NEW DRUGS

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Risankizumab

Approved indication: psoriasis

Skyrizi (Abbvie)
pre-filled syringes containing 75 mg/0.83 mL

The skin inflammation seen in psoriasis is immune-mediated. This has led to immunomodulating drugs becoming part of treatment. While methotrexate has been used for many years, cytokine modulating drugs such as adalimumab, a tumour necrosis factor inhibitor, and ustekinumab, an inhibitor of interleukins 12 and 23, are more recently available. The systemic treatments are usually prescribed for patients with moderate–severe psoriasis.

Risankizumab is a monoclonal antibody that binds to interleukin 23 to prevent the cytokine binding to its receptor. As interleukin 23 is involved in peripheral inflammation, particularly T-cell responses, inhibiting it aims to reduce the skin lesions of psoriasis.

The drug is injected subcutaneously. To give the recommended dose of 150 mg, two injections are needed at different sites. Lower doses are not required in patients with hepatic or renal impairment. Risankizumab is catabolised and has an elimination half-life of 28 days.

A phase II randomised trial studied different doses of risankizumab in 126 patients with moderate–severe chronic plaque psoriasis. They were injected at the start of the trial and then, depending on the dose, at four weeks and 16 weeks. Another group of 40 patients received treatment with ustekinumab. The primary end point was a reduction of at least 90% on the Psoriasis Area Severity Index (PASI) at week 12 of the trial. This was achieved by 77% of the patients injecting risankizumab 90 mg or 180 mg, compared with 40% of the ustekinumab group. The benefits of treatment were generally sustained for up to 20 weeks after the final injection.[1]

The phase III trials of risankizumab for moderate–severe plaque psoriasis used a dose of 150 mg given at baseline, at four weeks then every 12 weeks.[2,3] They also used a 90% reduction in the PASI as a main outcome for assessing efficacy.

The two UltIMMa trials allocated 997 patients (in a 3:1:1 ratio) to receive risankizumab, ustekinumab or placebo. At week 16 patients in the placebo group were switched to risankizumab. Most of the patients had previously received systemic treatments, including biological therapy. By 16 weeks the psoriasis was clear or almost clear in 84–88% of the risankizumab group with 75% achieving at least a 90% reduction in the PASI. This was a statistically superior outcome to ustekinumab and placebo. The PASI 90 was achieved by 42–48% of the ustekinumab group and 2–5% of the placebo group (see Table). Patients in the placebo group began to improve after they switched to risankizumab. By 52 weeks 78–85% of these patients had achieved a 90% reduction in the PASI. This was similar to the outcome (81–82%) for the patients who took risankizumab throughout the trial. Only 44–51% of the ustekinumab group achieved the same outcome.[2]

The IMMvent trial compared risankizumab with adalimumab in 605 patients. If the patients taking adalimumab had only had an intermediate response at 16 weeks, they were re-randomised to continue or switch to risankizumab. By week 16 there had been a reduction of at least 90% in the PASI score in 72% of the risankizumab group and 47% of the adalimumab group (see Table). The psoriasis was judged to be clear

Table **Sixteen-week efficacy of risankizumab in moderate–severe psoriasis**

Trial	Treatments (number of patients)	Proportion of patients achieving primary outcomes	
		PASI 90*	Clear or almost clear of psoriasis†
UltIMMa-1[2]	Risankizumab (304)	75.3%	87.8%
	Ustekinumab (100)	42%	63%
	Placebo (102)	4.9%	7.8%
UltIMMa-2[2]	Risankizumab (294)	74.8%	83.7%
	Ustekinumab (99)	47.5%	61.6%
	Placebo (98)	2%	5.1%
IMMvent[3]	Risankizumab (301)	72%	84%
	Adalimumab (304)	47%	60%

* PASI Psoriasis Area and Severity Index. PASI 90 is a 90% or greater reduction in the index
† Based on a physician's global assessment score

or almost clear in 84% and 60%. In the 109 patients who were re-randomised from the adalimumab group, 66% achieved the PASI 90 at 44 weeks after being switched to risankizumab, compared with 21% of those who continued adalimumab.[3]

Immunomodulation can increase the risk of infection. While infections are more frequent than with placebo, the rate with risankizumab seems similar to the rate with ustekinumab[2] and adalimumab. For example, in the UltIMMa-1 trial infections occurred in 25% of the risankizumab group, 20% of the ustekinumab group and 17% of the placebo group. Tuberculosis should be excluded before treatment.

Injecting an antibody can induce an immune response. After 52 weeks, up to 14% of patients may develop neutralising antibodies against risankizumab.

Approximately 70% of the patients in the trials were men. There is little information about the drug in pregnancy and lactation.

Evidence is emerging that targeting the interleukins rather than tumour necrosis factor may have greater efficacy. The comparison with ustekinumab suggests that the higher efficacy of risankizumab could be related to its more selective inhibition of interleukin 23. It is currently unknown how risankizumab will compare with other inhibitors of interleukin 23, such as guselkumab, that have also been approved for psoriasis. Further research is needed to establish the role of risankizumab. For example, should treatment be continued long term or stopped and restarted? Long-term data should also reveal if there is any increase in malignancy or problems related to immunogenicity.

manufacturer did not supply data

REFERENCES

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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.