

TABLE 103e-5 MOLECULARLY TARGETED AGENTS

Drug	Target	Adverse Events	Notes
<b>Diagnostically Guided Protein Kinase Antagonists</b>			
Imatinib	Bcr-Abl fusion protein (CML/ALL); c-kit mutants, PDGFR variants (GI stromal tumor; eosinophilic syndromes)	Nausea Periorbital edema Rare CHF QTc prolongation	Myelosuppression not frequent in solid tumor indications
Nilotinib	Bcr-Abl fusion protein (CML) and some imatinib-resistant variants	Interaction with CYP3A4-metabolized drugs CHF Hepatotoxicity Hypothyroidism	Chronic phase and in patients resistant to imatinib
Dasatinib	Bcr-Abl fusion protein (CML/ALL); wild-type and imatinib-resistant mutants	Myelosuppression (bleeding, infection) Pulmonary hypertension CHF Fluid retention QTc prolongation	Chronic phase and imatinib or nilotinib resistant
Bosutinib	Bcr-Abl fusion protein (CML); wild-type and imatinib-resistant mutants	Myelosuppression Hepatic QTc prolongation	Chronic phase and imatinib or nilotinib resistant
Ponatinib	T315I mutation of Bcr-Abl fusion protein (CML)	Clotting Hepatic CHF Pancreatitis Neuropathy Rash	
Gefitinib	First-line treatment of NSCLC with ATP site mutation of EGFR	Diarrhea Interstitial pneumonitis	In United States, only with prior documented benefit in second-line treatment of NSCLC
Erlotinib	First-line treatment of NSCLC with ATP site mutation of EGFR; second-line treatment of wild-type EGFR NSCLC	Rash Diarrhea Rare interstitial pneumonitis	1 h before, 2 h after meals
Afatinib	First-line treatment of NSCLC with ATP site mutation of EGFR	Diarrhea Cutaneous	Interacts with Pgp inhibitors
Crizotinib	EML4-Alk fusion protein	Interstitial pneumonitis Hepatic QTc prolongation Bradycardia	
Vemurafenib	<i>BRAF</i> V600E in melanoma	Nausea Rash Cutaneous Second cutaneous neoplasms	
Dabrafenib	<i>BRAF</i> V600E in melanoma	Cutaneous Second cutaneous neoplasms	
Trametinib	<i>BRAF</i> V600E in melanoma (both as single agent and in combination with dabrafenib)	Rash Diarrhea Lymphedema	In combination with dabrafenib, second neoplasms, hemorrhage, venous thrombosis, CHF, ocular, hyperglycemia
<b>Drug</b>	<b>Indication</b>	<b>Adverse Events</b>	<b>Notes</b>
<b>Diagnostically Guided Retinoid</b>			
Tretinoin	APL t(15,17)	Teratogenic Cutaneous	APL differentiation syndrome: pulmonary dysfunction/infiltrate, pleural/pericardial effusion, fever
<b>Nondiagnostically Guided Agents</b>			
<b>Retinoid</b>			
Bexarotene	Cutaneous T cell lymphoma	Hypercholesterolemia Hypertriglyceridemia Cutaneous Teratogenic	Central hypothyroidism

(Continued)