FFa 10

Phase I clinical trial of systemically administered TUSC2(FUS1)-nanoparticles mediating functional gene transfer in humans.

Evaluate

Dissent

Lu C, Stewart DJ, Lee JJ, Ji L, Ramesh R, Jayachandran G, ..., Grimm EA, Reuben JM, Baladandayuthapani V, Templeton NS, McMannis JD, Roth JA, +
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10 EXCEPTIONAL

06 Jun 2012 | Novel Drug Target, New Finding, Clinical Trial, Technical Advance

The clinical data generated in the report by Lu et al. involving 31 advanced lung cancer patients convincingly support clinical utilization of non-viral delivery mechanisms for safe systemic-targeted delivery of DNA plasmids to cancer patients with pulmonary disease.

A critical limitation of DNA-based therapeutics is delivery to the target cell population. Lu et al. in their paper in PLoS ONE demonstrated convincing proof of principle that tumor-specific delivery of DNA can be achieved via systemic infusion of a non-viral delivery vehicle. They specifically studied a therapy utilizing a non-viral DOTAP:cholesterol cationic nanoparticle delivery vehicle {1} to deliver an expressive TUSC2 (FUS1) plasmid to patients with advanced lung cancer {2}. They demonstrated in 31 patients safe delivery and expression of the intended transgene within primary and metastatic disease sites following systemic delivery in a subset of patients. Functional effect related to delivered transgene expression, as evidenced by induction of intrinsic pro-apoptotic signals, was also observed. These results are consistent with a prior publication utilizing the same DOTAP:cholesterol cationic nanoparticle for systemic delivery of another DNA plasmid (GNE gene) in a patient with a rare muscle disorder called hereditary inclusion body myopathy (see {3}, on which I am an author). Moreover, as pointed out by Lu et al. and others, multiple examples in preclinical testing have further supported successful systemic delivery and functional capacity involving several different experimental DNA therapeutics (see {2}, {4,5}, on which I am an author, and {6,7}). Trial registration: NCT00059605

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Competing interests
None declared