OAD, in absence of relevant toxicity. The primary endpoint was the rate of MR3 at 12 months. Key inclusion criteria: > 60 yrs old, chronic phase CML, intolerance or failure of any first-line TKI (2013 ELN criteria), absence of T315I or V299L mutation.

Results: Sixty-three patients have been enrolled. Median age: 73 yrs (range 60-90). Reasons for switching to BOS: intolerance 63%, resistance 37%. First-line TKI: imatinib 83%, DAS 11%, NIL 6%. All patients reached at least 1-year observation. Due to the emergency situation caused by SARS CoV2 spread in Italy, few data are still missing, but final results will be presented onsite. Maximum BOS dose: 400 mg OAD, 19%; 300 mg OAD, 76%; 200 mg OAD, 5%. At baseline, 17% of patients were already in MR3; MR3 rates at 3, 6 and 12 months were 44%, 54% and 59%, respectively. The cumulative rate of patients achieving or maintaining a MR3 by 12 months was 67%; patients achieving MR4 or MR4.5 by 12 months were 44% and 24%, respectively. Overall, 30%, 29% and 8% of patients had 1 log, 2 logs or > 3 logs reduction from baseline BCR-ABLIS transcript level (67% of patients had a molecular improvement from baseline). Selected adverse events: acute coronary syndromes, 4 patients; pericarditis, 2 patients; peripheral arterial thrombosis, 1 patient; no pleural effusions were observed. Events leading to permanent treatment discontinuation: 2 unrelated deaths, 7 adverse events, 4 unsatisfactory responses (without progressions), 1 second neoplasia. Fourty-nine patients are still on BOS at the last contact: 10% of them on 400 mg OAD, 61% on 300 mg OAD, 29% on 200 mg OAD.

Conclusions: These results trial showed that in elderly patients intolerant to or failing a first-line TKI BOS may be highly effective and better tolerated at a dose lower than 500 mg OAD, namely at 300 mg OAD.

P011

MARROW BCR-ABL+ ENDOTHELIAL CELLS SHARE MYELOID-LINEAGE ANTIGENS FORMING 2D AUTOCRINE BRANCHING PATTERNS *IN VITRO* THAT SUPPORT TKI-RESISTANT CML STEM/PROGENITOR CELLS

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BCR-ABL tyrosine kinase inhibitors (TKIs) approved for the treatment of chronic myeloid leukemia (CML) have adverse effects mostly including hemodynamic instability and pulmonary edema. Whilst imatinib prevents vascular leakage and edema formation, other TKIs such as dasatinib, nilotinib or ponatinib are much stronger associated with endothelial barrier dysfunction in endothelial cells (ECs) isolated from multiple ori-

P012

AUTOIMMUNE DISEASES AND MYELOID HEMATOLOGICAL DISORDERS: A POSSIBLE PATHOGENETIC RELATIONSHIP.

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Background: The association between autoimmune diseases (ADs) and lymphomas is well established; nonetheless, few studies have investigated the relationship between myeloid malignancies and ADs. In a series of more than 11,000 patients with myeloproliferative neoplasms (MPN), a Swedish group reported that a prior history of AD was significantly associated with a higher risk of MPN. More recently, our group showed that in chronic myeloid leukemia (CML) some genes correlated with AD (GLYPR1, PCARD, S100) were highly expressed at diagnosis and that the treatment with Imatinib impacted on the "inflammatory" profile of CML patients. Aim of the study: to investigate the frequency of myeloid malignancies, such as myelodysplastic syndromes (MDS) and chronic, either Philadelphia-positive (CML) or Philadelphia-negative (MPN), myeloproliferative disorders in patients with ADs, and to identify several distinctive clinical and biological features.

Methods: A retrospective systematic search through the electronic health records of the patients admitted at our Rheumatology of Pisa from 2009 to 2019 was performed to select those presenting with ADs and MDS or MPNs. Categorical variables were compared using chi square test and Fisher's test; continuous variables were compared using Student's t-test. A 2-tailed value of $p < 0.05$ was taken to indicate statistical significance.

Results: Out of the medical records of 5040 patients, we identified 112 patients (67 F: 45 M, mean age: 63 years) with ADs and hematological malignancies (2.2%): 41% with AD and MPN, 28% with AD and MDS, and 20% with AD and CML. No demographic differences were observed in the two subgroups. Regarding MDS, AR was the most common hematologic presenting finding, with diagnosis of refractory anemia with excess of blasts (RAEB I/II) done in 16% of cases. In the MPNs subgroup, 31% had a diagnosis of CML, 31% had a myelofibrosis (MF), 15% had an essential thrombocythemia (ET) and 13% a polycythemia vera (PV). The JAK2 V617F mutation was detected in 80%, 92%, and 61% of MF, PV, and ET patients respectively, and CALR was mutated in 15% of ET and in 10% of MF. Regarding the temporal appearance of ADs in respect of myeloid disorders, ADs preceded hematological diseases in 53% of all cases, especially in MPNs. Both kind of disorders were synchronously diagnosed in 35% of MDS and 32% of MPNs, while

in 45% of CML the hematological diagnosis anticipated that of AD. In MDS, the most commonly diagnosed ADs were seronegative arthritis (25%) and large and small vessel vasculitis (20%). In patients with MPNs, the most frequent diagnoses were connective tissue disorders (30%) and rheumatoid arthritis (26%); arteritis was more frequent in CML. The anti-Ro52 (TRIM21)-positive systemic connective tissue disorders were more frequently detected in MPN (55% *vs.* 22% of CML and MDS). Cardiovascular events were observed in 27% of patients: 23% in MDS, 25% in CML and 32% in MPNs, with a significant correlation with JAK2V617F mutation.

Conclusion: Our study is limited by its retrospective design. However, it showed that the frequency of MDS and MPNs in ADs is not negligible. It has been already reported that, under viral infection, TRIM21 is up-regulated by activation of the IFN/JAK/STAT pathway; interestingly, anti-Ro52 (TRIM21) were over-represented in our MPN cases, where the JAK/STAT signal is hyper activated. This might be a factor explaining the frequent association between ADs and MPN, and support the use of anti-JAK2 compounds as anti-inflammatory drugs.

tion observed in PMF patients. Finally, transcriptome analysis of CD34+ cells from PMF patients showed an alteration of SHH related genes expression. In conclusion, our data demonstrated an involvement of SHH pathway in the crosstalk between MSC and CD34+ cells in PMF. The inhibition of this pathway may constitute a promising strategy to counteract inflammation, osteosclerosis and fibrosis of the PMF patients.

P015

THE ROLE OF IGFB6 IN THE PATHOGENESIS OF BONE MARROW (BM) FIBROSIS IN MYELOPROLIFERATIVE DISEASE

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Primary Myelofibrosis (PMF) is a Philadelphia-negative chronic myeloproliferative neoplasm (MPN) characterized by the uncontrolled proliferation of bone marrow stem cells sometimes with an increase in