NEW DRUGS

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Tildrakizumab

Approved indication: psoriasis

Ilumya (Sun)
pre-filled syringes containing 100 mg/mL
Australian Medicines Handbook section 8.2, Drugs for psoriasis

Immune mechanisms are involved in the inflammation seen in psoriasis. Several pro-inflammatory cytokines, such as the interleukins, are implicated and this has led to the use of cytokine modulators when the psoriasis is severe enough to require systemic therapy. These include tumour necrosis factor alpha antagonists, such as etanercept, and the monoclonal antibodies ixekizumab, secukinumab and ustekinumab. Tildrakizumab is a monoclonal antibody which blocks the interaction of interleukin 23 with its receptor and this inhibits the release of pro-inflammatory cytokines.

Tildrakizumab has to be given by subcutaneous injection. The drug is slowly absorbed. In the recommended regimen of one injection followed by another after four weeks and then every 12 weeks, steady-state concentrations are reached at 16 weeks. The antibody is catabolised with a half-life of 23 days. No studies have been done in patients with hepatic or renal impairment.

A phase II trial studied several different doses of tildrakizumab in 355 patients with moderate–severe plaque psoriasis. To be included in the trial the patients had to have a Psoriasis Area and Severity Index (PASI) score of at least 12 (moderate severity). After 16 weeks this score had reduced by at least 75% in 33–74% of the patients. This response was significantly better than the 4% rate seen in a placebo group. At the recommended dose of tildrakizumab 100 mg, 62% of the patients had cleared or minimal psoriasis.[1]

The main trials of tildrakizumab (reSURFACE 1 and 2) studied doses of 100 mg and 200 mg in patients with moderate–severe plaque psoriasis (PASI score ≥12). The participants in reSURFACE 1 were randomised to tildrakizumab or placebo, while in reSURFACE 2 patients were randomised to tildrakizumab, etanercept or placebo (see Table). After 12 weeks the patients in the placebo groups were re-randomised to one of the tildrakizumab groups. The PASI score fell by at least 75% (PASI 75) in 6% of the placebo groups at 12 weeks. In contrast, this outcome was achieved by 61–64% of the patients given tildrakizumab 100 mg, 62–66% of those given 200 mg and 48% of the etanercept group. At 28 weeks the PASI 75 outcome was achieved by 73–82% of the patients who continued tildrakizumab and 54% of those taking etanercept. Favourable responses were also seen in 55–86% of the patients who switched from placebo. With tildrakizumab 100 mg, the psoriasis was clear or minimal in 55–58% of the patients at 12 weeks and in 65–66% of those who were treated for 28 weeks.[2]

During the phase III trials only about 1% of the patients discontinued tildrakizumab 100 mg because of adverse effects.[2] Common effects included injection-site reactions, nasopharyngitis and fatigue. Injecting an antibody that alters the immune response has some potentially serious adverse effects. Cancer was more frequent with tildrakizumab than placebo (0.2 vs 0%). During treatment 6.5% of the patients developed antibodies to tildrakizumab. This led to minor decreases in efficacy, but no apparent increase in adverse events. Tuberculosis should be excluded before treatment. Live vaccines should not be given during treatment and for at least 17 weeks afterwards.

In all clinical trials, 1994 people received tildrakizumab and the mean duration of treatment was 53.9 weeks. As psoriasis is a chronic disease, longer term safety data will be needed, including safety in pregnancy

Table **Twelve-week efficacy of tildrakizumab in psoriasis**[2]

	Trial						
	reSURFACE 1			reSURFACE 2			
Treatment	Tildrakizumab 100 mg	Tildrakizumab 200 mg	Placebo	Tildrakizumab 100 mg	Tildrakizumab 200 mg	Placebo	Etanercept 50 mg
Number of patients	309	308	155	307	314	156	313
PASI 75 response*	64%	62%	6%	61%	66%	6%	48%
Clear or minimal disease†	58%	59%	7%	55%	59%	4%	48%

* Proportion of patients achieving at least a 75% improvement in the Psoriasis Area and Severity Index
† Based on physician's global assessment

and lactation. Although the efficacy of tildrakizumab is probably similar to that of other monoclonal antibodies, its onset of action is slower. More patients will achieve a PASI 75 response with tildrakizumab than with etanercept, but the difference in patients with minimal or cleared psoriasis at 12 weeks is not statistically significant.[2]

TT manufacturer provided additional useful information

REFERENCES

1. Papp K, Thaçi D, Reich K, Riedl E, Langley RG, Krueger JG, et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. Br J Dermatol 2015;173:930-9. https://doi.org/10.1111/bjd.13932
2. Reich K, Papp KA, Blauvelt A, Tyring SK, Sinclair R, Thaçi D, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet 2017;390:276-88. https://doi.org/10.1016/S0140-6736(17)31279-5

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency.