PHARMACOLOGICAL STUDY FOR THE SCREENING OF PRIMARY MYELOFIBROSIS.

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Introduction

Primary myelofibrosis is characterized by uncontrolled proliferation and activation of fibroblasts under the influence of different signals transmitted by the abnormal megakaryocytes but also by various elements of the bone marrow microenvironment. Following this activation, fibroblasts will produce an abundant extracellular matrix, which eventually will replace the bone marrow and interfere with its normal operation.

Materials and methods.

Currently, the treatment of this disease is limited and mostly nonspecific. Therefore, the development of new therapeutic strategies is very important. Several clinical trials with promising results is based on the use of ruxolitinib, inhibitor of JAK2 tyrosine kinase, mutant myelofibrosis, in combination with an anti-fibrotic agent (#NCT01369498, NCT01981850#).

In this study, we present the screening of 1240 substances, drugs currently used in various diseases to identify those who will inhibit the activation and differentiation of fibroblast into myofibroblasts phenotype, extracellular matrix producer. It was used mesenchymal stem cell line SR-497 submited to inactivation process by hanging drops, which can be isolated from chemical, biological and physical stimuli. After inactivation, cells were exposed to drugs investigated.

Results.

After the screening, we obtained three substances which inhibited the proliferation and differentiation of fibroblast: cyclosporine, mycophenolate mofetil and bisphosphonate risedronate.

Conclusions.

Further, these three substances will be investigated individually, both established cell lines and primary cell lines isolated from patients with primary myelofibrosis.