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**Supplementary Table S1: Characteristics of included studies evaluating induction of endoscopic improvement, and/or endoscopic remission, and/or histologic improvement and/or histologic remission, and/or mucosal healing in ulcerative colitis.**

| AUTHOR | NCT NUMBER, NAME OF STUDY | TRIAL AND INTERVATION CHARACTERISTICS | AGE(MEAN) | MALE SEX (NUMBER %) | DISEASE DURATION (YEARS, MEAN (SD) | BIOLOGIC OR SMALL MOLECULE EXPERIENCE | ORAL GLUCOCORTICOSTEROIDS | DEFINITION OF OUTCOME |
|---|---|---|---|---|---|---|---|---|
| ADALIMUMAB | | | | | | | | |
| Suzuki et. al | NCT00853099, ULTRA-JAPAN, INDUCTION and MAINTENANCE | Induction :ADA-90,P-96 Maintenance:ADA-177,P-96 , treat straight through design | ADA:42.6 P:41.3 | ADA:61(67.8%),P:70(72.9%) | ADA:7.8±7.1, P:7.8±6.6 | ADA-0, P-0 | ADA-57(63.3%) P-58(60.4%) | Endoscopic Improvement MES ≤1 |
| Reinisch et. al | NCT00385736 , ULTRA-1,INDUCTION | Induction: ADA -130, P-130 | ADA:36.5 P:37 | ADA:63.8% P:63.1% | ADA:6.06 P:5.35 | ADA-0, P-0 | ADA-48(36.9%) P-55 (41.5%) | Endoscopic Improvement MES ≤1 |
| Sandborn et. al | NCT00408629, ULTRA -2,INDUCTION and MAINTENANCE | Induction:ADA-248 , P-246, Maintenance :ADA-248,P-246 ,treat straight through design | ADA :39.6,P:41.3 | ADA:142(57.3%) ,P:152(61.8%) | ADA:8.1±7.09, P:8.5±7.37 | ADA-98(39.1%) P-101(41.1%) | ADA-150(60.5%), P-140 (56.9%) | Endoscopic Improvement MES ≤1 |
| ETRASIMOD | | | | | | | | |
| Sandborn et. al | NCT03996369, ELEVATE UC12, INDUCTION | Induction: ETR-238 P-116 | ETR: 40.3 ,P:40.4 | ETR:135(57%),P:73(63%) | ETR:7.3, P:7.7 | ETR-89(37%), P-43(37%) | ETR-177(74%),P-98(84%), | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| Sandborn et. al | NCT03945188,ELEVATE UC 52 , INDUCTION and MAINTENANCE | Maintenance :ETR-289 , P-144, treat straight through design | ETR:41.2, P:38.9 | ETR:152(53%), P:88(61%) | ETR:7.5(8.0),P:5.9(5.5) | ETR-108(37%), P- 55(38%) | ETR-224(78%), P-101(70%) | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |

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|---|---|---|---|---|---|---|---|---|
| Wu et.al | NCT04176588-INDUCTION and MAINTENANCE | Induction: ETR-228, P-112 | NA | NA | NA | NA | NA | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| Takeuchi et.al | NCT04706793-ELEVATE JAPAN, INDUCTION and MAINTENANCE | Induction: ETR-32, P-16 Maintenance : ETR-32, P-16 treat straight through design | ETR:43.7, P:43,3 | ETR: 21(55.6%), P: 8(50%) | ETR:6.2, P: 6.0 | ETR-4(12.5%), P-9(56.3%) | NA | Endoscopic Improvement MES ≤1, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| Sandborn et. al | NCT02447302,OASIS , INDUCTION | Induction:ETR-54,P-50 | ETR:40.4, P:44.8, | ETR:27(54.0%), P: 32(59.3%) | ETR:6.2, P:8.6 | ETR:24(48%), P:30(55.5%) | ETR:18(36%), P:16(29.6%) | Endoscopic Improvement MES ≤1, Histologic Improvement Geboes <3.1, Histologic Remission Geboes <2 |
| FILGOTINIB | | | | | | | | |
| Feagan et. al | NCT02914522,SELECTION, INDUCTION and MAINTENANCE | Induction A P-137, Filgotinib 100 mg -277,Filgotinib 200 mg-245 Induction B P-142, Filgotinib 100 mg -285,Filgotinib 200 mg-262 Maintenance :Placebo 3 groups-93,91,99, Filgotinib 100 mg -179, Filgotinib 200 mg -202. Re-randomisation design | Induction A:P -41, Filgotinib 100 mg-42, Filgotinib 200 mg-42 Induction B:P-44, Filgotinib 100 mg-43, Filgotinib 200 mg-43 | Induction A:P -87(63.5%), Filgotinib 100 mg-157(56.7%),Filgotinib 200 mg-123(50.2%) Induction B: P-86(60.6%), Filgotinib 100 mg-186(65.3%), Filgotinib 200 mg-148(56.5%) | Induction A:P -6.4, Filgotinib 100 mg-6.7, Filgotinib 200 mg-7.2 Induction B:P-10.2, Filgotinib 100 mg-9.7, Filgotinib 200 mg-9.8 | Induction A:P -0, Filgotinib 100 mg-2, Filgotinib 200 mg-0 Induction B:P-139, Filgotinib 100 mg-283, Filgotinib 200 mg-259 | Induction A:P- 34, Filgotinib 100 mg-67, Filgotinib 200 mg-54 Induction B:P-51, Filgotinib 100 mg-103, Filgotinib 200 mg-94 | Endoscopic Improvement MES≤1 ,Ensoscopic Remission MES=0, Histologic Remission Geboes <2, Mucosal Healing =Endoscopic Improvement and Histologic Remission |
| GOLIMUMAB | | | | | | | | |
| Sandborn et. al | NCT00487539, PURSUIT -SC, INDUCTION | Induction: GOL-331 ,P-331 | GOL:40.0, P:39.0 | GOL:180(54.4%), P:175(52.9%) | GOL:6.4 ,P:6.0 | GOL-0, P-0 | GOL:47%, P:43% | Endoscopic Improvement MES ≤1 |
| INFLIXIMAB | | | | | | | | |
| Probert et. al | INDUCTION | Induction:IFX-23, P-20 | IFX:41, P:40 | NA | IFX:6.2,P:4.9 | IFX=0, P=0 | All patients | Endoscopic Remission -Baron score=0 |

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|---|---|---|---|---|---|---|---|---|
| Jiang et. al | INDUCTION and MAINTENANCE | Induction:IFX-41(34completed),P-41(22 completed) Maintenance:IFX-33, P-21 treat straight through design | IFX:34.3, P: 34.5 | IFX:26(63.4%),P:25(60.9%) | IFX:4.4,P:4.4 ,2 | IFX=0, P=0 | IFX:22(53.6%),P:21(51.2%) | Endoscopic Improvement MES ≤1 |
| CNTO312 | NCT01551290,INDUCTION and MAINTENANCE | Induction :IFX-50, P-49 Maintenance:IFX-50, P-49, treat straight through design | IFX:37, P: 37 | NA | IFX:3.7,P:3.7 | IFX=0, P=0 | IFX:30(60%), P:39(79.5%) | Endoscopic Improvement MES ≤1 |
| Rutgeerts et.al | NCT00036439-ACT1,INDUCTION and MAINTENANCE | Induction: IFX-121,P-121 treat straight through design | IFX:42.4,P:41.4 | IFX:78(64.5%) P:72(59.5%) | IFX:5.9, P:6.2, | IFX=0, P=0 | IFX:70(57.8%), P:79(65.2%) | Endoscopic Improvement MES ≤1 |
| Rutgeerts et.al | NCT00096655-ACT2,INDUCTION and MAINTENANCE | Induction :IFX-121,1-P-123 treat straight through design | IFX:40.5, P:39 | IFX:76(62.8%)1, P:71(57.7%) | IFX:6.7, P:6.5 | IFX=0, P=0 | IFX:60(49.5%), P:60(48.7%) | Endoscopic Improvement MES ≤1 |
| Kobayashi et. al | INDUCTION and MAINTENANCE | Induction :IFX-104,P-104 treat straight through design | IFX:40.0,P:37.8 | IFX:66(63.5%),P:67(64.4%) | IFX:8.1,P:7.1 | IFX=0, P=0 | IFX:68(65.4%), P:69(66.3%) | Endoscopic Improvement MES ≤1 |
| MIRIKIZUMAB | | | | | | | | |
| Haens et.al | NCT03518086-LUCENT 1,INDUCTION | Induction: MIRI-868, P-294 | MIRI:42.9, P:41.3 | MIRI:530(61.1%), P:165(56.1%) | MIRI:7.2, P:6.9 | MIRI:361(41.6%), P:118(40.1%) | MIRI:351(40.4%), P:113(38.4%) | Endoscopic Improvement MES ≤1, Mucosal Healing= Endoscopic - Histologic Improvement MES ≤1 and Geboes scoring system with neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue; |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sandborn et. al | NCT02589665, INDUCTION and MAINTENACE | Induction:MIRI-62, P-63 Maintenance Re-randomisation design | MIRI:43.4, P:42.6 | MIRI:37(59.7%), P:36(57.1%) | MIRI:9.0,P:9.5 | MIRI:40(64.5%), P:38(60%) | MIRI:25(40.3%), P:33(52.4%), | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Histologic Remission Geboes scoring system 0 for the neutrophils in lamina propria, neutrophils in epithelium, and erosion or ulceration parameters) |
| OZANIMOD | | | | | | | | |
| Sandborn et. al | NCT01647516-TOUCHSTONE, INDUCTION and MAINTENANCE | Induction:OZA-67, P-65, Maintenance treat straight through design | OZA:41.8, P:41.9 | OZA:48(72%), P:35(54%) | OZA:6.7, P:6.1 | OZA:13(19%), P:10(15%) | OZA:27(40%), P:24(37%) | Endoscopic Improvement MES ≤1, Histologic Remission Geboes<2 |
| Sandborn et. al | NCT02435992-TRUE NORTH, INDUCTION and MAINTENANCE | Induction:OZA-429, P-216, Maintenance Re-randomisation design | OZA:41.4, P:41.9 | OZA:245(57.1%), P:143(66.2%) | OZA:6.9, P:6.8 | OZA:204(47.5%), P:107(49.5%) | OZA:322(75.1%), P:62(75%) | Endoscopic Improvement MES ≤1, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| TOFACITINIB | | | | | | | | |
| Sandborn et. al | NCT00787202, INDUCTION | Induction: TOF-33, P-48 | TOF:43.2, P:42.5 | TOF:21(64%), P:23(48%) | TOF:10.9, P:8.8 | TOF:10(30%), P:15(31%) | TOF:19(58%), P:13(27%) | Endoscopic Remission MES=0 |
| Sandborn et. al | NCT01465763-OCTAVE 1, INDUCTION | Induction:TOF-476, P-122 | TOF:41.3, P:41.8 | TOF:277(58.2%), P:77(63.1%) | TOF:6.5,P:6.0 | TOF:254(53.4%), P:65(53.3%) | TOF:214(45.0%),P:58(47.5%) | Endoscopic Improvement MES≤1 Endoscopic Remission MES=0 |
| Sandborn et. al | NCT01458951-OCTAVE 2, INDUCTION | Induction:TOF-429, P-112 | TOF:41.1,P:40.4 | TOF:259(60.4%),P:55(49.1%) | TOF:6.0,P:6.2 | TOF:234(54.5%), P:65(58.0%) | TOF:198(46.2%),P:55(49.1%) | Endoscopic Improvement MES≤1 Endoscopic Remission MES=0 |
| UPADACITINIB | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|
| Sandborn et. al | NCT02819635, U-ACHIEVE-Induction-SUBSTUDY 1 | Induction:UPA-56, P-46 | UPA:37, P:40 | UPA:37(66.1%),P:29(63%) | UPA:6.46,P:5.19 | UPA:43(76.8%),P:35(76.1%) | UPA:29(51.8%),P:30(65.2%) | Endoscopic Improvement MES≤1 Endoscopic Remission MES=0, Histologic Improvement Any decrease in Geboes scoring system |
| Danese et.al | NCT02819635, U-ACHIEVE-Induction-SUBSTUDY 2 | Induction:UPA-319, P-154 | UPA:43.0,P:44.5 | UPA:198(62%),P:97(63%) | UPA:6.6, P:6.0 | UPA:168(53%), P:78(51%) | UPA:124(39%),P:61(40%) | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Histologic Improvement Any decrease in Geboes scoring system, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| Danese et.al | NCT03653026-U-ACCOMPLISH, INDUCTION | Induction:UPA-341, P-174 | UPA:40.0, P:42.0 | UPA:214(63%), P:107(61%) | UPA:5.6, P:4.9 | UPA:172(50%),P:89(51%) | UPA:120(35%),P:72(41%) | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Histologic Improvement Any decrease in Geboes scoring system, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| USTEKINUMAB | | | | | | | | |
| Sands et .al | NCT02407236-UNIFI, INDUCTION and MAINTENANCE | Induction:UST-322, P-319 Maintenance :UST-176,P-175 Re-randomisation design | UST:41.7, P:41.2 | UST:195(60.6%), P:197(61.8%) | UST:8.2, P:8.0 | UST:166(51.6%),P:161(50.5%) | UST:168(52.2%),P:157(49.2%) | Endoscopic Improvement MES ≤1, Histologic improvement Geboes scoring system 0-<5% neutrophils in epithelium, no crypt destruction, and no erosions or ulcerations or granulations |

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|---|---|---|---|---|---|---|---|---|
| VEDOLIZUMAB | | | | | | | | |
| Feagan et. al | NCT00783718-GEMINI I, INDUCTION and MAINTENANCE | Induction :VEDO-225,P-149, Maintenance:VEDO-122,P-126 Re-randomisation design | VEDO:40.1,P:41 | VEDO:132(58.7%),P:92(61.7%) | VEDO:6.1,P:7.1 | VEDO:95(42.2%),P:73(49%) | VEDO:79(35.1%),P:58(38.9%) | Endoscopic Improvement MES ≤1 |
| Motoya et.al | NCT02039505, INDUCTION and MAINTENANCE | Induction :VEDO-164, P-82, Maintenance:VEDO-41, P-42 Re-randomisation design | VEDO:42.3, P:44.0 | VEDO:99(60.4%), P:55(67.1%) | VEDO:7.2, P:8.6 | VEDO:85(51.8%), P:41(50.0%) | VEDO:31(18.9%), P:11(13.4%) | Endoscopic Improvement MES ≤1 |
| RISANKIZUMAB | | | | | | | | |
| Louis et.al | NCT03398148-INSPIRE, INDUCTION | Induction: RIS-650, P-325 | RIS:41.8, P;42.8 | RIS:385(59.2%), P:201(61.8%) | RIS:7.7, P:8.1 | NA | RIS:236(36.3%), P:112(34.5%) | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| GOLIMUMAB AND GUSELKUMAB | | | | | | | | |
| Feagan et .al | NCT03662542-VEGA, INDUCTION and MAINTENANCE | Induction:GOL-72, GUS-71, GOL/GUS-71, Maintenance treat straight through strategy | GOL:38.1, GUS:39.1, GOL/GUS:37.8 | GOL:42(58%), GUS:40(56%), GOL/GUS:34(48%) | GOL:4.7,GUS:5.4, GOL/GUS:4.6 | NA | NA | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Histologic Remission Geboes<2, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| GUSELKUMAB | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|
| Rubin et.al | NCT04033445-Quasar phase 3, INDUCTION and MAINTENANCE | Induction :Guselkumab 200mg-190, Guselkumab 100mg-188, P-190, Maintenance Re-randomisation design | NA | NA | NA | NA | NA | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Histologic Remission Geboes≤2, Histologic Improvement Geboes ≤3.1, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes ≤2 |
| Peyrin-Biroulet et.al | NCT04033435-QUASAR 2b, INDUCTION | Induction: GUS-101, P-105 | GUS:43.3, P:41.2 | GUS:60(59.4%),P:66(62.9%) | GUS:7.0,P:7.7 | GUS:53(52.4%), P:54(51.4%) | GUS:41(40.6%),P:40(38.1%) | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Mucosal healing = Endoscopic improvement and Histologic improvement Geboes score ≤3.1) |

ADA=Adalimumab, Baron score: 0- normal, 1- abnormal mucosal but not hemorrhagic, 2- friability, easy to bleeding , 3 -spontaneous bleeding, ETR=Etrasimod GOL=Golimumab, GUS=Guselkumab, IFX=Infliximab, MES=Mayo Endoscopic Score, MIRI=Mirikizumab, P=Placebo, OZA=Ozanimod, , RIS= Risankizumab TOF=Tofacitinib, UPA=Upadacitinib, , UST= Ustekinumab, VEDO=Vedolizumab

**Supplementary Table S2: Characteristics of included studies evaluating maintenance of endoscopic improvement, and/or endoscopic remission, and/or histologic improvement and/or histologic remission, and/or mucosal healing in ulcerative colitis.**

| AUTHOR | NCT NUMBER, NAME OF STUDY | TRIAL AND INTERVATION CHARACTERISTICS | AGE(MEAN) | MALE SEX (NUMBER %) | DISEASE DURATION (YEARS, MEAN (SD) | BIOLOGIC OR SMALL MOLECULE EXPERIENCE | ORAL GLUCOCORTICOSTEROIDS | DEFINITION OF OUTCOME |
|---|---|---|---|---|---|---|---|---|
| ADALIMUMAB | | | | | | | | |
| Suzuki et. al | NCT00853099, ULTRA-JAPAN, INDUCTION and MAINTENANCE | Induction :ADA-90,P-96 Maintenance:ADA-177,P-96 , treat straight through design | ADA:42.6 P:41.3 | ADA:61(67.8%),P:70(72.9%) | ADA:7.8±7.1, P:7.8±6.6 | ADA-0, P-0 | ADA-57(63.3%) P-58(60.4%) | Endoscopic Improvement MES ≤1 |
| Sandborn et. al | NCT00408629, ULTRA -2,INDUCTION and MAINTENANCE | Induction:ADA-248 , P-246, Maintenance :ADA-248,P-246 ,treat straight through design | ADA :39.6,P:41.3 | ADA:142(57.3%) ,P:152(61.8%) | ADA:8.1±7.09, P:8.5±7.37 | ADA-98(39.1%) P-101(41.1%) | ADA-150(60.5%), P-140 (56.9%) | Endoscopic Improvement MES ≤1 |
| ETRASIMOD | | | | | | | | |
| Sandborn et. al | NCT03945188,ELEVATE UC 52 , INDUCTION and MAINTENANCE | Maintenance :ETR-289 , P-144, treat straight through design | ETR:41.2, P:38.9 | ETR:152(53%), P:88(61%) | ETR:7.5(8.0),P:5.9(5.5) | ETR-108(37%), P- 55(38%) | ETR-224(78%), P-101(70%) | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| Takeuchi et.al | NCT04706793-ELEVATE JAPAN, INDUCTION and MAINTENANCE | Induction: ETR-32, P-16 Maintenance : ETR-32, P-16 treat straight through design | ETR:43.7, P:43,3 | ETR: 21(55.6%), P: 8(50%) | ETR:6.2, P: 6.0 | ETR-4(12.5%), P-9(56.3%) | NA | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |
| FILGOTINIB | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|
| Feagan et. al | NCT02914522,SELECTION, INDUCTION and MAINTENANCE | Induction A P-137, Filgotinib 100 mg -277,Filgotinib 200 mg-245 Induction B P-142, Filgotinib 100 mg -285,Filgotinib 200 mg-262 Maintenance :Placebo 3 groups-93,91,99, Filgotinib 100 mg -179, Filgotinib 200 mg -202. Re-randomisation design | Induction A:P -41, Filgotinib 100 mg-42, Filgotinib 200 mg-42 Induction B:P-44, Filgotinib 100 mg-43, Filgotinib 200 mg-43 | Induction A:P -87(63.5%), Filgotinib 100 mg-157(56.7%),Filgotinib 200 mg-123(50.2%) Induction B: P-86(60.6%), Filgotinib 100 mg-186(65.3%), Filgotinib 200 mg-148(56.5%) | Induction A:P -6.4, Filgotinib 100 mg-6.7, Filgotinib 200 mg-7.2 Induction B:P-10.2, Filgotinib 100 mg-9.7, Filgotinib 200 mg-9.8 | Induction A:P -0, Filgotinib 100 mg-2, Filgotinib 200 mg-0 Induction B:P-139, Filgotinib 100 mg-283, Filgotinib 200 mg-259 | Induction A:P- 34, Filgotinib 100 mg-67, Filgotinib 200 mg-54 Induction B:P-51, Filgotinib 100 mg-103, Filgotinib 200 mg-94 | Endoscopic Improvement MES≤1 ,Ensoscopic Remission MES=0, Histologic Remission Geboes <2, Mucosal Healing =Endoscopic Improvement and Histologic Remission |
| GOLIMUMAB | | | | | | | | |
| Hibi et.al | NCT01863771, PURSUIT-J, INDUCTION-OPEN LABEL and MAINTENANCE -DOUBLE BLINDED | Maintenance :GOL -32,P-31 | GOL:39.3,P:42.9 | GOL:19(59%), P:19(61%) | GOL:5.35, P:5,74 | GOL-0, P-0 | GOL:9(28%), 2-9(29%) | Endoscopic Improvement MES ≤1 |
| Sandborn et. al | NCT00488631, PURSUIT-M,MAINTENANCE only randomised | Maintenance :GOL-154, P-156, Re-randomisation design | GOL:39,1, P:40.2 | GOL:89(57.8%), P:75(48.1%) | GOL:7.2, P:-6.9 | GOL-0, P-0 | GOL-79(51.3%), P-83(53.2%) | Endoscopic Improvement MES ≤1 |
| INFLIXIMAB | | | | | | | | |
| Jiang et. al | INDUCTION and MAINTENANCE | Induction:IFX-41(34completed),P-41(22 completed) Maintenance:IFX-33, P-21 treat straight through design | IFX:34.3, P: 34.5 | IFX:26(63.4%),P:25(60.9%) | IFX:4.4,P:4.4 ,2 | IFX=0, P=0 | IFX:22(53.6%),P:21(51.2%) | Endoscopic Improvement MES ≤1 |
| CNTO312 | NCT01551290,INDUCTION and MAINTENANCE | Induction :IFX-50, P-49 Maintenance:IFX-50, P-49, treat straight through design | IFX:37, P: 37 | NA | IFX:3.7,P:3.7 | IFX=0, P=0 | IFX:30(60%), P:39(79.5%) | Endoscopic Improvement MES ≤1 |
| Rutgeerts et.al | NCT00036439-ACT1,INDUCTION and MAINTENANCE | Induction: IFX-121,P-121 treat straight through design | IFX:42.4,P:41.4 | IFX:78(64.5%) P:72(59.5%) | IFX:5.9, P:6.2, | IFX=0, P=0 | IFX:70(57.8%), P:79(65.2%) | Endoscopic Improvement MES ≤1 |
| Rutgeerts et.al | NCT00096655-ACT2,INDUCTION and MAINTENANCE | Induction :IFX-121,1-P-123 treat straight through design | IFX:40.5, P:39 | IFX:76(62.8%)1, P:71(57.7%) | IFX:6.7, P:6.5 | IFX=0, P=0 | IFX:60(49.5%), P:60(48.7%) | Endoscopic Improvement MES ≤1 |
| Kobayashi et. al | INDUCTION and MAINTENANCE | Induction :IFX-104,P-104 treat straight through design | IFX:40.0,P:37.8 | IFX:66(63.5%),P:67(64.4%) | IFX:8.1,P:7.1 | IFX=0, P=0 | IFX:68(65.4%), P:69(66.3%) | Endoscopic Improvement MES ≤1 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sands et .all | NCT04205643-LIBERTY-UC, MAINTENANCE | Maintenance :IFX-294, P-144, Re-randomisation design | IFX:37,P:39 | IFX:163(55.4%), P:83(57.6%) | IFX:6.09, P:6.8 | IFX:29(9.9%), P:13(9.0%) | IFX:120(40.8%), P:61(42.4%) | Endoscopic - Histologic Improvement MES ≤1 and RHI≤3 |
| MIRIKIZUMAB | | | | | | | | |
| Haens et.al | NCT03524092-LUCENT 2, MAINTENANCE | Maintenance:MIRI-365, P-179 Re-randomisation design | MIRI:43.4, P:41.2 | MIRI:214(58.6%), P:104(58.1%) | MIRI:6.9, P:6.7 | MIRI:128(35.1%), P:64(35.8%) | MIRI:135(37.0%), P:68(38.0%) | Endoscopic Improvement MES ≤1, Endoscopic - Histologic Improvement MES ≤1 and Geboes scoring system with neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue; |
| Sandborn et. al | NCT02589665, INDUCTION and MAINTENACE | Induction:MIRI-62, P-63 Maintenance Re-randomisation design | MIRI:43.4, P:42.6 | MIRI:37(59.7%), P:36(57.1%) | MIRI:9.0,P:9.5 | MIRI:40(64.5%), P:38(60%) | MIRI:25(40.3%), P:33(52.4%), | Endoscopic Improvement MES ≤1, Endoscopic Remission MES=0, Histologic Remission Geboes scoring system 0 for the neutrophils in lamina propria, neutrophils in epithelium, and erosion or ulceration parameters) |
| OZANIMOD | | | | | | | | |
| Sandborn et. al | NCT01647516-TOUCHSTONE, INDUCTION and MAINTENANCE | Induction:OZA-67, P-65, Maintenance treat straight through design | OZA:41.8, P:41.9 | OZA:48(72%), P:35(54%) | OZA:6.7, P:6.1 | OZA:13(19%), P:10(15%) | OZA:27(40%), P:24(37%) | Endoscopic Improvement MES ≤1, Histologic Remission Gebos<2 |
| Sandborn et. al | NCT02435992-TRUE NORTH, INDUCTION and MAINTENANCE | Induction:OZA-429, P-216, Maintenance Re-randomisation design | OZA:41.4, P:41.9 | OZA:245(57.1%), P:143(66.2%) | OZA:6.9, P:6.8 | OZA:204(47.5%), P:107(49.5%) | OZA:322(75.1%), P:62(75%) | Endoscopic Improvement MES ≤1, Mucosal Healing= Endoscopic Improvement and Histologic Remission by Geboes<2 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| TOFACITINIB | | | | | | | | |
| Sandborn et. al | NCT01458574-OCTAVE Sustain, MAINTENANCE | Maintenance:Tofacitinib 5mg-198, Tofacitinib 10mg-197, P-198, Re-randomisation design | Tofacitinib 5mg :41.9, Tofacitinib 10 mg:42.9, P:43.4 | Tofacitinib 5mg:103(52%), Tofacitinib 10 mg :110(55.8%), P:116(58.6%) | Tofacitinib 5mg:6.5, Tofacitinib 10mg:6.8,P:7.2 | Tofacitinib 5mg:90(45.5%), Tofacitinib 10 mg:101(51.3%),P:92(46.5%) | Tofacitinib 5mg :101(51.0%), Tofacitinib 10mg:87(44.2%),P:100(50.5%) | Endoscopic Improvement MES≤1 Endoscopic Remission MES=0 |
| UPADACITINIB | | | | | | | | |
| Danese et.al | NCT02819635, U-ACHIEVE-Maintenance -SUBSTUDY 3 | Maintenance:Upadacitinib 15mg-148,Upadacitinib 30mg-154, P-149 Re-randomisation design | Upadacitinib 15mg:40, Upadacitinib 30mg:41,P:40 | Upadacitinib 15mg:95(64%), Upadacitinib 30mg:86(56%), P:85(57%) | Upadacitinib 15mg:6.4, Upadacitinib 30mg:6.0, P:6.2 | Upadacitinib 15mg:71(48%), Upadacitinib 30mg:73(47%), P:81(54%) | Upadacitinib 15mg55(37%), Upadacitinib 30mg:57(37%), P:60(40%) | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| USTEKINUMAB | | | | | | | | |
| Sands et .al | NCT02407236-UNIFI, INDUCTION and MAINTENANCE | Induction:UST-322, P-319 Maintenance :UST-176,P-175 Re-randomisation design | UST:41.7, P:41.2 | UST:195(60.6%), P:197(61.8%) | UST:8.2, P:8.0 | UST:166(51.6%),P:161(50.5 %) | UST:168(52.2%),P:157(49.2%) | Endoscopic Improvement MES ≤1, Histologic improvement Geboes scoring system 0-<5% neutrophils in epithelium, no crypt destruction, and no erosions or ulcerations or granulations |
| VEDOLIZUMAB | | | | | | | | |
| Sands et .al | NCT02497469-VARSITY, INDUCTION and MAINTENANCE | ADA-386, VEDO-385 treat straight through design | ADA:40.5,VEDO:40.8 | ADA:216(56%), VEDO:234(60.8%) | ADA:6.4, VEDO:7.3 | ADA:81(21%), VEDO:80(20.8%) | ADA:140(36.3%), VEDO:139(36.1%) | Endoscopic Improvement MES ≤1, Histologic Remission Geboes Scoring System <2, Histologic Improvement Geboes Scoring System <3.2 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Feagan et. al | NCT00783718-GEMINI I, INDUCTION and MAINTENANCE | Induction :VEDO-225,P-149, Maintenance:VEDO-122,P-126 Re-randomisation design | VEDO:40.1,P:41 | VEDO:132(58.7%),P:92(61.7%) | VEDO:6.1,P:7.1 | VEDO:95(42.2%),P:73(49%) | VEDO:79(35.1%),P:58(38.9%) | Endoscopic Improvement MES ≤1 |
| Motoya et.al | NCT02039505, INDUCTION and MAINTENANCE | Induction :VEDO-164, P-82, Maintenance:VEDO-41, P-42 Re-randomisation design | VEDO:42.3, P:44.0 | VEDO:99(60.4%), P:55(67.1%) | VEDO:7.2, P:8.6 | VEDO:85(51.8%), P:41(50.0%) | VEDO:31(18.9%), P:11(13.4%) | Endoscopic Improvement MES ≤1 |
| Sandborn et. al | NCT02611830-VISIBLE I, INDUCTION and MAINTENANCE | Maintenance:Vedolizumab SC-106, Vedolizumab IV-54,P-56 Re-randomisation design | Vedolizumab SC:38.1, Vedolizumab IV:41.6, P:39.4 | Vedolizumab SC:65(61.3%), Vedolizumab IV:31(57.4%), P:34(60.7%) | Vedolizumab SC:8.0, Vedolizumab IV:8.2, P:7.4 | Vedolizumab SC :40(37.7%), Vedolizumab IV:24(44.4%), P:20(35.7%) | Vedolizumab SC:28(26.4%), Vedolizumab IV:21(38.9%), P:22(39.3%) | Endoscopic Improvement MES ≤1 |
| RISANKIZUMAB | | | | | | | | |
| Louis et.al | NCT03398135-COMMAND, MAINTENANCE | Maintenance :Risankizumab 180mg-179, Risankizumab 360mg-186, P-183 Re-randomisation design | Risankizumab 180 mg:40.9, Risankizumab 360mg:42.5, P:39.2 | Risankizumab 180mg:105(58.7%), Risankizumab 360mg :107(57.5%), P;101(55.2%) | Risankizumab180mg:8.5, Risankizumab 360mg:9.3, P:8.2 | NA | Risankizumab180mg:74(41.3%), Risankizumab360mg :59(31.7%), P:68(37.2%) | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| GOLIMUMAB AND GUSELKUMAB | | | | | | | | |
| Feagan et .al | NCT03662542-VEGA, INDUCTION and MAINTENANCE | Induction:GOL-72, GUS-71, GOL/GUS-71, Maintenance treat straight through strategy | GOL:38.1, GUS:39.1, GOL/GUS:37.8 | GOL:42(58%), GUS:40(56%), GOL/GUS:34(48%) | GOL:4.7,GUS:5.4, GOL/GUS:4.6 | NA | NA | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Histologic Remission Geboes<2, Mucosal Healing= Endoscopic Remission and Histologic Remission by Geboes<2 |
| GUSELKUMAB | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Rubin et.al | NCT04033445-Quasar phase 3, INDUCTION and MAINTENANCE | Induction :Guselkumab 200mg-190, Guselkumab 100mg-188, P-190, Maintenance Re-randomisation design | NA | NA | NA | NA | NA | Endoscopic Improvement MES ≤1, Ensoscopic Remission MES=0, Histologic Remission Geboes≤2, Mucosal Healing= Endoscopic Remission and HistologicRemission by Geboes ≤2 |

ADA=Adalimumab, Baron score: 0- normal, 1- abnormal mucosal but not hemorrhagic, 2- friability, easy to bleeding , 3 -spontaneous bleeding, ETR=Etrasimod GOL=Golimumab, GUS=Guselkumab, IFX=Infliximab, MES=Mayo Endoscopic Score, MIRI=Mirikizumab, P=Placebo, OZA=Ozanimod, , RIS= Risankizumab TOF=Tofacitinib, UPA=Upadacitinib, , UST= Ustekinumab

## Supplementary Table S3: Biologic molecules compared to placebo or other molecules for moderate to severe ulcerative colitis

**Patient or population:** moderate to severe ulcerative colitis
**Setting:** outpatient
**Intervention:** biologic molecules
**Comparison:** placebo or other molecules

| Outcomes | № of participants (studies) Follow-up | Certainty of the evidence (GRADE) | Relative effect (95% CI) | Anticipated absolute effects | |
|---|---|---|---|---|---|
| | | | | Risk with placebo or other molecules | Risk difference with biologic molecules |
| INDUCTION ENDOSCOPIC IMPROVEMT | 14369 (30 RCTs) | ⊕⊕◯◯ Low[a,b] | **RR 1.90** (1.67 to 2.13) | 191 per 1,000 | **172 more per 1,000** (128 more to 216 more) |
| INDUCTION MUCOSAL HEALING | 8225 (12 RCTs) | ⊕⊕◯◯ Low[c,d] | **RR 3.12** (2.22 to 4.23) | 77 per 1,000 | **163 more per 1,000** (94 more to 248 more) |
| MAINTENACE ENDOSCOPIC IMPROVEMENT TST | 3473 (13 RCTs) | ⊕⊕⊕◯ Moderate[e] | **RR 1.68** (1.28 to 2.10) | 252 per 1,000 | **171 more per 1,000** (71 more to 277 more) |
| MAINTENANCE ENDOSCOPIC IMPROVENT RR | 7738 (13 RCTs) | ⊕⊕◯◯ Low[f,g] | **RR 1.77** (1.53 to 2.01) | 287 per 1,000 | **221 more per 1,000** (152 more to 289 more) |
| MAINTENANCE MUCOSAL HEALING TST | 867 (3 RCTs) | ⊕⊕⊕◯ Moderate[h] | **RR 2.09** (1.02 to 3.81) | 96 per 1,000 | **105 more per 1,000** (2 more to 271 more) |
| MAINTENANCE MUCOSAL HEALING RR | 5511 (7 RCTs) | ⊕⊕⊕◯ Moderate[i] | **RR 1.92** (1.35 to 2.60) | 159 per 1,000 | **147 more per 1,000** (56 more to 255 more) |

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

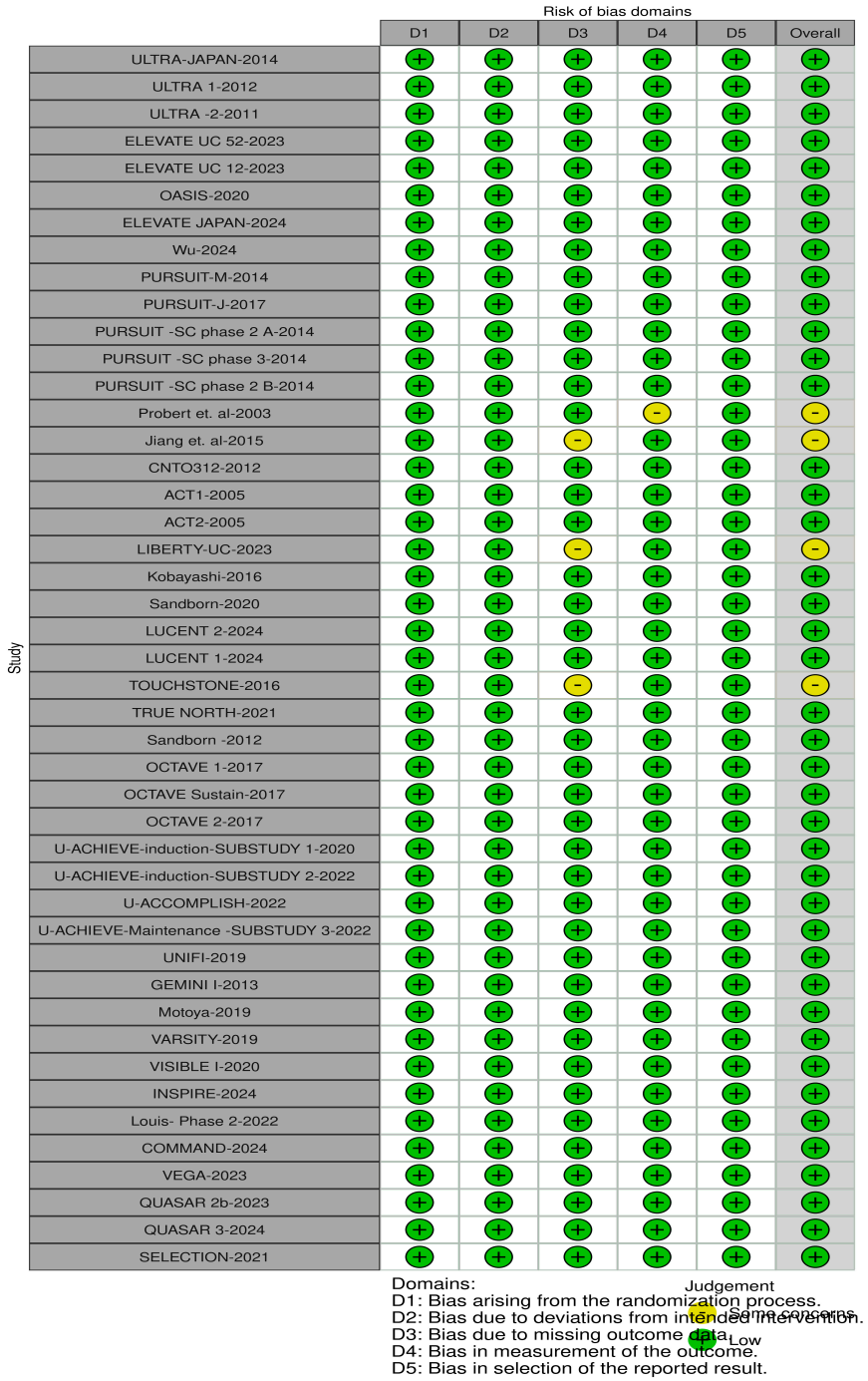
**CI:** confidence interval; **RR:** risk ratio ; **TST**: Treat straight through ; **RR**: Re-Randomization

**GRADE Working Group grades of evidence**
**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.
**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

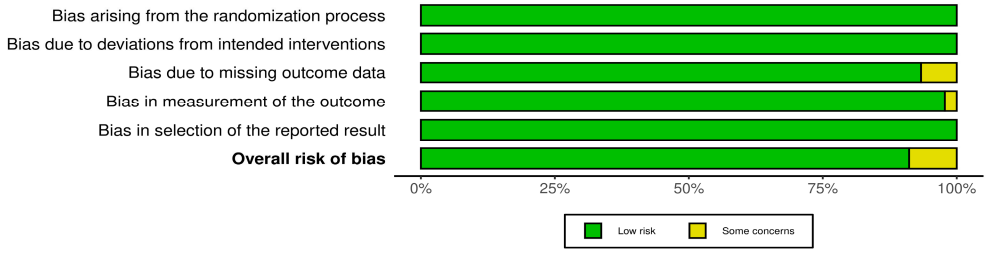
*Explanations*

a. Rated down for one level for inconsistency ($I^2$=71%)
b. Funnel plot asymmetry, p-value <0.05 in Eager's test
c. Rated down for one level for inconsistency ($I^2$=82%)
d. Funnel plot asymmetry , p-value <0.05 in Eager's test
e. Funnel plot asymmetry, p-value <0.05 in Eager's test
f. Rated down for one level for inconsistency($I^2$=61%).
g. Funnel plot asymmetry , p-value <0.05 in Eager's test
h. Lack of sufficient statistical power. Downgraded by 1 level for imprecision
i. Rated down due to Inconsistency ($I^2$=81%)

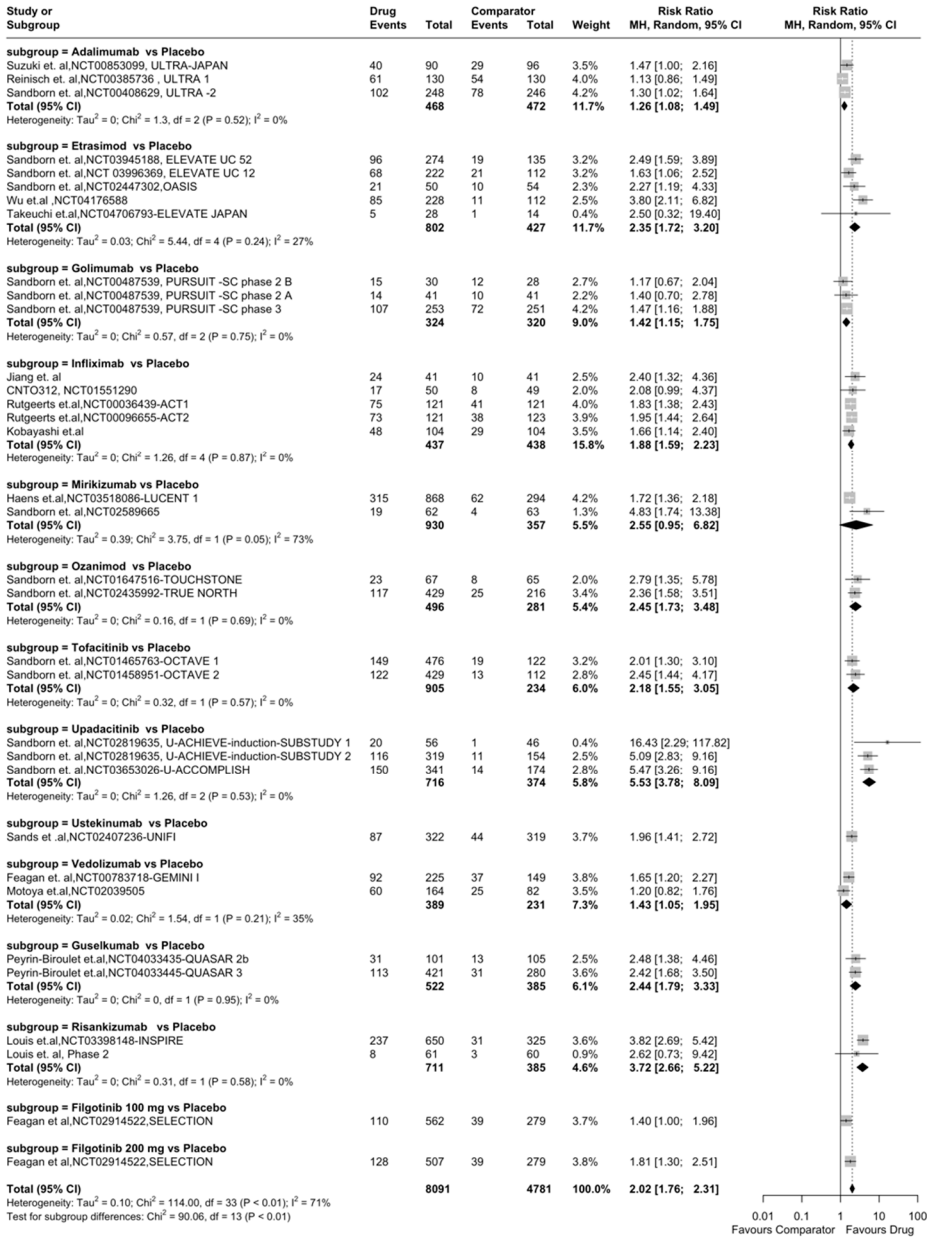
## Supplementary Figure S1: Risk of Bias assessment



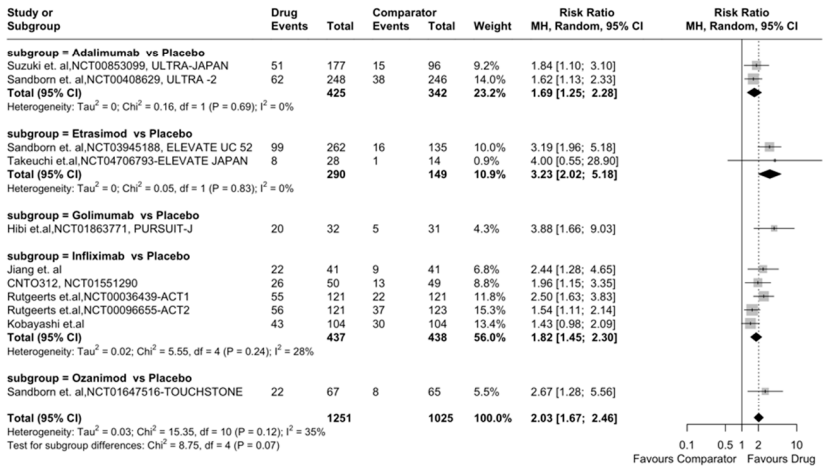
## Supplementary Figure S2: Risk of Bias assessment



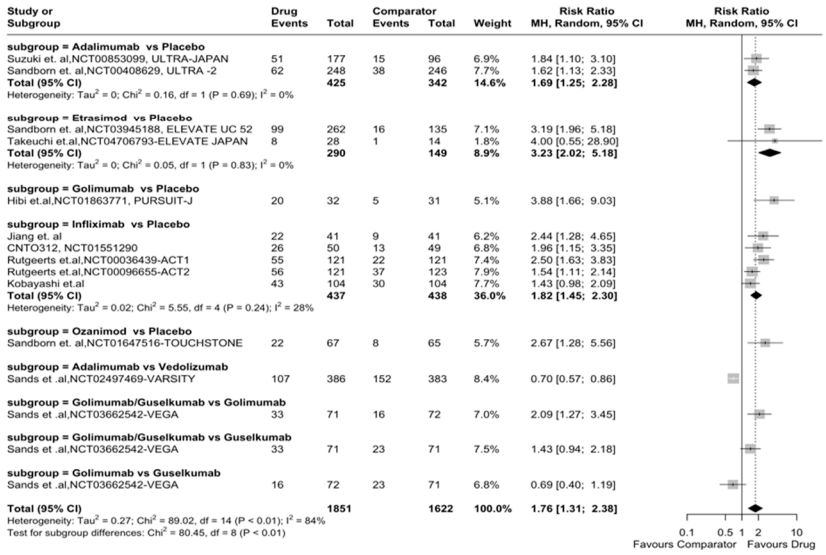
## Supplementary Figure S3: pair-wise meta-analysis for induction of endoscopic improvement (only drugs compared to placebo)



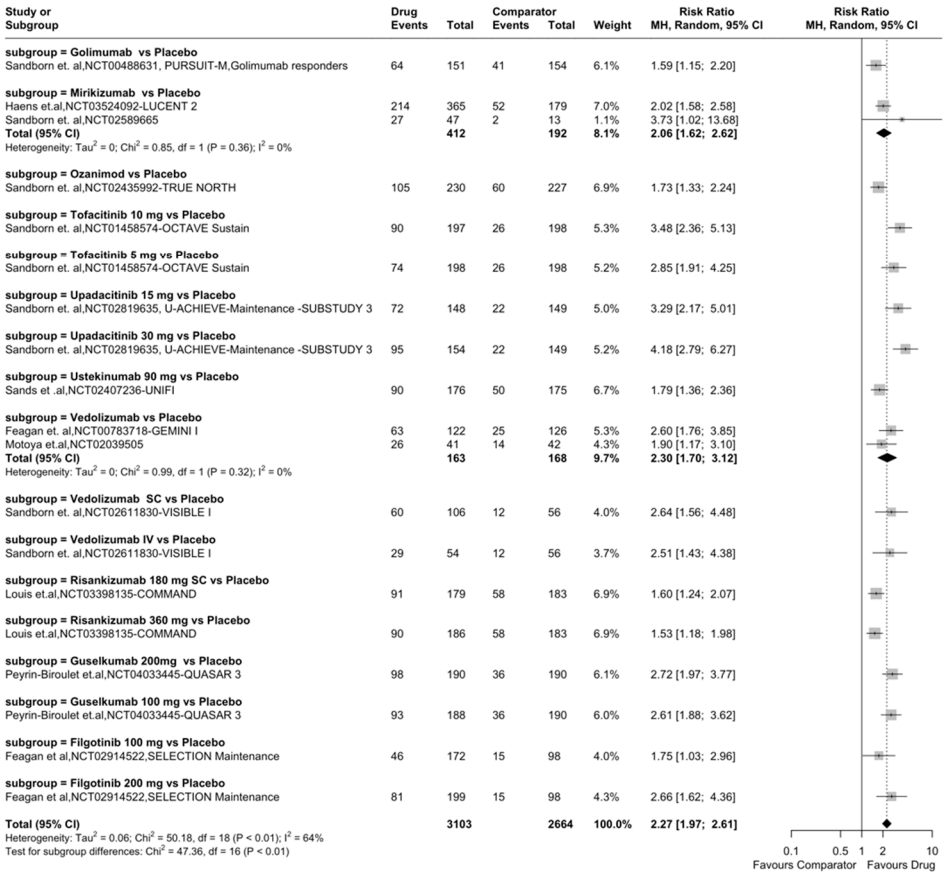
## Supplementary Figure S4: pair-wise meta-analysis for maintenance of endoscopic improvement in treat straight through trials (only drugs compared to placebo)



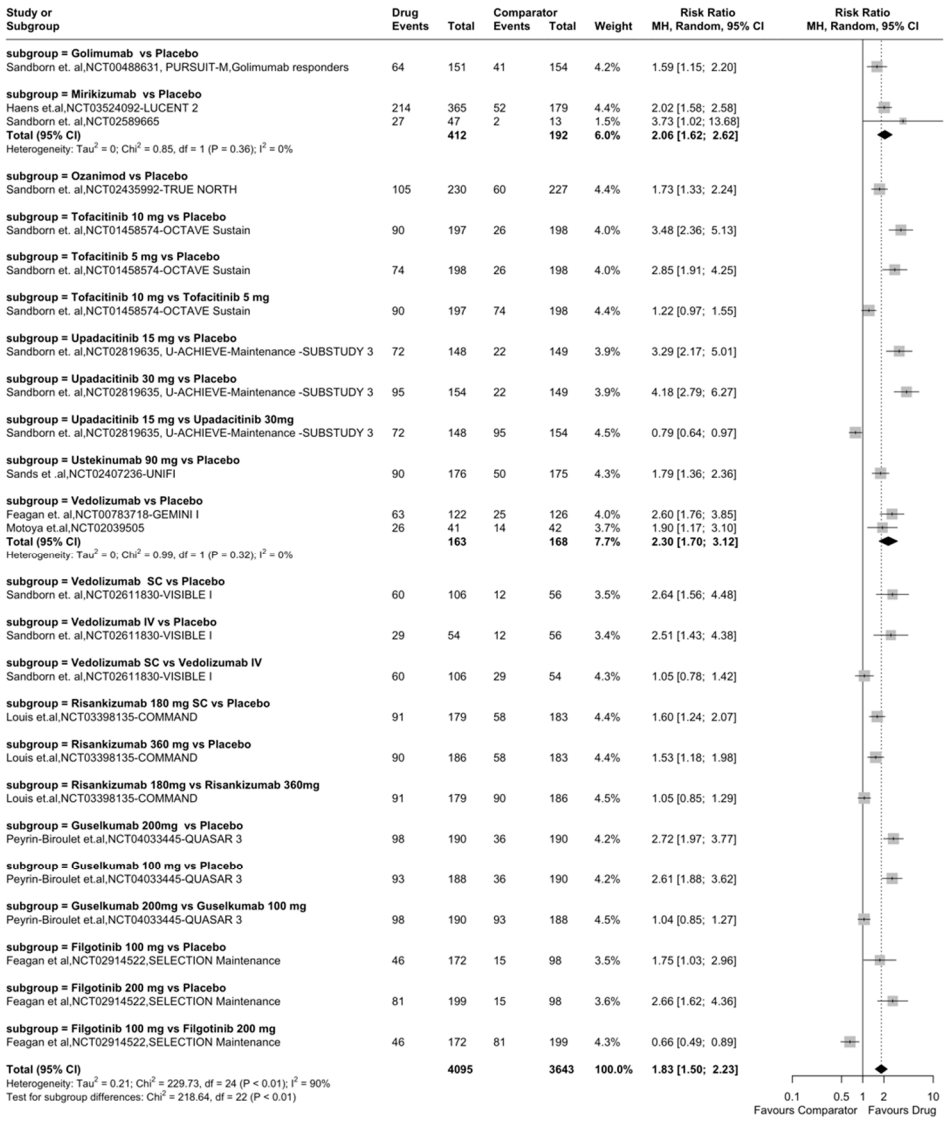
## Supplementary Figure S5: pair-wise meta-analysis for maintenance of endoscopic improvement in treat straight through trials



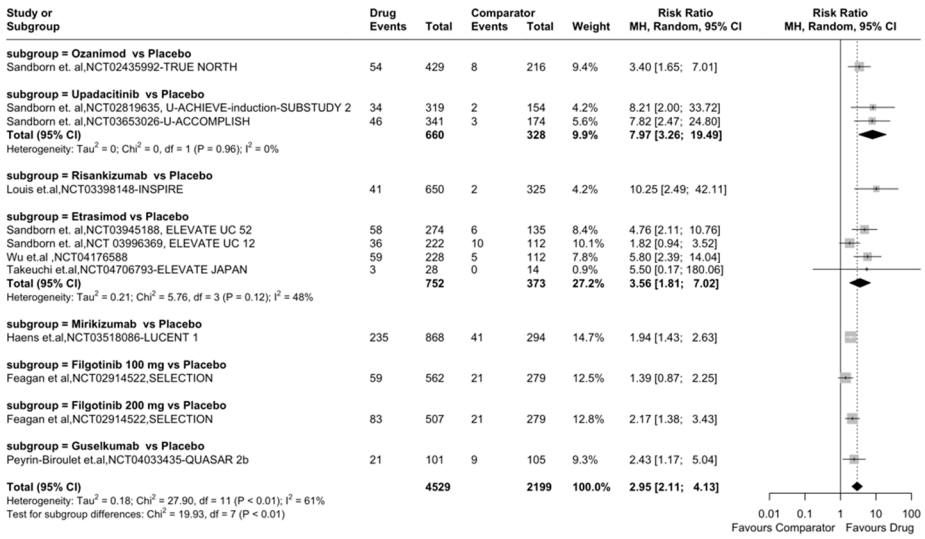
## Supplementary Figure S6: pair-wise meta-analysis for maintenance of endoscopic improvement in re-randomization only responders trials (only drugs compared to placebo)



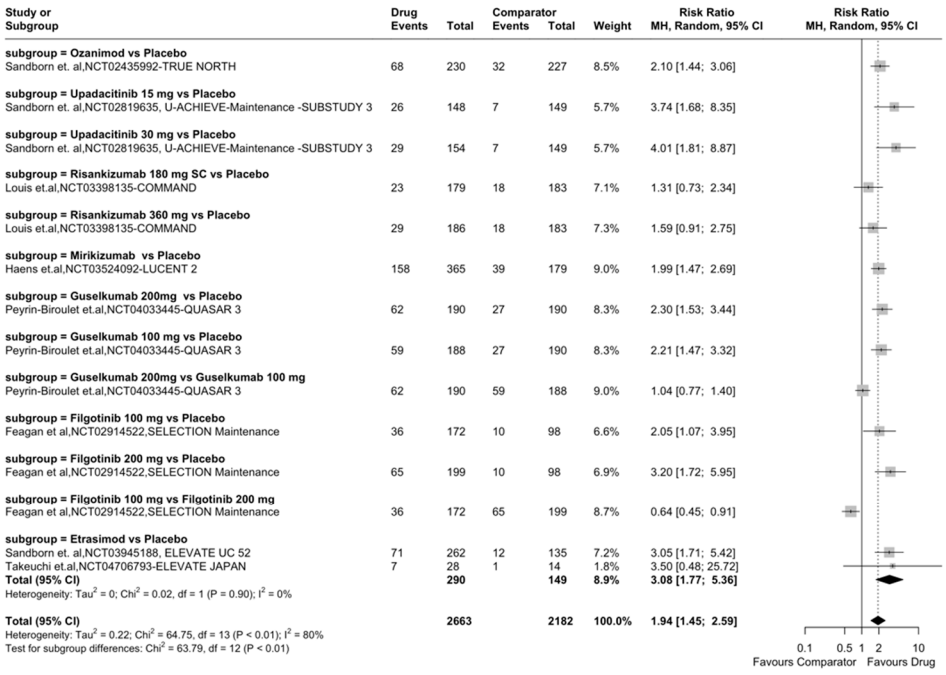
## Supplementary Figure S7: pair-wise meta-analysis for maintenance of endoscopic improvement in re-randomization only responders trials



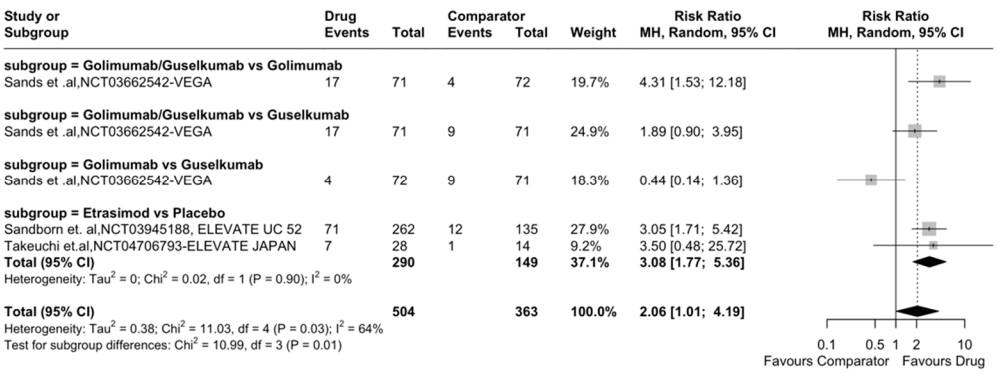
## Supplementary Figure S8: pair-wise meta-analysis for induction of mucosal healing (only drugs compared to placebo)



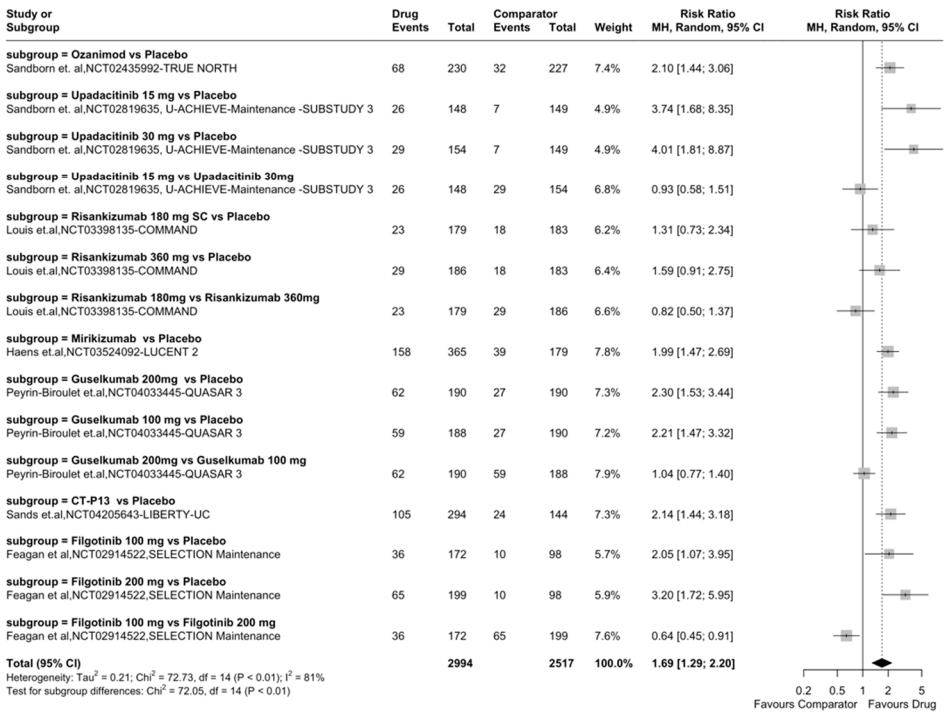
## Supplementary Figure S9: pair-wise meta-analysis for maintenance of mucosal healing (only drugs compared to placebo)



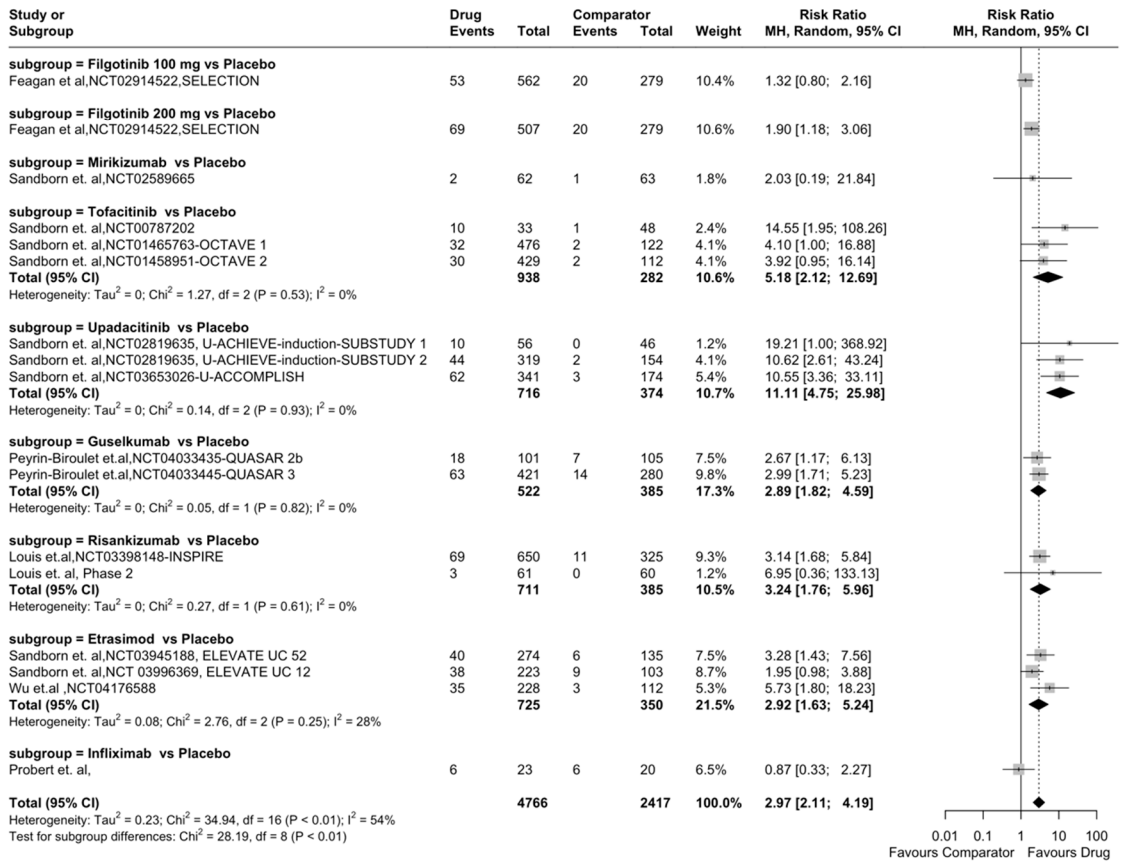
## Supplementary Figure S10: pair-wise meta-analysis for maintenance of mucosal healing in treat-straight-through trials(all drugs)



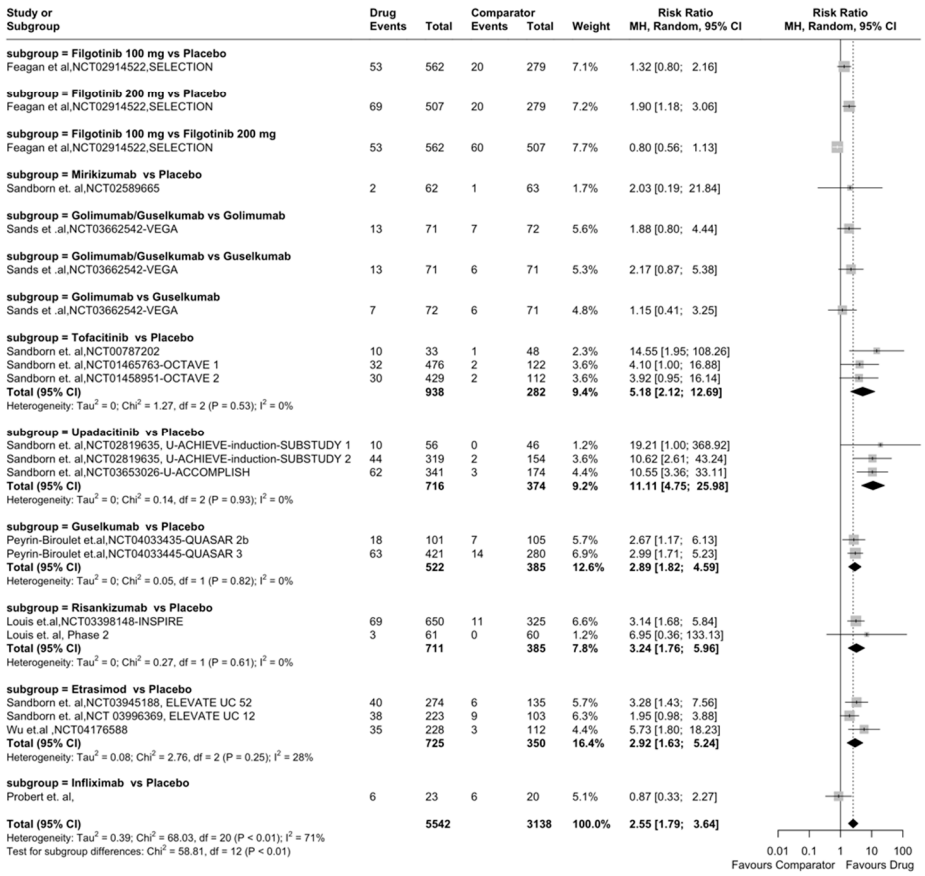
## Supplementary Figure S11: pair-wise meta-analysis for maintenance of mucosal healing in re-randomization only responders (all drugs)



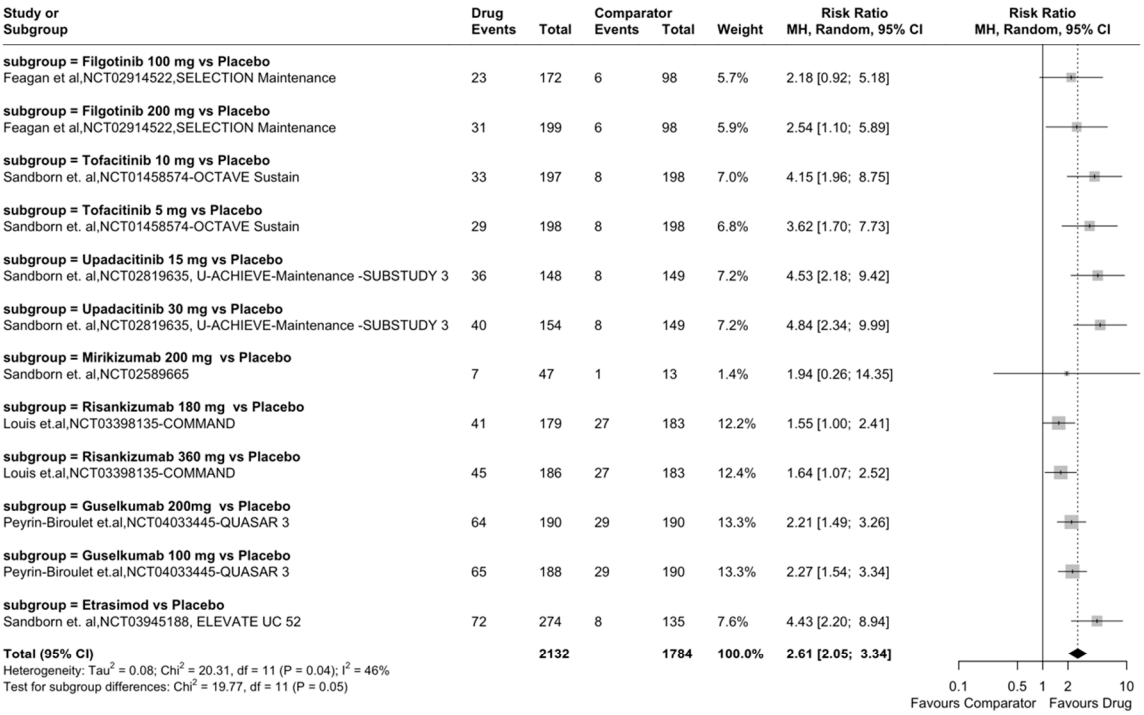
## Supplementary Figure S12: pair-wise meta-analysis for induction of endoscopic remission (only drugs compared to placebo)



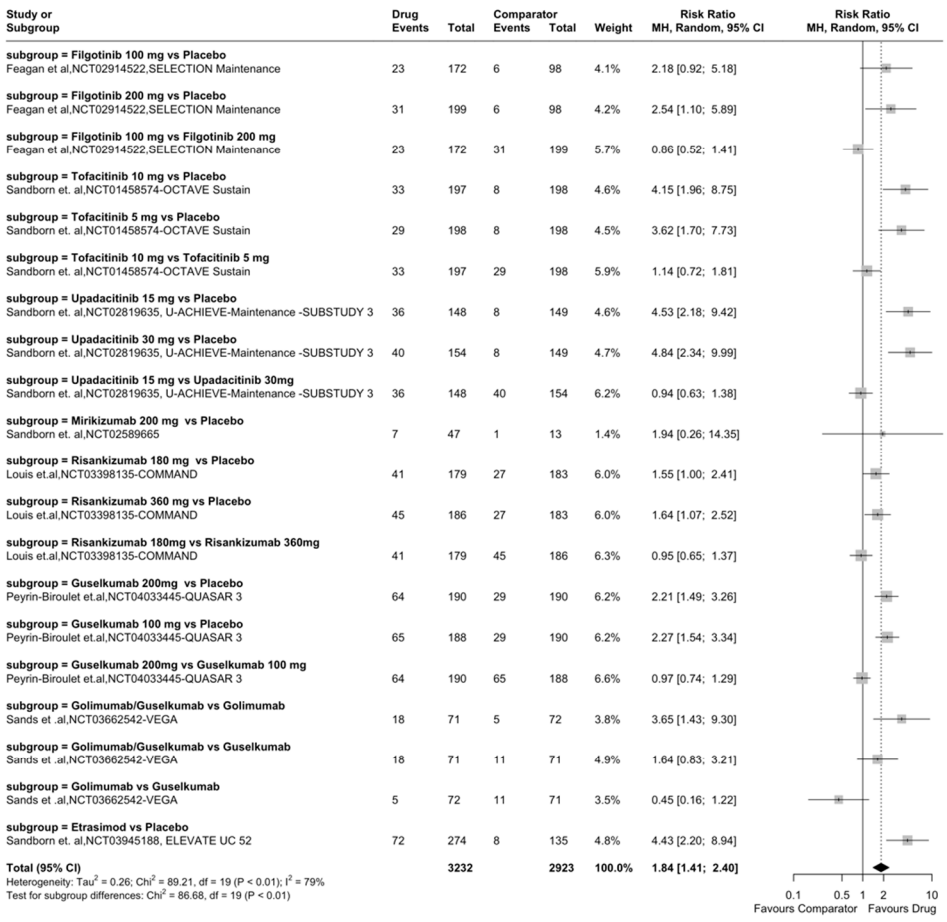
## Supplementary Figure S13: pair-wise meta-analysis for induction of endoscopic remission (all drugs)



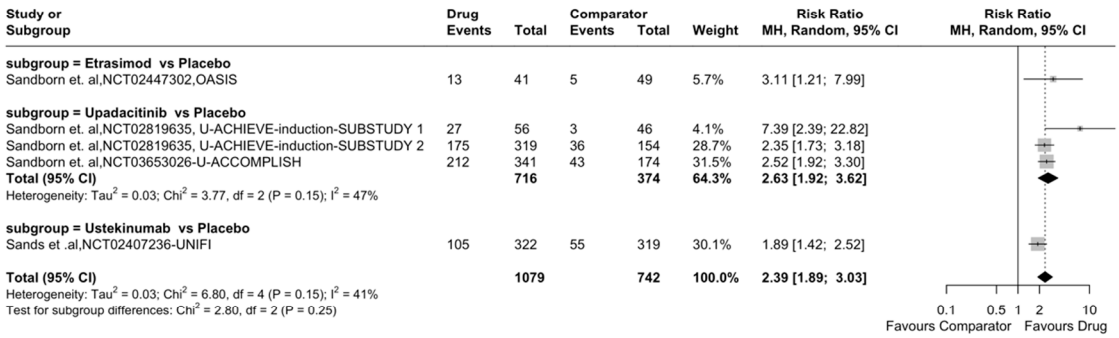
## Supplementary Figure S14: pair-wise meta-analysis for maintenance of endoscopic remission (only drugs compared to placebo)



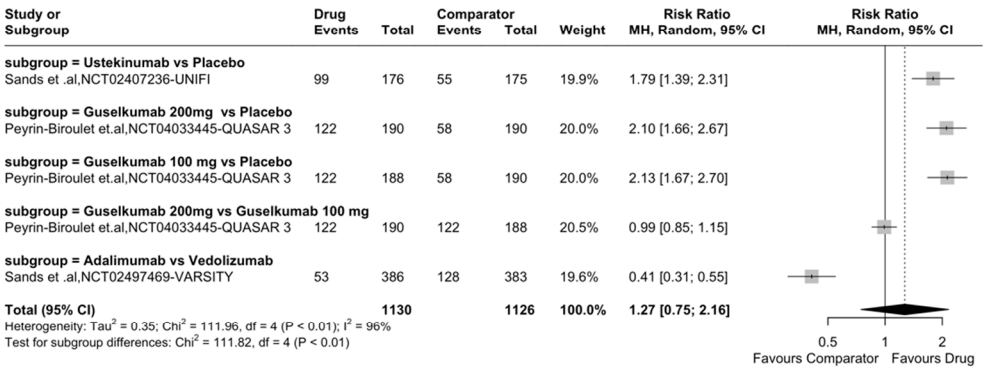
## Supplementary Figure S15: pair-wise meta-analysis for maintenance of endoscopic remission (all drugs)



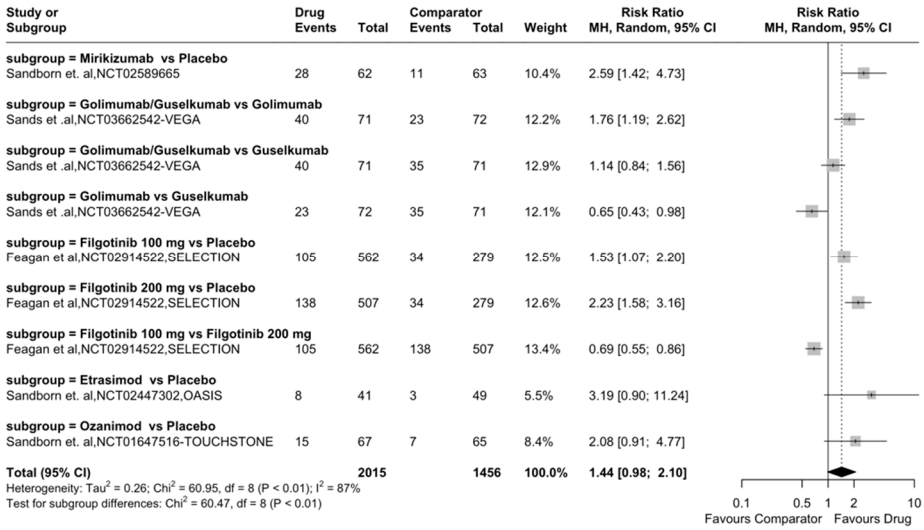
## Supplementary Figure S16: pair-wise meta-analysis for induction of histologic improvement



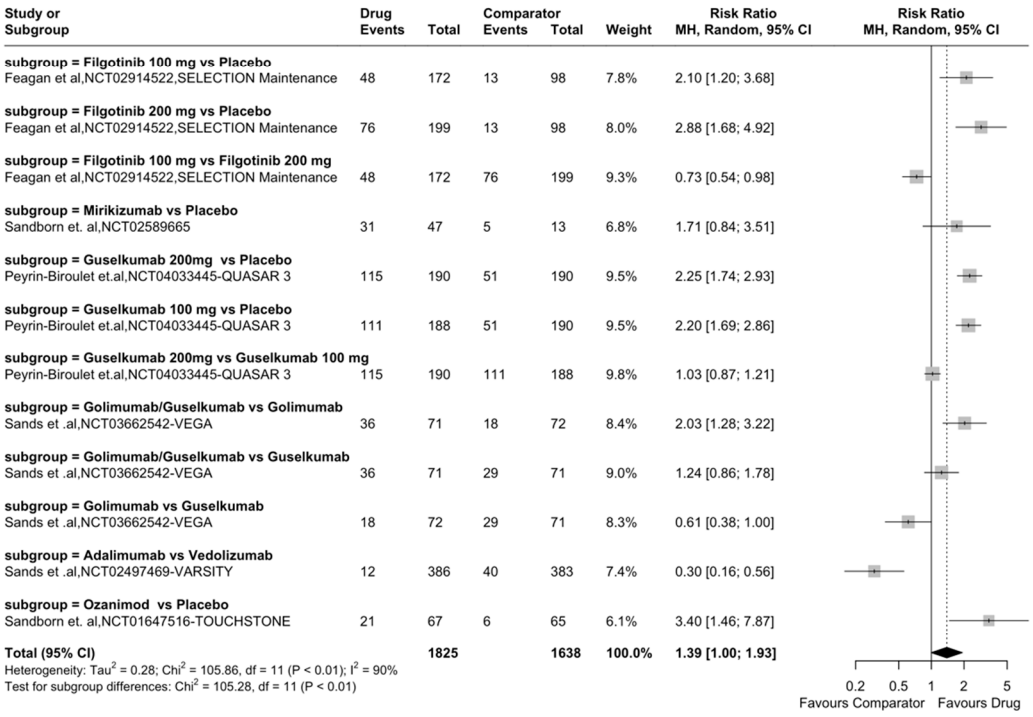
## Supplementary Figure S17: pair-wise meta-analysis for maintenance of histologic improvement



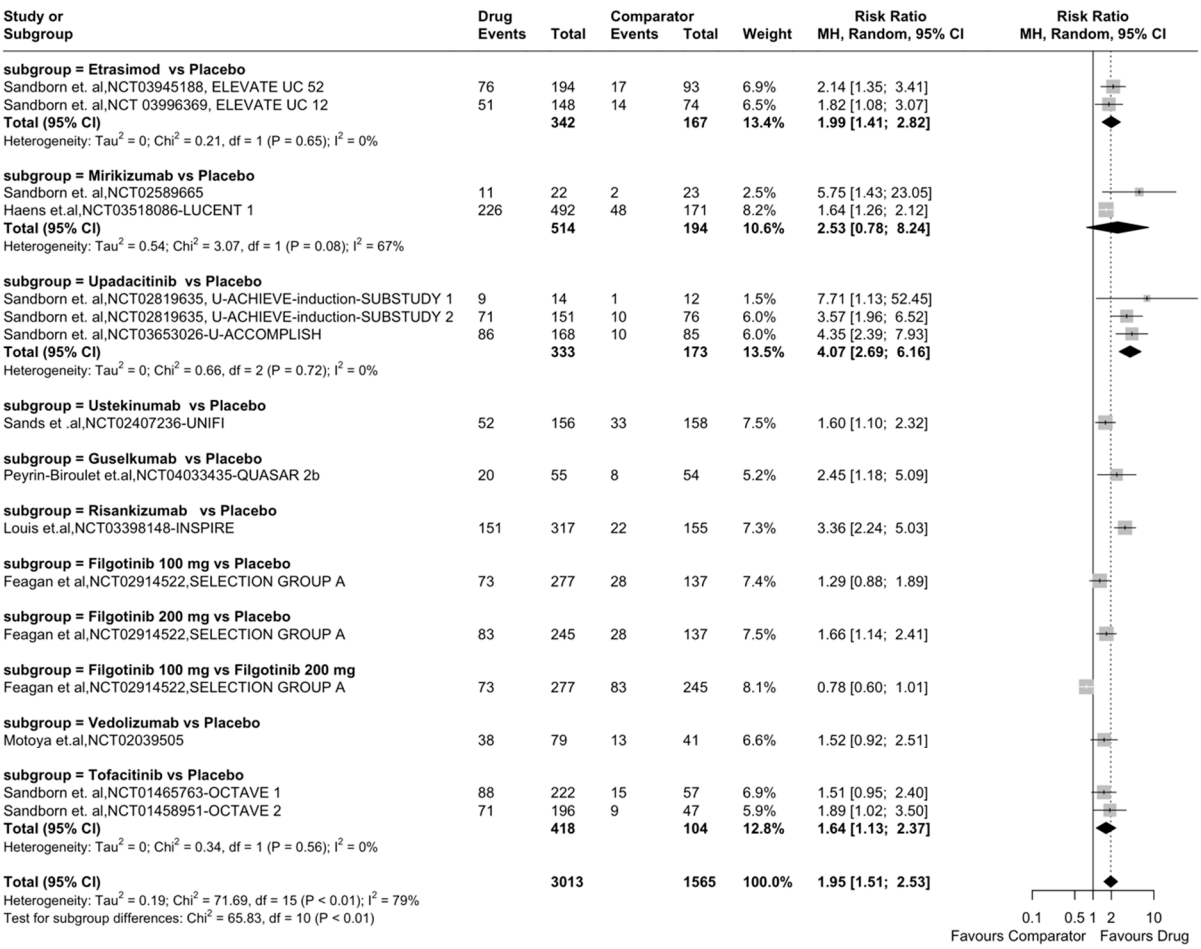
## Supplementary Figure S18: pair-wise meta-analysis for induction of histologic remission



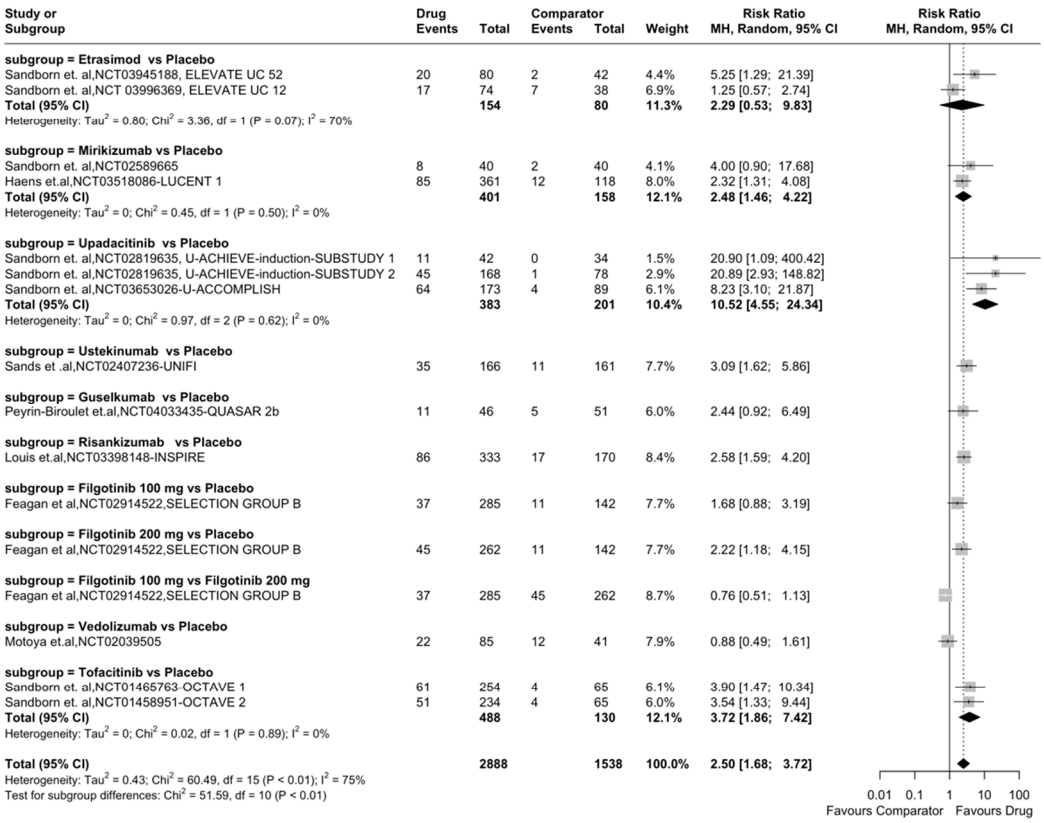
## Supplementary Figure S19: pair-wise meta-analysis for maintenance of histologic remission



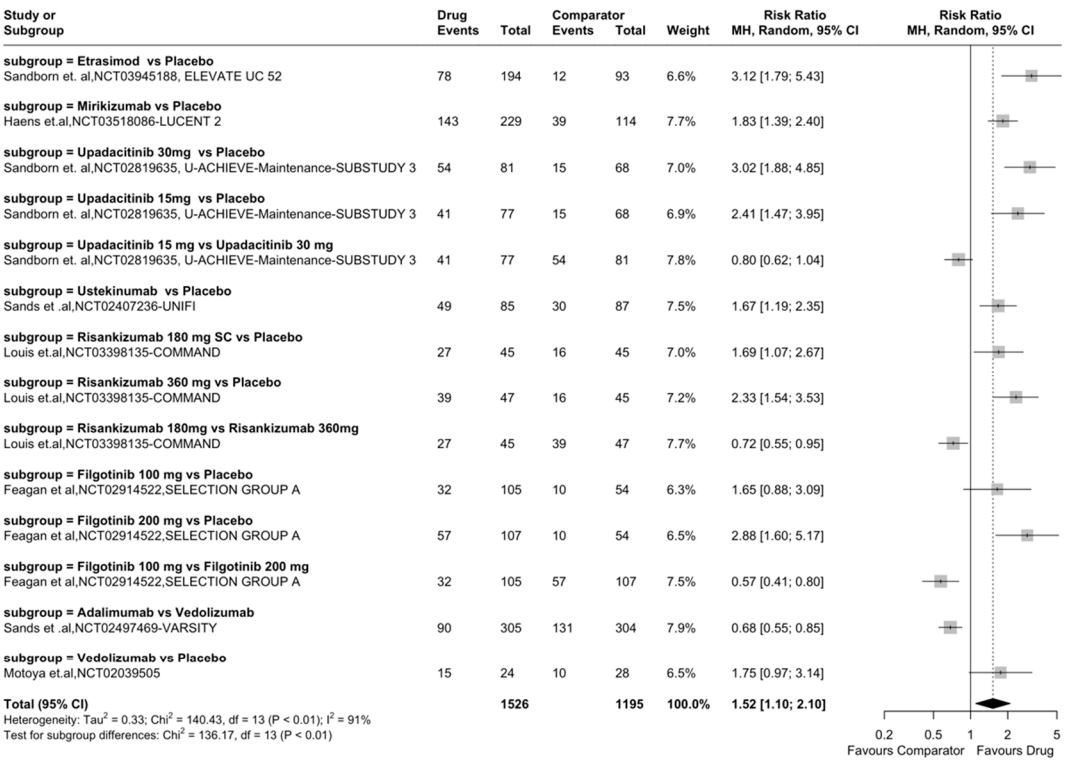
## Supplementary Figure S20: pair-wise meta-analysis for induction of endoscopic improvement in biologic-naïve and no previous biologic failure status patients



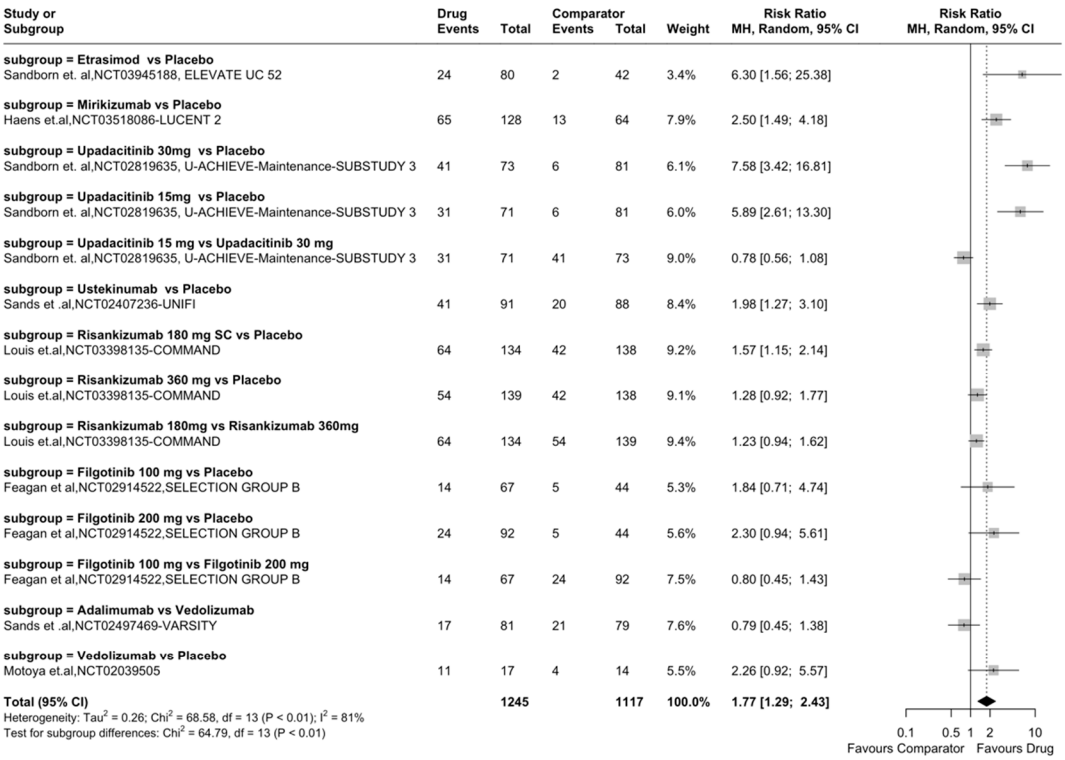
## Supplementary Figure S21: pair-wise meta-analysis for induction of endoscopic improvement in biologic-exposed and with previous biologic failure status patients



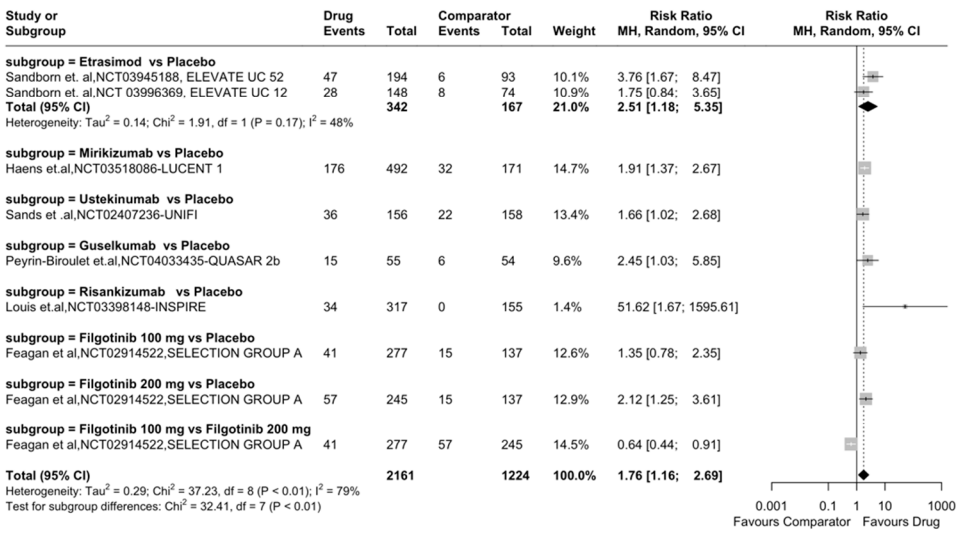
## Supplementary Figure S22: pair-wise meta-analysis for maintenance of endoscopic improvement in biologic-naïve and no previous biologic failure status patients



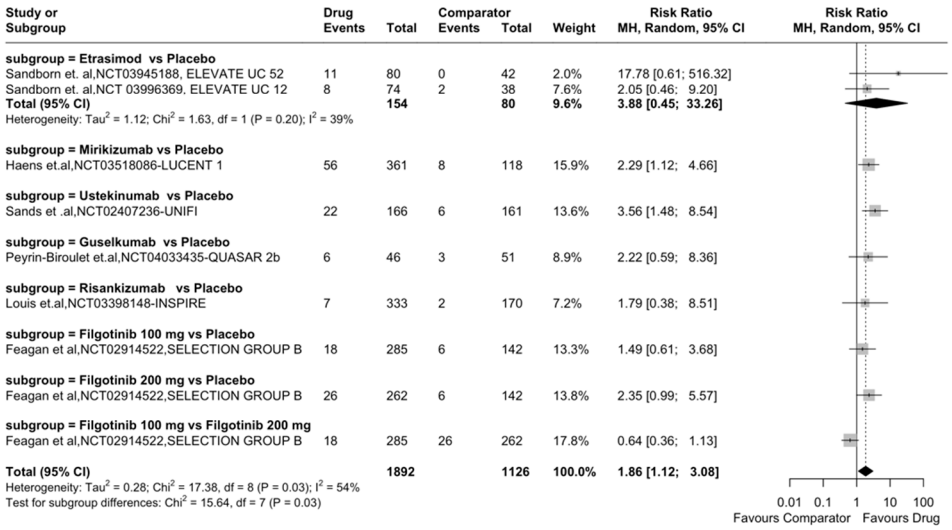
## Supplementary Figure S23: pair-wise meta-analysis for maintenance of endoscopic improvement in biologic-exposed and with previous biologic failure status patients



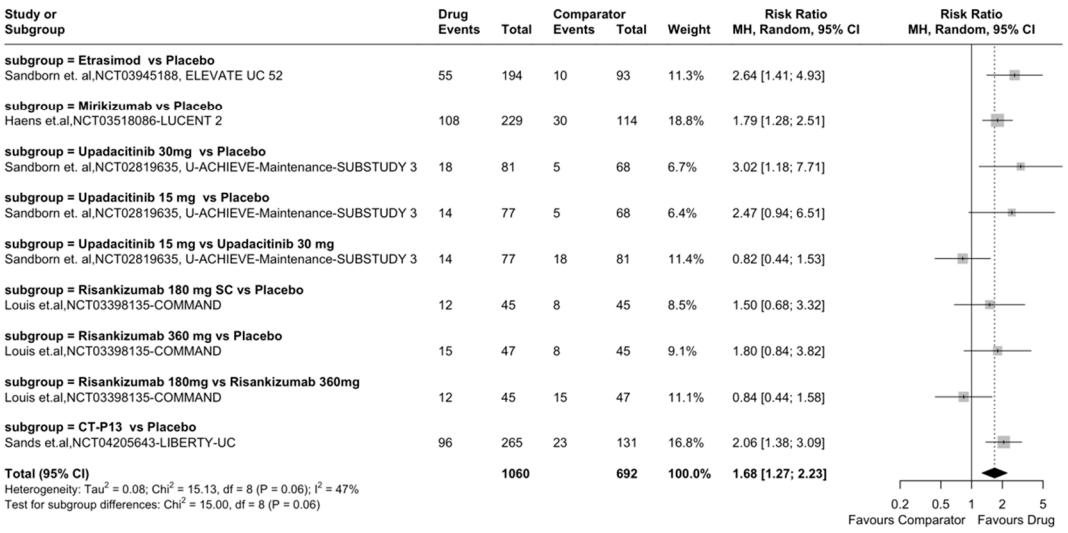
**Supplementary Figure S24: pair-wise meta-analysis for induction of mucosal healing in biologic-naïve and no previous biologic failure status patients**



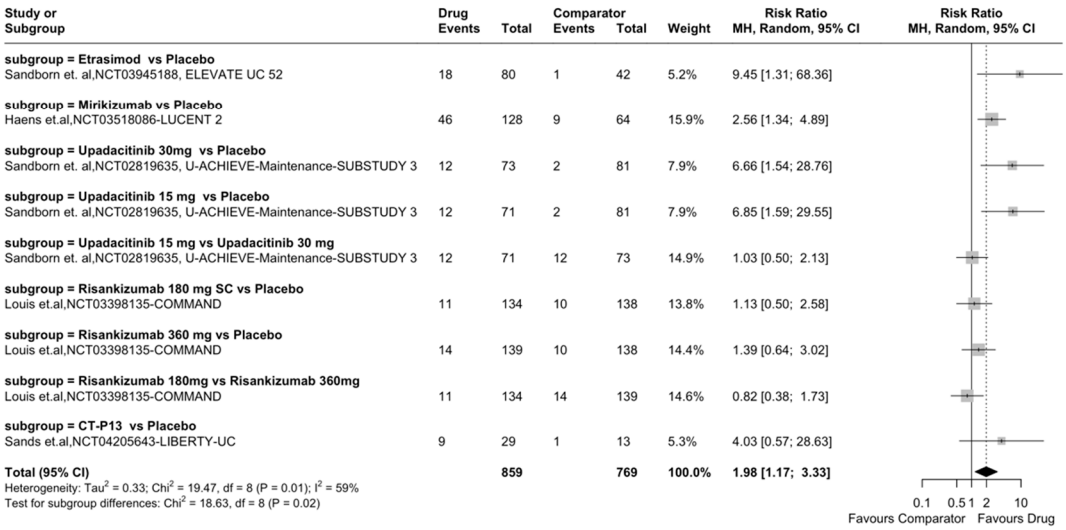
**Supplementary Figure S25: pair-wise meta-analysis for induction of mucosal healing in biologic-exposed and with previous biologic failure status patients**



**Supplementary Figure S24: pair-wise meta-analysis for maintenance of mucosal healing in biologic-naïve and no previous biologic failure status patients**



**Supplementary Figure S25: pair-wise meta-analysis for maintenance of mucosal healing in biologic-exposed and with previous biologic failure status patients**



Supplementary Table S4:
PRISMA checklist

| | | | |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | Page-1 |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Page-1 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page-2,3 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page-2,3 |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page-3 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page-3 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supplementary Appendix page 44-49 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 3 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 3 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page 3,4 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Supplementary Appendix page 3-15 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 3 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 4 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Page 3,4 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | NA |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | NA |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 4 |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 4 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 4 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 4 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 4 |

## Supplementary Table S4: PRISMA checklist

| | | | |
|---|---|---|---|
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 5 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Page 5 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplementary Tables S1 and S2 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supplementary Figure S1 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Table 1,2, Supplementary Figures S3-S25 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | NA |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Table 1,2, Supplementary Figures S3-S25 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | NA |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | NA |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | NA |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Supplementary Table S3 |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 10 |
| | 23b | Discuss any limitations of the evidence included in the review. | Page 11-12 |
| | 23c | Discuss any limitations of the review processes used. | Page 11-12 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Page 11 |
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 4 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 4 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Page 12 |
| Competing interests | 26 | Declare any competing interests of review authors. | Page 12 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 12 |

# Search Algorithm

**PubMed via Medline -1582**

1 Tumor necrosis factor inhibitor*[tw]

2 Tumour necrosis factor inhibitor*[tw]

3 "TNF-alpha antagonist*"[tw]

4 "Tumor Necrosis Factor Alpha Blocking Agent*" [tw]

5 "Tumour Necrosis Factor Alpha Blocking Agent*" [tw]

6 TNF inhibitor* [tw]

7 TNF-a blocker*[tw]

8 "anti-TNF agent*" [tw]

9 Infliximab [tw]

10 Remicade [tw]

11 Inflectra [tw]

12 CT-P 13 [tw]

13 Adalimumab [tw]

14 Humira [tw]

15 Golimumab [tw]

16 Simponi [tw]

17 Vedolizumab [tw]

18 Entyvio [tw]

19 Tofacitinib [tw]

20 Xeljanz [tw]

21 ustekinumab [tw]

22 Stelara [tw]

23 etrolizumab [tw]

24 filgotinib [tw]

25 ozanimod [tw]

26 *upadacitinib* [tw]

27 etrasimod

28 mirikizumab

29 jak inhibitor* [tw]

30 anti-integrin [tw]

31 Anti-Interleukin [tw]

32 Guselkumab[tw]

33 Tremfya [tw]

34 Risankizumab[tw]

35 Skyrizi [tw]

36 OR/1-35

37 Ulcerative colitis [mh]

38 Proctocolitis [mh]

39 Proctitis [mh]

40 Pancolitis [tw]

41 rectitis [tw]

42 proctocolitis [tw]

43 procto-colitis [tw]

44 colorectitis [tw]

45 rectocolitis [tw]

46 recto-sigmoiditis [tw]

47 rectosigmoiditis [tw]

48 procto-sigmoiditis [tw]

49 proctosigmoiditis [tw]

50 proctitis [tw]

51 ((Ulcer* or total or sub-total or subtotal or extensive or left-sided or universal) AND colitis) [tw]

52 OR/ 37-51

53 Randomised controlled trial [mh]

54 randomized controlled trial [mh]

55 Double Blind Method [mh]

56 Single Blind Method [mh]

57 Random Allocation [mh]

58 clinical trial [mh]

59 ((singl* or doub* or treb* or tripl*) AND (blind or mask) [tw]

60 clinical trial phase i [tw]

61 clinical trial phase ii [tw]

62 clinical trial phase iii [tw]

63 clinical trial phase iv [tw]

64 controlled clinical trial [tw]

65 randomized controlled trial [tw]

66 randomised controlled trial [tw]

67 multicenter study [tw]

68 clinical trial [tw]

69 random* [tw]

70 randomly allocated [tw]

71 OR/53-70

72 36 AND 52 AND 71

**Embase via Ovid-2793 search until 27/04/2024 due to no access**

1 TNF-alpha antagonist$.mp.

2 TNF inhibitor$.mp

3 TNF-a blocker$.mp

4 Infliximab.mp

5 Remicade.mp.

6 Inflectra .mp.

7 CT-P 13.mp

8 Adalimumab .mp.

9 Humira.mp.

10 Golimumab.mp.

11 Simponi.mp.

12 Vedolizumab.mp.

13 Entyvio.mp.

14 Tofacitinib .mp.

15 Xeljanz .mp.

16 ustekinumab .mp.

17 Stelara.mp.

18 etrolizumab.mp.

19 filgotinib.mp.

20 ozanimod.mp.

21 *upadacitinib*.mp.

22 jak inhibitor$.mp

23 anti-integrin.mp

24 Anti-Interleukin.mp

25 OR/1-24

26 ulcerative colitis.mp or ulcerative colitis/

27 proctocolitis.mp or proctocolitis/

28 proctosigmoiditis .mp.

29 procto-sigmoiditis .mp.

30 rectosigmoiditis .mp.

31 recto-sigmoiditis .mp.

32 rectocolitis.mp.

33 colorectitis .mp.

34 procto-colitis .mp.

35 proctocolitis .mp.

36 rectitis .mp.

37 OR/ 26-36

38 Randomised controlled trial/

39 Single blind procedure/

40 Double blind procedure/

41 Randomi?ed controlled trial$.mp.

42 Rct. mp.

43 Random allocation.mp

44 Single blind$.mp

45 Double blind$.mp

46 Triple blind$.mp

47 OR/38-46

49 25 AND 37 AND 47

**CENTRAL -Cochrane Library-1072**

1 Tumour necrosis factor inhibitor

2 TNF-alpha antagonist

3 TNF inhibitor

4 TNF-a blocker

5 Infliximab

6 Remicade

7 Inflectra

8 CT-P 13

9 Adalimumab

10 Humira

11 Golimumab

12 Simponi

13 Vedolizumab

14 Entyvio

15 Tofacitinib

16 Xeljanz

17 ustekinumab

18 Stelara

19 etrolizumab

20 filgotinib

21 ozanimod

22 *upadacitinib*

23 jak inhibitor

24 anti-integrin

25 Anti-Interleukin

26 Risankizumab

27 Skyrizi

28 Guselkumab

29 Tremfya

30 OR/1-29

31 MeSH descriptor: [Colitis, Ulcerative] explode all trees

32 MeSH descriptor [Proctitis] explode all trees

33 (total or sub-total or subtotal or extensive or left-sided or universal) AND colitis

34 Pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis
35 OR/ 31-34
36 30 AND 35 in Cochrane Reviews, Cochrane Protocols and Trials

**WEB OF SCIENCE-1947**

#1 ALL=((Ulcerative colitis OR Proctocolitis OR Proctitis OR Pancolitis OR rectitis OR proctocolitis OR "procto-colitis" OR colorectitis OR rectocolitis OR "recto-sigmoiditis" OR rectosigmoiditis OR "procto-sigmoiditis" OR proctosigmoiditis OR proctitis OR (Ulcer* AND (total OR sub-total OR subtotal OR extensive OR left-sided OR universal) AND colitis)))

#2 ALL=((Randomised controlled trial OR randomized controlled trial OR "Double Blind Method" OR "Single Blind Method" OR "Random Allocation" OR "clinical trial" OR (singl* OR doub* OR treb* OR tripl*) AND (blind OR mask) OR "clinical trial phase i" OR "clinical trial phase ii" OR "clinical trial phase iii" OR "clinical trial phase iv" OR "controlled clinical trial" OR "randomized controlled trial" OR "randomised controlled trial" OR "multicenter study" OR random* OR "randomly allocated"))

#3 ALL=((Tumor necrosis factor inhibitor* OR Tumour necrosis factor inhibitor* OR "TNF-alpha antagonist*" OR "Tumor Necrosis Factor Alpha Blocking Agent*" OR "Tumour Necrosis Factor Alpha Blocking Agent*" OR TNF inhibitor* OR "TNF-a blocker*" OR "anti-TNF agent*" OR Infliximab OR Remicade OR Inflectra OR "CT-P 13" OR Adalimumab OR Humira OR Golimumab OR Simponi OR Vedolizumab OR Entyvio OR Tofacitinib OR Xeljanz OR ustekinumab OR Stelara OR etrolizumab OR filgotinib OR ozanimod OR upadacitinib OR "jak inhibitor*" OR "Risankizumab" OR "Guselkumab" "anti-integrin" OR "Anti-Interleukin"))