

# 4<sup>th</sup> International Conference and Exhibition on Cell & Gene Therapy

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## Retroviral replicating vectors for gene therapy of cancer: Gene therapy as precision medicine

Retroviral replicating vectors (RRV) can deliver transgenes efficiently and selectively to tumors as they only infect mitotic cells and are normally restricted by innate and adaptive immune mechanisms which are down-regulated in cancer. Toca 511 (vocimageneamiretrorepvec) is an RRV encoding an optimized yeast cytosine deaminase (CD) prodrug-activator enzyme which converts an anti-fungal pro drug 5-fluorocytosine (5-FC) to the anti-cancer drug 5-fluorouracil (5-FU). Tumor-specific spread and CD expression by Toca 511 enables orally-administered Toca FC (extended-release 5-FC formulation) to be converted into 5-FU directly within infected tumors thereby avoiding adverse effects associated with systemic chemotherapy including generalized immunosuppression. In preclinical models, RRV integration into the cancer genome results in viral persistence within tumors and enables repeated killing of proliferating cancer cells over multiple pro drug cycles achieving long-term survival benefit and induction of durable anti-tumor immune responses. Toca 511+Toca FC is currently being investigated in multi-center Phase 1 dose-escalation clinical trials for recurrent primary brain cancer with the vector administered by direct intratumoral injection, injection into the resection cavity walls or intravenously. Cumulatively, >90 patients have been treated to date and all dose levels have been safe and well-tolerated. Viral and CD protein, DNA and RNA were confirmed in post-treatment tumor resection tissues indicating viral spread and persistence with all three routes of administration. MRI changes consistent with tumor response have been observed. Median overall survival and progression-free survival data have surpassed historical benchmarks. Based on these encouraging results, a randomized controlled Phase 2/3 trial is underway (NCT02414165).

## Biography

Noriyuki Kasahara is a Professor of Cell Biology & Pathology at the University of Miami and Co-Leader of the Viral Oncology Program at the Sylvester Comprehensive Cancer Center. He is also Adjunct Professor at the University of California, Los Angeles where he was Director of the UCLA Vector Core Facility for the past decade. He has more than 25 years of experience and has authored more than 125 peer-reviewed articles in the field of gene therapy and genetic engineering and pioneered the development of tumor-selective retroviral replicating vectors (RRV) for gene therapy of cancer, now in first-in-human multi-center clinical trials sponsored by Tocagen Inc.

## Notes: