NEW DRUGS

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Cemiplimab

Approved indications: Cutaneous squamous cell carcinoma, basal cell carcinoma, non-small cell lung cancer

Libtayo (Sanofi)
350 mg concentrate for dilution

Programmed death-ligands 1 and 2 can be expressed by tumour cells or cells within the tumour microenvironment. When these ligands bind with programmed cell death-1 (PD-1), an immune checkpoint, T-cell function is downregulated. By causing dysregulation of T-cell function, tumours can then evade the immune response. Immunotherapy to block the ligands from binding to the PD-1 receptor is therefore an attractive antitumour treatment approach. Cemiplimab is a fully human immunoglobulin G4 monoclonal antibody that binds to the PD-1 receptor. By inhibiting its interaction with the ligands, T-cell responses are stimulated.

Cemiplimab is indicated for two types of skin cancer in Australia. These are cutaneous squamous cell carcinoma in adults who cannot undergo curative surgery or curative radiation, and basal cell carcinoma in adults previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate. Cemiplimab is also indicated for the first-line treatment of certain locally advanced or metastatic non-small cell lung cancers. Its approval for locally advanced disease is only for patients who cannot undergo surgical resection or definitive chemoradiation.

Cemiplimab must be diluted before being given as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity occurs. Steady-state exposure is achieved after approximately four months of treatment. The drug's elimination is similar to that of other antibodies, with a half-life of 20 days. No dose adjustments are recommended, but data are limited in patients with severe hepatic or renal impairment.

In two open-label phase II trials, patients with cutaneous squamous cell carcinoma were given 3 mg/kg intravenous cemiplimab every two weeks, which has been shown to have similar pharmacokinetics to the dose approved for use in Australia.[1] This regimen induced a complete or partial response in 34 of 78 patients (44%) with locally advanced disease[1] and in 28 of 59 patients (47%) with metastases.[2]

For locally advanced basal cell carcinoma, an open-label phase II trial showed that 26 of 84 patients (31%) achieved a complete or partial response to 350 mg intravenous cemiplimab given every three weeks.[3] The results for patients with metastatic basal cell carcinoma have not yet been reported.[3] In a conference presentation on an interim analysis of the metastatic basal cell carcinoma cohort, cemiplimab was reported to have induced a complete or partial response in six of 28 patients (21.4%).[4]

Cemiplimab for non-small cell lung cancer was studied in an open-label phase III trial. Patients were randomised to receive 350 mg intravenous cemiplimab given every three weeks or chemotherapy. There was a complete or partial response to cemiplimab in 111 of 283 patients (39%) compared with 57 of 280 patients (20%) who received chemotherapy. The median progression-free survival was 8.2 months with cemiplimab and 5.7 months with chemotherapy. The median overall survival was 14.2 months with chemotherapy, but the median had not been reached with cemiplimab.[5]

As cemiplimab acts on the immune system, it can cause immune-related adverse effects. These include pneumonitis, hepatitis, colitis and endocrinopathies such as hypothyroidism, or more rarely, adrenal or cortical insufficiency. Non-physiological doses of systemic corticosteroids and immunosuppressants should be avoided before starting cemiplimab. However, they can be used after starting treatment to manage immune-mediated adverse reactions. Cemiplimab can also cause severe infusion-related reactions. Doses can be modified and infusions can be discontinued to manage immune-related and infusion-related adverse reactions. Other common adverse events found in clinical trials were fatigue, diarrhoea and hypertension. Cemiplimab is generally well tolerated, with variable rates of discontinuation due to adverse events (7–62%) and low rates of treatment-related death (0–8.2%) found in the trials.

Women should use effective contraception during and for at least four months after treatment. No effects on fertility were observed in animal studies. There are no safety and efficacy data for cemiplimab in children and pregnant women, although animal studies have shown that cemiplimab can cause fetal toxicity. Women should avoid breastfeeding during and for at least four months after treatment.

Cemiplimab appears to have a manageable safety profile in patients with cutaneous squamous cell carcinoma, basal cell carcinoma and non-small cell lung cancer. In Australia, the drug's approval is only provisional for metastatic and locally advanced cutaneous squamous cell carcinoma and metastatic basal cell carcinoma. The trials for these cancers included small numbers of participants and some doses that were different to the recommended dose in Australia. There have been no head-to-head studies

comparing cemiplimab with other immune checkpoint inhibitors approved for similar indications. Further clinical data are needed to confirm any long-term benefit of cemiplimab.

REFERENCES

1. Migden MR, Khushalani NI, Chang ALS, Lewis KD, Schmults CD, Hernandez-Aya L, et al. Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. Lancet Oncol 2020;21:294–305. https://doi.org/10.1016/s1470-2045(19)30728-4
2. Migden MR, Rischin D, Schmults CD, Guminski A, Hauschild A, Lewis KD, et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. N Engl J Med 2018;379:341–51. https://doi.org/10.1056/nejmoa1805131
3. Stratigos AJ, Sekulic A, Peris K, Bechter O, Prey S, Kaatz M, et al. Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy: an open-label, multi-centre, single-arm, phase 2 trial. Lancet Oncol 2021;22:848–57. https://doi.org/10.1016/S1470-2045(21)00126-1
4. Lewis K, Peris K, Sekulic A, Stratigos A, Dunn L, Eroglu Z, et al. Interim analysis of phase 2 results for cemiplimab in patients with metastatic basal cell carcinoma (mBCC) who progressed on or are intolerant to hedgehog inhibitors (HHIs). SKIN The Journal of Cutaneous Medicine 2021;5:s3. https://doi.org/10.25251/skin.5.supp.3
5. Sezer A, Kilickap S, Gümüş M, Bondarenko I, Özgüroğlu M, Gogishvili M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. Lancet 2021;397:592–604. https://doi.org/10.1016/s0140-6736(21)00228-2

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.