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 | Medium  2 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=143  1 meta-analysis  (N=190) | Medium  RCT and meta-analysis/  fair | Unknown, single study | Direct | Imprecise | Higher rates of diarrhea and increased ALT levels for LEF vs. placebo  LEF had higher withdrawals due to AEs | Insufficient |
| **SFZ vs. placebo**  1 meta-analysis (N=434) | Medium  meta-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 | Medium  RCT/2 fair | Consistent | Direct | Imprecise | Infusion reactions with ADA; worsened psoriasis with placebo | Low |
| **ETN vs. placebo**  2 RCT N=265 | Medium  RCT/2 fair | Consistent | Direct | Imprecise | No difference in adverse events except for more ISRs with ETN | Low |
| **GOL vs. placebo**  1 RCT N=405 | Medium  RCT/1fair | Unknown, single study | Direct | Imprecise | More infections and malignancies for GOL than placebo | Insufficient |
| **INF vs. placebo**  2 RCT N=304 | Medium  RCT/2 fair | Consistent | Direct | Imprecise | No differences in adverse events for INF and placebo | Insufficient |
| **TNF Inhibitors vs. placebo**  1 meta-analysis (N=882) | Medium  meta-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