Editorial

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Anti-Cancer Drugs 2010, **21 (suppl 1)**:S1–S2

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The main challenge of cancer research is to find an agent that kills malignant cells but spares normal tissue as much as possible. In the last few years, as our understanding of the mechanisms involved in malignancy has increased, specific molecules required for tumor growth have been identified and new agents that inhibit these targets have been developed and approved for treatment. This 'targeted therapy' has become a milestone in cancer treatment because it allows more specific destruction of tumor cells and reduces unwanted side effects on normal tissue [1].

Receptor tyrosine kinases (RTKs) play a key role in tumor growth and survival [2]. After the success of early tyrosine kinase inhibitors such as imatinib in cancer treatment, many of these drugs are now being developed. Although the use of targeted therapies is relatively recent, in the last few years the focus has changed from finding compounds that act on a single target to developing drugs that can inhibit several molecules. Sunitinib, a tyrosine kinase inhibitor, is an example of this new focus. Sunitinib was rationally designed to inhibit multiple RTKs, including vascular endothelial growth factor receptors, platelet-derived growth factor receptors and the c-KIT receptor. Consequently, sunitinib affects most of the processes involved in tumor growth, including angiogenesis and metastasis [1,3,4].

Agents acting at several targets, such as sunitinib, have a broader spectrum of activity than single-target agents. It is now evident that these multitarget drugs potentially have greater antitumor activity than single-target drugs, while retaining acceptable toxicity profiles [5]. A further potential benefit of multitarget agents is that resistance, which can occur with single-target tyrosine kinase inhibitors because of activation of alternative RTK pathways, is less likely to arise [1,6]. Treatment with multitarget agents can also reduce the number of drugs a patient has to take, which in turn decreases the risk of drug–drug interactions and toxicity, and increases patient compliance.

Sunitinib has recently been approved by the European Union for the first-line or second-line treatment of metastatic renal cell carcinoma (RCC) and in patients with advanced gastrointestinal stromal tumors who have failed or are intolerant to imatinib. Targeted therapies, such as sunitinib, have greatly improved the prognosis for patients with these types of cancer. In patients with metastatic RCC, progression-free survival has more than doubled, compared with when cytokines were used for treatment [7]. Similarly, in patients with advanced gastrointestinal stromal tumors, the 1-year overall survival rate has increased to almost 90% with the introduction of targeted therapies [7].

Understanding the mechanism of action of these targeted therapies is important for maximizing their efficacy. On account of its multitarget activity, sunitinib has the potential to be used in a range of solid tumor types. Indeed, sunitinib is currently being evaluated in a broad clinical programme across different types of tumors. Challenges for the future use of multitarget therapies, including sunitinib, include developing strategies to assess which patients are most likely to benefit from which treatments, optimizing dosing regimens, managing treatment-related adverse effects and minimizing further the potential for drug resistance. The ability to tailor treatment to individual patients and tumor types may involve combining sunitinib with other targeted therapies or chemotherapy [6]. Currently, clinical trials are investigating some of these issues, including the use of multitarget agents in combination and their role in first-line and adjuvant treatment.

The development of multitarget agents such as sunitinib is a major step forward in the treatment of cancer. These agents provide an example of how understanding of biology can be used to develop a clinically effective drug. It is hoped that these targeted therapies will help greatly with the fight against cancer, and allow it to become a manageable disease. However, further research is still required to be able to fully understand these agents and use them to the best effect.

This supplement to Anti-Cancer Drugs reviews the role of angiogenesis in cancer and summarizes both the preclinical activity and the clinical development of sunitinib, including early clinical trials, phase I and pharmacological trials and its late clinical development. It also contains a review of biomarker and functional imaging studies and concludes with a discussion of the role of the combination of antiangiogenics and chemoradiotherapy regimens and future directions. Four

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case reports depicting the use of sunitinib in patients with different cancer types (RCC, breast and colorectal cancer) are also discussed.

Conflicts of interest: none.

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