IDH1/2 (isocitrate dehydrogenase) mutations

Isocitrate dehydrogenase is an enzyme that catalyzes conversion of isocitrate to α-keto-glutarate. First discovered in glioblastoma,[1] heterozygous mutations in the *IDH1* and *IDH2* genes have leter been described in acute myeloid leukemia (AML)[2,3] and in myeloproliferative neoplasms (MPNs).[4–6] *IDH* mutations most often involve codon 132 in *IDH1* and codons 172 and 140 in *IDH2*. Mutated enzymes acquire the capacity to transform α-keto-glutarate in (R)-2-hydroxyglutarate which interferes with the function of other enzymes, such as TET2. This explains why *IDH* and *TET2* mutations are mutually exclusive.[7] *IDH* mutations lead to a decrease of the production of 5-hydroxymethylcytosine and an increase of the methylation of cytosines located in certain regions of the genome (this phenomenon is involved in the repression of target genes expression). Although the impact of *IDH1/2* mutations in hematopoietic stem and progenitors cells is unknown, it is probable that the events triggered are similar to those resulting from *TET2* mutations.

In MPNs, *IDH1/2* mutations are rare during the chronic phase (0.8%, 1.9%, 1% and 4.2% of cases of essential thrombocythaemia (ET), polycythaemia vera (PV), post-ET/PV myelofibrosis, and primary myelofibrosis (PMF), respectively). They are more frequent in blast crisis (21.6-31%).[4–6] Thus, *IDH1/2* mutations are associated with accelerated forms of MPN, although their role in the initiation or progression toward acute myeloid leukemia remains to be defined. *IDH* mutations could be associated with unfavorable prognostic in MPN chronic phase[8] and in blast crisis.[6]

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