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SINGLE-DOSE PHARMACOKINETICS OF NEVIRAPINE (BI-RG-587).

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Objective: To determine an appropriate oral dose and schedule for administration of nevirapine in a chronic dosing and preliminary efficacy trial.

Methods: Nevirapine is a non-nucleoside HIV-1 specific reverse transcriptase inhibitor with IC $_{50}$ of 40 nM (10 ng/ml) in cell culture. Rising single oral doses were administered after an overnight fast to groups of three HIV infected volunteers with CD4 counts < 400 cells/ul. Plasma samples were obtained at 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 28, 32, 48 and where possible, 72-75 hrs. after dosing. All urine output was also collected over the 0-4, 4-8, 8-12, 12-16, 16-24, 24-32 and 32-48 hour intervals after dosing. Nevirapine concentrations were assayed by HPLC. The assay is accurate within 10% for concentrations >/= 25 ng/ml.

Results: Detectable plasma levels were obtained at all dose levels tested. Pharmacokinetic analysis will be presented.

Conclusion: The dose and schedule for subsequent clinical trials was based on this data.

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Interferon-Inducing Activity of Curantyl in Volunteers

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There are some data illustrating that a number of coronary-active drugs, for example Curantyl (Dipyridamole), possess interferon-inducing activity. Interferon inducers may be useful in the prevention of influenza and acute respiratory infections of patients with chronic ischemic coronary disorders. Interferon-inducing activity of Curantyl was studied in three groups of volunteers of 19-25 years old who were treated with Curantyl. The first group (10 persons) was given Curantyl 25 mg, 3 times a day (total dose: 75 mg). The second group (10 persons) was given Curantyl 75 mg, 3 times a day (total dose: 225 mg). The third group (11 persons) was given placebo, 1 tablet 3 times a day. Curantyl at the above mentioned doses did not stimulate the production of endogenous interferon. Interferon titers in the volunteers' sera did not exceed basis level at 6 hr, 12 hr, 24 hr, 7 and 14 days after administration of the compound per os. Yet, using the appropriate laboratory techniques, some distinct cardiotropic and anti-aggregative effects were detected with the sera of the Dipyridamole-treated volunteers.