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Perspectives and Commentaries

Therapy of Herpes zoster Infections

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(A COMMENT ON: Wildiers J, De Clercq E. Oral (*E*)-5-(2-bromovinyl)-2′-deoxyuridine treatment of severe Herpes zoster in cancer patients. *Eur J Cancer Clin Oncol* 1984, **20**, 471–476.)

A DECADE ago there were no effective antiviral agents for the treatment of Herpes zoster in the immunosuppressed cancer patient. Now there are three, with other promising agents on the horizon. The report by Wildiers and De Clercq suggests that oral (*E*)-5-(2-bromovinyl)-2′-deoxyuridine (BVDU) may prove to be one of these promising agents. In their study they show that when administered at a dose of 7.5 mg/kg/day for 5 days, BVDU is well tolerated, and most patients recover quickly from their Herpes zoster infection. What they do not show, as they readily admit, is BVDU efficacy in this disorder. Most patients with Herpes zoster and cancer recover quickly with no therapy, and whether BVDU is any better than placebo remains to be demonstrated.

Intravenous vidarabine has been the most carefully studied drug in varicella-zoster virus infections among cancer patients [1, 2]. Two double-blind, placebo-controlled trials have evaluated vidarabine's role in Herpes zoster. In the initial 'cross-over' study, patients taking vidarabine (10 mg/kg/day for 5 days) had a more rapid cessation of viral shedding and acceleration of cutaneous healing. Benefits occurred primarily in patients with lymphoreticular neoplasms who were treated within 6 days of initial lesions. The second trial did not employ a cross-over design, thus allowing an evaluation of long-term complications. Patients were eligible for participation only if lesions had been present for 72 hr or less. In this trial, in addition to local benefit, vidarabine decreased distal cutaneous dissemination from 24 to 8% and visceral dissemination from 19 to 5%. Duration of postherpetic neuralgia was also significantly shorter in vidarabine recipients.

The efficacy of interferon alpha has been studied in three randomized placebo-controlled studies [3]. In the third study, which used the highest dose of interferon alpha (5.1×10^5 U/kg day), the drug slowed progression of disease in the primary dermatome and eliminated distal cutaneous spread. When the three studies were taken together, interferon could also be demonstrated to decrease the frequency of visceral dissemination and to hasten resolution of pain.

Controlled trials of intravenous acyclovir also demonstrate beneficial effects on the course of Herpes zoster in the immunocompromised host [4]. At doses of 1500 mg/m^2 for 7 days, acyclovir retarded the spread of both localized and cutaneous zoster and reduced the frequency of visceral zoster. All three drugs also show efficacy in chicken pox among cancer patients [5–7].

Each of these agents has potential toxicity, and the controlled trials have included only parenterally administered compounds. Current efforts are directed toward use of antivirals that do not require hospitalization for administration. In the U.S.A. outpatient trials comparing oral acyclovir, intramuscular vidarabine monophosphate and placebo are planned. Studies evaluating intramuscular recombinant interferons in ambulatory patients are also underway. Oral BVDU has greater potency against varicella-zoster virus *in vitro* than vidarabine or acyclovir, and can be given orally. The next step in its evaluation should be to subject BVDU to rigorously controlled studies against placebo and other antivirals. These trials should be multicentered to

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allow for enrollment of sufficient numbers of homogeneous patients for proper evaluation. Efforts should be to enroll patients at greatest risk, i.e. those with lymphoreticular neoplasms, within 72 hr of lesion onset. Patients should be monitored acutely for healing, acute pain, cutaneous and visceral dissemination, virus shedding and both drug levels and drug toxicity. Study subjects should be followed for long enough periods to evaluate effects on post-herpetic neuralgia as well. Only in this comprehensive and controlled fashion can the ultimate place of BVDU in the treatment of Herpes zoster in cancer patients be clarified.

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