Targeted Drug Therapies: Beyond Blood Counts and Chemistries

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For many decades, traditional chemotherapy, or cytotoxic chemotherapy, has been the mainstay of cancer treatment. These drugs affect rapidly dividing cells throughout the body. Although cancer cells tend to grow faster, there are many healthy cells in the body that also divide and grow quickly, such as hair follicles, bone marrow cells, and cells of the gastrointestinal (GI) tract (National Cancer Institute, 2022a). Correspondingly, patients who receive traditional chemotherapies can experience the classic toxicities of alopecia; GI tract side effects such as nausea and vomiting; and myelosuppression, which may lead to fatigue, infections, and easy bruising and bleeding. Targeted therapies are treatments that target specific genes and proteins that help cancer cells survive and grow (National Cancer Institute, 2022b). Targeted therapies include small molecule inhibitors and immune checkpoint inhibitors. These two targeted therapies have become more common in the treatment of cancer because of better patient tolerability as compared with traditional chemotherapy. Although targeted therapies have expanded treatment options for many patients, they come with distinct side effects of their own.

Small Molecule Inhibitors
Small molecule inhibitors target proteins within cancer cells that may be overexpressed or mutated. There are many target receptors for small molecule inhibitors, with one of the most common being the receptor tyrosine kinase. The receptor tyrosine kinases play a role in cell-to-cell communication and control a range of complex biologic functions (cell growth, motility, differentiation, and metabolism). Consequently, acquired dysregulation of the receptor tyrosine kinase pathway leads to a disruption in the homeostasis of cell proliferation and cell death, the result of which is induced oncogenesis (Du & Lovly, 2018).

By the nature of their size, small molecule inhibitors vary in their target selectivity. Small molecule inhibitors can be categorized as selective inhibitors or as multitarget inhibitors. The first U.S. Food and Drug Administration–approved small molecule inhibitor in 2001 was imatinib, a selective BCR-ABL1 kinase inhibitor (Liu et al., 2022). The BCR-ABL1 tyrosine kinase created by the Philadelphia chromosome translocation variant is seen in individuals with certain forms of leukemia (Liu et al., 2022). Imatinib is indicated as a first-line treatment for newly diagnosed adults and pediatric patients with Philadelphia chromosome–positive chronic myeloid leukemia.