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What is new in myelofibrosis?

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The discovery of JAK2 mutation a decade ago has marked a crucial change in our understanding and knowledge of the pathogenesis, prognosis and management of myeloproliferative disorders, particularly Myelofibrosis. Since then, new mutations have been identified and added as prognostic factors in the international scoring system. A new group of drugs have been developed to target the main pathways involved in Myelofibrosis. Ruxolitinib was the first JAK2 inhibitor that demonstrated rapid symptomatic improvement and spleen reduction as reflected in the COMFORT I-II studies. Furthermore, a recent study reported the efficacy and safety of Ruxolitinib therapy in COMFORT I patients after three years. In recent years, new medications are under investigation as single agent or in combination with Ruxolitinib such as Pacritinib (JAK2-*FLT3* inhibitor), Panobinostat (Pan-Deacetylase inhibitor) or Smo inhibitors. The preliminary results of these drugs showed promising responses in splenomegaly reduction, improvement in symptoms and reduction in JAK2 mutant allele; although important side effects have also been described for these drugs. On the other hand, Myelofibrosis presents with significant fibrosis in the bone marrow that affects the haematopoiesis and as a consequence, patients develop marked cytopenias and related symptoms. Recently, a new specific anti-fibrotic activity agent is under investigation in a few clinical trials. The current landscape of therapy for Myelofibrosis is based on JAK2 inhibitors however, promising agents may contribute to achieve our final goal of cure in this disease, probably with a combination strategy.

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Expression and prognostic impact of long non-coding RNAs in acute myeloid leukemia

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Long noncoding RNAs (lncRNAs) are transcripts longer than 200 nucleotides located within the intergenic stretches or overlapping antisense transcripts of protein coding genes. The lncRNAs are involved in numerous biological roles including imprinting, epigenetic regulation, apoptosis and cell-cycle. To determine whether lncRNAs are associated with clinical features and recurrent mutations in older patients (aged ≥60 years) with cytogenetically normal (CN) acute myeloid leukemia (AML), we evaluated lncRNA expression in 148 untreated older CN-AML cases using a custom microarray platform. An independent set of 71 untreated older CN-AML patients was used to validate the outcome scores using RNA-seq. Distinctive lncRNA profiles were found associated with selected mutations such as *FLT3* internal tandem duplications (*FLT3*-ITD) and *NPM1, CEBPA, IDH2, ASXL1* and *RUNX1* mutations. Using the lncRNAs most associated with event-free survival in a training cohort of 148 older CN-AML patients we derived lncRNA score comprised of 48 lncRNAs. Patients with an unfavorable compared with favorable lncRNA score had a lower complete response (CR) rate [P<0.001, odds ratio (OR)=0.14, 54% vs. 89%], shorter disease-free survival (DFS) [P<0.001, hazard ratio (HR)=2.88] and overall survival (OS) (P<0.001, HR=2.95). The validation set analyses confirmed these results (CR, P=0.03; DFS, P=0.009; OS, P=0.009). Multivariable analyses for CR, DFS and OS identified the lncRNA score as an independent marker for outcome. The functional impact of several lncRNAs was investigated and data will be presented at the meeting. In conclusion, lncRNA expression in AML is closely associated with recurrent mutations. A small subset of lncRNAs is correlated strongly with treatment response and survival.

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