# The importance of a personalized therapy in Gastrointestinal stromal tumor prognosis

S. Angelini[1], G. Ravegnini[1], P. Hrelia[1],M.A. Pantaleo[2], G. Biasco[2], G. Cantelli-Forti[3]

[1]Dept. of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy
[2]Dept. of Specialized, Experimental & Diagnostic Medicine, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy
[3]Dept. for Life Quality Studies, University of Bologna, Rimini, Italy

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract. The molecular mechanism of GIST formation is among the best characterized of all human tumors. Activating mutations of the c-Kit-kinase (KIT), a member of the receptor tyrosine kinase III family, are present in 80% of GISTs. Gain-of-function mutations of platelet-derived growth factor receptor A (PDGFRA), a member of the same kinase family, are present in 35% of GISTs that lack KIT mutations. In a small subset of patients, the disease does not harbor any mutations on these receptors and is defined as wild type (WT). To date imatinib , the most important tyrosine Kinase inhibitor (TKI), represents the gold standard therapy and the only first line treatment. Cancer handling has been considered for a long time a difficult and crucial question for clinicians and oncologists due to in part to the myriad of treatment options and, on the other side, due to the lack of patient specific information. However it is certain that in the final clinical outcome two major actors are involved. Indeed on one hand there is the somatic DNA; on the other hands there is the germinal DNA. Both are involved in the final resulting response of a cancer patient to chemotherapic agents. Besides KIT and PDGFRA there are no biomarkers to predict the response to TKI and both somatic and germinal DNA influence the clinical response. Two approaches can describe the involvement of these two main players in imatinib response: i) identification of novel mutation through Next Generation Sequencing (NGS) in somatic DNA; ii) DMET assay to evaluate 1936 pharmacogenetic variants in 231 genes in germline DNA. NGS techniques are widely used to explore different areas in the study of cancer, including identification of driver mutations and measurement of tumor heterogeneity, Techniques with low sensitivity, as sanger sequencing with a sensitivity of 30%, are not able to detect low frequencies mutations and consequently are not useful for this purpose. In this view, NGS techniques, with a deep sensitivity, represent a precious tool, able to detect low frequencies mutations and variations in order to achieve the goal of a personalized medicine for GIST patients. DMET assay represents a precious and important tool. Indeed understanding the common variation in genes encoding for drug metabolism enzymes and drug transporters has the potential to significantly impact clinical research by predicting the impact of an individual's genetic variation on metabolic capacity.