Phase I Study of Safety and Immunogenicity of a Survivin Long Peptide Vaccine (SurVaxM) in Patients with Survivin Positive Metastatic Neuroendocrine Tumors (NETs)

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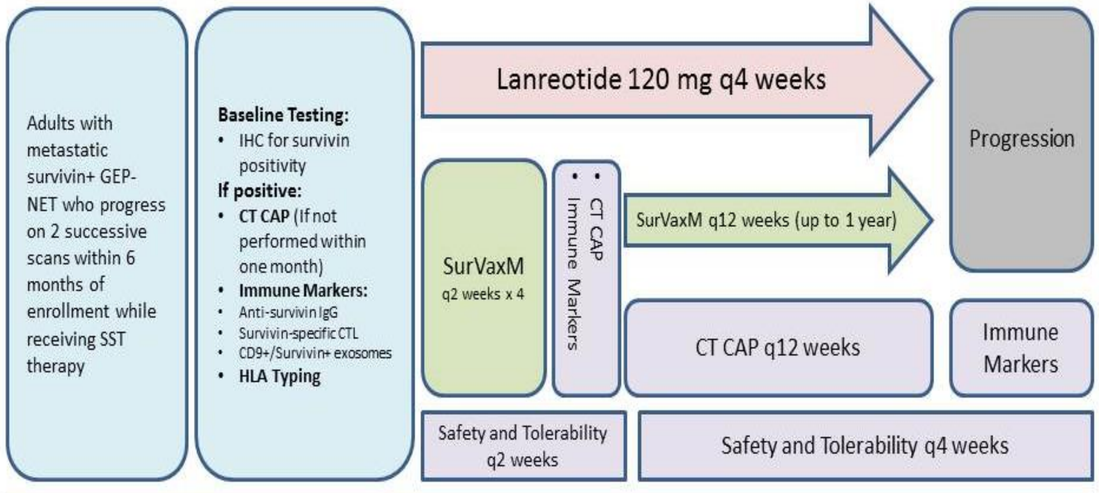
Background

- Metastatic NETs have a poor prognosis and there are limited options after 1st-line treatment with somatostatin analogues (SSA)/chemotherapy. Therefore, new therapies are urgently needed.
- Survivin is an intracellular protein that alters cell division, function of cell death proteases and inhibits apoptosis. It is undetectable in adult cells and expressed in many tumors, making it an ideal target.
- SurVaxM is a 15 amino acid synthetic peptide vaccine. It stimulates antigen presentation via intracellular cell-surface target recognition and induces CD8+ & CD4+ T cells and IgG production. It was well tolerated in a phase I trial in recurrent glioma pts (Fenstermaker et al., Neurooncol; 2014). Prelim analysis from a phase II study in glioma pts showed its efficacy (Ahluwalia et al., Neurooncol; 2018).
- Targeting survivin in NETs is based on our work with tissue microarrays from gastroenteropancreatic (GEP) and lung NETs that showed that its expression correlated with a worse OS (Hanif et al., Oncotarget 2020).
- We have an ongoing single-arm phase I trial evaluating the safety and immunogenicity of SurVaxM in metastatic NETs.

Methods

- Ten eligible patients with any grade metastatic GEP or lung origin NETs that are survivin positive by immunohistochemistry and have progression on SSA within the last 6 months on two CT scans >4 weeks apart per RECIST v1.1 are being enrolled

Trial Schema



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Methods (continued)

- Patients receive a fixed dose of 500 mcg of SurVaxM in Montanide ISA 51 subcutaneously along with 100 mcg of GM-CSF q2 weeks X 4 doses. SSA continued at the same dose as before. Patients free of progression and toxicity at six months get extra doses of SurVaxM q12 weeks, up to 1 year.
- Subjects are assessed continuously for safety per NCI CTCAEv5.0. Response assessment via CT scans per RECIST v1.1 q12 weeks.
- Primary objective is to assess safety of SurVaxM +/- SSA. Secondary objectives are to assess overall response rate, progression free survival, duration of response and vaccine immunological response (anti-survivin antibody titers and survivin-specific CD8 T-cell responses).

Statistical Analysis

- Safety analysis is per Pocock stopping boundary with the assumption of true toxicity of 0.2 and unacceptable toxicity of 0.3 at a significance level of 0.05.

Study Status

- To this date, eight patients were screened out of which five patients were enrolled. Currently, two patients remain on the study.

Ongoing Related Research

- Exosomes can play a role in stimulating angiogenesis, tumor cell migration, cell proliferation and modulate tumor invasiveness. Circulating exosomes may be indicative of disease status and response to therapy.
- We are exploring the role of survivin-expressing plasma derived exosomes (PDEs) as a biomarker in patients with GEP NETs.
- Plasma (n=17) was obtained pre-and post-treatment with SSAs. Exosomes were isolated by size exclusion chromatography (qEV, Izon, 35nm columns). Exosomes were phenotyped using imaging flow cytometer (Image StreamX Mark II; AMNIS/Millipore, Billerica, MA) for exosome-markers (tetraspanins: CD9/CD63/CD81), NET-specific markers (chromogranin neuron-specific enolase, synaptophysin) and survivin. Associations between phenotypes and progression-free survival and overall survival were evaluated using Cox regression models.

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