Phase I Safety and Pharmacokinetic Study of Systemic p53 Gene Therapy (SGT-53) using Immunolipoplexes Targeted by Anti-Transferrin Receptor (TfR) Single Chain Antibody Fragment (scFv): Updated Results

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Deletion or mutation of the p53 'gatekeeper' gene, located at chromosome 17p13, has been documented in ≥50% of clinical cancers and pre-clinical studies have demonstrated tumor regression following p53 reactivation, providing the rationale for this p53 restoration study. SGT-53 is a lipoplex comprised of cationic DOTAP/DOPE liposome, surface decorated with an anti-TfR scFv, encapsulating a wt p53 DNA sequence in a plasmid backbone, in a fixed constituent ratio designed for systemic delivery. The first patient was treated at 1.2 mg DNA/1 hour IV infusion and experienced adverse events (AE) including grades 3 hypertension and fever and grade 2 hyperglycemia which, although successfully managed, resulted in protocol modification to include hydration, prophylactic anti-complement (indomethacin), anti-inflammatory (dexamethasone, acetoaminophen, indomethacin), and anti-histamine (famotidine, diphenhydramine) medication, overnight observation for first infusion, and cohort 1 dose de-escalation to 0.6 mg DNA with cohort expansion. Subsequent patients have been treated twice weekly x 5 weeks with dose escalated through 0.6 mg DNA/1 hour (n=3) IV , 1.2 mg DNA/1 hour (n=1), 2.4 mg DNA/1.5 hours (n=1), and 3.6 mg DNA/2 hours (n=4) at which dose tumor localization of exogenous p53 was demonstrated triggering cohort expansion to 6 patients. Subsequent AE were limited to grade 1 (fatigue, fever, neutropenia, leucopenia, thrombocytopenia, headache, hypotension, chills, tachycardia, pleural effusion, cough, dizziness, and anorexia) and grade 2 (fatigue, dehydration diarrhea, hypotension, fever, anemia, neutropenia, leucopenia, elevated AST/ALT, and headache) without evidence of dose relationship. Dose-dependent transgene expression (PCR) was detected at 0.6 mg DNA and 3.6 mg DNA. A partial response (PR, RECIST) was documented at 0.6 mg DNA (adenoid cystic carcinoma) and a second infusion cycle delivered. Clinical and laboratory results will be updated at the meeting.