**Supplementary Table 1. Search Strategy in Pubmed**

|  |  |
| --- | --- |
| ID | Query |
| # 1 | ((etanercept or anti-TNF therapy)) AND clinical trial Schema: nomesh |
| # 2 | (ankylosing spondylitis) AND anti tumor necrosis factor therapy |
| # 3 | ((ankylosing spondylitis) AND etanercept) OR anti tumor necrosis factor therapy |
| # 4 | ((etanercept and ankylosing spondylitis)) AND randomized controlled trial |
| # 5 | ((25 mg and etanercept)) OR 50mg etanercept |
| # 6 | (TNF blocker) OR ((etanercept) AND randomized controlled trial) |
| # 7 | (etanercept) AND randomized controlled trial |
| # 8 | etanercept or anti-TNF therapy |
| # 9 | etanercept |
| # 10 | etanercept and ankylosing spondylitis or anti-TNF therapy Filters: Clinical Trial; Randomized Controlled Trial |
| # 11 | etanercept and ankylosing spondylitis or anti-TNF therapy Filters: Clinical Trial |
| # 12 | etanercept and ankylosing spondylitis or anti-TNF therapy |
| # 13 | etanercept and ankylosing spondylitis or anti-TNF |
| # 14 | etanercept and ankylosing spondylitis and anti-TNF |
| # 15 | etanercept and ankylosing spondylitis |
| # 16 | etanercept ankylosing |
| # 17 | etanercept dosing period ankylosing |
| # 18 | treatment pattern of etanercept and ankylosing |
| # 19 | persistence of etanercept and ankylosing |
| # 20 | duration of etanercept and ankylosing |
| # 21 | duration of etanercept |
| # 22 | antidrug antibodies etanercept |
| # 23 | 25 mg and etanercept |
| # 24 | dose and etanercept |
| # 25 | dose separation and etanercept Schema: all |
| # 26 | dose separation and etanercept |
| # 27 | benefit of dose separation and etanercept Schema: all |
| # 28 | benefit of dose separation and etanercept |
| # 29 | pharmacokinetic and etanercept |

**Supplementary Table 2. Meta-analysis of efficacy evaluated by BASFI and BASDAI scores**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome | Subgroups | Test for overall effect | |  | Heterogeneity | |
|  |  | MD (95% CI) | *p*-value |  | *I* 2 (%)a | *p*-valueb |
| BASFI | Dose-related |  |  |  |  |  |
|  | 25 mgc | -2.90 (-7.10, -1.30) | 0.18 |  | 99 | <0.00001 |
|  | 50 mgd | -1.83 (-4.11, -0.45) | 0.12 |  | Not applicable |  |
|  | Duration-related |  |  |  |  |  |
|  | Less than 12 weekse | -11.21 (-11.63, -10.79) | <0.00001 |  | 100 | <0.00001 |
|  | 12 weeks | -0.60 (-0.65, -0.55) | 0.00001 |  | 88 |  |
|  | More than 12 weekse | 0.01 (-0.83, 0.84) | 0.99 |  | 92 | <0.00001 |
| BASDAI |  | -9.94 (-26.33, 6.45) | 0.23 |  | 100 | <0.00001 |

95% CI, 95% confidence interval; MD, mean difference

a. *I2* > 40% denotes statistical heterogeneity between the studies.

b. *p* < 0.10 in the chi-squared test denotes statistical heterogeneity between the studies.

c. 25 mg: etanercept dosing at 25 mg twice weekly.

d. 50 mg: etanercept dosing at 50 mg once weekly.

e. Period of etanercept dosing.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 3. Meta-analysis of safety** | | | | | | |
| Outcomes | Subgroups | Heterogeneity |  |  | Test for overall effect | |
|  |  | *I* 2 (%) | *p*-value a |  | RR (95% CI) | *p*-value |
| Serious adverse reactions | Dose-related |  |  |  |  |  |
|  | 25 mg | 0 | 0.79 |  | 1.58 (0.68–3.68) | 0.28 |
|  | 50 mg | 0 | 0.40 |  | 1.89 (0.52–6.92) | 0.34 |
|  | Duration-related |  |  |  |  |  |
|  | 12 weeks | 0 | 0.63 |  | 1.85 (0.53–6.45) | 0.34 |
|  | More than 12 weeks | Not applicable |  |  | 1.87 (0.61–5.73) | 0.27 |
| Upper respiratory tract infection | Dose-related |  |  |  |  |  |
|  | 25 mg | 48 | 0.13 |  | 1.15 (0.82–1.62) | 0.42 |
|  | 50 mg | Not applicable |  |  | 0.56 (0.23–1.36) | 0.20 |
|  | Duration-related |  |  |  |  |  |
|  | Less than 12 weeks | Not applicable |  |  | 1.25 (0.29–5.41) | 0.77 |
|  | 12 weeks | Not applicable |  |  | 0.54 (0.22–1.32) | 0.18 |
|  | More than 12 weeks | 55 | 0.14 |  | 1.54(0.86–2.75) | 0.14 |

95% CI, 95% confidence interval; RR, risk ratio

a. *p* < 0.10 in the chi-squared test denotes statistical heterogeneity between the studies.

b. 25 mg; 25-mg twice-weekly etanercept dosing.

c. 50 mg; 50-mg once-weekly etanercept dosing.

d. Period of etanercept dosing.