# INTERFERON- ALFA AS A FIRST- AND SECOND-LINE TREATMENT OPTION IN PRIMARY MYELOFIBROSIS

Nina Sghibneva-Bobeico MD [1,2],Vasile Musteata MD, PhD [1,2], Maria Robu MD, PhD [1,2], Larisa Musteata MD, PhD [1,2], Elena Covalschi MD, [1,2].

1. Department of Hematology, Institute of Oncology, Chisinau, Republic of Moldova;

2 . State University of Medicine and Pharmacy "N. Testemitanu", Chisinau, Republic of Moldova.

## INTRODUCTION

Primary myelofibrosis (PMF) is a clonal, myeloproliferative neoplasm Ph-negative MPN that is known for its aggressive, rapid progression and poor prognosis. Clinical manifestations depend of stage of PM. Pre-fibrotic PM is characterized mostly by leukocytosis and thrombocytosis in CBC and the normal sizes of spleen. The classical clinical manifestations such as massive splenomegaly, anemia and thrombocytopenia of overt-fibrotic PM are well known, but hardly to solve. Bone marrow transplantation is the only treatment option that is currently curative despite the medications that are accessible. Pre-PMF management is still a subject of discussion. Although hydroxycarbamide and interferon alfa are still often used today to regulate blood count and bone marrow cellularity. Over 30 years ago, interferon alfa was first used to treat myeloproliferative neoplasms (MPNs). However, due to its adverse effect profile and lack of official regulatory authorization for the treatment of MPN, its initial use was restricted. Given its ability to change illness with corresponding genetic and histological responses, the use of interferon in MPNs is the focus of new study. The creation of pegylated formulations and, more recently, ropeginterferon alfa-2b, has contributed to increased interferon use and better tolerance [1].

## AIM

Evaluation of the effectiveness of interferon- alfa as a first- and second-line treatment option for PRE-PMF.

## METHOD

DESIGN. This was a single-center cohort study.

SETTING. All patients are from the in-day haematological department of the Oncological Institute of the Republic of Moldova.

PARTICIPANTS: We analysed the response to treatment with interferon- alfa in 14 patients of PRE-PMF with thrombocytosis and leucocytosis in complete blood count (CBC). They were at low risk according to Dynamic International Prognostic Scoring System score. Eastern Cooperative Oncology Group status was equal to 0-1. All patients were divided into 2 groups according to the treatment line.

The median age was 41,5 and 57,4 years, respectively.

## RESULTS

The best results were obtained in the first group, which started the immunotherapy as a first-line treatment. Four (57,1%) patients showed excellent results: regression of splenomegaly and normalization of CBC. Stabilization of tumor process was obtained in 14,3% of cases. Normalization of CBC and a decrease in spleen size were obtained in 3 (42,8%) patients from the second group. 28,6% of patients from the second group interrupted treatment due to drug intolerance. 14,3 % of patients from the first group and 14,3% of patients from the second group had a tendency toward normalization of the level of platelets and leukocytes, but finally the response was not received, and the patients were transferred to another treatment.

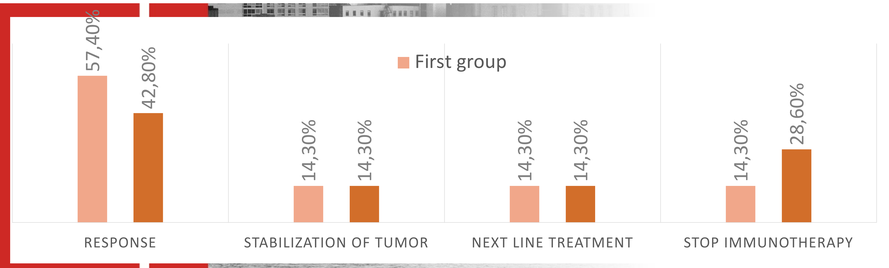



Fig. 1. Results of immunotherapy

## DISCUSSIONS

Interest in interferon alfa has greatly increased its effectiveness, achieved by many years of practice. Interferon alfa has recently been demonstrated to induce deep molecular remissions and normalization of the bone marrow in PV, which may persist even after immunotherapy is stopped. In considering this, a new era of growing curiosity in the use of Interferon alfa in the treatment of patients with PV, ET, and the hyperproliferative phase of PMF is most likely to begin in the upcoming years [2]. IFN treatment has been shown to reduce the allele burden of driver mutations in patients with essential thrombocytosis (ET) and polycythemia vera (PV), suggesting a disease-modifying effect. Interferon has been shown to have multiple anti-proliferative, pro-apoptotic, and immunomodulatory effects on hematopoietic progenitor and immune cells in the bone marrow [3-8].

## CONCLUSIONS

The immunotherapy proved to be an effective first- and second- line treatment option for PM. Due to its ability to recover the BM, interferon- alfa remains a successful therapy for PM in prefibrotic stage and, thus, should be indicated as the first-line treatment approach.

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