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Adalimumab
In Psoriatic Arthritis

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Contents

Abstract

▲ Adalimumab, a fully human monoclonal antibody, is a tumour necrosis factor antagonist that has been investigated for efficacy in psoriatic arthritis, based on well-established use of the drug in rheumatoid arthritis.

▲ In well-controlled Phase III trials, adalimumab (40 mg administered subcutaneously every other week) has shown efficacy in adult patients with psoriatic arthritis who had an inadequate response to previous treatment with NSAIDs (24-week ADEPT trial; n = 313) or disease-modifying antirheumatic drugs (12-week study; n = 100).

▲ In these trials, adalimumab recipients experienced a significantly greater improvement in arthritis response ($p < 0.001$ in the ADEPT trial, and $p \leq 0.05$ in the smaller study) than placebo recipients, as assessed by the ACR20, ACR50 and ACR70 response rates.

▲ There was radiographic evidence of progressive joint damage in the placebo group but not the adalimumab group at 24 weeks in the ADEPT trial, according to the mean total Sharp score modified for psoriatic arthritis.

▲ The signs and symptoms of psoriasis in patients with psoriatic arthritis were clinically and statistically more improved with adalimumab than with placebo, according to the PASI responses, at 12 and 24 weeks in the ADEPT trial (e.g. PASI50 rate 75% vs 12% at 24 weeks; $p < 0.001$).

▲ Adalimumab was generally well-tolerated in clinical trials of psoriatic arthritis; the adverse event profile appears to be similar to that associated with use of the drug in rheumatoid arthritis.

Features and properties of adalimumab (Humira®)	
Featured indication	
Psoriatic arthritis	
Mechanism of action	
Tumour necrosis factor antagonism	
Dosage and administration	
Recommended dose	40 mg
Route	Subcutaneous
Frequency	Every other week
Steady-state pharmacokinetics of subcutaneous adalimumab (40 mg every other week in patients with rheumatoid arthritis)	
Peak serum concentration (C_{max})	7.7 μg/mL
Time to C_{max}	≈90 hours
Bioavailability	64%
Volume of distribution	4.7–6.0 L
Terminal half-life	≈2 weeks
Adverse events in patients with psoriatic or rheumatoid arthritis (incidence ≥10%)	
Most frequently reported	Injection-site reactions, upper respiratory tract infection, headache, rash and sinusitis

It is estimated that approximately one-third of patients with psoriasis develop joint disease associated with their condition.[1,2] Psoriatic arthritis is generally less severe than rheumatoid arthritis, but there is joint and bone erosion and structural damage in approximately 40% of patients and psoriatic spondylitis (possibly leading to axial skeletal damage) in 20–40% of affected patients.[3] Radiographic evidence at 2 years after disease diagnosis suggests a relatively early onset of damage,[4] and timely diagnosis and treatment may limit the associated functional limitations and deformity that contribute to the debility and impaired health-related quality of life in patients with this condition.[3-5]

There are few trials evaluating disease-modifying antirheumatic drugs (DMARDs) for the treatment of psoriatic arthritis and their use in this disease is based on evidence of their efficacy in patients with rheumatoid arthritis. In a meta-analysis of trials in psoriatic arthritis, oral sulfasalazine and high-dose parenteral methotrexate (too toxic by current standards) were the only agents with proven efficacy,[2] although cyclosporin has also typically been used; however, these agents do not appear to benefit axial disease and there is no evidence of them delaying disease progression.[6]

With evidence of raised concentrations of tumour necrosis factor (TNF) in psoriatic skin and synovial tissue and fluid,[7] and the use of TNF antagonists in other autoimmune diseases,[8,9] these agents (including etanercept, infliximab and adalimumab) have been investigated for the treatment of psoriatic arthritis.

This profile focuses on the clinical evidence for the use of the fully human monoclonal IgG1 antibody and TNF antagonist adalimumab (Humira®)[1] for the treatment of psoriatic arthritis, and briefly summarises the relevant pharmacodynamic and pharmacokinetic properties of this agent.

1. Pharmacodynamic Profile

The pharmacodynamics of adalimumab have been examined in relation to the drug's activity in rheumatoid arthritis, and some findings are considered relevant in characterising the activity of adalimumab in the treatment of psoriatic arthritis. The majority of data in this section are summarised from reviews of adalimumab,[10,11] TNF inhibition and the pathophysiology of psoriatic arthritis.[5]

Elevated TNF concentrations in psoriatic skin and synovial tissue and fluid may play a key role in the pathogenesis of psoriatic arthritis; recent studies indicate that treatment that decreases TNF concentrations appears to improve psoriatic arthritis.[5] Adalimumab binds specifically to TNF; this prevents the binding of TNF to the p55 and p75 receptors, which inhibits the release of the proinflammatory cytokines (including TNF) that contribute to the joint damage characteristic of inflammatory arthritic conditions.[7,11]

- In patients with rheumatoid arthritis, a single dose of intravenous (IV) adalimumab (1–10 mg/kg), but not placebo, significantly increased mean systemic total concentrations of TNF (possibly indicating the presence of TNF/adalimumab complexes); mean systemic concentrations of TNF messenger RNA were unchanged, but p55 and p75 soluble TNF receptor concentrations were significantly decreased from baseline.[10]

- There were also reduced serum concentrations of some other cytokines (interleukin [IL]-1β mRNA, IL-1 receptor antagonist and IL-6)[10,11] within 24 hours of a single IV dose of adalimumab (1–10 mg/kg); concentrations remained below baseline values through 14 days.[10]

- Adalimumab reduced (from baseline) concentrations of matrix metalloproteases (MMP-1 and -3) and other markers of cartilage and synovium turnover at 24 weeks in patients with rheumatoid arthritis. The drug also reduced concentrations of adhesion molecules (responsible for leukocyte migration) and C-reactive protein, and reduced erythrocyte sedimentation rate (both indicative of reduced acute-phase inflammation).[10]

- Immune function in patients with rheumatoid arthritis was not adversely affected by adalimumab

1 The use of trade names is for identification purposes only and does not imply endorsement.

treatment. Recipients of subcutaneous adalimumab (20 mg weekly or 40 mg every other week for 24 weeks) had slightly increased peripheral lymphocyte percentages (indicated by a slight increase in memory CD4+ and CD8+ T cells and CD19+ B cells; no data reported), but no difference in percentages of CD3+, CD4+, CD8+ or CD25+ T cells, compared with patients receiving placebo (both groups received methotrexate).[12]

- Anti-adalimumab antibody development in 12% of patients with rheumatoid arthritis receiving adalimumab monotherapy in clinical trials[13] may partly account for the lower ACR (defined in table I) response rates that were observed with monotherapy administered every other week than were observed with weekly treatment.[14] Only 1% of patients receiving adalimumab in combination with methotrexate developed antibodies, but the clinical significance of these observations is not clear[13,15] (see also section 2).

2. Pharmacokinetic Profile

There are no pharmacokinetic data for adalimumab in patients with psoriatic arthritis, but relevant properties of the drug have been investigated in patients with rheumatoid arthritis; values in this population are reported to be similar to those in healthy volunteers.[16] Data presented here are summarised from reports of single-[17] or multiple-[18] dose studies in patients with rheumatoid arthritis receiving adalimumab as monotherapy[17,18] or combination therapy with oral methotrexate,[18] from reviews of the pharmacokinetics of TNF antagonists[19,20] and from the manufacturer's prescribing information.[16] Unless otherwise stated, adalimumab was administered subcutaneously at a dosage of 40 mg every other week. There are no pharmacokinetic data for adalimumab recipients with impaired renal or hepatic function.[16]

- The slow absorption and elimination rates of adalimumab contribute to favourable steady-state pharmacokinetics; the concentration-time profile is smooth and uniform, and safe maximum concentrations, and trough concentrations higher than the minimum effective concentration, are maintained.[19,21]

- The volume of distribution was 4.7–6.0 L and in multiple-dose studies, there was no evidence of accumulation of the drug over time.[16] The average absolute bioavailability of adalimumab is 64%.[16]

- In patients with rheumatoid arthritis who received adalimumab monotherapy, mean maximum plasma drug concentration (C_{max}) at steady state was 7.70 μg/mL and mean time to C_{max} (t_{max}) was

Table I. Selected endpoint measures used in trials of psoriatic arthritis[22,24,32]

Endpoint	Measure	
Arthritis response	ACR20/50/70	American College of Rheumatology response criteria. ACR20, ACR50 and ACR70 represent a ≥20%, ≥50% and ≥70% improvement in tender and swollen joint counts and three of five other relevant clinical measures
	PsARC	Psoriatic Arthritis Response Criteria (modified). A response is defined by an improvement of ≥30% in at least one of the joint counts (swollen or tender), improvements in Patient's Global Assessment or Physician's Global Assessment by one point on a visual analogue scale (instead of Likert scale in original PsARC), and no worsening of any measure
Joint damage	Modified total Sharp score	Sharp score (originally for rheumatoid arthritis) modified for psoriatic arthritis. For radiographic evidence of progressive structural damage (score increase) to the hands and feet. Composite score of joint erosion (score 0–5 at 54 sites) and joint space narrowing (score 0–4 at 48 sites)
Skin disease	PASI	Psoriasis Area and Severity Index. A composite measure of psoriasis symptoms and body surface area involved (scale 0–72). Score reduction represents improvement. A PASI50, PASI75 or PASI90 response represents a ≥50%, ≥75% or ≥90% improvement
Disability	HAQ DI	Health Assessment Questionnaire Disability Index. Scale 0–3. Score reduction represents improvement
Quality of life	SF-36	Short Form 36 Health Survey scoring eight individual domains and Physical and Mental Component Summary scores. Score increase represents improvement
	DLQI	Dermatology Life Quality Index. An 11-item self-administered questionnaire; scale 0–30. Score increase represents improvement

≈90 hours;[18] the mean minimum serum concentration (C_{min}) at steady state was 3.8 μg/mL, the average serum concentration was 5.5 μg/mL and the mean area under the plasma concentration-time curve (AUC) for the 14-day dose interval was 1832 μg • h/mL.[18]

- In patients receiving adalimumab with oral methotrexate background therapy (dose not stated), mean C_{min}, C_{max} and average serum concentrations of adalimumab were 5.83 μg/mL, 9.97 μg/mL and 7.63 μg/mL, respectively.[18] Mean t_{max} was 83.2 hours and mean AUC for the 14-day dose interval was 2563 μg • h/mL.[18]
- Concentrations of adalimumab in the synovial fluid of five patients with rheumatoid arthritis were 31–96% of those in serum.[16]
- Mean terminal elimination half-life was approximately 2 weeks.[16] There was a trend for the apparent clearance of adalimumab to be higher in the presence of anti-adalimumab antibodies (see also section 1) and lower in elderly patients.[16]
- Following the coadministration of therapeutic dosages of methotrexate (dosage and route not specified), apparent clearance of multiple doses of adalimumab was reduced by 44%,[16] but no dosage adjustments are required to accommodate this increased exposure.

3. Clinical Efficacy

The efficacy of adalimumab (40 mg subcutaneously every other week) has been investigated in two Phase III randomised, double-blind, placebo-controlled, multicentre clinical trials[22,23] in patients aged ≥18 years with moderate to severely active psoriatic arthritis (defined as the presence of at least three swollen joints and at least three tender or painful joints). The report of the large (n = 313) 24-week pivotal study in patients with an inadequate response to NSAIDs (ADEPT; ADalimumab Effectiveness in Psoriatic arthritis Trial) has been fully published[22] (with further detail in abstracts[24,25]) and that of the smaller (n = 100) 12-week trial in patients with an inadequate response to DMARDs is available as an abstract and poster.[23]

In the ADEPT trial, enrolled patients had active psoriatic skin lesions or a documented history of psoriasis, and were stratified by methotrexate use and degree of psoriasis (≥3% or <3% of body surface area).[22] The dosage and route of administration were not specified; orally (or subcutaneously) administered methotrexate is commonly used as background therapy in psoriatic arthritis. Baseline characteristics for adalimumab and placebo recipients were similar: mean age ≈49 years, concentration of C-reactive protein 1.4 mg/dL indicating significant inflammation, arthritic disease duration 9.8 and 9.2 years, psoriasis duration 17 years, methotrexate coadministration in 51% and 50% of patients (no other DMARDs permitted), and proportion of patients with psoriasis affecting at least 3% of body surface area 46% and 43%. Efficacy analyses were based on patients who received at least one dose of study drug (intention-to-treat population).[22]

Selected endpoint measures (and their abbreviations) used in trials of psoriatic arthritis are shown in table I. The primary efficacy endpoints in the ADEPT trial were the ACR20 response rate at week 12[22] and the change in modified total Sharp score at week 24.[22,24] Secondary endpoints included further joint disease assessment (using other ACR measures and PsARC),[22] severity of skin disease in patients with ≥3% body surface area affected by psoriasis (PASI)[22] and the assessment of disability (according to the HAQ DI).[22]

Subanalyses of the ADEPT trial (published as abstracts and posters[25-30]) assessed the response according to the coadministration (n = 77) or not (n = 74) of oral methotrexate (total n = 151),[27,31] the affect of adalimumab on quality of life (according to SF-36 and DLQI)[25] and health state utility (n = 313),[26] and the results of the 24-week, open-label extension phase of the trial (total trial duration 48 weeks).[28,29] In the extension phase, all patients received adalimumab 40 mg every other week; after 12 weeks of this phase, patients with an inadequate response to the drug could increase the dosage to 40 mg every week.[28].

The enrolment of patients in the smaller trial[23] was based on current or historical lack of response to

DMARDs.[23] The primary endpoint was ACR20 response at week 12, and secondary endpoints included an assessment of disability (HAQ DI) and, in those patients with psoriasis, assessments of their skin disease (according to a target lesion evaluation and the Physician's Global Assessment for psoriasis).

Arthritis - Signs and Symptoms

- The improvement in arthritis response was significantly greater with adalimumab than with placebo in both major trials of patients with psoriatic arthritis.[22,23]
- In the ADEPT trial, there was a significantly greater improvement in arthritis in adalimumab (n = 151) than in placebo recipients (n = 162) at 12 weeks, as assessed by ACR20 response rate (coprimary endpoint; 58% vs 14%; $p < 0.001$) [figure 1].[22]
- In this trial, secondary assessments of joint disease (ACR20 at 24 weeks and ACR50 and ACR70 at 12 and 24 weeks) were also significantly (all $p < 0.001$) improved with adalimumab compared with placebo (figure 1).[22]
- ACR responses developed rapidly, and response rates were significantly different between groups for ACR20 and ACR50 at week 2 (27% vs 6% and 11% vs 0%; $p < 0.001$ for both) and ACR70 at week 4 (7% vs 1%; $p = 0.002$).[22]
- PsARC response rates for adalimumab recipients and placebo recipients were 62% versus 26% at 12 weeks and 60% versus 23% at 24 weeks (significance not reported).[22]
- In the smaller trial (in patients not adequately responsive to DMARDs),[23] the ACR20 (primary endpoint), ACR 50 and ACR70 response rates at 12 weeks were significantly greater with adalimumab (n = 51) than with placebo (n = 49) [figure 1]; treatment groups were well-matched at baseline, except for the degree of inflammation, indicated by the concentration of C-reactive protein (1.0 in the adalimumab group vs 1.6 in the placebo group; $p < 0.05$).[23]
- Arthritis responses to adalimumab treatment that were demonstrated in the double-blind phase of the ADEPT trial were further improved by another 24 weeks of treatment (open-label) with the agent.[28] The group originally randomised to adalimumab in the double-blind phase continued to improve

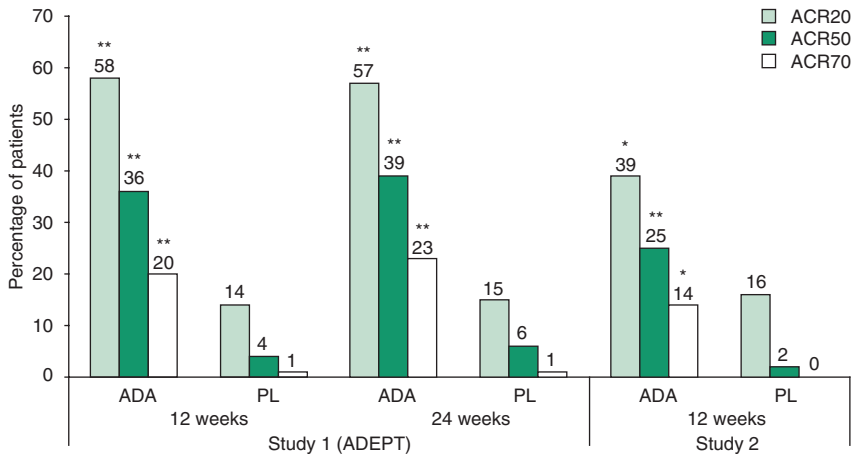

Fig. 1. Efficacy of subcutaneous adalimumab (ADA) in adult patients with psoriatic arthritis. Data from two randomised, double-blind, multicentre Phase III clinical trials of adalimumab (40 mg every other week) or placebo (PL) in patients with moderate to severely active disease (one report fully published,[22] one available as an abstract and poster[23]). Study 1 (ADEPT): patients with an inadequate response to NSAIDs received ADA (n = 151) or PL (n = 162) for 24 weeks.[22] Study 2: patients with an inadequate response to DMARDs received ADA (n = 51) or PL (n = 49) for 12 weeks.[23] ACR20, ACR50 and ACR70 represent a 20%, 50% and 70% improvement in arthritis response according to the American College of Rheumatology (ACR) criteria. * $p \leq 0.05$, ** $p < 0.001$ vs PL.

(ACR20, ACR50 and ACR70 response rates at 24 weeks were 57%, 39% and 23%, and at 48 weeks were 61%, 46% and 31%); the responses in the group originally randomised to placebo improved from 15%, 6% and 1% at 24 weeks to 54%, 37% and 21% at 48 weeks.[28]

Arthritis - Joint Damage

- Adalimumab inhibited joint damage (as assessed by the mean change in modified total Sharp score; coprimary endpoint), whereas placebo did not, in patients in the ADEPT trial, and the difference was statistically significant.[22] The between-group difference at 24 weeks was significant (mean change with adalimumab −0.2 [inhibition] vs mean change with placebo +1.0 [progression]; $p < 0.001$); the component scores of the Sharp score, joint erosion and joint space narrowing scores, were also reduced significantly more with adalimumab than with placebo (mean change 0.0 vs +0.6 and −0.2 vs +0.4; $p < 0.001$ for both).[22]
- At 24 weeks, 3-fold as many placebo as adalimumab recipients experienced an increase of >0.5 in modified total Sharp score (28.9% vs 9%), and 3-fold as many adalimumab as placebo recipients had a score decrease of >0.5 (18.8% vs 5.3%). The percentages of patients with no change in score was similar for the two groups.[24]
- The reduction in progressive joint destruction demonstrated in the double-blind phase of the ADEPT trial, was maintained during the open-label extension phase, in patients who received active treatment in both phases; the mean change in modified Sharp score over 48 weeks was 0.1.[29] As discussed, patients originally randomised to placebo had greater radiographic evidence of progressive structural damage than adalimumab recipients during the 24-week, double-blind phase, but when switched to adalimumab for the 24-week extension phase, they experienced inhibition of progression similar to that of patients who received active treatment for 48 weeks.[29]

Psoriasis

- Adalimumab improved symptoms of psoriasis among patients with ≥3% body surface area affected by psoriasis in the ADEPT trial.[22] Significantly more adalimumab recipients (n = 69) experienced an improvement in their skin condition than placebo recipients (n = 69) at 24 weeks (PASI50, PASI75 and PASI90 response rates were 75%, 59% and 42% vs 12%, 1% and 0% for placebo recipients; $p < 0.001$ for all comparisons) [figure 2], and the difference was significant from as early as week 4 (PASI75 response rate 16% vs 3%; $p = 0.009$). Baseline values for PASI were 7.4 and 8.3 for the respective treatment groups.[22]
- In this trial, adalimumab treatment also reduced the impact of the patient's skin disease on daily activities significantly more than placebo; at week 24, the DLQI was decreased by 6.1 versus 0.7 ($p < 0.001$), from respective baseline values of 8.6 and 10.3.[22]
- The improvements in skin disease in the adalimumab group were maintained during the open-label phase of the ADEPT trial;[28] at 48 weeks, PASI50, PASI75 and PASI90 rates were 70%, 58% and 46% for adalimumab-only recipients.

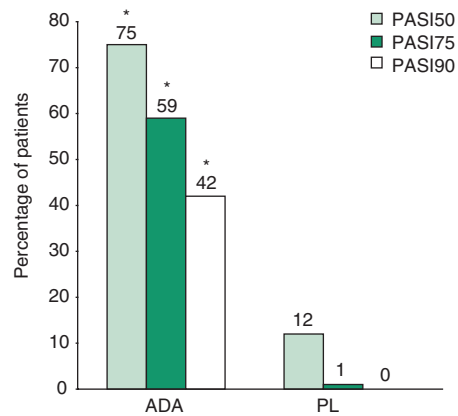

Fig. 2. Skin responses to adalimumab (ADA) in patients with psoriatic arthritis. Data from the ADEPT trial[22] in patients with moderate to severely active disease and and an inadequate response to NSAIDs. In the 24-week randomised, double-blind phase, patients received ADA 40 mg every other week (n = 151) or placebo (PL) [n = 162]. PASI50, PASI75 and PASI90 represent a 50%, 75% and 90% improvement in psoriasis, according to the PASI (Psoriasis Area and Severity Index). * $p \leq 0.001$ vs PL.

Patients originally randomised to placebo then receiving adalimumab from weeks 24–48 achieved response rates of 76%, 63% and 47%. In both groups, responses were similar for patients with mild psoriasis (baseline PASI scores <10) and those with moderate to severe psoriasis (baseline PASI scores ≥10).[30]

- There was also a significantly better psoriasis response with adalimumab than with placebo in patients with an inadequate response to DMARDs. Target lesions in 40.6% of adalimumab recipients versus 6.7% of placebo recipients ($p \leq 0.01$) were considered clear or almost clear according to the Physician's Global Assessment, and the mean reduction in target lesion score (estimated from a graph) was −45 in adalimumab recipients versus 0 in placebo recipients.[23]

Disability and Quality of Life

- The quality of life of adalimumab recipients was significantly improved compared with that of placebo recipients in the ADEPT trial. Seven of eight individual SF-36 domain scores (i.e. for all domains except mental health) were significantly improved in the adalimumab compared with the placebo group at week 24,[25] and these improvements, other than for role-emotional, were also clinically significant (according to definitions for rheumatoid arthritis). Likewise, there was a significant improvement in the Physical Component Summary score in the adalimumab compared with the placebo group (increase was 9.3 vs 1.4 at both 12 and 24 weeks [from baseline values of 33.2 and 33.3]; $p < 0.001$), but not in the the Mental Component Summary score (1.8 vs 0.6 at week 24).[22] Baseline Physical and Mental Component summary scores on the SF-36 indicated marked physical disability in both groups but almost normal mental health scores compared with a healthy population, which may explain the difference in physical and mental score results.[22]
- Overall, patients showed a greater improvement in health state utility with 24 weeks of adalimumab treatment than with placebo in this trial, as estimated by the Short Form 6D, a preference-based utility instrument using the Brazier algorithm of responses to the SF-36 (improvement 10.6% vs 2.9%; $p < 0.01$).[26,31] Patients who had a PsARC response (vs no response) and patients who had ≥3% (vs <3%) body surface area affected by psoriasis had greater improvements in this parameter (p-values not reported).
- There was a significantly greater and sustained improvement in disability for adalimumab recipients compared with placebo recipients in the ADEPT study; the HAQ DI score reduction of 0.4 versus 0.1 ($p < 0.001$) at week 12 (from a baseline score of 1.0 in each group) was maintained at week 24.[22]
- Disability was also significantly more improved with adalimumab than with placebo in the trial of patients not adequately responsive to DMARDs;[23] mean change from baseline to 12 weeks was −0.3 versus −0.1 ($p \leq 0.01$).

Adalimumab Coadministered with Methotrexate

- In the ADEPT trial, the arthritis response was similar for recipients of adalimumab plus methotrexate and those receiving adalimumab monotherapy (ACR20, 50 and 70 response rates at 24 weeks were 59%, 42% and 23% vs 55%, 36% and 22%).[27] There was also no difference in disability improvements (according to the HAQ DI) between treatment groups.[27] However, skin symptoms improved more with combination treatment than with monotherapy; PASI50, 75 or 90 response rates were numerically higher (but not statistically significantly so) with combination treatment (n = 29) than with monotherapy (n = 40) [86%, 72% and 52% vs 70%, 53% and 35%].[27,28]

4. Tolerability

The tolerability profile of adalimumab has primarily been derived from the 24-week pivotal trial in patients with psoriatic arthritis discussed in section 3.[22] Additional data from the pooled analysis of clinical trials in patients with rheumatoid arthritis that is detailed in the manufacturer's prescribing information is relevant,[16] as there is to date a larger body of tolerability data for adalimumab in patients

with rheumatoid arthritis, than there is for patients with psoriatic arthritis.

- Adalimumab was generally well-tolerated by patients with psoriatic arthritis,[22] with a similar incidence of adverse events as that with placebo. The tolerability profile of adalimumab appears to be similar in patients with rheumatoid arthritis to that in patients with psoriatic arthritis.[16]

- In patients with rheumatoid arthritis, the incidence of serious infections in placebo-controlled studies of adalimumab was 0.04 per patient-year with adalimumab versus 0.02 per patient-year with placebo.[16] As with all TNF antagonists,[33] the manufacturer's prescribing information for adalimumab carries a warning for the development of serious infections (including tuberculosis and other opportunistic infections) while receiving the drug. Further warnings, also common to all TNF antagonists, pertain to the onset or exacerbation of demyelinating disease and malignancies.[16,33] Worsening of congestive heart failure has also been reported with adalimumab treatment.[16]

- The most frequently reported adverse events in adalimumab recipients and placebo recipients in the pivotal clinical trial of psoriatic arthritis were upper respiratory tract infection (12.6% vs 14.8%) and nasopharyngitis (9.9% vs 9.3%).[22] Other adverse events included injection-site reactions, headache, hypertension, arthralgia, diarrhoea and aggravation of psoriatic arthropathy or psoriasis; these events occurred in 3–10% of patients in each treatment group.[22]

- The most common adverse reaction to adalimumab (in trials in patients with rheumatoid arthritis) was injection-site reactions (involving erythema and/or itching, haemorrhage, pain or swelling) [20% vs 14% with placebo], most of which were mild and did not prompt treatment discontinuation.[16] The incidence of other adverse events with adalimumab versus placebo were upper respiratory tract infection (17% vs 13%), headache (12% vs 8%), rash (12% vs 6%), sinusitis (11% vs 9%), and gastrointestinal symptoms, abnormal laboratory test, accidental injury, back pain, urinary tract infection and hypertension (all ≤10% in any treatment group).[16]

- Serious adverse events occurred in 5 of 151 adalimumab recipients (vs 7 of 162 placebo recipients) with psoriatic arthritis, but only one of five active treatment discontinuations was because of a serious adverse event (viral meningitis); two others were for nonserious events, and the other two were because of laboratory value abnormalities (low platelet count, and elevated liver function results in patient also receiving methotrexate).[22] One placebo recipient withdrew from treatment (because of aggravated psoriasis).

- In four double-blind studies in patients with rheumatoid arthritis, the discontinuation rates for adverse events were 7% and 4% for adalimumab and placebo recipients.[16] The most common events responsible were clinical flare reaction (0.7%), rash (0.3%) and pneumonia (0.3%).

5. Dosage and Administration

The recommended dosage for adalimumab is 40 mg subcutaneously every other week, which can be administered with methotrexate or other DMARDs.[16] Further details concerning the administration of adalimumab (including warnings common to all TNF antagonists concerning the development of serious infections, demyelinating disease and/or malignancies)[33] are included in the manufacturer's prescribing information.[16]

6. Adalimumab in Psoriatic Arthritis: Current Status

Adalimumab is approved in the US for reducing signs and symptoms of active arthritis in adult patients with psoriatic arthritis, and in the EU for the treatment of adults with active and progressive psoriatic arthritis when the response to previously administered DMARDs has been inadequate.

In well-controlled 12- and 24-week clinical trials, adalimumab was generally well-tolerated, but, as with all TNF antagonists, vigilance with regard to the long-term tolerability of the drug is recommended. In these trials, adalimumab reduced signs and

symptoms of arthritis and inhibited progression of structural damage in patients with psoriatic arthritis who had experienced an inadequate arthritis response to NSAIDs or DMARDs. Adalimumab also significantly improved the symptoms of the concurrent skin disease in these patients.

Disclosure

During the peer review process, the manufacturer of the agent under review was offered an opportunity to comment on this article; changes based on any comments received were made on the basis of scientific and editorial merit.

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