Bioavailability of Tyrosine Kinase Inhibitors: An Added Component of Assessment

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The growing prominence of tyrosine kinase inhibitors (TKIs) as treatment for malignancies prompts oncology nurses to expand the scope of their patient assessment. Because TKIs as oral agents have a different bioavailability than parenteral agents, factors that alter drug absorption and metabolism can have a measurable effect on the amount of active, available drug when TKIs are prescribed. In relation to TKIs as cancer therapies and intended dosing, this article reviews three drug absorption and metabolism factors: changes in stomach pH, as well as P-glycoprotein and cytochrome P450 interactions.

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Key words: targeted therapies; tyrosine kinase inhibitors; drug interactions

Digital Object Identifier: 10.1188/14.CJON.714-716

Patient assessment in oncology nursing has focused on side effects associated with traditional cytotoxic chemotherapeutic agents, including myelosuppression (e.g., neutropenia, thrombocytopenia, anemia), gastrointestinal toxicity (e.g., nausea, vomiting, diarrhea, gastritis), cutaneous toxicity, and constitutional symptoms (e.g., fatigue, pain, malaise). In addition, the assessment for a few drug-specific toxicities has included taxane-induced neuropathy or cisplatin-associated hearing loss.

The growing prominence of tyrosine kinase inhibitors (TKIs) in the oncology pharmaceutical arsenal has triggered a shift in what is considered to be a standard assessment. Targeted therapies have expanded the spectrum of side effects in scope and diversity. Therefore, with targeted therapies, the assessment template includes a wider range of considerations when monitoring and educating patients.

Factors Affecting Tyrosine Kinase Drug Delivery

The bioavailability of TKIs as oral agents differs from their bioavailability as parenteral agents. Bioavailability is defined as the "rate and extent to which the active ingredient . . . is absorbed from a drug product and becomes available at the site of action" (U.S. Department of Health and Human Services, U.S. Food and Drug Administration [FDA], & Center for Drug Evaluation and Research, 2013, p. 3). More simply, bioavailability is the proportion of administered drug that becomes active.

Parenteral administration is associated with a high rate of bioavailability because IV administration allows for the immediate entry of the administered drug into systemic circulation. In addition, parenteral administration generally is associated with consistent pharmacokinetics and absorption. Oral medications, however, must be absorbed across the gastrointestinal mucosa and processed by gastric and intestinal enzymes, then metabolized in the liver. Along this path, oral medications are transformed from insoluble forms to more absorbable, soluble forms (Polovich, Olsen, & LeFebvre, 2014). Factors that alter drug absorption and metabolism can have a measurable affect on the amount of active, available drug. Three specific altering factors are changes in stomach pH, as well as P-glycoprotein (P-gp) and cytochrome P450 (CYP) interactions.

Changes in Stomach pH

Stomach acidity, measured in pH, has a direct impact on the bioavailability of orally administered agents such as TKIs. Oral medications are formulated to dissolve into soluble, ionized forms at specific pH levels inherent in the human body. Concomitant use of acid-suppressing agents (e.g., proton pump inhibitors [PPIs], H_2 antagonists, antacids) will shift the stomach environment to a higher pH, making it less acidic and, therefore, affecting the chemical availability. For example, erlotinib becomes more soluble in a mildly acidic environment (pH 5.42) (Genentech, 2013). As a PPI, omeprazole will reduce the acidity of the gastric environment and alter the solubility of erlotinib, effectively reducing its chemical availability. The concomitant use of PPIs, such as 40 mg of omeprazole once daily, will decrease the maximum concentration of erlotinib to 61%, which is a dose reduction of 39% (van Leeuwen, van Gelder, Mathijssen, & Jansman, 2014).

Because the concomitant use of acid-reducing agents can adversely affect the accuracy of target dosing of TKIs,