Acute Myeloid Leukemia and Its Targeted Therapy

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Abstract

Leukemia is a malignant clonal disease of hematopoietic stem cells, also known as "blood cancer." Leukemia cells proliferate and accumulate in bone marrow and other hematopoietic tissues due to uncontrolled proliferation, differentiation disorders, and blocked apoptosis, and infiltrate other non-hematopoietic tissues and organs, while inhibiting normal hematopoietic function.

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Leukemia is a malignant clonal disease of hematopoietic stem cells, also known as "blood cancer." Leukemia cells proliferate and accumulate in bone marrow and other hematopoietic tissues due to uncontrolled proliferation, differentiation disorders, and blocked apoptosis, and infiltrate other non-hematopoietic tissues and organs, while inhibiting normal hematopoietic function.

Leukemia is divided into acute and chronic leukemia according to the onset of onset. The differentiation of acute leukemia cells is arrested at an early stage. The primary and early-stage cells are dominant, and the disease develops rapidly, with a course of several months. Chronic leukemia cells differentiate well, mainly in naive or mature cells, with slow development and several years of disease.

In recent years, with the continuous introduction of new targeted drugs, leukemia clinical treatment has achieved breakthrough results, this article counts these four types of leukemia targeted therapeutic drugs.

AML (acute myeloid leukemia)

AML is the most common acute leukemia in adults, and it is also one of the poor control of common blood tumors. The recurrence rate is very high. Before the emergence of targeted drugs, AML patients usually first perform "induction chemotherapy." "Commonly used 3 + 7 standard chemotherapy (cytarabine 7 days plus 3 days of anthracycline antibiotics), followed by intensive consolidation chemotherapy or allogeneic hematopoietic stem cell transplantation. However, only a few patients with AML can successfully perform bone marrow. Most of them may not only respond to chemotherapy but also progress to relapsed or refractory AML, with a very low 5-year survival rate.

In May 2000, Pfizer Gemtuzumab ozogamicin (Mylotarg) received accelerated approval as the first independent treatment for elderly patients with relapsed CD33-positive AML, becoming the first targeted drug for patients with AML. However, subsequent confirmatory clinical trials withdrew from

the market in 2010 due to safety and efficacy issues, but Pfizer later explored the low-dose clinical effects of the drug, which was re-approved by the FDA in September 2017 for new diagnostic CD33-positive Treatment of adult AML patients, relapsed and refractory AML patients over 2 years of age.

Since 2017, the FDA has approved new AML targeted therapies such as Novartis Midostaurin, New Base/agios Enasidenib and agios ivosidenib (see table below), which brings new hope for the treatment of AML patients.

AML targeted therapy

Midostaurin inhibits a variety of key enzymes such as FLT3 and KIT during cell growth, interferes with cancer cell growth and proliferation, and is approved by the FDA for use in combination with chemotherapy in the treatment of FLT3-positive acute myeloid leukemia patients. Approximately 17%-34% of AML patients have FLT3 mutations, and these patients develop rapidly and have a high recurrence rate. In a phase III clinical trial called PARIFY, Midostaurin combined with cytarabine + soft red For the newly diagnosed patients with FLT3+AML, the risk of death was reduced by 23% compared with chemotherapy alone, and the median event-free survival was significantly improved (8.2 months vs 3.0 months).

Enasidenib is the first isocitrate dehydrogenase 2 (IDH2) inhibitor for patients with relapsed and refractory AML who carry IDH2 mutations. The proportion of IDH2 mutations in AML patients is approximately 8% to 19%. The drug was marketed based on a 199-person I/II single-arm clinical trial with 19% of Enasidenib's complete response over 6 months, with a median response time of 8.2 months, median survival in complete response population It is 19.7 months.

Ivosidenib is an inhibitor of the IDH1 enzyme for the relapsed and refractory AML patients with IDH1 mutations, and ID-10 mutations in 6-10% of AML patients. In a one-arm Phase I clinical trial, 500 mg of Ivosidenib daily produced a 30% complete response in patients with IDH1 mutations with a median response time of 8.2 months. The overall objective response rate was 42% and the median response time was 6.5 months.

Author Bio

Established in 2004, Creative Biolabs is highly specialized in advanced antibody biochemistry and engineering. With more than a decade of exploration and expansion, our current research and service capacity covers the entire new drug discovery and development pipeline, ranging from early discovery, preclinical evaluations, cGMP manufacturing, to clinical trials. As an international cooperation, we have established offices all around the globe with more than 200 well-trained full-time scientists and technicians, who work closely with our customers and research partners to develop new medicines for a better, healthier world.