

## SUPPLEMENT MATERIAL

### Supplement appendix 1

#### **PUBMED:**

- #1 Rheumatoid Arthritis[MeSH Terms]
- #2 Interstitial Lung Disease[MeSH Terms]
- #3 Interstitial Pneumonia[Title/Abstract]
- #4 Interstitial Pneumonitis[Title/Abstract]
- #5 #2 OR #3 OR #4
- #6 #1 AND #5
- #7 Tumor Necrosis Factor-alpha[MeSH Terms]
- #8 Etanercept[MeSH Terms]
- #9 TNF Receptor Fusion Protein [Title/Abstract]
- #10 Enbrel[Title/Abstract]
- #11 Infliximab[MeSH Terms]
- #12 Remicade[Title/Abstract]
- #13 Adalimumab[MeSH Terms]
- #14 Humira[Title/Abstract]
- #15 D2E7 Antibody[Title/Abstract]
- #16 Certolizumab[MeSH Terms]
- #17 Cimzia[Title/Abstract]
- #18 Golimumab[MeSH Terms]
- #19 Simponi[Title/Abstract]
- #20 Tocilizumab[MeSH Terms]
- #21 Receptors, Interleukin-6[MeSH Terms]
- #22 Monoclonal antibody[Title/Abstract]
- #23 Actemra[Title/Abstract]
- #24 Roactemra[Title/Abstract]
- #25 Rituximab[MeSH Terms]
- #26 CD20 Antibody, Rituximab [Title/Abstract]
- #27 Mabthera[Title/Abstract]
- #28 Rituxan[Title/Abstract]
- #29 Abatacept[MeSH Terms]
- #30 CTLA-4-Ig[Title/Abstract]
- #31 Orencia[Title/Abstract]
- #32 Janus kinase inhibitor[MeSH Terms]
- #33 Janus kinase[MeSH Terms]
- #34 Janus kinase 1 inhibitor[Title/Abstract]
- #35 Janus kinase 2 inhibitor[Title/Abstract]
- #36 Janus kinase 3 inhibitor[Title/Abstract]
- #37 Tofacitinib[MeSH Terms]
- #38 Xeljanz[Title/Abstract]
- #39 CP-690550[Title/Abstract]

- #40 Baricitinib[MeSH Terms]
- #41 Olumiant[Title/Abstract]
- #42 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41
- #43 #6 AND #42
- #44 Filters English
- #45 Filters humans

**EMBASE:**

- 1 exp Rheumatoid Arthritis/
- 2 exp Interstitial Lung Disease/
- 3 Etanercept/
- 4 Etanercept.tw.
- 5 TNF Receptor Fusion Protein.tw.
- 6 Enbrel.tw.
- 7 Infliximab/
- 8 Infliximab.tw.
- 9 Remicade.tw.
- 10 Adalimumab/
- 11 Adalimumab.tw.
- 12 Humira.tw.
- 13 D2E7 Antibody.tw.
- 14 Certolizumab pegol/
- 15 Certolizumab.tw.
- 16 Cimzia.tw.
- 17 Golimumab/
- 18 Golimumab.tw.
- 19 Simponi.tw.
- 20 Tocilizumab/
- 21 Tocilizumab.tw.
- 22 Monoclonal antibody.tw.
- 23 Actemra.tw.
- 24 Roactemra.tw.
- 25 Rituximab/
- 26 Rituximab.tw.
- 27 CD20 Antibody, Rituximab.tw.
- 28 Mabthera.tw.
- 29 Rituxan.tw.
- 30 Abatacept/
- 31 Abatacept.tw.
- 32 CTLA-4-Ig.tw.
- 33 Orencia.tw.

- 34 Janus kinase inhibitor/
- 35 Janus kinase/
- 36 Janus kinase 1 inhibitor/
- 37 Janus kinase 2 inhibitor/
- 38 Janus kinase 3 inhibitor/
- 39 Tofacitinib/
- 40 Tofacitinib.tw.
- 41 Xeljanz.tw.
- 42 CP-690550.tw.
- 43 Baricitinib/
- 44 Baricitinib.tw.
- 45 Olumiant.tw.
- 46 INCB-028050.tw.
- 47 LY-3009104.tw
- 48 1 and 2
- 49 or/3-47
- 50 48 and 49
- 51 limit 50 to english language
- 52 limit 51 to human

#### **the Cochrane Library**

- 1 MeSH descriptor: [Arthritis, Rheumatoid] explode all trees
- 2 MeSH descriptor: [Lung Disease, Interstitial] explode all trees
- 3 MeSH descriptor: [Antibodies, Monoclonal] explode all trees
- 4 MeSH descriptor: [Monokines] explode all trees
- 5 MeSH descriptor: [Receptors, Interleukin-6] explode all trees
- 6 MeSH descriptor: [Tumor Necrosis Factor-alpha] explode all trees
- 7 MeSH descriptor: [Immunoglobulin g] explode all trees
- 8 MeSH descriptor: [Immunoconjugates] explode all trees
- 9 MeSH descriptor: [Polyethylene Glycols] explode all trees
- 10 MeSH descriptor: [Immunoglobulin Fab Fragments] explode all trees
- 11 MeSH descriptor: [T-Lymphocytes] explode all trees
- 12 MeSH descriptor: [Janus kinase] explode all trees
- 12 (Etanercept):ti,ab,kw
- 13 (TNF Receptor Fusion Protein):ti,ab,kw
- 14 (Enbrel.tw):ti,ab,kw
- 15 (Infliximab):ti,ab,kw
- 16 (Remicade):ti,ab,kw
- 17 (Adalimumab):ti,ab,kw
- 18 (Humira):ti,ab,kw
- 19 (D2E7 Antibody):ti,ab,kw
- 20 (Certolizumab):ti,ab,kw

- 21 (Cimzia):ti,ab,kw
- 22 (Golimumab):ti,ab,kw
- 23 (Simponi):ti,ab,kw
- 24 (Tocilizumab):ti,ab,kw
- 25 (Actemra):ti,ab,kw
- 26 (Roactemra):ti,ab,kw
- 27 (Rituximab):ti,ab,kw
- 28 (CD20 Antibody, Rituximab):ti,ab,kw
- 29 (Mabthera):ti,ab,kw
- 30 (Rituxan):ti,ab,kw
- 31 (Abatacept):ti,ab,kw
- 32 (CTLA-4):ti,ab,kw
- 33 (Orencia):ti,ab,kw
- 34 (Janus kinase inhibitor):ti,ab,kw
- 35 (Tofacitinib):ti,ab,kw
- 36 (Xeljanz):ti,ab,kw
- 37 (CP-690550):ti,ab,kw
- 38 (Baricitinib):ti,ab,kw
- 39 (Olumiant):ti,ab,kw
- 40 (INCB-028050):ti,ab,kw
- 41 (LY-3009104):ti,ab,kw
- 42 (#1 AND #2)
- 43 (#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41)
- 44 (#42 AND #43)
- 45 (limit 44 to in trials)

**Web of Science:**

- #1 TS=(Arthritis, Rheumatoid\*)
- #2 TS=(Lung Disease, Interstitial\*)
- #3 TS=(Interstitial Pneumonia\*)
- #4 TS=(Interstitial Pneumonitis\*)
- #5 #2 OR #3 OR #4 ((TS=(Lung Disease, Interstitial\*)) OR TS=(Interstitial Pneumonia\*)) OR TS=(Interstitial Pneumonitis\*)
- #6 #1 AND #5
- #7 TS=(Etanercept\*)
- #8 TS=(TNF Receptor Fusion Protein\*)
- #9 TS=(Enbrel\*)
- #10 TS=(Infliximab\*)
- #11 TS=(Remicade\*)
- #12 TS=(Adalimumab\*)

- #13 TS=(Humira\*)
- #14 TS=(D2E7 Antibody\*)
- #15 TS=(Certolizumab\*)
- #16 TS=(Cimzia\*)
- #17 TS=(Golimumab\*)
- #18 TS=(Simponi\*)
- #19 TS=(Tocilizumab\*)
- #20 TS=(Monoclonal antibody\*)
- #21 TS=(Actemra\*)
- #22 TS=(Roactemra\*)
- #23 TS=(Rituximab\*)
- #24 TS=(CD20 Antibody, Rituximab\*)
- #25 TS=(Mabthera\*)
- #26 TS=(Rituxan\*)
- #27 TS=(Abatacept\*)
- #28 TS=(CTLA-4\*)
- #29 TS=(Orencia\*)
- #30 TS=(Janus kinase inhibitor\*)
- #33 TS=(Janus kinase\*)
- #37 TS=(Tofacitinib\*)
- #38 TS=(Xeljanz\*)
- #39 TS=(CP-690550\*)
- #40 TS=(Baricitinib\*)
- #41 TS=(Olumiant\*)
- #42 #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41
- #43 #6 AND #42
- #44 #6 AND #42 **and** English (Languages)
- #45 #6 AND #42 **and** English (Languages) **and** Humans (MeSH Headings)

**Supplement Table 1.** Details of the Newcastle-Ottawa Scale in all included studies

Study	Selection				Comparability control for important factor	Outcomes			Scores
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study		Assessment of outcomes	Follow-up long enough for outcomes to occur*	Adequacy of follow-up of cohorts†	
Atienza-Mateo 2020 <sup>1</sup>	0	0	1	1	1	1	0	1	5
Cassone 2020 <sup>2</sup>	1	1	1	1	1	1	1	1	8
d'Alessandro 2020 <sup>3</sup>	1	1	1	1	1	0	0	1	6
Detorakis 2016 <sup>4</sup>	1	1	1	1	2	1	0	1	8
Dixon 2010 <sup>5</sup>	1	1	1	1	1	1	1	1	8
Druce 2017 <sup>6</sup>	1	1	1	1	1	1	1	1	8
Duarte 2019 <sup>7</sup>	1	1	1	1	1	1	1	0	7
Fernández-Díaz 2020 <sup>8</sup>	1	1	1	1	2	1	1	0	8
Fui 2019 <sup>9</sup>	1	1	1	1	1	1	0	1	7
Koo 2015 <sup>10</sup>	1	1	1	1	1	0	1	1	7
Kurata 2019 <sup>11</sup>	1	1	1	1	2	1	0	1	8
Manfredi 2019 <sup>12</sup>	1	1	1	1	1	1	1	1	8
Matteson 2012 <sup>13</sup>	1	1	1	1	2	1	0	0	7
Mena-Vázquez 2022 <sup>14</sup>	1	1	1	1	2	1	1	1	9
Narváez 2020 <sup>15</sup>	1	1	1	1	1	1	1	0	7
Tardella 2022 <sup>16</sup>	1	1	1	1	1	1	0	1	7
Yusof 2017 <sup>17</sup>	1	1	1	1	1	0	1	0	6

\* If the follow-up time have been more than 20 months, the follow-up was considered as long enough.

† If the number of patients >80% at the end of follow-up, the cohort was considered to be adequacy.

## References

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**Supplement Table 2.** Summary of findings and certainty of evidence for efficacy

	Summary of findings		Certainty of evidence				Certainty of evidence
	No of participants (No of trials)	Mean difference (95% CI)	Study design	Inconsistency	Imprecision	Small study effects	
<b>FVC</b>							
ABA	243 (3)	0.37 (-2.29 to 3.03)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
RTX	124 (7)	-4.62 (-8.90 to -0.33)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
TCZ	25 (1)	3.00 (-7.89 to 13.89)	Downgraded*	Not downgraded	Downgraded†	Downgraded‡	Very low
TNFis	42 (1)	-0.36 (-8.70 to 7.98)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
JAKis	31 (1)	-1.59 (-6.84 to 3.66)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
<b>DLCO</b>							
ABA	177 (2)	-0.65 (-3.58 to 2.28)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
RTX	77 (4)	0.01 (-4.16 to 4.17)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
TCZ	25 (1)	1.50 (-9.83 to 12.83)	Downgraded*	Not downgraded	Downgraded†	Downgraded‡	Very low
JAKis	31 (1)	-3.03 (-8.17 to 2.11)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
<b>FEV1</b>	75 (3)	0.16 (-5.85 to 6.17)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
<b>Non-progression rate of HRCT</b>							
ABA	216 (3)	0.804 (0.747 to 0.856)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
RTX	102 (5)	0.661 (0.542 to 0.773)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
TCZ	28 (1)	0.929 (0.765 to 0.991)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
JAKis	31 (1)	0.839 (0.663 to 0.945)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
NA	23 (1)	0.696 (0.471 to 0.868)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
<b>Case fatality rate</b>							
ABA	263(1)	0.008 (0.001 to 0.027)	Downgraded*	Not downgraded	Not downgraded	Downgraded‡	Low
RTX	117 (3)	0.165 (0.100 to 0.240)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate
TNFis	632 (3)	0.064 (0.045 to 0.085)	Downgraded*	Not downgraded	Not downgraded	Not downgraded	Moderate

FVC, forced vital capacity; DLCO, diffusion lung capacity for carbon monoxide; FEV1, forced expiratory volume in the first second; HRCT, high-resolution computed tomography; ABA, abatacept; RTX, rituximab; TCZ, tocilizumab; TNFis, tumor necrosis factor inhibitors; JAKis, Janus kinase inhibitors

\* Downgraded by one level because studies were cohort studies with a one-level reduction in evidence level

† Downgraded by one level because the limits of the 95% confidence interval were 20 points different to smallest worthwhile effect

‡ Downgraded by one level owing to small study bias