Role of molecular analysis in the adjuvant treatment of gastrointestinal stromal tumours: It is time to define it

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Abstract

Sendur et al pointed out the attention on the importance of mutational analysis for adjuvant treatment of gastrointestinal stromal tumor (GIST) in an article published in World Journal of Gastroenterology. In particular, they suggested that the optimal dose and duration of adjuvant therapy could be defined by the mutational status of the primary disease. This comment would underline the importance of centralised laboratories, given the increasingly important role of molecular analysis in the work-flow of all GIST, and the need of retrospective analyses for subgroups population stratified for the mutational status from the available studies in the adjuvant setting, in order to define the role of mutational analysis in choosing the optimal dose and duration of adjuvant therapy.

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TO THE EDITOR

We read with great interest the article by Sendur et al [1] entitled “Is exon mutation analysis needed for adjuvant treatment of gastrointestinal stromal tumor?”, that has been recently published in the January issue (2013) of World Journal of Gastroenterology. The authors pointed out the likely importance of mutational analysis for guiding...
It has been recently identified a subgroup of PDGFRA WT GIST, characterized by germline and somatic mutations in succinate dehydrogenase (SDH) subunits B, C and A and defined in different ways as $SDH$-deficient GIST, or type-2 or pediatric-type GIST$^{[24-27]}$. These patients have in common several pathological and clinical features, such as the epithelioid pattern, the multifocal presentation, the female prevalence, the gastric primary tumor localization, and the indolent course of disease despite the presence of lymph nodes and liver metastases up-front and independently to standard prognostic parameters. Moreover it seems that they have also a questionable sensitivity to imatinib. Given their indolent behaviour when metastatic, $KIT/PDGFRA$ WT GIST $SDH$-deficient may not benefit from adjuvant treatment irrespective to the standard risk stratification, whereas more aggressive $KIT/PDGFRA$ WT GIST without $SDH$-impairment, may be probably considered as all mutated GIST.

Therefore also the effect of adjuvant imatinib on $KIT/PDGFRA$ WT GIST may be variable and clinical decision-making should be individualised case by case taking into account various molecular data and shared with the patient$^{[17]}$.

In conclusion, given the increasingly important role of molecular analysis in the work-flow of all GIST, centralised laboratories should be widely warranted. Furthermore, the special attention pointed up by the authors on the “optimal dose” and the “duration” of adjuvant treatment defined by the mutational status of the primary disease should be used at first for the decision to suggest or not the imatinib treatment in this setting. Finally, since prospective clinical trials with large series for definitely defining the role of mutational analysis for patients stratification, dose selection and treatment duration in the adjuvant setting, are difficult because the rarity of disease, retrospective analyses for subgroups population stratified for the mutational status from the available studies in the adjuvant setting are necessary.

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