Casirivimab and imdevimab

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Approved indication: COVID-19

Ronapreve (Roche)
casirivimab 120 mg/mL and imdevimab 120 mg/mL co-packaged in single-dose or multidose vials

Despite the provisional approval of remdesivir and sotrovimab for COVID-19 in Australia, there remains an urgent need for effective treatment and prophylaxis. Regimens combining casirivimab and imdevimab have now been provisionally approved for use in adults and adolescents 12 years and older, weighing at least 40 kg. These drugs are indicated for infected patients who have an elevated risk of progressing to severe COVID-19, but who do not need supplemental oxygen. Casirivimab and imdevimab have also been approved for post-exposure prophylaxis in individuals who are unvaccinated or have a medical condition that makes them unlikely to be protected by vaccination. The combination is not intended to be used as a substitute for vaccination against COVID-19.

Casirivimab and imdevimab are human monoclonal antibodies that target distinct epitopes of the spike protein of SARS-CoV-2. They block the virus from binding to the receptors on human cells. The aim of using two antibodies is to reduce the risk of viral resistance.

The drugs can be given together as an intravenous infusion or as separate subcutaneous injections. Doses for treatment and single-dose prophylaxis are casirivimab 600 mg and imdevimab 600 mg. If there is an ongoing need for prophylaxis, lower subsequent doses are given once every four weeks. For infection, the intravenous route is strongly recommended. Treatment should begin as soon as possible after a positive test for SARS-CoV-2 and not later than seven days after the onset of initial symptoms. Prophylaxis should be given as soon as possible after exposure to SARS-CoV-2.

The median times to reach the maximum serum concentrations following subcutaneous injection are 6.6 days for casirivimab and 6.5 days for imdevimab. Casirivimab and imdevimab are expected to be eliminated like other immunoglobulins. The half-lives are 30 days for casirivimab and 26 days for imdevimab. The effects of severe renal impairment or moderate-to-severe hepatic impairment are currently unclear. The antibodies are not renally excreted or metabolised by cytochrome P450 enzymes so pharmacokinetic interactions with concomitant drugs are unlikely. There have been no formal drug–drug interaction studies. As casirivimab and imdevimab bind to the spike protein that forms the basis of all COVID-19 vaccines, they may interfere with the development of effective immune responses to COVID-19 vaccines. These vaccines should therefore not be administered for at least 90 days after the antibodies.

There is an ongoing, placebo-controlled, clinical trial involving outpatients with confirmed COVID-19. An initial analysis of data from 275 symptomatic patients showed that intravenous casirivimab and imdevimab reduced the SARS-CoV-2 viral load. The largest effect was in patients with a high viral load, with most of the reduction occurring in the 48 hours following infusion. Patients who received the combination also reported fewer medical visits within the first 29 days (3% vs 6%).[1] Subsequent data from this trial showed a reduction in the viral load. COVID-19-related hospitalisation or death from any cause occurred in seven of 736 patients (1%) who received 1200 mg of the combination versus 24 of 748 patients who received a placebo (3.2%).[2]

A phase III trial studied subcutaneous casirivimab and imdevimab to prevent post-exposure infection in uninfected close contacts with household exposure to infected individuals. Overall, during a 28-day observation period, subcutaneous prophylaxis prevented symptomatic COVID-19 compared to placebo. Eleven of 753 patients (1.5%) who received the antibodies and 59 of 752 patients (7.8%) who received a placebo developed symptomatic COVID-19. Among these symptomatic patients, the median time to symptom resolution was shorter and the duration of a high viral load (more than 10^4 copies/mL) was shorter in the patients who received prophylaxis.[3]

Another part of this phase III trial investigated subcutaneous casirivimab and imdevimab for preventing progression in people with asymptomatic COVID-19 and household exposure to infected individuals. The combination reduced the progression to symptomatic infection. Symptoms developed in 29 of 100 participants (29%) who received the combination, compared with 44 of 104 participants (42.3%) given a placebo. The combination also reduced the duration of high viral loads, corresponding to a reduction in symptom duration of 5.6 days compared to placebo.[4]

Most of the adverse events encountered in the trials of intravenous and subcutaneous treatment were related to COVID-19. Injecting or infusing antibodies can cause hypersensitivity reactions. These reactions may include nausea, chills, dizziness or syncope, rash, urticaria and flushing. Anaphylaxis is rare.

The safety and efficacy of casirivimab and imdevimab in children and pregnant women are unknown.

Provisional approval of these drugs in Australia has been granted based on short-term efficacy and safety

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

data. Continued approval for COVID-19 will depend on the evidence of longer term efficacy and safety. There will be a need to monitor for the emergence of viral variants that are resistant to the combination of casirivimab and imdevimab. The combination is unlikely to be effective against the Omicron variant.[5]

TT manufacturer provided additional useful information

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, the European Medicines Agency and the Therapeutic Goods Administration.