Dose-escalated cetuximab tolerated in colorectal cancer

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(HealthDay) -- For patients with irinotecan-refractory metastatic colorectal cancer (CRC), dose escalation of cetuximab is well tolerated and may improve response and disease control rates, but patients experience more grade ≥2 skin reactions, according to a study published online July 2 in the *Journal of Clinical Oncology*.

Eric Van Cutsem, M.D., Ph.D., of University Hospital Gasthuisberg in Leuven, Belgium, and colleagues investigated the effect of cetuximab dose escalation in 157 intent-to-treat patients with irinotecan-refractory metastatic CRC. Following 21 days of standard-dose (400 mg/m^2 initial dose, then 250 mg/m^2 per week) treatment, participants who developed no or mild skin reactions (grade ≤1) at the standard dose were randomly

allocated to standard-dose (45 patients) or dose-escalated (44 patients; up to 500 mg/m^2 per week) cetuximab. Patients with skin reactions grade ≥2 continued with standard-dose cetuximab and irinotecan.

The researchers found that the pharmacokinetic profiles were predictable across the dose range assessed. Cetuximab up to 500 mg/m^2 per week was well tolerated, with comparable grade 3 and 4 adverse events between the groups. There was an increase in grade ≥2 skin reactions for the dose-escalation versus the standard-dosing group (59 versus 38 percent). Although some evidence for improved response rate (30 versus 16 percent) and disease control rate (70 versus 58 percent) was noted with dose escalation, no overall survival benefit was found. Patients with *KRAS* wild-type, compared with *KRAS* mutant tumors, had increased response rate with dose escalation versus standard dosing.

"Cetuximab serum concentrations increased predictably with dose. Higher dose levels were well tolerated," the authors write. "The possible indication for improved efficacy in the dose-escalation group warrants further investigation."

Several authors disclosed financial ties to pharmaceutical companies, including Merck KGaA, which funded the study.

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