Table I-3. Strength of evidence for adverse events

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| --- | --- | --- | --- | --- | --- | --- |
| **Number of Studies; # of Subjects** | **Risk of Bias****Design/ Quality** | **Consistency** | **Directness** | **Precision** | **Results** | **Strength of Evidence** |
| **Biologic DMARD vs. Biologic DMARD** |  |
| **ADA vs. ETN vs. INF**2 observational N=827 | Medium2 cohort/1 fair, 1 good | Consistent | Direct  | Imprecise  | ETN had lower risk of withdrawals due to AEs than INF. Concomitant MTX lowered withdrawals. | Low |
| **Oral DMARD vs. placebo** |  |
| **LEF vs. placebo**1 RCT N=1431 meta-analysis(N=190)  | MediumRCT and meta-analysis/fair | Unknown, single study | Direct | Imprecise  | Higher rates of diarrhea and increased ALT levels for LEF vs. placeboLEF had higher withdrawals due to AEs | Insufficient |
| **SFZ vs. placebo**1 meta-analysis (N=434)  | Mediummeta-analysis/fair | Consistent | Direct  | Imprecise  | SFZ had more withdrawals due to AEs than placebo, but not statistically significant | Insufficient |
| **Biologic DMARD vs. placebo** |  |
| **ADA vs. placebo**2 RCT N=415 | MediumRCT/2 fair | Consistent | Direct  | Imprecise  | Infusion reactions with ADA; worsened psoriasis with placebo | Low |
| **ETN vs. placebo** 2 RCT N=265 | MediumRCT/2 fair | Consistent | Direct | Imprecise | No difference in adverse events except for more ISRs with ETN | Low |
| **GOL vs. placebo**1 RCT N=405 | MediumRCT/1fair | Unknown, single study | Direct  | Imprecise  | More infections and malignancies for GOL than placebo | Insufficient |
| **INF vs. placebo** 2 RCT N=304 | MediumRCT/2 fair | Consistent | Direct | Imprecise  | No differences in adverse events for INF and placebo | Insufficient |
| **TNF Inhibitors vs. placebo**1 meta-analysis (N=882)  | Mediummeta-analysis/fair | Consistent | Direct | Imprecise  | TNF inhibitors as class had more withdrawals due to AEs than placebo, but not statistically significant | Insufficient |

ADA = adalimumab; AE = adverse event; ALT = alanine aminotransferase; DMARD = disease-modifying antirheumatic drug; ETN = etanercept; GOL = golilumab; INF = infliximiab; ISR = injection site reaction; LEF = leflunomide; MTX = methotrexate; N = total sample size; RCT = randomized controlled trial; vs. = versus