCT, parallel arms with a 8-week run-in period | Start year: 2000Duration of assigned treatment: 12 months | EuropeMulticenter | No | CD only, CDAI (150-400), mild-moderate disease, other criteria |
| Summers, 197956 | RCT, parallel arms | Start year: 1971Duration of assigned treatment: 24 months | USMulticenter | No | Adults, CD only, CDAI (<150), inactive disease, not pregnant, no abscess, no obstructive symptoms with strictures, no history of TB, other criteria |
| Sutherland, 1997117 | RCT, parallel arms | Start year: 1990Duration of assigned treatment: 11 months | North AmericaMulticenter | YesYes | Adults, CD only, no previous surgery (proctocolectomy or history of >3 resections in the last 10 years), CDAI (<150), no use of azathioprine, 6-MP or cyclosporine in past 90 days, steroids in past 30 days, mesalamine or metronidazole in past 7 days, perianal fistulizing, no short bowel syndrome, no cancer, other criteria |
| Thomson, 1990224 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 12 months | North America, Europe, AfricaMulticenter | YesYes | Pediatrics, CD only, CDAI (<150), no use of azathioprine, metronidazole, no ostomy, no obstructive symptoms with strictures, other criteria |
| Thomson, 1995120 | RCT, parallel arms | Start year: 1988Duration of assigned treatment: 12 months | US, North America, Europe, Asia, AfricaMulticenter | YesNo | Adults, CD only, no previous surgery (ileostomy, colostomy, or bowel resection with >100 cm of bowel removed; or bowel resection in past 3 months), CDAI (<150), no use of azathioprine, immunomodulators or systemic corticosteroids in past month, not pregnant, not nursing, using adequate contraception, no short bowel syndrome, no obstructive symptoms with strictures, no cancer, other criteria |
| Wellmann W, 1988126 | RCT, parallel arms | Start year: NRDuration of assigned treatment: 1 year | EuropeNumber of centers NR | YesYes | CD only, CDAI (<120), in remission for >3 months, no use of corticosteroids, corticosteroids in past 3 months, inactive disease |

Abbreviations: 6-MP = 6-mercaptopurine; CD = Crohn’s disease; CDAI = Crohn’s Disease Activity Index; HBI = Harvey-Bradshaw Index; NA = not applicable; NR = not reported; RCT = randomized controlled trial; TAS = Trial of Adjunctive Sulfasalazine in Crohn's disease; TB = tuberculosis; US = United States