



BRIGHAM AND  
WOMEN'S HOSPITAL



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October 28, 2014

Alice Chen, M.D.  
Senior Clinical Investigator  
Investigational Drug Branch  
CTEP, DCTD, NCI

Re: Career Development PTMA of Panagiotis Konstantinopoulos, M.D.  
Institutional Commitment Letter

Dear Dr. Chen (Alice):

I am writing to confirm Dana-Farber institutional support for the proposed trial of Gemcitabine/Cisplatin +/- VX-970 in platinum-resistant ovarian cancer, proposed by Dr. Panagiotis (Panos) Konstantinopoulos, as well as other trials of VX-970 in which Panos has expressed interest, including a trial in platinum-sensitive disease and a trial of VX-970 in combination with topotecan.

Panos will lead a trial that will represent a collaboration of the Early Drug Development Center, of which I am the Director, as well as the Susan Smith Center for Women's Cancers, where Dr. Ursula Matulonis serves as co-Director. The Programs will together provide a Research Nurse and a data manager to assist in the care and data collection of enrolled patients and will provide overall regulatory support for the trial, including communications with NCI-CTEP, the CIRB and any other collaborating sites that join the trial within the ETCTN network.

Panos will have access to statisticians affiliated with the Experimental Therapeutics and Gyn Programs, who are members of the Biostatistics Core of the Dana-Farber/Harvard Cancer Center and are members of our ETCTN site. Additionally, he will also work with Dr. Jeffrey Supko, Director of the Dana-Farber/Harvard Cancer Center Pharmacology Core, in order to derive and report plasma pharmacokinetic data as required by his studies.

He will also interact closely with scientists and technicians of the Brigham and Women's Hospital Pathology Core, the Center for DNA Damage and Repair (CDDR), the Center for Cancer Precision Medicine (CCPM) and the Center for Advanced Molecular Diagnostics (CAMD) in the conduct of a VX-970 trial. Pathologists and Research Scientists in the Brigham Pathology Core and the CDDR will assist with integrated and exploratory biomarkers. Members

of the CCPM and CAMD are part of the DFCI/BWH/Broad Genomics Hub for the ETCTN and will assist with genomic analyses, including targeted NextGen sequencing, whole exome sequencing or whole transcriptome sequencing, depending on the final clinical trial design. In this regard, Panos will work with Drs. Scott Rodig, Alan D'Andrea, Levi Garraway and Neal Lindeman, all of whom will provide tutelage and support for the conduct of his study. In particular, interaction with the CAMD will permit identification of patients with tumors harboring *CCNE1* amplification or *ATM* mutation, who may be prime candidates for the clinical trial; interaction with the team of Levi Garraway will facilitate whole exome sequencing and other genomic analyses that can define the homologous recombination repair-proficiency of tumors from patients enrolled to an ovarian cancer study.

In summary, substantial resources from our ETCTN site will contribute to the conduct of a VX-970 trial that Panos will lead. The Early Drug Development Center, the Susan Smith Center for Women's Cancers and the Department of Medical Oncology are all committed to his successful execution of a trial, and we look forward to fully supporting him in this endeavor.

Sincerely,

A handwritten signature in cursive script that reads "Geoffrey Shapiro". The signature is written in black ink and is positioned below the word "Sincerely,".

Geoffrey Shapiro, M.D., Ph.D.