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Letter to Editor

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Maintenance Therapy or Metronomic Treatment Replacement Intravenous Phase in Acute Lymphoblastic Leukemia During COVID-19 Pandemic: New Strategy

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1. Letter to Editor

Coronavirus pandemic has prompted physicians and healthcare providers to change the treatment for cancer patients, especially those with acute lymphoblastic leukemia. During the Covid19 pandemic, oncologists around the world must choose the best strategy for these immunocompromised patients to reduce coronavirus infection and maximize patient survival.

Conventional chemotherapy with intravenous formulation may cause severe neutropenia and cause fever and infection in various parts of the body. COVID-19 pneumonia may occur in 16% of patients undergoing chemotherapy. The infection also mimics the symptoms of CMV pneumonia or pulmonary aspergillosis and P.Carini's pneumonia. The first solution for oncology patients is simply to stop standard treatment or delay treatment to overcome the dangerous course of coronavirus, but this strategy is more specific to solid tumors [1].

However, this option is not suitable for acute leukemia, especially symptomatic patients who need immediate treatment to improve their quality of life and survival. It makes sense for these cancer patients to be tested repeatedly.

However, it is not possible to perform serology and airway sampling methods for PCR during patient visits worldwide, especially in low- and middle-income countries.

In addition, classical chemotherapy requires hospitalization in patients, and Howard has an intravenous and second cannula for infusion, which increases the risk of COVID 19 with pulmonary complications. In this paper, an oral chemotherapy formula could replace intravenous chemotherapy, and we will evaluate this theory in this paper.

ALL chemotherapy protocols include two different stages, including pre-injection and maintenance injections, which mainly include oral chemotherapy agents.

Maintenance chemotherapy is an important part of the treatment of Acute Lymphoblastic Leukemia (ALL) in children to prevent recurrence by eliminating the Minimum Residual Disease (MRD). ALL chemotherapy is based on the oral daily dose of 6-dose low-dose of mercaptopurine and weekly low-dose, monthly intravenous methotrexate, and intravenous vincristine for a period of 2 to 3 years [2].

At low doses, conventional chemotherapy is the same as metronomic chemotherapy with changes in the immune system and Anti-Angiogenic Effects in ALL patients [3].

In molecular picture, elevated CEC and EMP levels in peripheral blood can be thought of as indicative of endothelial damage and

vascular dysfunction. Circulation of Endothelial Cells (CEC), Endothelial Progenitor Cells (EPC) and endothelial microfibers (EMP), which are environmental indicators of vascular endothelial integrity in peripheral blood cells, are effective in maintaining therapeutic maintenance.

A decrease in these cellular biomarkers and an increase in THBS-1 levels indicate that maintenance will reduce the activity of the endothelium and increase its resting state. The mechanisms by which maintenance therapy uses this anti-endothelial effect are unclear, but several points can be made. The direct effect on endothelial cells has already been demonstrated for 3 anticancer drugs involved in ALL protocols. VEGF levels remain low and unchanged during treatment with maintenance. Therefore, it is unlikely that VEGF will play a key role in these settings [4].

In contrast, a significant increase in THBS-1 levels is a disinfectant and an effective mediator of MC efficacy. Platelets may not be involved.

Medtronic Chemotherapy (MC), which relies on frequent administration of chemotherapy in low doses, is significantly less tolerable than the maximum dose, and medications are used without long-term interruptions, which are usually uncomplicated. It is used as an alternative to high-dose conjunctival chemotherapy [5].

In 2019, vinorelbine was introduced as a valuable option for the treatment of patients with weak lung cancer during the Covid19 period [6] but experienced in the administration of MC during COVID-19 epidemics is very rare, especially in fluid tumors such as ALL.

Conventional high-dose chemotherapy during COVID-19 and infection during the suppression of the immune system is a challenge for oncologists.

MCT with oral 6-mercaptopurine is an effective treatment option in elderly AML patients with minimal toxicity.

Therefore, maintenance therapy in leukemia can have effects such as metronomic and is a type of multifunctional treatment. Maintenance therapy in children with ALL is not only pharmacologically but also mechanically a type of inhibitory therapy that works, at least with a relative reduction in endothelial activity [7].

Long-term routine chemotherapy in ALL as well as COVID-19 both cause lymphopenia. Therefore, oncologists should reduce the degree of lymphopenia to increase patient survival during the epidemic.

A logical alternative to AIDS-related malignancies, which is similar to lymphopenia in COVID-19 patients, is metronomic chemotherapy in developing countries, which reduces the toxicity of injecting chemotherapy drugs in high doses [8]. Therefore, maybe MC or maintenance therapy during these same lymphogenic situation was an effective alternative strategy. But *how long we allow to continue this accessory method?*

The bone marrow production cycle is equivalent to 90-120 days, equivalent to the lifespan of the RBC, which is a long time. Instead of intravenous high-dose chemotherapy, we suggest the maintenance phase for 3-4 months in a patient whose disease is under control, or more precisely, when the MRD is negative, or below 0.01%.

Using MRD level is an effective tool for changing treatment strategy and using new anti-leukemia strategy. With this method, the optimal start of the injection and maintenance phase identify *which patient can benefit from the main treatment or which patient, instead of the injection stage, replace the alternative strategy?* The effect of MC on endothelial integrity and vascular components is a major factor in the effectiveness of this method.

However, there is no change in the number of T cells because of therapeutic treatment, which suggests that T cell regulation is not involved in the long-term control of ALL. Other immune cells, such as dendritic cells or myeloid-derived suppressor cells, may be affected by maintenance [9].

In summary because of the mechanism of maintenance therapy is very similar to MC, which increases the patient's survival by reducing the power of chemotherapy and its toxicity. We recommend that a part of maintenance chemotherapy replace injectable phase medications in MRD negative ALL patients during COVID-19 pandemic, temporarily (maximum 3-4 months) and at the end of treatment to reduce this period of the entire course of maintenance phase.

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