Abstract 019

INNOVATIVE TREATMENTS FOR MYELOFIBROSIS

Aysu Timuroğlu

Atatürk University Faculty Of Medicine, Türkiye

Myelofibrosis (MF) is a Philadelphia chromosome-negative chronic myeloproliferative neoplasm characterized by fibrosis in the bone marrow, cytopenias and extramedullary hematopoiesis (1). In the 2022 International Consensus Classification (ICC) and the 5th edition of the World Health Organization (WHO) classification, myelofibrosis is subclassified as prefibrotic and overt primary myelofibrosis (2). The 2022 WHO or ICC criteria should be used for PMF diagnosis. The disease is a clonal stem cell disorder, with the most common genetic mutations are JAK2 V617F (60%), MPL (13.6%) and calreticulin (CALR) (22-35%). Approximately 90% of PMF patients have these mutations, while triple-negative cases have non-driver mutations. Chromosomal abnormalities may also be observed in PMF (1, 3-5). After diagnosis, prognostic risk scoring is performed for the treatment and management of patients. Symptoms are assessed using the myeloproliferative neoplasm symptom assessment form. IPSS, DIPSS, DIPSS Plus, MIPSS70, MIPSS70+v2, and GIPSS are the scoring systems used in PMF. Patients are divided into low/high risk groups, the reatment planning is based on this and patient's symptoms (6-7). The only curative and survival-enhancing treatment method in PMF is allogeneic hematopoietic stem cell transplantation (ASCT), which has high mortality and morbidity rates. In high-risk PMF patients, the treatment decision is primarily shaped by whether the patient is a candidate for ASCT. Treatments other than ASCT are currently aimed more at palliative care, controlling symptoms, and reducing spleen size (2). In patients with low-risk PMF who are asymptomatic, they may be observed only or included in a clinical trial. In symptomatic patients, hydroxyurea, ruxolitinib, or interferon may be used, or enter a clinical trial (2). In PMF, treatment decisions related to symptoms are made by considering anemia, splenomegaly, and constitutional symptoms. Especially in patients with prominent anemia, androgens, prednisolone, lenalidomide, thalidomide, and pomalidomide may be preferred if the patient does not have splenomegaly. New studies are investigating the efficacy of combining ruxolitinib with immunomodulatory agents. The efficacy of erythropoiesis-stimulating agents is limited, and studies show that luspatercept has a low effect in PMF patients. Momelotinib and pacritinib are also other treatment options for these patients and they have positive effects on increasing erythropoietic activity, splenomegaly and constitutional symptoms (2,3,8,9). In patients with anemia, splenomegaly, and constitutional symptoms, momelotinib should be the first choice. If splenomegaly is present alone, hydroxyurea, interferon, or ruxolitinib may be preferred. In patients resistant to ruxolitinib, fedratinib or momelotinib is preferred, while pacritinib is recommended in thrombocytopenic cases (2,10-13). There are studies on many agents planned for use alone or in combination with ruxolitinib in PMF patients. Studies exist on pelabresib, navitoclax, parsaclisib, pegylated interferon alpha, selinexor and luspatarcept in combination with ruxolitinib, and ongoing studies exist on the use of navtemadlin, bomedemstat, RUV120, and imetelstat as single agents in PMF treatment. The preliminary analysis report of these studies at the 2022 American Society of Hematology annual meeting. There is also a preclinical study on monoclonal antibody therapy (INCA 033989) specifically targeting mutant CALR, which has been shown to be effective in thrombocytosis (2).

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Abstract 020

CURRENT TREATMENT APPROACHES IN ELDERLY PATIENTS WITH ACUTE MYELOID LEUKEMIA

Fatma Arikan

Marmara University Pendik Training and Research Hospital, Türkiye

Acute myeloid leukemia (AML) is the most common acute leukemia in adults, with a median age at diagnosis of 68 years. Estimated 5-year survival differs significantly by age and is <10% for patients older than 60 years (1). Older patients represent highly heterogeneous group and require careful evaluation of comorbidities and frailty. When selecting a treatment plan for older patients, physicians must carefully weigh the risk of adverse events and the potential impact on quality of life (QOL) against possible survival benefits. They are generally unsuitable for curative treatment options such as intensive chemotherapy and hematopoietic stem cell transplantation. Consequently, treatment strategies aimed at improving outcomes and patient compliance continue to evolve. Lower intensity regimens include hypomethylating agents (HMA), such as azacitidine or decitabine, or low-dose cytarabine (LDAC). The introduction of azacitidine in 2012 and decitabine in 2015 significantly transformed the treatment landscape for these patients (2-4). However, HMA monotherapy has been associated with remission rates of 30% or less and survival of under one year (2, 5). As HMA therapy is considered the standard backbone for AML patients unfit for intensive chemotherapy, the majority of phase III trials have been designed to evaluate novel agents in combination with HMA versus HMA alone. In 2018, azacitidine and venetoclax combination was approved for patients with newly diagnosed AML aged ≥75 years old or ineligible for intensive chemotherapy (6). The VIALE-A trial demonstrated improved overall survival (OS) with venetoclax-azacitidine versus plasebo-azacitidine (14.7 and 9.6 months, respectively). Moreover, with long term follow-up, patients achieving CR/CRi with measurable residual disease (MRD) negativity had a longer median OS (34.2 months) compared to those without MRD response (18.7 months) (7). Profound cytopenias accompanied by concurrent infections, bone marrow evaluations during treatment cycles to evaluate cellularity, treatment delays, and prolonged hospitalizations are frequently observed. Nevertheless, due to its manageable side effect profile and a protocol allowing dose and schedule modifications,