

Clinical trials of anti-hCG cancer vaccines

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hCG is expressed by many common cancers and may play a role in cancer progression. Vaccine approaches targeting tumor-associated hCG have been tested in clinical trials. A synthetic peptide immunogen corresponding to the carboxy terminal peptide (CTP) of the beta subunit of hCG, CTP37-DT, was developed to avoid the possibility of cross-reactive autoimmunity with the beta subunit of LH. Immunogenicity was achieved by conjugating the peptide to diphtheria toxoid. In the initial phase I study in patients with metastatic cancers, intramuscular (i.m.) injections of up to 2 mg of CTP37-DT were administered with nor-muramyl dipeptide (MDP) adjuvant in squalene/mannide mono-oleate without evidence of systemic toxicity. Anti-hCG IgG antibody was elicited and was detectable for more than 10 months. A dose-response relationship was not evident, though the highest level of antibody was achieved with the 2 mg dose. Cellular immune responses to hCG were not detectable. CTP37-DT was also tested in a phase I study in patients with metastatic cancers combined with the nonionic copolymer adjuvant, CRL1005, which has been shown to promote cellular immune responses in aqueous solution. Injections of up to 75 mg of CRL1005 in combination with 1 mg CTP37-DT i.m. were well tolerated. Anti-hCG IgG antibody was elicited, though at lower levels than that observed with MDP in water-in-oil formulation. Immunization with CRL1005 did result in the induction of cellular immune responses to the CTP and to hCG in some patients. CTP37-DT with MDP in squalene/mannide mono-oleate was subsequently investigated in a phase II study in patients with metastatic colorectal cancer who were randomized to receive i.m. injections of either 0.5 or 2 mg. Significant differences in anti-hCG antibody response and survival were not observed between the low- and high-dose groups. Patients who developed antibody levels higher than or equal to the median value exhibited a median survival of 45 weeks compared with 24 weeks for patients who developed levels lower than the median. In contrast, no significant difference was observed when comparing survival based upon the levels of diphtheria toxoid antibody that developed. A second generation synthetic peptide vaccine, CTP-Loop-DT, which targets the "loop" region of beta-hCG as well as the CTP was evaluated in a phase II study in patients with advanced pancreatic cancer who were randomized to receive CTP-Loop-DT alone or to CTP-Loop-DT plus gemcitabine chemotherapy. Immunizations were well tolerated, and patients developed antibody to the CTP and to the loop domains. Gemcitabine did not significantly influence antibody response. One-year survival was 14% with CTP-Loop-DT and 30% with CTP-Loop-DT plus gemcitabine. These clinical trials have indicated that synthetic peptide immunogens targeting hCG are safe and effective in eliciting anti-hCG antibody in patients with cancer. They support further study of hCG vaccines in cancer.