

Tyrosine Kinase Inhibitors

Tyrosine kinase inhibitors (TKIs) are a form of targeted therapy that blocks the action of tyrosine kinase enzymes in cells. TKIs disrupt the signaling pathways that protein kinases use to control cell growth and division. This prevents cancer cells from growing and multiplying. TKIs can be used alone or in combination with other treatments, such as chemotherapy. TKIs are administered orally, and generic names commonly end in the suffix *-nib*. The U.S. Food and Drug Administration has approved more than 50 TKIs.

Examples

- Osimertinib: targets epidermal growth factor receptor (EGFR); used in non-small cell lung cancer (NSCLC)
- Ibrutinib: targets Bruton tyrosine kinase (BTK); used in chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), and graft-versus-host disease
- Axitinib: targets vascular endothelial growth factor receptor (VEGFR); used in advanced renal cell carcinoma (RCC)
- Trametinib: targets MEK1/2; used in melanoma

Side Effects

- Nontraditional side effect profile compared to cytotoxic agents
 - Side effects are dose dependent and occur at different frequencies depending on the drug.
 - Not all side effects are associated with every TKI.
- General: fatigue, arthralgia, muscle cramping
- Ocular: conjunctivitis, keratitis
- Integumentary: acneiform rash; photosensitivity; hair, skin, and nail changes
- Hepatic: elevated liver function tests (LFTs)
- Gastrointestinal: nausea, vomiting, diarrhea, constipation, fistula/perforation
- Hematologic: neutropenia, thrombocytopenia, anemia
- Pulmonary: pneumonitis, pulmonary edema
- Cardiovascular: hypertension, QT prolongation, dysrhythmias, myocardial toxicities
- Renal: syndrome of inappropriate antidiuretic hormone secretion (SIADH), electrolyte abnormalities, acute kidney injury
- Pancreatic: pancreatitis, elevated amylase/lipase

Pre- and Postadministration Considerations

- Monitor blood counts closely and reference treatment parameters.
- Conduct baseline and symptom assessment to closely monitor for side effects and report or intervene early.
- TKIs have a high propensity for drug–drug interactions.
 - Medications can inhibit or induce enzymes in the cytochrome P450 (CYP) pathway, leading to interactions.

- Interactions could lead to adverse reactions or therapeutic failures due to over- or underexposure.
- Complete a thorough medication reconciliation and provide education.
- The price of TKI therapy ranges \$5,000–\$10,000 per month, and the financial burden may contribute to nonadherence. Discuss financial burdens during education.

Patient and Caregiver Education Considerations

Providers should have a conversation with patients and caregivers relaying medication information, what to expect during treatment, side effects, home medications for side effect management, discharge instructions, when to notify the healthcare team of adverse effects, and emergency contact information for providers.

References

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