Potential use of imatinib mesylate in ocular melanoma and liposarcoma expressing immunohistochemical c-KIT (CD117)

KIT is a transmembrane tyrosine kinase receptor in which the extracellular portion binds a ligand known as stem-cell factor and the intracellular portion contains the kinase enzymatic domain. KIT is similar in structure to several other receptor tyrosine kinases with oncogenic capabilities, including platelet-derived growth factor receptors (PDGF-R) A and B [1]. KIT activation normally occurs when two adjacent receptors are brought together through binding to ligand dimers; this process, known as homodimerization, is accompanied by structural changes in the receptors, resulting in activation of the KIT kinase domain. The activated kinases then cross phosphorylate tyrosine residues in the opposed homodimer partner, leading to additional KIT structural alterations and further activation of the receptor [2]. The phosphotyrosines also serve as binding sites for various cell-signaling proteins. These steps culminate in the activation of cell-signaling cascades that control crucial cell functions, such as proliferation, adhesion, apoptosis and differentiation [3, 4].

KIT is frequently mutated and activated in gastrointestinal stromal tumor (GIST), while PDGF-R is expressed in most other sarcomas [5]. We determined c-KIT expression and concentration with Dako CD117 (DK-2600 Glostrup, Denmark) antibody in three cases of ocular melanoma (OM) and two of retroperitoneal liposarcoma (RL). We found positive immunoreactivity for CD117 in all three OM patients and one RL. We decided to treat these patients with palliative imatinib mesylate (IM), a tyrosine kinase inhibitor of KIT and PDGF-R.

Case 1: A 29-year-old female with liver, skin, lung and lymph nodes metastases from OM, heavily pretreated with chemo-immunotherapy, intrarterial fotemustine and tamoxifen. She was in a terminal condition and received IM 200 mg b.i.d. She died after 2 weeks of therapy with increased cholestatis parameters, but reduction of ascites.

Case 2: A 31-year-old male with liver, lung, central nervous system, skin, bone and lymph nodes metastases from OM, who failed chemo-immunotherapy and vaccine therapy. He received IM 200 mg b.i.d. with partial remission of lymph nodes in the neck, but no change in the other lesions. He died after 3 weeks of treatment, because of brain metastases.

Case 3: A 45-year-old female with massive liver metastases from OM. She refused IM for more conventional approaches (intra-arterial hepatic chemotherapy and immunotherapy). She is strictly followed, and we are considering IM at progression.

Case 4: A 71-year-old male with liver and peritoneum metastases from RL, who had been previously treated with three radical tumor resections and intraperitoneal cisplatin chemotherapy. He underwent IM 200 mg b.i.d. After 3 months of therapy, he is showing clear improvement in performance status, body weight gain (5 kg) and withdrawal of analgesic medications; abdominal computed tomography scan has shown evidence of stable disease. He presented with grade 2 neutropenia, grade 2 diarrhea, and two consecutive pleural effusions, cytologically negative, probably due to IM.

We conclude that the effect of IM should be assessed in OM and RL patients with positive immunohistochemical c-KIT (CD117) expression. IM might be a potential therapeutic strategy for these patients.


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References