A Standing Ovation for a Change in How We Treat Patients With Cancer—Forever

By Daniel D. Von Hoff, MD, FACP, and J. Lyle Bootman, PhD

This year's annual meeting of the American Society of Clinical Oncology was history in the making as data were presented that indicated the dramatic regression of gastrointestinal stromal tumors (GIST) when treated with the new agent STI-571.[1] These spectacular responses[1,2] are linked to the effectiveness of STI-571 against tumors that are positive (on immunohistochemistry) for c-*kit* (C117). As it turns out, GISTs, which have heretofore been uniformly unresponsive to any therapy and essentially uniformly fatal, actually arise from the cells of Cajal which constituently express increased levels of c-*kit* (C117+).

This excellent targeted therapy was built on the pioneering work of Brian Druker, MD, and colleagues,[3] who originally developed STI-571 as a superb inhibitor of the mutated *bcr-abl* tyrosine kinase which is present in chronic myelogenous leukemia (CML).[3] Indeed, STI-571 has caused tumor remissions in patients with CML—even to the extent of the elimination of Philadelphia chromosome in patients' white cells (a sensitive indicator that the malignant clone is probably eliminated in these patients). As it turns out, STI-571 not only inhibits the *bcr-abl* tyrosine kinase in CML cells, but also inhibits c-*kit* and platelet derived growth factor receptor kinase that is present in a small percentage of other types of tumors (eg, small-cell lung cancer, glioblastoma multiforme, ovarian cancer, and others). Thus, if any of those targets are present in an individual patient's tumor, it is possible that STI-571 will have activity against the patient's tumor. Also of great importance is the fact that STI-571 is an oral medication which, aside from occasional mild myelosuppression, has virtually no major side effects.

This work is making a reality of what all antitumor drug developers and oncologists everywhere have dreamed would be possible. STI-571 and many new agents like it are tailored for the molecular abnormalities (targets) present in a patient's tumor with resulting spectacular efficacies and essentially no side effects.

This work by Druker and colleagues[1-3] sets a new standard for how we will approach our patients, and how drug development must now proceed. It will be particularly helpful to the special care of the elderly with cancer, as discussed so well in this issue of *Oncology Spectrums*. The work by Druker and colleagues deserves our admiration, our standing ovation, and our appreciation for how much of a difference this will make for humankind. OS

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REFERENCES

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