



PIC QUESTION OF THE WEEK: 4/23/07

Q: Can the antineoplastic agent irinotecan be administered orally?

A: Irinotecan (Camptosar[®]) is an antineoplastic agent indicated for the treatment metastatic carcinoma of the colon or rectum. Unlabeled indications include the treatment of cervical, lung (small cell and non-small cell), gastric, pancreatic, and breast cancers, leukemia, lymphoma, and a variety of other solid tumors. It is one of two topoisomerase I inhibitors now commercially available (the other is topotecan; Hycamtin[®]). Though currently available only for intravenous (I.V.) injection, the oral route has been investigated for several years. There are potentially several advantages to this method of administration. First, it reduces patient inconvenience by eliminating the need for frequent office visits for I.V. infusions. In addition, sustained exposure to the oral formulation appears to reduce the frequency of hematological toxicities such as bone marrow suppression, leucopenia, and thrombocytopenia. Lastly, the oral route decreases treatment costs while maintaining a pharmacokinetic profile similar to the parenteral form. A number of pharmacokinetic studies indicate that the drug is rapidly and relatively well absorbed by mouth. However, oral dosage might be limited due to potentially severe diarrhea. This adverse effect also occurs with the parenteral route. Several oral formulations of irinotecan have been evaluated including powder-filled capsules, semi-solid matrix capsules, and a reconstituted solution made from the current I.V. product. One of these phase I trials compared the kinetic profile of an *orally* administered I.V. formulation versus I.V. *injection* in 39 pediatric patients. The appropriate dose of reconstituted irinotecan was placed in pre-filled oral syringes with a designated stability of 21 days under refrigeration. The caregiver was instructed to mix each dose with cranberry-grape juice just prior to administration. The study also investigated the effects of the antimicrobial cefixime on the kinetics and dose escalation of oral irinotecan. Cefixime reduces levels of beta-glucuronidase producing bacteria in the gastrointestinal tract, thus, limiting the conversion of irinotecan's inactive (SN-38G) glucuronide metabolite back to its active, non-conjugated form (SN-38). The authors concluded that irinotecan is relatively well absorbed by mouth, but its kinetics and tolerance can be improved by simultaneous use of cefixime. Progress in the development of an oral irinotecan formulation continues and such a dosage form may be soon available.

References:

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