Tailored treatment options for patients with psoriasis and psoriatic arthritis – literature review of established and new biologic therapies

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Abstract

Background
The diverse clinical picture of Psoriatic Arthritis (PsA) suggests the need to identify suitable therapies to address the different clinical manifestations.
Review
We set out to review the current literature regarding the use of biological therapies for the treatment of psoriasis and PsA. Literature searches were performed for different classes of biological agents: Anti-TNF (Adalimumab, Etanercept, Infliximab, Golimumab, Certolizumab), Anti-IL12/IL23 (Ustekinumab), Anti-co-stimulatory Molecule (Abatacept), Phosphodiesterase-4-Inhibitor (Apremilast), Anti-IL17 (Secukinumab, Brodalumab, Ixekizumab), T-Cell Modulators (Alefacept, Efalizumab), Anti-IL6 (Tocilizumab), Janus-Kinase-Inhibitor (Tofacitinib), Anti-CD20 (Rituximab). Papers with the highest level of clinical evidence were analysed to look at responses to psoriasis (as measured by the PASI75 response), PsA (ACR20 response), and extra-articular manifestations such as enthesitis and dactylitis scoring, and nail disease improvement. The effect on radiographic progression and patient quality of life was also analysed.
Discussion
The majority of the biologics showed efficacy for skin psoriasis and peripheral arthritis. Efficacy for enthesitis, dactylitis and nail disease was seen in some, but only a few improved sacroiliitis and spinal disease.
Conclusion
Recommendations could be made for Ustekinumab or Secukinumab (if at a higher dose or IV) being used as a 2nd line biologic in anti-TNF failures, and there is evidence for switching anti-TNF drugs if a patient fails their first anti-TNF treatment.

Introduction

The diverse clinical picture of PsA suggests the need to identify suitable therapies to address different combinations of clinical manifestations. Tailoring the available treatment options according to the disease phenotype is needed to ensure the use of a minimal combination of drugs for a maximal therapeutic effect (1). Conventional treatments for PsA have limited efficacy for nail disease, enthesitis or axial involvement, and some are unable to control moderate and severe peripheral joint and skin disease. For the first time, the introduction of biologic treatments offered the possibility of controlling multiple aspects of these diseases using a single drug, minimising the need for additional therapies.

Materials and Methods

A systematic literature research of MEDLINE (via PubMed) and EMBASE data bases (from July 2000 to March 2015) was performed to identify randomised controlled trials (RCT) that reported the efficacy of different biologic therapies in psoriasis and PsA. We used the following MeSH terms: Anti-TNF treatments (adalimumab, etanercept, infliximab, golimumab, certolizumab), Anti-IL12/23 (ustekinumab), Anti-co-stimulatory molecule (abatacept), Phosphodiesterase-4-inhibitor (apremilast), Anti-IL17 (secukinumab, brodalumab, ixekizumab,), Anti-IL6 (tocilizumab), T-cell modulator (alefacept), Anti-CD11a (efalizumab), Janus-kinase-inhibitor (tofacitinib), Anti-CD20 (rituximab), Anti-CD6 (itolizumab), and psoriasis and psoriatic arthritis. Only papers in English were selected. SE and BT screened all titles and abstracts for potential inclusion.

We identified 1718 papers including RCT of biologic treatments in psoriasis and PsA. Duplications or papers analysing the same RCT were excluded. Congress abstracts and case reports were included only for the new emerging therapies, because of the lack of clinical trial data available.

We selected 88 papers, which were analysed in detail, out of which 40 papers were included in table 1.

Results

The table below includes a summary of biologic treatments and their efficacy for different clinical manifestations in PsA and psoriasis, using the following level of evidence classification (Oxford Centre of Evidence-based Medicine, 2009):

1a: Systematic reviews (with homogeneity) of randomized controlled trials
1b: Individual randomized controlled trials (with narrow confidence interval)
1c: “All or none” randomized controlled trials
2a: Systematic reviews (with homogeneity) of cohort studies
2b: Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)
2c: "Outcomes" Research; ecological studies
3a: Systematic review (with homogeneity) of case-control studies
3b: Individual case-control study
4: Case-series (and poor quality cohort and case-control studies)
5: Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Treatment	Peripheral Arthritis	Sacroiliitis & Spinal Disease	Enthesitis	Dactylitis	Nail Involvement	Skin Psoriasis
ADALIMUMAB	YES (*1a)				YES (*1a)	YES (*1a)
ETANERCEPT	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)
ABATACEPT	YES (*1b)	NO (*1b)- study in AS				YES (*1b)
APREMILAST	YES (*1a)		YES (*1b)	YES (*1b)	YES (*1b)	YES (*1a)
ALEFACEPT						YES (*1a)
EFALIZUMAB (withdrawn)	NO (*1b)					YES (*1a)
BRODALUMAB	YES (*1b)	YES (*1b)	NO (*1b)	NO (*1b)		
INFLIXIMAB	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)
IXEKIZUMAB	Ongoing study		Ongoing study	Ongoing study	Ongoing study	YES (*1a)
CERTOLIZUMAB	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)
GOLIMUMAB	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)
ITOLIZUMAB	Planned studies	Planned studies	Planned studies	Planned studies	Planned studies	YES (*1b)
RITUXIMAB	NO (*1b)		YES (*1b)	NO (*1b)		
SECUKINUMAB	YES (*1a)	YES (*1a)	YES (*1a)	YES (*1a)		
TOCILIZUMAB	YES (*4)	NO (*1b)				YES(pustular psoriasis) (*4)
TOFACITINIB	Ongoing studies	Under recruitment in AS	Ongoing studies	Ongoing studies		YES (*1a)
USTEKINUMAB	YES (*1a)	YES (*1b)	YES (*1b)	YES (*1b)		YES (*1a)

Discussion

The new biologics reassuringly showed similar control of peripheral joint symptoms (indirect comparison showed the following percentages of ACR 20 response: Ustekinumab 90 mg, 42%; Secukinumab 300 mg, 54%; Brodalumab 280 mg, 64%: Abatacept 10 mg/kg, 48%; Apremilast 20 mg daily, 43.5%, which is comparable to Infliximab 5 mg/kg, 65%; Certolizumab 200 mg e.o.w., 58%; Golimumab 100 mg monthly, 61%; Adalimumab 58%, Etanercept 25 mg twice weekly, 59%).

Different aspects of the disease activity, such as dactylitis and enthesitis, were effectively controlled by anti TNF therapy, and also by Ustekinumab and Secukinumab.

The axial involvement also responded to therapy with Ustekinumab and Secukinumab.

The nail involvement, enthesitis and dactylitis associated were all improved with treatment with Apremilast and Secukinumab, (along with Infliximab, Certolizumab, Etanercept, Adalimumab and Golimumab).

Optimising therapy for those patients who failed anti-TNF treatments is one of the main challenges. Dose adjustment of Secukinumab showed the best response in PsA patients previously treated with anti TNF therapy (2).

The response to a second anti TNF agent, in patients with PsA who failed the first anti TNF, is significantly lower (3); the use of other biologic treatments with different mechanisms of action is therefore currently considered a better option.

Conclusion

1. Ustekinumab can be used as second line biologic in psoriatic and PsA patients who failed TNF treatments (level of evidence 1b)
2. Secukinumab at higher dose (300 mg) and with additional IV loading dose is effective in PsA patients who failed anti TNF therapy (level of evidence 1b)
3. The use of a second anti TNF therapy can be effective in patients who failed the first anti TNF treatment (Certolizumab and Golimumab, level of evidence 1b; Infliximab and Adalimumab and Etanercept- level of evidence 2b)

It is difficult to establish an algorithm for sequential biologic treatment in PsA patients who failed the first biologic, due to of lack of evidence of efficacy of the majority of new drugs as second line biologic therapies.

References

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