

## Tyrosine Kinases: promising targets for cancer chemotherapy

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### Abstract

Cancer chemotherapy has been one of the major medical advances in the last few decades. However, the drugs used for this therapy have a narrow therapeutic index, and often the responses produced are only just palliative as well as unpredictable. In contrast, targeted therapy that has been introduced in recent years is directed against cancer-specific molecules and signaling pathways and thus has more limited nonspecific toxicities. Tyrosine kinases are an especially important target because they play an important role in the modulation of growth factor signaling. This review focuses on small molecule inhibitors of tyrosine kinase. They compete with the ATP binding site of the catalytic domain of several oncogenic tyrosine kinases. They are orally active, small molecules that have a favorable safety profile and can be easily combined with other forms of chemotherapy or radiation therapy. Several tyrosine kinase inhibitors (TKIs) have been found to have effective antitumor activity and have been approved or are in clinical trials. The inhibitors discussed in this manuscript are imatinib mesylate (STI571; Gleevec), gefitinib (Iressa), erlotinib (OSI-1774; Tarceva), lapatinib (GW-572016), canertinib (CI-1033), semaxinib (SU5416), vatalanib (PTK787/ZK222584), sorafenib (BAY 43-9006), sunitinib (SU11248), and leflunomide (SU101). TKIs are thus an important new class of targeted therapy that interfere with specific cell signaling pathways and thus allow target-specific therapy for selected malignancies. The pharmacological properties and anticancer activities of these inhibitors are discussed in this review. Use of these targeted therapies is not without limitations such as the development of resistance and the lack of tumor response in the general population. The availability of newer inhibitors and improved patient selection will help overcome these problems in the future.

**Keywords:** Kinase; Protein kinase; Kinase inhibitors; Cancer therapy

### Introduction

Kinase is a type of enzyme that transfers phosphate groups from high-energy donor molecules, such as ATPs to specific substrates, a process referred to as phosphorylation. Kinases are part of the larger family of phosphotransferases. Kinases are not to be confused with