Drug Class Review

Targeted Immune Modulators

Final Update 5 Report

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Update 3: March 2012
Update 2: November 2009
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STRUCTURED ABSTRACT

Purpose

We systematically compared the efficacy, effectiveness, and harms (adverse events) of abatacept, adalimumab, alefacept, anakinra, apremilast, canakinumab, certolizumab pegol, etanercept, golimumab, infliximab, natalizumab, rituximab, secukinumab tocilizumab, tofacitinib, ustekinumab, and vedolizumab in patients with rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, ulcerative colitis, and plaque psoriasis.

Data Sources

To identify published studies, we searched PubMed, EMBASE, CINAHL, Centre for Reviews and Dissemination, The Cochrane Library, and International Pharmaceutical Abstracts up to 2016 (January). We also searched the US Food and Drug Administration Center for Drug Evaluation and Research website for additional unpublished data, requested dossiers of information from pharmaceutical manufacturers, and retrieved relevant citations from reference lists of included studies.

Review Methods

Study selection, data abstraction, validity assessment, grading the strength of the evidence, and data synthesis were all carried out according to standard streamlined Drug Effectiveness Review Project methods.

Results and Conclusion

For rheumatoid arthritis, we did not find any direct evidence for most comparisons among approved targeted immune modulators. Results indicate similar efficacy between targeted immune modulators if direct head-to-head trials were available (low or insufficient strength of evidence). Most of the comparisons are based on single-study evidence and it is likely that future trials will change these estimates.

A single head-to-head randomized trial for psoriatic arthritis indicates equivalent efficacy between adalimumab, etanercept, and infliximab (insufficient strength of evidence).

For Crohn's disease, one open-label trial suggested higher discontinuation rates because of adverse events or loss of response for adalimumab than infliximab. A second open-label trial did not identify any differences in endoscopic, histological, or clinical recurrence rates following curative ileocolonic resection (insufficient strength of evidence).

For plaque psoriasis four head-to-head trials report that secukinumab is superior to ustekinumab; both secukinumab and ustekinumab are superior to etanercept; and tofacitinib is equivalent to etanercept in treating plaque psoriasis (low strength of evidence for all comparisons).

We did not find any head-to-head evidence for the treatment of ankylosing spondylitis and ulcerative colitis in adults. Likewise, no head-to-head evidence was available for juvenile idiopathic arthritis, psoriatic arthritis, Crohn's disease, ulcerative colitis, or plaque psoriasis in children.

The most comparative evidence on harms was available for the tumor necrosis factor inhibitors adalimumab, etanercept, and infliximab. Infliximab consistently had a higher risk

of serious infections and discontinuation because of adverse events than abatacept, adalimumab and etanercept (moderate strength of evidence.

Injection site or infusion reactions were less frequent for patients receiving abatacept compared with adalimumab and infliximab (low strength of evidence). Etanercept had a higher risk for injection site reactions than adalimumab, secukinumab, and ustekinumab (low strength of evidence)

Evidence that infliximab has a higher comparative risk for serious infections compared with abatacept, adalimumab, and etanercept was moderate strength. For tuberculosis specifically, low strength evidence suggests a greater risk with adalimumab and infliximab compared with etanercept. For herpes zoster, low strength evidence suggests no differences.

The strength of evidence comparing the risk of malignancy with targeted immune modulators is low strength; however it suggests no differences exist.

High strength of evidence shows that the combination of 2 targeted immune modulators leads to higher risks of serious adverse events, withdrawal due to adverse events, and serious infections without additional therapeutic benefit.

Direct evidence on the comparative risk of any adverse events associated with targeted immune modulators in children does not exist and therefore is insufficient strength to make conclusions.

One trial suggests no difference between adalimumab or tocilizumamb for the subgroups age, gender, duration of disease, and use of previous disease-modifying therapy (insufficient strength of evidence).