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POSTER ABSTRACTS

631.CHRONIC MYELOID LEUKEMIA: BIOLOGY AND PATHOPHYSIOLOGY, EXCLUDING THERAPY

Clinical and Molecular Characterization of Triple-Negative Essential Thrombocythemia: Data from the Prospective Spanish Registry of Essential Thrombocythemia

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Triple-negative Essential Thrombocythemia (TN-ET) accounts for up to 10-20% of patients with a histological diagnosis of ET. Despite being considered an indolent disease, it remains a diagnostic and therapeutic challenge as it can be confused with non-clonal thrombocytosis and its prognostic factors and management are not standardized.

Objectives

The aim of this study was to evaluate the utility of a Next Generation Sequencing (NGS) panel targeting recurrently mutated genes in myeloid pathology for detecting genetic variants in patients diagnosed with TN-ET and to assess the significance

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of these variants in the risk of thrombosis and hemorrhage, progression to Acute Leukemia (AL) or Myelofibrosis (MF), and overall survival.

Materials and Methods

Data from 151 TN-ET patients with confirmed biopsy and NGS sequencing from the Spanish Registry of Essential Thrombocythemia of the Spanish Group of Philadelphia-Negative Myeloproliferative Neoplasms was obtained. This registry includes information on diagnosis, molecular biology, clinical characteristics, and molecular biology. In addition, 39 patients whose molecular diagnosis was performed at the Molecular Biology Laboratory of the Hematology Department at Hospital Universitario 12 de Octubre, Madrid, Spain were included. This last panel included the genes: ANKRD26, ASXL1, ATG2B, BCOR, BCORL1, CALR, CBL, CEBPA, CSF3R, CUX1, DDX41, DNMT3A, EGLN1, EPAS1, EPOR, ETNK1, ETV6, EZH2, FLT3, GATA2, GNAS, GNB1, GSKIP, IDH1, IDH2, JAK2, KDM6A, KIT, KMT2A, KRAS, MBD4, MPL, NF1, NFE2, NPM1, NRAS, PHF6, PPM1D, PRPF8, PTPN11, RAD21, RIT1, RRAS, RUNX1, SAMD9, SAMD9L, SETBP1, SF3A1, SF3B1, SH2B3, SMC1A, SMC3, SRSF2, STAG2, TERC, TERT, TET2, THPO, TP53, U2AF1, VHL, WT1, ZRSR2. Statistical analyses were performed using SPSS v.29.0.

Results

A canonical mutation was detected in 20 out of the 190 studied patients, (*JAK2* V617F n=13, *CALR* n=3 and *MPL* n=4) being discarded from subsequent studies. Among the other 170 samples, 206 genetic variants were detected in a total of 86 patients (median 2, range 1-9). A total of 39 pathogenic (P) or probably pathogenic (PP) variants were found in 28 patients, whereas 59 uncertain significance (US) and 108 benign (B) variants were found in 44 and 54 patients, respectively. The distribution of genes in which P/PP/US variants were detected is shown in Figure 1.

Patients with P /PP mutations had a statistically higher age compared to the remaining (50 vs. 64.8 years; p <0.001). The prevalence of males was higher in the group where P/PP mutations were detected (57.14% vs. 28.87%; p=0.004). No differences were found regarding cardiovascular comorbidity or symptomatology at diagnosis, but the P/PP group presented a higher frequency of thrombosis prior to diagnosis (28.57% vs. 5.64%; p=0.001). There were no differences in hemoglobin, leukocyte, or platelet counts at diagnosis according to the presence of P/PP variants. The presence of P/PP mutations was associated with a higher risk of progression to AL and a lower overall survival. A higher risk of thrombosis or progression to MF was not found (Figure 2).

No differences were found in the risk of thrombosis, transformation, or overall survival between patients with or without the presence of US, PB or B variants.

Conclusions

The use of NGS technology is useful for the diagnosis and prognostication of TN-ET. The detection of P/PP mutations in patients diagnosed with TN-ET is associated with a higher risk of transformation to AL and lower overall survival, but not with higher risk of thrombosis or progression to MF. It is necessary to evaluate the individual risk of each of these mutations and the potential prognostic role of variants of US.

Disclosures Hernandez Boluda: Pfizer, BMS, Incyte, and Novartis: Membership on an entity's Board of Directors or advisory committees. Gómez-Casares: Astellas: Research Funding; GSK: Consultancy, Membership on an entity's Board of Directors or advisory committees; AbbVie: Consultancy, Membership on an entity's Board of Directors or advisory committees; Novartis: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; Incyte: Research Funding; Pfizer: Consultancy, Membership on an entity's Board of Directors or advisory committees; Amgen: Research Funding; Gilead: Other: Training support; Janssen: Other: Training support; AstraZeneca: Other: Training support. Ferrer Marin: Novartis Farmaceutica SA: Honoraria; Celgene S.L.U: Consultancy; INCYTE BIOSCIENCES INTERNATIONAL SARL: Honoraria, Research Funding; CTI BioPharma Corp., a Sobi company: Research Funding. García Gutiérrez: Pfizer: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; Incyte: Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; BMS: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; Novartis: Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding. Alonso-Dominguez: AVM Biotech: Research Funding; Astrazeneca: Research Funding; Astellas: Consultancy, Research Funding; GlaxoSmithKline: Research Funding; Novartis: Current equity holder in private company, Other: Travel/Accommodations/Expenses, Research Funding; Bristol Myers Squibb: Research Funding; Amgen: Research Funding; Incyte: Research Funding; Pfizer: Other: Travel/Accommodations/Expenses, Research Funding; Celgene: Research Funding; Kronos Bio: Research Funding; OnoPharma: Research Funding. Martinez Lopez: Pfizer: Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; BMS: Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; Incyte: Membership on an entity's Board of Directors or advisory committees, Research Funding; Sanofi: Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; Janssen: Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding. Ayala: Novartis: Consultancy, Speakers Bureau; Incyte: Consultancy; Astellas, BMS: Speakers Bureau. Alvarez-Larran: AOP: Consultancy.

Figure 1. Distribution of Myeloid Genes with P, PP or US variants detected among the 170 samples without canonical mutations.



Most Frequent Genes In Which P, PP or US variants were detected

Figure 2. A. Overall Survival, B. Risk of Thrombosis, C. Risk of Progression to Myelofibrosis and D. Risk of Progression to Acute Leukemia among patients with and without P or PP variants in NGS study.



Figure 1

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