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Poster presentations

Antiretroviral activity of aminothiols, WR2721 and WR1065

Miriam C Poirier*[1], Gene M Shearer[1], Andrew W Hardy[1], Ofelia A Olivero[1], Dale M Walker[2] and Vernon E Walker[2]

Address: [1]National Cancer Institute, National Institutes of Health, Bethesda Maryland, 20892, USA and [2]Lovelace Respiratory Research Institute, Albuquerque, New Mexico, 87108, USA

* Corresponding author

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The aminothiol drug WR2721 (amifostine, Ethyol), and its free-thiol metabolite WR1065, are cytoprotective agents. Ethyol is licensed to attenuate toxicity in cancer patients receiving chemo- and radiation-therapy. We found that WR1065 mitigates Zidovudine (AZT)-induced mutagenesis, and designed studies to ascertain that AZT antiretroviral activity was not altered in the presence of this aminothiol. Fresh peripheral blood mononuclear cells were cultured with phytohemaglutinin (PHA) for 48 hr. The resulting PHA-stimulated blasts were infected for 2 hr with HIV-1BZ-167 before the addition of AZT, WR1065, or Ethyol dephosphorylated by preincubation with alkaline phosphatase. Cells were cultured for an additional 72 hr and assayed for cytotoxicity (trypan blue) and HIV-1 replication (p24 ELISA kit). AZT concentrations of 0.8, 3.0, and 5.0 μM inhibited virus replication by 85–96%, and the same AZT doses combined with 5–26 μM WR1065 inhibited virus replication by 91–97%. When tested alone, AZT at 7.75 μM inhibited virus replication by 96.7 ± 5.1% (mean ± SD, n = 4) with 54 ± 15% target cell survival. Ethyol at 50 μM inhibited virus replication by 75.4 ± 16.6% (mean ± SD, n = 4) and cell survival was 53 ± 19%. Similarly, WR1065 concentrations of 50 and 100 μM blocked virus replication by 83.2 ± 18.6% (n = 5) and 92.0 ± 11.0% (n = 5), respectively, with cell survival at 55 ± 22% and 42 ± 18%, respectively. The data show that Ethyol and WR1065 do not compromise the antiretroviral efficacy of AZT. Interestingly, when used alone, these aminothiols also substantially inhibit HIV-1 replication. (Supported in part by R01 CA95741 to VEW; patent pending).