Vaccination of prostate cancer patients with modified vaccinia Ankara delivering the tumor antigen 5T4 (TroVax®): a phase II trial

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Aims: The attenuated vaccinia virus, modified vaccinia Ankara (MVA), has been engineered to deliver the tumor antigen 5T4 (TroVax®). More than 85% of primary prostate cancer and 3 of 3 metastatic specimens overexpress 5T4 antigen. TroVax® has been evaluated in a phase II trial in hormone refractory prostate cancer (HRPC) patients in which the cancer vaccine was administered either alone or in combination with granulocyte macrophage–colony stimulating factor (GM-CSF). GM-CSF is involved in the enhancement of T-cell priming via effects on dendritic cells. The comparative potency of this approach to elicit an immune response and to further determine the impact of such a response on signs of clinical benefit as defined by PSA reduction and delay in time to disease progression (TTP) was determined.

Methods: Eligibility included HRPC patients with progressive disease, any prior therapy, and adequate physiologic parameters. The dosage regimen of MVA 5T4 consists of 1 intramuscular injections (5x108 pfu) during week 1, 2, 5, 6, 9, 13, 17, 21, 29, 37, and 45. GM-CSF is given at 250 µg/m2 (maximum 500 µg) 14 days on, 14 days off by subcutaneous injection. PSA and imaging studies will occur every 8 weeks. 5T4-specific cellular and humoral responses were monitored throughout the study.

Results: 27 patients with metastatic HRPC were treated with TroVax alone (n=14) or TroVax® plus GM-CSF (n=13). TroVax® was well tolerated with no serious adverse

events attributed to vaccination. Of 24 immunologically evaluable patients, all mounted 5T4-specific antibody responses. Periods of disease stabilization from 2 to >10 months were observed. TTP was significantly greater in patients who mounted 5T4-specific cellular responses compared to those who did not (5.6 vs 2.3 months respectively).

Conclusions: The combination of GM-CSF with TroVax® showed similar clinical or immunological responses to TroVax® alone. The high frequency of 5T4-specific immune responses and correlation with enhanced TTP is encouraging and warrants further investigation. Indeed, an ongoing trial is investigating the combinination of TroVax® plus taxotere as initial therapy versus taxotere alone. Patients who progress on taxotere alone, will then be treated with TroVax®.

Topic of Abstract: Tumor vaccines

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