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Treatment of anogenital warts with recombinant Interferon gamma: results of two multicenter placebo-controlled clinical trials. G.Gross[1], K.W.Degen[2], G.Fierlbeck[3], M.Hilgarth[4], L.Kowalzick[1], H.Pfister[5], A.Roussaki[1], T.Rufli[6], H.Schöfer[7], C.Stetter[8], J.Brzoska[8].
Universities of [1]Hamburg, [2]Düsseldorf, [3]Tübingen, [4]Freiburg, [5]Erlangen, [6]Basel, [7]Frankfurt; [8] Bioferon, Laupheim (Germany).

166 patients suffering from histologically and virologically proved anogenital warts (disease duration 3 months to 3 years) were enrolled in two placebo-controlled double-blind clinical trials concerning the efficacy of systemically (subcutaneously) applied recombinant interferon gamma (rIFN-γ). Treatment consisted in 50µg (about 1 MU) or 100µg (about 2 MU), respectively, daily for 7 days followed by an observation period without therapy of 4 weeks. Response was defined as complete or partial ($\geq$ 50%) remission without formation of new lesions. Evaluable patients (41 out of 44 in the 50µg trial and 109 out of 122 in the 100µg trial) received 3 to 4 therapy cycles or had complete or partial remission or showed progressive disease earlier. In the rIFN-γ groups the response rates were 60% in the 50µg trial and 53% in the 100µg trial comparing with 33% or 31%, respectively, in the placebo groups ($p < 0.05$). Side effects were mild consisting mainly of flu-like symptoms, with significant differences between rIFN-γ and placebo only in the 100µg trial. Our results indicate that low doses of rIFN-γ applied systemically and given cyclically are effective in the treatment of multiple anogenital warts.

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Synthesis and In Vivo Anti-RNA-Viral Evaluation of a Phosphoramidate Derivative of 6-Azauridine; Orotidylic Acid Decarboxylase Inhibitors, Pyrazofurin and 6-Azauridine; and 2-Thio-6-azauridine and its Triacetate. B. Gabrielsen, T.P. Monath, J.T. Rankin, J.W. Huggins, D.F. Kefauver, (U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, USA 21702), C.D. Kwong, C.A. Krauth, J.A. Secrist III, (Southern Research Institute, Birmingham, AL, USA, 35255), J.H. Huffman, D.F. Smee and R.W. Sidwell (Utah State University, Logan, UT, USA, 84322).

The title compounds demonstrated in vitro antiviral activity against the flavivirus, Japanese encephalitis virus (JE), the bunyavirus, Punta Toro virus (PT), and the alphavirus, Venezuelan equine encephalomyelitis virus, (VEE). 6-Azauridine-5'-monophosphate (5'-MP) is known to inhibit orotidylic acid decarboxylase (ODCase). Therefore, 5'-(ethylmethoxyalanyl)phosphoramidyl-6-azauridine was synthesized as a potential precursor of 6-azauridine-5'-MP. This phosphoramidate, 6-azauridine, and 2',3'-5'-tri-O-acetyl-2-thio-6-azauridine moderately increased numbers of survivors when administered (i.p., bid x 4) to PT virus-infected mice. Other indicators of viral pathogenesis were unaffected. 2-Thio-6-azauridine by itself was ineffective. Administration (i.p., bid x 5) of 0.63 and 0.3 mg/kg/day of pyrazofurin at 4 and 24 hr post-virus inoculation significantly increased survival and reduced viral pathogenesis in PT virus-infected mice. There was no increased survival when non-toxic doses of 2-thio-6-azauridine, 6-azauridine (or its 2',3',5'-triacetate), or pyrazofurin were administered (i.p., bid x 6) to JE virus-infected mice 6 hr before virus inoculation. 2-Thio-6-azauridine was also ineffective when evaluated in the murine VEE model. Supported in part by U.S. Army Medical Research Acquisition Activity Contracts Nos. DAMD 17-91-C-1034 and DAMD 17-91-C-1030.