Blinatumomab

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Approved indication: acute lymphoblastic leukaemia

Blincyto (Amgen)
glass vials containing 38.5 micrograms powder for reconstitution
Australian Medicines Handbook section 14.2.1

Blinatumomab is indicated for adults with Philadelphia chromosome-negative relapsed or refractory acute lymphoblastic leukaemia. It is a dual-action antibody that binds to CD19 expressed on all B cells (including acute lymphoblastic leukaemia cells) and CD3 on T cells. When these molecules are bound at the same time, the drug acts as a bridge between the T and B cells. This interaction activates the T cells and causes them to produce cytolytic proteins and inflammatory cytokines which kill normal and malignant B cells.

Blinatumomab is thought to be catabolised. Its mean half-life is 2.1 hours. The drug is not expected to affect cytochrome P450 enzymes but drug interaction studies have not been done.

Approval of this drug is based on one main study of 189 patients.[1] This was an open-label phase III trial with no comparator. Enrolled patients had relapsed or refractory disease with a bone marrow blast count of at least 10%. At baseline, over two-thirds of patients had a blast count of 50% or more. Blinatumomab was administered by continuous infusion in four-week cycles followed by a two-week treatment-free interval. Patients received the drug for a median of 42 days. Those with more rapidly progressing disease were given dexamethasone before treatment to reduce the incidence of severe cytokine release syndrome.

The primary outcome of the trial was a complete response (5% or less blasts in bone marrow, no evidence of disease and full recovery of peripheral blood counts) or a complete response with a partial recovery of blood counts, within the first two treatment cycles. After treatment, 33% of patients had a complete response, 10% had a complete response with a partial recovery of blood counts and 48% did not respond. The median overall survival of all participants was 6.1 months (95% confidence interval 4.2–7.5 months).[1]

In a safety cohort of 475 patients, adverse events were very common. The most serious events included infusion-related reactions (67% of patients), infections (63%), fever (60%), headache (34%), febrile neutropenia (28%), peripheral oedema (26%), nausea (24%), hypokalaemia (24%), constipation (21%), anaemia (20%), cough (19%), diarrhoea (18%), tremor (18%), neutropenia (18%), abdominal pain (17%), insomnia (15%), fatigue (15%) and chills (15%). Blood monitoring is recommended during treatment because of the haematological effects. Severe neurological events also occurred with blinatumomab and included encephalopathy, convulsions, speech disorders, confusion and problems with coordination and balance.

During the trial 23 patients died because of an adverse event. Fatalities were due to sepsis, pneumonias, and infections caused by *Fusarium*, *Aspergillus*, *Candida*, *Escherichia coli* and enterococci.[1] As patients are immunocompromised, live virus vaccines are not recommended during, and for at least two weeks before, treatment.

Blinatumomab comes with a boxed warning about life-threatening cytokine release syndrome and neurological toxicities, and reactivation of JC virus infection. Treatment should be stopped immediately if any one of these is suspected.

A third of patients with Philadelphia chromosome-negative relapsed or refractory acute lymphoblastic leukaemia had a complete response to blinatumomab. However, it is difficult to know how this benefit compares to conventional chemotherapy as there was no comparator in the trial. Serious adverse effects commonly occurred and were fatal for 12% of patients.

[T] manufacturer provided the product information

REFERENCE

1. Topp MS, Gokbuget N, Stein AS, Zugmaier G, O'Brien S, Bargou RC, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. Lancet Oncol 2015;16:57-66. http://dx.doi.org/10.1016/S1470-2045(14)71170-2

The Transparency Score ([T]) 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 (www.fda.gov) and the European Medicines Agency (www.ema.europa.eu).