Simplified Dosage Zidovudine Treatment of Asymptomatic HIV-infected Subjects. J.M.A. Lange[1], F. de Wolf[1,2], P. Cload[3], J. Houweling[2], J. de Gans[1], J. Mulder[2], P.T.A. Schellekens[1,4], R.A. Coutinho[2], A.P. Fiddian[3], J. van der Noordaa[1], J. Goudsmit[1]; [1]Academic Medical Center, University of Amsterdam, The Netherlands; [2]Municipal Health Service, Amsterdam; [3]Wellcome Research Laboratories, Beckenham, U.K.; [4]Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands.

18 long-term HIV-antigenemic men without symptoms (CDC group II) or with PGL only (CDC group III) were treated for 16-24 weeks with different dosage schedules of zidovudine, ± acyclovir. Zidovudine dosages used were: 250 mg 6-hourly, 500 mg 6-hourly, and 500 mg 12-hourly. A decline in serum HIV-Ag levels was seen in 17 men; in 13 the decline was statistically significant in a monotone trend analysis, and in 9 HIV-Ag levels declined below cut-off values. Acyclovir treatment alone or in addition did not appear to influence HIV-Ag levels. In 7 untreated men HIV-Ag levels rose or remained stable during follow-up. In 10/18 zidovudine-treated subjects the CD4+ cell count at the end of the study period was at least $0.2 \times 10^9/l$ above the initial value (statistically significant in 2 men), and in 2 it had declined. In none of the 7 untreated men was the CD4+ cell count at 24 weeks $> 0.1 \times 10^9/l$ above the initial value, and in 3 it had declined. Subjective adverse reactions to the study drugs were infrequent and mild. Symptoms attributable to anemia occurred in 2 subjects. Serious leuco- or neutropenia did not develop in any of the men. Long-term follow-up data will be presented.

Intranasal Tolerance of Recombinant Interferon-αCon1 in Healthy Volunteers. F. Hayden, D. Innes, S. Mills, and P. Levine, Univ. of Virginia, Charlottesville, Virginia, USA.

Intranasal administration of recombinant interferon-α2(rIFN-α2) causes dose-related nasal irritation (stuffiness, dryness, blood in mucus, ulcers/erosions) and mucosal lymphocytic infiltration. Histologic alterations have been documented at dosages as low as 3 MU/day and as early as 4 days after initiating exposure. To determine the relation between tolerance, antiviral activity, and protein content, we assessed the long-term tolerability of an IFN-α analog, rIFN-αCon1, which has ∿10-fold higher specific activity (3×10^9 U/mg of protein) than rIFN-α2 (2×10^8 U/mg). In a double-blind trial 119 adults were randomly assigned to receive daily sprays of placebo(n=30) or rIFN-αCon1 3 MU(n=29), 9 MU(n=30), or 30 MU(n=30) per day for 25 consecutive days. Fifty-nine subjects were dropped during treatment because of abnormal nasal exams(n=56) or irritative symptoms (n=3). The fraction of drop-outs in the placebo group (23%) was significantly ($p<0.05$) different from that in the 3 MU(55%), 9 MU(70%), or 30 MU(63%) groups. Nasal mucosal biopsies collected 1-3 days after completing spray use detected moderate or marked lymphocytic infiltration in 10% of placebo(n=10), 87% of 3 MU(n=8), 85% of 9 MU(n=13), and 73% of 30 MU(n=11) subjects ($p \leq 0.01$, placebo vs each rIFN- Con1 group). All 3 dose levels of rIFN-αCon1 were associated with significant clinical and histopathologic signs of nasal irritation. The findings suggest that IFN-αCon1 would not have a more favorable therapeutic index than rIFN-α2 and that the risk of nasal irritation relates more closely to the antiviral activity than the protein content of the rIFN-α administered.