

In the REGARD trial, patients were randomised to ramucirumab monotherapy (8 mg/kg fortnightly) or placebo. All participants received best supportive care. Although median overall survival times were generally shorter in this trial, ramucirumab significantly prolonged survival compared with placebo (5.2 months vs 3.8 months) (see Table).²

In the RAINBOW trial, the most common adverse events with ramucirumab were fatigue (56.8%), neutropenia (54.4%), decreased appetite (40%), abdominal pain (36%), nausea (35.1%), leucopenia (33.9%), diarrhoea (32.4%), epistaxis (30.6%), vomiting (26.9%), peripheral oedema (25%), hypertension (23.8%), stomatitis (18%), proteinuria (16.5%) and thrombocytopenia (13.1%). All of these events were more common with ramucirumab than with placebo. There were six deaths that were thought to be related to ramucirumab plus paclitaxel. Causes included sepsis, septic shock, malabsorption, gastrointestinal haemorrhage and pulmonary embolism.¹

The most common adverse events with ramucirumab in the REGARD trial included fatigue (35.5%), abdominal pain (28.8%), decreased appetite (24.1%), vomiting (19.9%), hypertension (16.1%) and bleeding (12.7%). The five deaths thought to be related to ramucirumab were due to myocardial infarction, gastric haemorrhage, intestinal perforation (2 cases) and pneumonia.²

As hypertension can be a problem with ramucirumab, blood pressure should be monitored regularly. If it occurs, treatment should be interrupted until blood pressure is controlled.


Although patients with a history of thromboembolic events or gastrointestinal bleeding were excluded, myocardial infarction, cardiac arrest, cerebrovascular accident, cerebral ischaemia, gastrointestinal perforations and gastrointestinal bleeding have been reported with ramucirumab. These events have been fatal in some cases and treatment should be stopped if patients show symptoms. Blood clotting should be monitored in those with an increased risk of bleeding. Regular blood counts are also important as neutropenia was common with combination ramucirumab therapy.

As ramucirumab can affect angiogenesis, the drug could potentially reduce wound healing. Treatment should be stopped four weeks before elective surgery and only started again after adequate healing.

Interactions with other drugs have not been observed with ramucirumab. The drug is diluted and given by intravenous infusion over 60 minutes. Infusion reactions can occur and are more common during the first and second infusion. Premedication to prevent infusion reactions is recommended.

Antibodies to ramucirumab were detected in 2–3% of patients. However, these were found not to be neutralising antibodies.^{1,2}

Although ramucirumab improves the survival times of patients with advanced or metastatic gastric cancer, the benefit is modest. In the trials, median survival was prolonged by 8–9 weeks with ramucirumab and paclitaxel, and by 5–6 weeks with ramucirumab alone. Adverse reactions are common with ramucirumab and some are fatal so patient monitoring is essential.

 manufacturer did not respond to request for data

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Secukinumab

Aust Prescr 2016;39:64–6

<http://dx.doi.org/10.18773/austprescr.2016.011>

First published online 19 November 2015

Approved indication: psoriasis

Cosentyx (Novartis)

prefilled syringe or pen containing 150 mg/mL for injection

Australian Medicines Handbook section 8.2

Psoriasis is known to be an immune-mediated inflammatory skin disease. While many patients can be managed with topical treatments, systemic therapy may be needed in patients with moderate or severe disease. Severe plaque psoriasis has been treated with tumour necrosis factor antagonists such as etanercept, and immunosuppressant drugs such as methotrexate, cyclosporin and ustekinumab.

Like ustekinumab, secukinumab is a monoclonal antibody produced by genetic engineering. It binds with the cytokine interleukin 17A. This prevents interleukin 17A from binding to its receptors thereby modifying immune and inflammatory responses.

Secukinumab has to be injected. As the recommended dose is 300 mg, two subcutaneous injections are required. It then takes approximately

six days to reach the peak concentration. Monthly injections produce a steady state after 24 weeks of treatment. As secukinumab is an antibody, it is probably catabolised like other peptides. It has a half-life of 22–31 days.

A placebo-controlled trial (ERASURE) studied 150 mg and 300 mg doses of secukinumab injected weekly for five weeks then once every four weeks. Although the 737 patients were followed up for 52 weeks, the primary end points were assessed after 12 weeks. These end points were the investigators' global assessments and a reduction in the Psoriasis Area and Severity Index (PASI). A reduction of at least 75% of the PASI score was achieved by significantly more of the patients taking secukinumab (see Table). A 100% reduction was achieved by 28.6% of the patients injecting 300 mg, 12.8% of those injecting 150 mg, but only 0.8% of the placebo group. These significant differences were reflected in the investigators' global assessments.¹

Another placebo-controlled trial (FIXTURE), involving 1306 patients, studied the same regimens, but included subcutaneous etanercept as an active control. These patients were also followed up for 52 weeks and efficacy was assessed at week 12. The response to secukinumab was significantly greater than the response to placebo and etanercept whether assessed by the PASI or the investigator (see Table). There was a 100% reduction in the PASI score in 24.1% of the secukinumab 300 mg group and 14.4% of the 150 mg group, compared with 4.3% of the etanercept group and none of the placebo group.¹

Table Efficacy of secukinumab in plaque psoriasis¹

Trial	Treatment (patients)	Proportion achieving primary end point †
ERASURE	secukinumab	
	300 mg (245)	81.6%
	150 mg (243)	71.6%
	placebo (246)	4.5%
FIXTURE	secukinumab	
	300 mg (323)	77.1%
	150 mg (327)	67.0%
	etanercept	
	50 mg (323)	44.0%
	placebo (324)	4.9%

† The primary end point was the proportion of patients, at 12 weeks, who had a reduction from baseline of at least 75% on the (0–72) Psoriasis Area and Severity Index (PASI).

In both trials response to therapy was sustained in most (72–84%) patients treated for up to 52 weeks. The statistically significant advantage over etanercept was also maintained.¹

Two trials have studied the feasibility of patients injecting themselves using prefilled devices. A total of 359 patients were randomised. They injected themselves with secukinumab 150 mg or 300 mg, or a placebo weekly for five weeks and then monthly, with efficacy assessed at 12 weeks. In the trial of prefilled syringes, a reduction of 75% on the PASI score was achieved by 75.9% of patients injecting 300 mg, 69.5% of those injecting 150 mg and none of the placebo group.² The corresponding responses in the trial of an autoinjector pen were 86.7%, 71.7% and 3.3%.³ All the patients were able to use the devices.

The main adverse effects reported in the trials were nasopharyngitis and other upper respiratory symptoms. Patients taking secukinumab were also more prone to develop diarrhoea than those taking placebo. Neutropenia developed in 1% of patients.¹ As secukinumab affects the immune system, there is an increased risk of infections such as candidiasis and oral herpes. Patients should be tested for tuberculosis before treatment. Live vaccines should not be given. Patients can have hypersensitivity reactions to secukinumab, but only 1% of patients developed antibodies to the drug during a year of treatment. There are no studies of drug interactions and secukinumab has not been assessed in pregnant or breastfeeding women.

Secukinumab has been shown to be effective for the treatment of plaque psoriasis for at least 52 weeks. Longer term studies will report on the efficacy and safety of continued treatment. While secukinumab appears to have an advantage over etanercept, the full results of a comparison with ustekinumab in 676 patients were not published at the time of writing. Results at 16 weeks showed a 90% improvement in the PASI score for 79% of the secukinumab group and 57.6% of the ustekinumab group.⁴ Other drugs acting on interleukin 17A are also likely to emerge in the future.

TT manufacturer provided additional useful information

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NEW DRUGS

A:

ANSWERS
TO SELF-TEST
QUESTIONS

- | | |
|---------|---------|
| 1 False | 2 True |
| 3 False | 4 False |
| 5 False | 6 True |

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The Transparency score (T) is explained in 'New drugs: transparency', *Aust Prescr* 2014;37:27.

- * At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).
- † At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).
- ^ At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm).

Correction

How to manage warfarin therapy

Aust Prescr 2015;38:44-8

In the section on 'Maintenance therapy', the phrase 'and some complementary medicines such as St John's wort' has been removed from the list of drugs that may increase INR, because St John's wort decreases INR.

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