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A Comprehensive Review in Novel Therapeutics in Acute Leukemia

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Abstract: In recent years, acute leukemia has become a challenging disease for children, adolescents and adults, so there are always different treatments; None of them are considered as a definitive treatment for this disease. Finding treatments that have fewer side effects and more results has always been one of the most important and recently discussed challenges. The production of vaccines for the prevention and treatment of cancer has always been one of the candidates for the treatment of various cancers, and recently the companies Estraznika and Pfizer have achieved very good results. These days, new therapies called gene therapy have been introduced, which have shown promising results. T cell therapy is one of these treatments that has shown very good results and is currently undergoing clinical phases in various cancers, especially acute leukemias, in the United States of America. On the other hand, science-based therapy Virology is underway as virus therapy, which is undergoing animal testing and clinical trials for various cancers and viruses. It is hoped that viruses can be used as allies in the fight against cancer. With the help of microbiology, this problem has reached acceptable results and they have been able to study the microbiomes of leukemia patients and find out the results that contribute to a successful chemotherapy treatment. In this article, we aim to explore new treatments for acute leukemia and examine the results of different trials and different clinical phases. It is hoped that with the advancement of science, the treatment of leukemia patients will always be possible.

KEYWORDS: Acute Leukemia, cancer vaccine, virotherapy, nanomedicine therapy, immunotherapy

INTRODUCTION

Acute leukemia (AL) is a type of leukemia that originates from the bone marrow (BM). Due to the abnormally rapid growth of white blood cells, patients often experience fatigue, bleeding, bruising, fever, and a weakened immune system. According to lineage, AL can be classified as acute lymphocytic leukemia (B) (B-ALL), acute T-cell lymphocytic leukemia (T-ALL), and acute myelogenous leukemia (AML). Leads to bone marrow disorders Most patients experience fatigue, bleeding, bruising, and weakened immune systems due to the abnormally rapid growth of white blood cells Acute leukemia can be classified as acute B-cell lymphocytic leukemia, leukemia Acute T-cell lymphocytes and ultimately acute myelogenous leukemia Acute lymphocytic leukemia is more common in children, while acute myeloid leukemia is a more common type of acute leukemia in the elderly [5-1] CAR T Cell Therapy is one of the Recent treatments for acute leukemia have been in the clinical stages for other cancers and have produced significant clinical responses to specific subsets of leukemia or B-cell lymphoma, but there are limitations. And barriers such as tumor resistance to CAR structures are still problematic. [6] This acute leukemia has also been used. Nano-based targeted therapies have also been used for various diseases, including cancer, and various drugs have completed or completed their clinical phase, but these therapies are known as complementary therapies; Therefore, considering the mechanisms of suppression of the immune system as a contributing factor in treatment, combining cancer vaccines with other immune therapies, or in other words, the use of complementary therapies for the treatment of cancer, seems to be more effective [7]. Has been proposed for target therapy; Oncolytic virus therapy is one of these therapies that tests its trials and clinical phases for various viruses and cancers and faces challenges such as not getting infected with the virus because according to the principles of oncolytic virus as a virus Genetically engineered is defined and, unlike the gene therapy itself, the virus is used, which can selectively multiply in cancer cells and kill them without damaging normal tissues. [8]

But apart from the new therapies, the current therapies also have challenges. One of these challenges is to reduce the side effects of the treatments, which has been made possible by examining the intestinal microbiome.

Nano AML

Therapeutic management of AML disease involves the induction of chemotherapy and the recovery phase. Higher invasive treatment, such as allogeneic bone marrow transplantation, is performed for high-risk patients. Recommended treatments for patients in induction failure, clinical trials, low-intensity treatment, azacitidine (HCT, allogeneic decitabine, or supportive therapy) [9] Most AML patients are over 60 years old, and many receive light supportive or chemotherapy. The reason for the toxicity and unclear efficacy of invasive treatment is recommended.The 5-day low-dose treatment with Decitabine has the same outcome as the initial treatment in elderly AML patients, and its acceptable toxicity and mortality are 30 days [10,11]. The combination of talacotuzumab and decitabine is less beneficial than decitabine alone in elderly patients with AML [12]. The monosomal and complex karyotypes were Azacitidine, which saw a 46-46% reduction in the risk of death in patients treated with this drug compared to patients with conventional care regimens [13,14], the rate of MRD in 80% of patients after receiving 4 courses Azacitidine therapy, in the absence of relapse Hematologic, decreased or remained constant. Even with azacitidine re-treatment in most patients, hematologic relapses were unavoidable [101006]. Treatment with azacitidine for 32 days for 32 days is safe and can also be used for at least 4 periods after allogeneic transplantation for AML / MDS patients undergoing severe treatment [9]. We can also see more benefits after more cycles. [17] In addition, nanotechnology has made the treatment of many cancers, such as acute myeloblastic leukemia (AML), easier and more accurate than the above methods. . Three nanotechnology methods can be used to treat blood malignancies, which are: 1. Organic nanoparticles such as dendrimers, polymer particles and Lipid Based NPs. Inorganic nanoparticles such as iron particles, QDs, carbon-based particles and mesoporous silica. Nano-hybrid [18,19], for the treatment of acute myeloblastic leukemia (AML) there are two)chemotherapy and immunological methods [20]. Organic nano method can be used for both diagnosis and treatment of this disease, which is combined with the above two methods. The only disadvantage of using Nanomedicine is that it causes small subcellular damage to organ damage [21]. In this cancer, abnormal blood cells multiply uncontrollably and can invade and infect other organs. Using nanocarriers, anti-cancer drugs can be targeted into infected tissues and cells, and by increasing the half-life of the drug, reducing the dosage form, and minimizing drug interactions and drug toxicity, the therapeutic efficacy can be specifically addressed. Maximized [22,23]. In one study, a comparison was made between treating AML patients who did not qualify for invasive chemotherapy, between the effect of a single drug and the same drug with a nanoparticle. The incidence of fibril neutropenia was also much higher than in patients treated with Azacitin alone [24]; As a result, AML management methods with ventoclus-based compounds are expected to evolve and be considered more seriously over the next few years. [25] For this reason, the production of a precursor from nanoparticles called -CD-44targeted glutathione-sensitive hyaluronic acid mercaptopourin was provided. According to the evidence obtained, this prodrug of nanoparticles has very low side effects as well as high suppressive power of OCI / AML2 tumors in leukemia, which has made it a very functional and effective drug nanoparticle [26]. In another study, it was observed that the two molecules CD44 and NF-KB were much more expressed in leukemia patients than in normal people (25 times) [18].

For the treatment of leukemia patients, an incapsulated PTL nanoparticle called nano-antiCD44 encapsulating PTL was designed which acted on the NF-KB molecule and reduced cell proliferation in this molecule by 50% and was very effective in treating the disease [27]. Another drug that is very effective in treating AML, called Vorinostat, was tested and found to inhibit the activity of HDAC class 1 and 2 enzymes at nanomolar concentrations and induce cytotoxic activity at micromolar concentrations. A protein-based nanomedicine from Vorinostat encapsulated by human serum albumin, which increases the solubility and enhances the effect of the drug, and the combination of this drug with DNMTi increases the therapeutic efficacy [28,29]

CAR T cell Therapy AML

AML is a heterogeneous blood malignancy that often has a poor prognosis and has the highest annual death rate from leukemia. High levels of CD123 and CD33 have been observed in these patients, with CD123 being the most common antigen in AML. [30,31,32] But despite numerous treatments for AML, there are still refractory AMLs. [33] In AML cells, the 13-CD protein is highly expressed, targeting cancer cells Strongly destroyed. But direct targeting of CD13 can cause toxicity to human HSCS and other normal cells. [34] However, the use of CAR T + CD19 (which is effective in treating CD19 + B cell leukemia) can limit the expression of CD13, CD19, and CD123 proteins in cancer cells without having cytotoxicity. Studies have shown that concomitant use of SB vectors with CAR T not only increases the effectiveness of CAR T, but also reduces costs. However, there are limitations for SB, including low gene transfer and toxicity to T cells. [35,36,37] In addition, the use of ScFv also affects CAR T cytotoxicity. [38] Most CAR T cells today use anti-human SCFV extracted from mice. [39] One of the problems in treating AML with CAR T is the lack of appropriate antigen. Because FIt3Lg stimulates cell proliferation in AML, disruption of the FIt3Lg binding site in Flt3 may inhibit blast cell proliferation. [40] More generally, problems with AML treatment with CAR T include cases such as Antigenic Heterogeneity and On-Target Off-Tumor Toxicity. [41] GMP was examined there and showed higher sensitivity to FLT3 CAR T cells in the laboratory. Therefore, to prevent cytotoxicity, FLT3 CAR can be modified by having an induction-switching switch with retoximab. Or after AML eradication, reduce FLT3 CAR cells to recover bone marrow [42]. Molecule 1 - CLL is present on the surface of AML cells but not on the surface of normal HSCS cells, so it is considered as a safe antigen for CAR T to kill AML cells as well as LSCS. [36] No toxicity has been reported for CAR T against 1 CLL for CD34 and CD38 + cells. CLL is expressed in myeloid cells, so CAR anti-1 CLL cells effectively destroyed AML blasts so that they had the same toxicity as HL60 under the

same conditions. Overall, CAR T against 1 CLL shows excellent efficacy in the treatment of AML in vivo and has no life-threatening side effects. [43] Research has also shown that CD28 / CD27 excitatory signals can reduce the persistence of CAR T against CLL1. [44] UniCAR T in combination with TM123 has been shown to be effective in killing leukemia + CD123 cells and has been shown to reduce side effects. Treatment of HSPCs with UniCAR-T guided by TM123 resulted in lysis of HSPCs expressing CD123 in the laboratory, but this is transient and canceled by removal of TM123. The combination of CAR T anti-CD123 with AZA has also been shown to be effective in the treatment of AML without tissue damage and hematopoietic insufficiency. [45,46] CD7-specific CAR T cells effectively invade CD7-expressing AML cells without cytotoxicity to normal myeloid and erythroid cells. In fact, CD7 CAR Ts are a transient treatment and provide the conditions for stem cell transplantation, which terminates CAR T activity and resets NK cells and T lymphocytes. [47] Finally, it can be noted that despite advances in the use of T CAR cell therapy in this disease, AML has been obscure to some extent due to the lack of truly specific surface antigens [48]

Virotherapy AML

In blood diseases treated with systemic OVT, virus-mediated immunotherapy is performed, which includes tumor cells and responsive immune cells. The first injection of CVA21 (which shows anti-tumor responses in blood diseases) stimulated ISG and increased the expression of CD69 (CD69 on lymph nodes, causing cell migration and uptake of nutrients and preservation of lymphocytes) on CD4 + T cells. , NK and TCD8 + became on day 3 but decreased until day 22. CVA21 showed a high capacity for immunotherapy responses that, through ICAM-1 and dendritic plasmacytoid cells, was able to activate NKs, which could be a lethal pathway for malignant cells. Combining CVA21 with other immunotherapies and injecting it seems to be effective in treating AML and MM [49]. Another case in point is Reovirus, a RNA virus that mainly signals cells Hyperactivity, for example, infects the Ras pathway. In using the reovirus for extracorporeal clearance, MM cells were incompletely cleaved and only 50% of the MM cells were effectively cleaved. There were no follicular and burkit lymphoma cells. Therefore, in conclusion, reovirus may have therapeutic potential in some hematologic malignancies, but its efficacy should be evaluated in further clinical trials [50]

Vaccine AML

Immune cells are used to identify tumor cells that are difficult to target because of the immune mechanism. Based on the efforts made and considering the complexity of immune suppression mechanisms, the use of combination therapy as a combination of cancer vaccines with other immunotherapy seems to be more effective [51] in a vaccine study aimed at cells NKT and their combination with anti-4-1BB resulted in the survival of all mice with MLL AML because the vaccine in combination with anti-4-1BB activates CD8 + T and produces IFN-y, which clears the tumor. It is done by increasing CD8 + T and IFNY. But after combination treatment of 1-anti-PD and anti-4-1BB, 40-60% of mice survived. Vaccine and anti-4-1BB alone, either in combination or 1-anti-PD, increased AML tumor clearance in some mice, but the tumor gradually grew in some mice that did not respond to the vaccine. Evidence has shown that delays in the use of 1-anti-PD can counteract the therapeutic effect. Therapeutic response to NKT and anti-4-1BB vaccination cleared the tumor in all affected organs of infected mice, including blood, bone marrow and spleen [52,53] A clinical trial using SVF cells incubated with vaccine virus It was performed to treat 26 patients with AML, which showed that the combination of SVF and ACAM2000 was safe, and that inflammatory symptoms associated with the virus were seen in most patients within 2 weeks of treatment. Skin rash and viral DNA survival in the blood were among the signs of vaccine virus survival in the body after treatment. In some patients, the combination of this virus with inhibition of checkpoints caused the death of tumors, but it should still be evaluated in a larger population [54,55]. In one study, a measles vaccine was used to treat AML patients. Leukemic blasts in patients were lysed by MeV, and although they were susceptible to the virus, CD46 levels were either normal or decreased. Addition of 5-FC enhances the tumorigenic effects of MeV-SCD but is less commonly used in treatment due to its gastrointestinal toxicity and low potency. [56] IL-15 DCS has been shown to be able to inhibit 75 T cells. Which indicates its anti-tumor activity with 15-IL secretion. The DC vaccine in combination with anti-1-PD drugs further affects AML cells. T 75 cells in these patients are susceptible to stimulation of 15-IL DC, especially in the presence of IPP. Unlike aB T cells, T 75 cells are not dependent on the tissue compatibility complex and antigen-presenting cells [57,58]. The combination of IL-15 / IL-15Ra arteriodimer with CD80 in autologous leukemic cells as a vaccine seems to be an effective treatment for AML and expression of 15-IL in AML vaccines stimulates immunity and reduces toxicity. It becomes a cell. Mice with more severe AML responded to the 32Dp210-IL-15 / IL-15Ra / CD80 vaccine, which allowed them to survive longer and eradicate leukemia. [59,60] The DC vaccine targets WT1 with the ability to increase the immunity of non-leukemic T cells in AML patients, and CD8 + cells with WT1 remove the remaining tumor cells and reduce the recurrence of AML [61]. WT1 vaccination was performed on 22 AML patients which was effective and no mortality was reported [62,63]

In a phase safety test DCP-001 vaccination was evaluated in patients with advanced AML. MRD after chemotherapy is a major challenge in the treatment of AML. This vaccine has the ability to stimulate cellular and humoral immunity. The vaccine was injected every 4 weeks and 2 weeks, and the result was that elderly patients with stable and adjusted immune systems showed a greater response to the vaccine. "DCP-001 vaccination was effective in patients with safe elderly AML. In patients with CR and stable levels of blood T cells, it caused long-term survival (36 months). Therefore, it can be an effective therapeutic approach in the treatment of AML for complete recovery after chemotherapy [64]. Therefore, in an article, the use of hUC - MSCS as a carrier

for reoviruses in the treatment of AML was investigated. Reovirus infection caused the secretion of inflammatory cytokines from hUC - MSCS, especially CXCL10, which increased the antitumor effect of the virus. In fact, hUC-MSCS prevented the reovirus from being neutralized by high-titer antiviral antibodies and also facilitated the transmission of the reovirus to tumor cells. But in general, the role of hUC - MSCS as an antitumor needs further study. MSCS, along with reovirus, infiltrated lymphocytes into tumor cells and reduced immunosuppression. According to the results, reovirus activated AKT and SAPK / JNK and also increased the expression of CXCR4 and CXCR7 in hUC - MSCS and it seems that AKT plays an important role in cell migration and virus replication [65,66] in An experiment with a nanoparticle vaccine coated with an antigen-rich AML cell membrane (AMCNP) has been investigated to treat tumors and improve inhibition of cancer recurrence. The vaccine also protects against AML and cancer-specific T cell responses. Increase blood. It has more advantages than WCL vaccines. In the bone marrow and liver of mice vaccinated with AMCNP, much fewer leukemia cells were observed than in mice vaccinated with WCL. The AMCNP vaccine made here is multi-antigen and fully personalized, eliminating the need to identify neo-antigens. These vaccines can be combined with a variety of adjuvants [67,68].

MRD 9 fact, TRAIL-coated ZA4-oncovirus adenovirus -SZU vaccine (to enhance tumor targeting ability) showed strong antitumor effect against AML as well as combination zA4 with Rh2 treatment of leukemia and BALB / C cell transplantation Increased mice [30]. In one experiment, tumor cells were treated with DACA and a new conjugate TLR7 agonist 106-SZU. Cells conjugated to 106-SZU relative to DAC perform DC maturation and T activity in vitro against tumor cells and inhibit them. That is, combining the DAC with 106-SZU, in addition to activating TLR7, has the ability to deliver tumor antigen to DCs to remove tumors by binding TLR7 to the DC surface. DAC-AML-106 shows potential therapeutic effect in combination with PDI or PDL1 monoclonal antibody [69] Combining VSV virus with CAR T showed that T cells have the ability to load VSV and protect it against the immune system have . Experiments on NSG mice showed that loading high doses of VSV virus on CD8 + T cm had a stronger anti-leukemic effect than VSV alone. Therefore, the combination of an oncolytic virus with effective human tumor-specific immune cells as virus carriers could have a significant therapeutic effect compared to monotherapy [70]. It can be noted that the development of nanotechnologies in recent years has provided potential strategies to improve cancer immunotherapy, and its important advantages, as mentioned earlier, include the precise targeting of specific cell types in the design of cancer vaccines and Delivery of safety modifiers used [71]

CAR t - cell therapy for ALL

The treatment of patients with Acute Lymphoblastic Leukemia (ALL) using CAR - T cells as a new approach has been considered by many researchers. Among the numerous CAR - T receptors, CD19 receptor has been studied as an effective receptor for CAR - T, especially in the treatment of patients with recurrent B - ALL patients after transplantation with poor prognosis [72,73]. Anti-CD19 CAR-T is rare and non-hematologic diseases such as MDS, hypogammaglobulinemia and hypoglycemia have been observed in some cases [74]. In a report, mild neurotoxicity with lower degrees and severe neurotoxicity with higher degrees was observed for -Anti CD19 CAR-T, with factors such as pre-treatment disease level and stimulatory agonists such as N-methyl-D-aspartate (NMDA) receptor quinoa. Acid and glutamate in bone marrow are involved in neurotoxicity [75]. In patients with Relapsed / Refractory Acute (r / rALL Lymphoblastic Leukemia) and Non-Hodgkin Lymphoma (NHL) treated with CAR T, cases of CMV and RSV infection with pneumonia were reported, which did not pose a serious risk because most of these infections It was observed in the first days of CAR T injection and in hospital conditions [76]. CRS (Cytokine release syndrome) has also been reported as a result of effective treatment of recurrent B - ALL individuals after transplantation with CAR T cells [77]. The use of blinatumomab before CAR T treatment reduces the recovery and development of MRD, thereby reducing the effect of CAR T on B - ALL treatment [78,79] AUTO3 as a type of CAR T designed to target CD19 and CD22 has been shown to be effective in the treatment of children with r / r BALL simultaneously with a dose of 106 CAR T - cells 23 Kg. Although the use of AUTO3 has side effects such as neutropenia, anemia, thrombocytopenia, fever, but causes complete recovery (CR) or minimal residual disease (MRD) [80]. Also, treatment with CD22 CAR T after treatment with CD19 CAR T increases the function of CD19 CAR T and the half-life of CAR T, so the use of CD19 and CD22 can show potential effects in the treatment of patients B - ALL [81] KTE - X19 to As a type of autologous CAR T CD1919, in the treatment of r / r B - ALL patients despite complications such as fever (42%), hypotension (40%), decreased platelet count (33%), anemia (31%) Hypophosphatemia (31%), hypoxia (24%), encephalopathy (22%), neutropenia fever (22%) and a decrease in neutrophil count (22%) in some patients result in complete or minimal remission of the disease [82 The other two receptors for CAR T, including CD28 and 4-1BB, show an antitumor response in ALL patients with mild side effects, but these two have different response patterns. [83

vaccine for ALL

Potential for ALL treatment. One of the vaccines that has the ability to activate the immune system and kill tumor cells without side effects is the IPSC-based vaccine. This vaccine demonstrates anti-tumor effects against T-ALL by delivering it to T cells via DCs. [84] . For example, the use of Epstein-Barr virus-specific cytotoxic T cells (EBV CTL) can reduce neurotoxicity and CRS (cytokine release syndrome) and GVHD due to CAR T injection, thereby increasing the persistence of CAR Ts in the body. [85] CAR T cells with the epidermal growth factor receptor pathway substrate vaccine 8 (Eps8 - DCS peptide - derived dendritic cell), reduce cell death due to CAR T injection and its side effects, thus increasing its shelf life in the body. This vaccine induces anti-

tumor effects by increasing the secretion of 2-IL and TNF-α and increases the proliferation of T cells and the persistence of CAR T in the body, thus overcoming recurrent leukemia cells [86]

Nano medicine for ALL

A nanoparticle called novel CHC-SDS was made, which increased the hydrophobicity of the SDS fraction and also increased the pyrazoline H3Tm04 without encapsulation [87,88]. According to experiments, these nanoparticles are compatible with the living and non-toxic tissue environment, and CHC-SDS nanocapsules are a very good delivery system for a variety of pyrazoline-derived and hydrophobic drugs [87]. In one experiment, 737-ABT and IRAK1 / 4 inhibitors were inserted into a capsule of Polyethylene glycol modified poly nanoparticles, which had a double effect in inducing T-ALL apoptosis compared to the combination of IRAK1 / 4 and AB37-737 solution. Also, IC50 for -IRAK / ABT NPS was twice as low as for free combination drugs in Jurkat cells [89]. In another experiment, the effect of active thiol polymers on cell relationship and nanoparticle adsorption was studied and it was found that thiol-reactive star polymers contain mPEG brush corona, which contains some diethylene glycol brush moieties that improve cells. Leukemia becomes delirium [90]. Another nanoparticle that is very suitable for the treatment of ALL was called BSA / ASN25% / Pol407, which performed very well in intravenous injection and protected ammonium against free enzymes, which prevents hyperammonemia [91 , 92]. A new therapeutic strategy against ALL was the fabrication of DOX-PMs-NPMBP nanoparticles, which significantly inhibited tumor growth in ALL and also showed no systematic toxicity after treatment [93]. One of the markers in the malignant membrane of malignant cells, including B - LL, is CD19, and a nanoparticle called CD19 - PEG - MTN / DOX was made, which forced the CD19 + B - LL cell into the apoptor, but Not toxic to normal cells. After treatment with DOX / nanoparticle, CD19 - PEG - MTN Bax 6 - and NALM post-apoptotic proteins were dramatically upregulated and anti-apoptotic proteins such as 70 Bcl2, MCL - 1, HSP, were downregulated Indicating the activation of the apoptotic pathway by nanomedicines [94]

Virotherapy for ALL

Virus therapy for leukemia is still in need of further research; But this treatment, along with other treatments, has had good results. In a simultaneous study using rituximab, oncolytic measles virus was used, which boosted the immune system; On the other hand, increasing the effectiveness of oncolytic viruses has become one of the challenges that currently the use of bone marrow stem cells as carriers of oncolytic virus and the use of antibodies against it to prevent toxicity is one of the best methods. Measles was contracted here from the oncolytic virus. [95,96]

Microbiome AML, ALL

Intestinal barrier is a vulnerable site in patients who have received intensive chemotherapy and in patients with hematologic malignancies, intestinal microbiota disorder has been well established with chemotherapy and broad-spectrum antibiotics [97]. Maintaining high microbial diversity and metabolites produced by these microbiota in the intestine helps reduce toxicity and initiation of chemotherapy reduces this diversity and several complications [98,99]. For example, short-chain fatty acids (SCFAS) are microbial metabolites that are derived from dietary fiber in the colon and play an important role in body health. Butyrate is one of the most important SCFASs, which is the epithelial food source and reduces the inflammatory response of the intestine by inhibiting the production of cytokines, and Lachnospiraceae species, which are usually part of the intestinal microbiota and produce butyrate, are reduced by starting chemotherapy [100,101]. Indole compounds, which have antioxidant and anti-inflammatory effects, are also produced from tryptophan metabolites by intestinal microbiota, especially Commensal clostridium and E. coli, which are significantly reduced in patients with acute leukemia undergoing induced chemotherapy [102]. Overgrowth of Enterococcaceae species is also seen at the start of chemotherapy, which may cause acute GVHD and ulcerative colitis by compromising intestinal epithelial integrity and stimulating macrophage activation. In the past, an increase in the incidence of enterococci has been reported as a strong predictor of infectious complications in ALL children and adult AML [98,99]. In addition, the spread of Akkermansia species in the gut increases the risk of neutropenia (NF) in patients with acute leukemia receiving intensive chemotherapy, and adult AML patients with the first febrile neutropenia after intensive chemotherapy have a significant reduction in microbiota diversity. Intestines show [99,102]. Bloodstream Infection (BSI) pathogens are said to be the leading cause of death in ALL patients, and microbiota is a major source of BSI-causing pathogens in immunocompromised patients, and functional changes in intestinal bacteria in ALL patients may be possible. Increase BSI [101]

AFMT (Autologous Stool Microbiota Transfer) is one of the methods of intestinal microbial repair in patients with acute leukemia, after AFMT in AML patients who underwent chemotherapy and broad-spectrum antibiotics. Ruminococcaceae were observed. However, further research has shown that allogeneic FMT (fecal matter transferred from a healthy person to a person with intestinal microbiome disorder to repair and regenerate diseased microbiome) is safer than AFMT, and that the use of FMT is safer. It is effective in hematological malignancies for reducing infections related to chemotherapy and hematopoietic stem cell transplantation [103,104]. In general, intestinal microbiota play an important role in the recovery status of patients with acute leukemia [105]

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