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Famciclovir: Effect on Pain in Herpes Zoster

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Famciclovir has been shown to reduce significantly the duration of post-herpetic neuralgia (PHN). The definition of PHN used, pain following healing of the cutaneous lesions, is a widely accepted definiton, but there are numerous other definitions reported in the literature. We have, therefore, analysed the data from the 419 patient placebo-controlled famciclovir study to determine, firstly, whether cutaneous healing time influences rate of loss of pain, and secondly, to investigate loss of chronic pain using a number of alternative definitions. The results of these investigations showed that time to healing of cutaneous lesions did not correlate with time to loss of pain. The effect of famciclovir on pain was further investigated by measuring the rate of pain loss from enrollment in three groups of patients: those who experienced pain a) following healing, b) for 30 days or more and c) for 3 months or more. In all three analyses, famciclovir treated patients lost pain significantly faster than placebo recipients. For example, patients who had pain for 3 months or more lost pain approximately 2.5 times faster when treated with 500mg famciclovir tid ($p = 0.048$) compared with placebo. In conclusion, since there is no correlation between cutaneous healing and loss of pain, defining PHN as pain following healing of the rash is valid, and the significant reduction in duration of PHN reported previously using this definition was further supported by alternative analyses for time to loss of pain.

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Covariates in Herpes Zoster and Interpretation of Clinical Trial Data.

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Famciclovir has been shown to accelerate cutaneous healing and significantly reduce the duration of post-herpetic neuralgia (PHN). Various factors, such as age, duration of rash at start of treatment and severity of pain, are thought to affect the outcome of antiviral therapy of shingles. Data from a 419 patient placebo-controlled study was analysed using the Cox Proportional Hazards Model to determine which factors were significant covariates. We found that duration and severity of rash at start of study medication, age and severity of pain at enrollment were significant covariates for loss of zoster-associated pain (ZAP), but that only the first three were significant covariates for cutaneous lesion healing. When these significant covariates were fitted into the model, famciclovir significantly reduced the duration of all pain (ZAP) and the duration of PHN. The predictive value of covariates for the development of chronic pain (PHN) will be discussed. Of these covariates, age has been clearly shown to influence chronic pain (PHN), and in the famciclovir trial, placebo treated patients aged 50 years or more had a median duration of PHN of 163 days. However, in the same age group of patients who received famciclovir at 500mg or 750mg tid, the median duration of PHN was reduced to 63 days which was close to what appears to be the natural rate of resolution in patients aged <50 years. Covariates identified in this famciclovir trial illustrate the importance of treating patients as soon after rash onset as possible, and show that age is a very important factor influencing the course of the disease. We conclude that covariate analysis can provide additional valuable data to assess antivirals in the management of herpes zoster. By controlling for important covariates, the significant beneficial effect that famciclovir has on PHN was further substantiated.