Final results of phase I trial of GMCSF gene-TGFβ2 antisense gene autologous tumor cell (TAG) vaccine in advanced cancer

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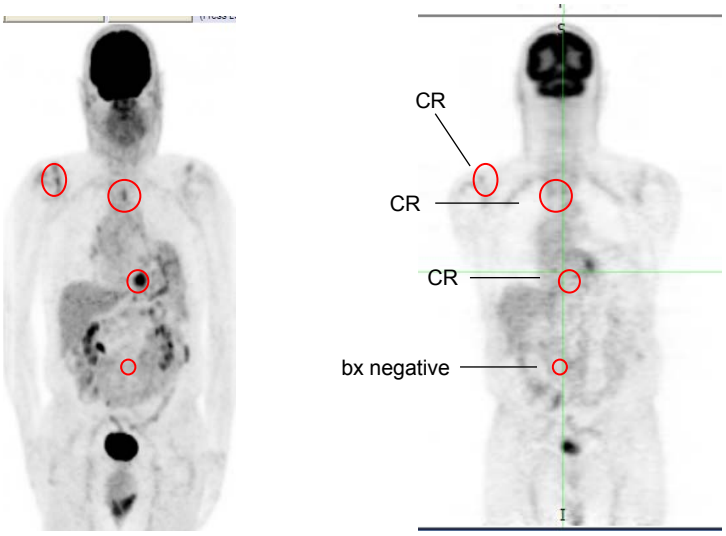
Both GMCSF gene transduced vaccine and TGFβ2 antisense gene vaccine, in separate trials, have demonstrated beneficial effects without evidence of toxicity in advanced cancer patients. The GMCSF transgene directly stimulates increased expression of tumor antigen(s) and enhances dendritic cell migration to the vaccination site. TGFβ2 blockade following intracellular TGFβ2 antisense gene expression reduces production of immune inhibiting activity at the vaccine site. We recently completed a phase I clinical investigation of the combined GMCSF/TGFβ2 antisense TAG vaccine under BB IND 13650. Nineteen patients [6/13, M/F; median age 58 yrs; median number prior chemotherapy regimens 2; cancer: melanoma (3), lung (2), colon (4), breast (2), neuroendocrine (4), other (4)] have received between 1 and 12 vaccinations. Harvested malignant tissue was processed to a single cell suspension, and cells were transfected via electroporation with our novel TAG expression vector and irradiated (median number vaccines/patient, 10). Patients received monthly intradermal injections in two dosing cohorts ($1x10^7$ cells/injection or $2.5x10^7$ cells/injection) for a minimum of 4 months. No grade 3, 4 toxic events related to therapy were observed in the 19 treated patients. One patient was unevaluable for response due to discontinuation after one month related to travel difficulty. Sixteen of 18 patients maintained stable disease for 3 months. Two patients maintained stable disease for one year; a third (melanoma) achieved complete response (CR) and remains in CR now 18 months after first vaccination (Figure 1).

Conclusion: GMP manufacturing of TAG vaccine is feasible, safety is achieved and evidence of clinical benefit is demonstrated.

Figure 1



07/07/08
pre TAG baseline

10/05/09
post TAG