EP662 ANALYSIS OF MYELOID MUTATIONS IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA AND THEIR ASSOCIATION WITH ADVERSE EVENTS AND RELAPSE AFTER DISCONTINUATION.

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Background: Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by the presence of the BCR-ABL1 fusion gene and is treated using tyrosine kinase inhibitors (TKI). The development of new technologies such as next-generation sequencing (NGS) has led to major advances in the understanding of CML pathogenesis. Molecular studies are beginning to reveal genetic profiles associated with adverse events among patients with CML, including thrombotic events, resistance and/or intolerance to TKI and risk of progression. Moreover, the majority of studies on TKI discontinuation show that approximately half of patients maintain treatment-free remission (TFR), but the factors that determine this are yet to be elucidated. Aims: Study the mutational profile of CML patients and its association with the development of adverse events and maintenance of TFR after TKI discontinuation.

Methods: We retrospectively analyzed 200 ng genomic DNA extracted from peripheral blood at diagnosis of 63 CML patients subsequently treated with TKI with a minimum follow-up of 3 years. NGS was performed with the MiSeq (Illumina) platform using the targeted panel Myeloid Solution™ (SOPHiA GENETICS). Only variants with VAF≥2%, MAF6 months) vs early relapse (6 months while 7 (29.2%) had early relapse. There was no difference between the patients who relapsed vs those who maintained TFR, or between early and late relapse in terms of myeloid mutations.

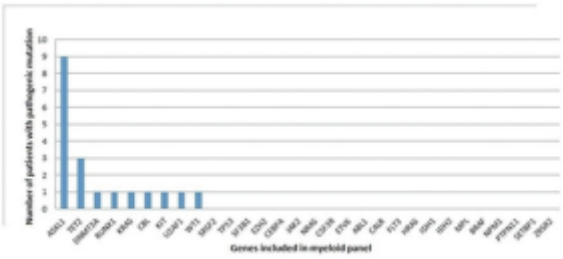

Figure 1. Pathogenic mutations detected in a series of 63 patients with CML.

Summary/Conclusion: Less than a quarter of the CML patients analyzed presented pathogenic mutations. These results contrast with those observed in the BCR-ABL1-negative myeloproliferative neoplasms, of whom approximately 50% present mutations (besides the driver genes) and with a higher average VAF. Although patients with thrombotic events presented a higher incidence of myeloid mutations, these differences were not significant. Our results suggest that myeloid mutations are not predictive of TFR or relapse following TKI discontinuation. Larger series are needed to determine whether these mutations are associated with TKI resistance or blastic phase evolution.