trials, myocardial infarctions were more frequent with nintedanib than placebo (1.6 vs 0.5%).

Conclusion

Idiopathic pulmonary fibrosis has a poor prognosis, so reducing the decline in lung function is a benefit. However, in a pooled analysis of the INPULSIS trials, nintedanib had no significant advantage over placebo in preventing acute exacerbations in pulmonary fibrosis or in health-related quality of life.[1]

In non-small cell lung cancer adding nintedanib to docetaxel increases progression-free survival, but the median overall survival is not significantly increased unless the cancer is an adenocarcinoma. The median overall survival for patients with an adenocarcinoma given the combination was 12.6 months compared with 10.3 months for patients treated with docetaxel alone. Pemetrexed is another drug that can be used to treat non-small cell lung cancer. In March 2015 the Pharmaceutical Benefits Advisory Committee concluded that an indirect comparison did not show that the effectiveness of nintedanib and docetaxel was non-inferior to pemetrexed.[3]

T T manufacturer provided additional useful information

REFERENCES *†A

1. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, et al.; INPULSIS Trial Investigators. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med 2014;370:2071-82. http://dx.doi.org/10.1056/NEJMoa1402584
2. Reck M, Kaiser R, Mellemgaard A, Douillard JY, Orlov S, Krzakowski M, et al.; LUME-Lung 1 Study Group. Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomised controlled trial. Lancet Oncol 2014;15:143-55. http://dx.doi.org/10.1016/S1470-2045(13)70586-2
3. Pharmaceutical Benefits Advisory Committee. Public Summary Document – March 2015 PBAC meeting. Nintedanib, 100 mg capsule, 60; 150 mg capsule, 60; Ofev®. Canberra: Australian Government Department of Health; 2015. www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2015-03/nintedanib-caps-ofev-psd1-2015-03 [cited 2016 Feb 12]

Ramucirumab

Aust Prescr 2016;39:63–4
http://dx.doi.org/10.18773/austprescr.2016.030
First published online 22 February 2016

Approved indication: gastric cancer

Cyramza (Eli Lilly)
vials containing 100 mg in 10 mL and 500 mg in 50 mL as concentrate
Australian Medicines Handbook section 14.2.1

Ramucirumab is indicated for patients with advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma when the disease has progressed after cytotoxic chemotherapy. This drug is used in combination with paclitaxel or as monotherapy if paclitaxel cannot be given.

Ramucirumab is a monoclonal antibody that binds to the vascular endothelial growth factor (VEGF) receptor 2. This blocks the binding of several vascular endothelial growth factors (A, C and D) to the receptor. Signalling mediated by these growth factors in endothelial cells is important in the progression of gastric cancer.

The efficacy and safety of ramucirumab has been assessed in two trials – RAINBOW[1] and REGARD.[2] The trials enrolled patients who had locally advanced or metastatic gastric adenocarcinoma which had progressed after chemotherapy with platinum, fluoropyrimidine or both. Patients with a history of arterial thromboembolic events, gastrointestinal bleeding, or uncontrolled hypertension were excluded from the trials. Participants received treatment until their disease progressed (confirmed by radiography) or they had unacceptable adverse effects. In both trials, the primary end point was overall survival.

The RAINBOW trial randomised patients to ramucirumab plus paclitaxel or placebo plus paclitaxel. Ramucirumab (8 mg/kg) or placebo was given on day 1 and 15 and paclitaxel (80 mg/m^2) was given on days 1, 8 and 15 of a 28-day cycle. Median overall survival was significantly longer in the ramucirumab arm than in the placebo arm (9.6 vs 7.4 months) (see Table).[1]

Table **Efficacy of ramucirumab alone and in combination with paclitaxel for gastric cancer**

RAINBOW trial [1]	**Ramucirumab + paclitaxel**	**Placebo + paclitaxel**
Number of patients	330	335
Median duration of treatment	18 weeks	12 weeks
Median duration of overall survival	9.6 months	7.4 months
Overall survival at 12 months	40%	30%
Median progression-free survival	4.4 months	2.9 months
REGARD trial [2]	**Ramucirumab**	**Placebo**
Number of patients	238	117
Median duration of treatment	8 weeks	6 weeks
Median duration of overall survival	5.2 months	3.8 months
Overall survival at 12 months	17.6%	11.8%
Median progression-free survival	2.1 months	1.3 months

NEW DRUGS

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%), epitaxis (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

REFERENCES *†

1. Wilke H, Muro K, Van Cutsem E, Oh SC, Bodoky G, Shimada Y, et al.; RAINBOW Study Group. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. Lancet Oncol 2014;15:1224-35. http://dx.doi.org/10.1016/S1470-2045(14)70420-6
2. Fuchs CS, Tomasek J, Yong CJ, Dumitru F, Passalacqua R, Goswami C, et al.; REGARD Trial Investigators. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 2014;383:31-9. http://dx.doi.org/10.1016/S0140-6736(13)61719-5

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