Limb Infusion an Option for In-Transit Melanoma

BY DAMIAN McNAMARA

PALM BEACH, FLA. — Regional chemotherapy via isolated limb infusion is an acceptable and minimally invasive alternative to hyperthermic isolated limb perfusion to combat in-transit extremity melanoma, according to a review.

"Perfusion is appropriate with lymph node involvement. For all others, infusion should be considered," Dr. Georgia M. Beasley said. She, Dr. Douglas S. Tyler, and their colleagues reviewed response and toxicity for 166 isolated limb infusions in 157 patients with advanced extremity melanoma. At 3 months after the infusion of melphalan, patients' responses were fairly evenly divided among complete response, partial response, and no response. In cases when the melphalan dose was adjusted for ideal body weight (IBW), the rate of grade 3 or higher toxicity fell more than half, with no effect on complete response rate.

Melphalan (Alkeran) was administered at eight centers, representing the majority of institutions performing limb infusions in the United States, Dr. Beasley said at the annual meeting of the Southern Surgical Association.

Patients received melphalan at doses of 7.5 mg/L for advanced melanoma of the lower extremity and 10 mg/L for the upper extremity. Mean ischemic time was 72 minutes. Papaverine was also administered in 60% of procedures. "We currently recommend use of papaverine in conjunction with adjustment of melphalan for ideal body weight to minimize toxicity," Dr. Beasley said.

Among the 122 evaluable patients, 31% experienced a complete response at 3 months according to RECIST (Response Evaluation Criteria in Solid Tumors), modified for cutaneous lesions. Another 33% of patients had a partial response, and 36% did not respond at 3 months. The complete response rate for hyperthermic isolated limb perfusion is generally accepted to be 40%-80%, Dr. Beasley said. Discussant Dr. Kirby I. Bland drew attention to the 36% rate of nonresponders. "You were still unable to control local disease in [almost] 40% of that population," said Dr. Bland, chair of the surgery department at the University of Alabama at Birmingham.

"For extensive in-transit disease in the lower extremity, I would recommend infusion, even though one-third of patients are not expected to have a response," responded Dr. Beasley, a first-year general surgery resident at Duke University Medical Center, Durham, N.C. "This allows reservation of perfusion for those who do not respond. Also, repeat perfusions are more difficult to do."

Dr. Beasley said that 36% of cases were associated with grade 3 or higher clinical toxicity. In 42% of the procedures, melphalan was adjusted for IBW. This modification reduced grade 3 or greater toxicities from 47% to 21%. At the same time, it did not alter the complete response rate. "By the end of the series, we were correcting everyone [at Duke] for ideal body weight," Dr. Beasley said. She cautioned that the dose adjustment did reduce the partial response rate, however.

Limb infusion and perfusion exhibit major differences in the rates of grade 5 toxicity, Dr. Beasley said. Even though one limb infusion patient had an amputation, the rate of grade 5 toxicity "appears to be nearly 10-fold higher with perfusion," based on all the published data for isolated limb infusion. The study did not directly compare rates of grade 3 and 4 toxicity in infusion and perfusion, but the rates appear to be somewhat similar, she said, with dose correction for IBW significantly reducing toxicity.

"How many patients had compartment syndrome, and what are your recommendations for monitoring?" asked Dr. Kelly M. McMasters, a study discussant and chair of surgery at the University of Louisville (Ky.). Nine cases of compartment syndrome were reported, Dr. Beasley replied. She recommended daily creatine phosphokinase measurements and close clinical monitoring.

Only two U.S. studies previously assessed isolated limb infusion, with both reporting single-center experience (Ann. Surg. Oncol. 2008;15:2195-205; Ann. Surg. Oncol. 2006;13:1123-9).

None of the researchers in the current study had any relevant disclosures. ■