FLT-PET/CT for the Prediction of Response to ANG-1005 Therapy in Patients with Brain Metastases from Breast Cancer

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Background
- 18F-FLT (3’ Fluoro 3’ deoxythymidine)-PET imaging is a novel imaging study and a tool for measuring in vivo tumor cell proliferation.
- FLT is an analog of thymidine. Retention of FLT by the cells reflects DNA synthesis.
- ANG1005 (formerly called GRN1005) is a peptide-drug conjugate being developed for targeted treatment of brain metastases (Cremophor-free formulation).
- It consists of 3 molecules of paclitaxel covalently linked to Angiopep-2 designed to cross the blood brain barrier via LDL receptor related peptide (LRP) transport system.
- ANG1005 therapy was administered intravenously at 550 mg/m^2 every 21 days progressing of intra-cranial disease or unacceptable toxicity. All patients underwent FLT PET/CT imaging before and after 1 cycle of therapy with ANG1005. For (18F) FLT-PET/CT scan: Volumes of Interest were drawn in target brain metastases: SUVmax (80% Threshold : average value of the maximum 20% pixels), SUVmax, % of Change pre-post therapy, % of change (using SUVmax), % of change (using T/Normal ratio). Patients underwent dynamic brain imaging over 30 min and then a static whole body PET scan at 1 hour post-injection. We calculated the % of change before and after therapy, considering significant response if the % of change was larger than 20%.

Study Objectives
- Primary Objective: Determine whether one cycle of therapy ANG1005 is associated with a significant change in FLT-PET uptake.
- Key Secondary Objectives:
  1. Determine whether change in the FLT-PET/CT uptake after 1 cycle of therapy with ANG1005 is associated with intracranial tumor response.
  2. Compare brain metastasis detection by standard contrast-enhanced MRI vs. FLT PET/CT vs. dynamic contrast MRI.

Study Design & Methods
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Results
- FLT PET/CT Baseline (09/06/2012)
  - SUVmax = 2.91

- PET/CT before 1 cycle of therapy with ANG1005.

- FLT PET/CT after 1 cycle of therapy with ANG1005.
  - SUVmax = 2.29

- FLT / Normal ratio change was significant (using T:Normal ratio).

- FLT PET/CT vs. dynamic contrast MRI imaging study and a tool for measuring in vivo tumor cell proliferation.
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