TABLE 55-4 COMMONLY USED TARGETED THERAPY AGENTS

DRUG	CANCERS TREATED	TARGETS	COMMON SIDE EFFECTS
MONOCLONAL ANTIBODIES			
Alemtuzumab	CLL	CD52	Myelosuppression, fever, rash
Bevacizumab	Colorectal, renal, lung	VEGF	Hypertension, proteinuria, bleeding, thromboembolism
Cetuximab	Colorectal	EGFR	Rash
Ipilimumab	Metastatic melanoma	CTLA4	Cytokine release storm
Ofatumumab	CLL	CD20	Rash, diarrhea, respiratory tract infections
Panitumumab	Colorectal	EGFR	Rash
Pertuzumab	Breast	HER2	Rash, diarrhea
Rituximab	NHL	CD20	Infusional reaction, skin reactions
Trastuzumab	Breast	HER2/Neu	Infusional reaction, congestive heart failure
SIGNAL TRANSDUCTION INHIBITORS			
Axitinib	Renal	VEGF, PDGF, KIT	Hypertension, hand-foot syndrome, diarrhea
Crizotinib	Lung	EML4-ALK	Edema, diarrhea
Dasatinib	CML	BCR-ABL	Myelosuppression, pleural effusions
Imatinib	CML, GIST	BCR-ABL	Diarrhea, fluid retention, myelosuppression
Erlotinib	Lung, pancreas	EGFR tyrosine kinase	Rash, diarrhea
Gefitinib	Lung	EGFR tyrosine kinase	Rash, hypertension
Lapatinib	Breast	HER2, EGFR	Rash, diarrhea
Regorafenib	GIST, colorectal	VEGF	Hypertension, hepatotoxicity, dysphonia
Sunitinib	Renal, GIST	VEGF, PDGF, KIT	Rash, diarrhea, fatigue
Sorafenib	Liver, renal	VEGF, PDGF, KIT	Hypertension, fatigue, diarrhea, hand-foot syndrome
Vandetanib	Medullary thyroid	VEGF, EGFR, RET	Rash, abdominal pain, diarrhea
Vemurafenib	Melanoma	BRAF	Rash, skin lesions, arthralgia
OTHERS			
All-*trans*-retinoic-acid	Acute promyelocytic leukemia	Differentiating agent	Vitamin A toxicity, retinoic acid syndrome, hyperlipidemia
Azacitidine	Myelodysplasia	Hypomethylating agent	Myelosuppression, injection site reactions
Bortezomib	Lymphoma, myeloma	Proteasome inhibitor	Rash, nausea, emesis, neuropathy
Everolimus	Renal, breast, neuroendocrine	mTOR inhibitor	Hyperglycemia, diarrhea, fatigue

CLL, Chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; CTLA4, cytotoxic T lymphocyte–associated protein 4; EGFR, epidermal growth factor receptor; GIST, gastrointestinal stromal tumor; mTOR, mammalian target of rafampin; NHL, non-Hodgkin's lymphoma; VEGF, vascular endothelial growth factor.

combined with standard chemotherapy in advanced colorectal cancer. Similarly, the EGFR antagonists, cetuximab and panitumumab, increase the efficacy of irinotecan-based chemotherapy in colorectal cancer and that of definitive radiation therapy in oropharyngeal cancers. The availability of these agents has increased the number of drug combinations that can be used in particular cancers. For example, multiple combinations of chemotherapy and targeted therapy are now available for the treatment of advanced colon cancer. Correspondingly, the median survival time of patients with this disease has doubled.

Biologic and Immunologic Therapy

Cytokines that use host immunomodulatory effects as their primary mechanism of action are classified as *biologic response modifiers* or *biologic agents*. Monoclonal antibodies are sometimes classified as biologic agents, although here they have been reviewed under targeted therapy (see earlier discussion). Interferons are commonly used in CML, although they are not as successful as imatinib in inducing responses. Interferons are also used for the treatment of hairy cell leukemia, Kaposi's sarcoma, and selected melanomas and renal cell carcinomas. Interleukin-2 (IL-2) functions as a T-cell growth factor and induces lymphokine-activated and natural killer cell activity. IL-2 can induce responses in 10% to 20% of patients with metastatic melanoma or renal cell carcinoma. In a minority of these patients, responses are complete and last for years. However, IL-2 has toxicity—in particular, a capillary leak syndrome that leads to hypotension, edema, renal insufficiency, and even death.

Immunotherapy agents act by altering the host immune response to the tumor. Cancer vaccines, such as the dendritic cell vaccine sipuleucel-T for prostate cancer, are primed to target cells with specific tumor antigens. Molecules that achieve immune checkpoint blockade have some benefit in melanoma. These agents block T-cell inhibitory molecules such as cytotoxic T lymphocyte–associated protein 4 and programmed cell death 1, thereby releasing T-cells to actively target cancer cells.

Personalized Medicine

The field of oncology is rapidly moving toward an era in which individual patient biospecimens can be evaluated using advanced techniques to reveal specific molecular aberrations that can then be targeted with precise therapeutic agents. Such an approach is referred to by various names, including *precision* or *personalized medicine* and *genomics-driven therapeutics*. The time and costs involved in analyzing the whole genome from a patient's tumor are now much reduced and continue to fall rapidly. In addition to DNA, whole transcriptome (RNA), epigenome (DNA methylation), and single-nucleotide polymorphism (SNP array) analyses can also be performed. Several cancers have already been sequenced completely. Such work creates "reference libraries" against which a patient's tumor can be tested. Based on findings from such analyses, specific drugs or regimens can be recommended for individual patients. Currently used assays include a 21-gene expression profile in breast cancer, *KRAS* in colorectal cancer, *EGFR* and *EML4-ALK* in lung cancer, and *BRAF* in melanoma. Such evaluation of tumor tissues allows patients to