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Commentary

A Review of Efficacy and Safety of Tyrosine Kinase Inhibitors in the Treatment of Chronic Myeloid Leukemia

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DESCRIPTION

Chronic Myelocytic Leukemia (CML) is a common blood disease, and its pathogenesis is the production of a new pathogenic gene BCR-ABL gene by chromosomal ectopic mutation [1]. This gene can cause excessive proliferation of white blood cells, inhibit the normal distribution of white blood cells, and cause the consumption of other normal blood cells, thereby affecting various antibodies and life functions. Tyrosine Kinase Inhibitors (TKIs) mainly inhibit the progression and occurrence of CML by blocking the signal transduction pathways related to tyrosine kinase receptor molecules [2,3]. However, TKIs can also combine with other protein kinases and cause a series of adverse reactions through targeted or off-target mechanisms [4]. Therefore, CML patients need to weigh the known adverse effects and efficacy of each drug before medication [5].

Efficacy

Recently, the authors conducted a network meta-analysis on the efficacy and safety of nilotinib, bosutinib, radotinib, dasatinib, imatinib and flumatinib [6-16], and the results showed that the efficacy of the second-generation TKIs was better than that of the first-generation TKIs imatinib. Dasatinib and nilotinib are easier to achieve molecular biological response, and flumatinib is easier to achieve cytogenetic response. Dasatinib 100 mg and flumatinib 600 mg were more effective in achieving 3-month Extramedullary Relapse (EMR) and 12-month Deep Molecular Response (DMR), which confirmed that patients with earlier early molecular response were more likely to achieve deep molecular response. In terms of survival data, 1-year Progression-Free Survival (PFS) of flumatinib was significantly better than that of the other five drugs, which may be related to the higher molecular structure selectivity of flumatinib. Therefore, patients are recommended to use flumatinib in order to obtain better quality of life based on the results of this study.

Safety

Although TKIs improve the prognosis of CML patients, they are not without safety concerns and potential adverse effects. The adverse reactions associated with different TKIs vary in severity and require routine monitoring and dose adjustment. The risk rates of cardiovascular events, pleural effusion and pancreatic events were higher in second-generation TKIs. In addition, studies have found that bosutinib and dasatinib have lower safety, and are prone to severe pleural effusion, resulting in a high discontinuation rate. Nilotinib has a lower discontinuation rate than the other five drugs. The adverse reaction of flumatinib was diarrhea, and the harm degree was low. Therefore, optimal treatment must be individualized, taking into account the patient's age, comorbidities, and risk factors.

Factors influencing the choice of TKI treatment

Disease stage, mutation status, risk scores (Sokal, Hasford and EUTOS scores) and patient comorbidities affect the choice of individual patients for TKIs treatment [17]. In addition, given the high cost of novel TKIs drugs, the affordability and accessibility of TKIs drugs play a crucial role in their utilization.

Future research

The following areas warrant further investigation to improve our understanding of TKIs in CML patients:

- Development of predictive biomarkers to identify patients who are likely to benefit most from specific TKIs.
- New strategies to mitigate or prevent TKIs related adverse effects.
- Identification of new targets and innovative drug therapies to overcome drug resistance and increase treatment options.
- TKIs withdrawal and treatment-free remission studies to reduce the treatment burden of patients and achieve stable deep molecular response.

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CONCLUSION

Over the past two decades, the advent of TKIs has greatly improved the prognosis and life expectancy of patients with CML. Network meta-analysis helps us to understand the comparative efficacy and safety of different TKIs. As we continue to advance in the field of targeted therapy for CML, there is promise in the future for personalized treatment approaches, novel drugs, and strategies to minimize treatment-related adverse effects and resistance.

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