Porter v. Tap Pharmaceutical, et al Doc. 583

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

M.D.L. NO. 1430
CIVIL ACTION NO. 01-10861

IN RE LUPRON® MARKETING AND
SALES PRACTICES LITIGATION

MEMORANDUM ACKNOWLEDGING THE RECEIPT AND REVIEW OF THE A. DAVID MAZZONE SECOND ANNUAL RESEARCH AWARDS PROGRESS and ACCOUNTING REPORT #5

December 18, 2013

STEARNS, DJ.

On October 8, 2013, Dr. Philip Kantoff of the Dana-Farber/Harvard Cancer Center (DF/HCC), the principal investigator for the A. David Mazzone Research Awards Program, and co-principal investigator, Dr. Jonathan Simon, President of the Prostate Cancer Foundation (PCF), submitted Progress and Accounting Report #5 for the court's review. The Report covers the period from August of 2012 to July of 2013. As the Report notes, the Mazzone Awards Program is now in its third year and currently supports the work of 93 investigators involved in twenty-seven separate prostate cancer research projects. Twenty-three of these projects are funded through DF/HCC and four through PCF Challenge Awards. Nine new projects were undertaken in 2013 through DF/HCC and one through PCF. The Report summarizes the scientific progress and financial accountings for the twenty-eight active projects and the DF/HCC Post-Bacc

Dockets.Justia.com

training (CURE) award funded through the Mazzone Research Program during the reporting year.[1, 2]

In the 2013 cycle, the scientific review committee established through DF/HCC received and peer reviewed 50 proposals from 48 institutions involving 163 researchers. It awarded nine grants involving 36 researchers from eleven institutions. PCF received and peer reviewed 62 proposals and awarded one grant which involves eight researchers. In July of 2013, the initial DF/HCC and PCF award recipients completed their second year of research, while the 2012 award recipients finished their first full year of research. Each of the award recipients has submitted the required scientific progress and financial reports for review by Dr. Kantoff and the Program's Science Advisory Board. As the Program matures, it has begun to show solid scientific accomplishments. The court has taken the following examples from Dr. Kantoff's extensive Report.

---

[1] The Report notes that Career Development grantee Dr. Kathryn Wilson (phosphorus and calcium intake, tumor microenvironment and prostate cancer progression), received an extension of her grant to October 23, 2013, and for this period has submitted a partial progress report.

[2] Lupron-Treatable Diseases and Conditions grantee Dr. Jose Teixeira (preclinical in vivo studies investigating the efficacy of mTOR inhibitors for uterine fibroids) relocated during the reporting period to Michigan State University but will continue to collaborate on the in vivo studies project. Dr. Aaron Styer (Massachusetts General Hospital) replaced Dr. Teixeira as the principal investigator on June 1, 2013. Dr. Styer's progress and accounting reports will be reviewed for the next annual submission to the court.

(1) Career Development Principal Investigator David Miyamoto (Massachusetts General Hospital) published as lead author the article: *Androgen receptor signaling in circulating tumor cells as a marker of hormonally responsive prostate cancer*, Cancer Discovery, 2:995-1003 (2012). The article describes the development of a single cell immunofluorescence-based assay for measurement of androgen receptor (AR) activity, and explores the feasibility of measuring AR activity in circulating tumor cells as a biomarker to monitor and predict responses to second line hormonal therapy in CRPC.

(2) Disparities Research Principal Investigator Nancy Keating (Harvard Medical School) co-authored the article: *Explaining racial differences in prostate cancer mortality*, Cancer Sept. 2012 1;118(17):4280-9. The article explores the reasons for a higher incidence of prostate cancer mortality among black males and low-income males, and the palliative effects of more frequent PSA screening, aggressive treatment approaches, and greater vitamin D intake.

(3) High Impact Principal Investigator Levi Garraway (Dana--Farber Cancer Institute) utilized a prostate cancer cell model (LNCaP) that requires androgen for survival to perform genome scale small-hairpin RNA (shRNA) screens to identify genes whose silencing (loss-of-function) allow

cells to proliferate in the absence of androgen, as well as in the presence of enzalutamide (MDV3100), a drug that interferes with the function of the androgen receptor. Among other genes, Dr. Garraway and his colleagues identified two regulatory subunits of a large enzymatic complex operant in the cell, the loss of which enables LNCaP cells to grow despite the lack of androgen. This enzymatic complex (PP2A) regulates signaling pathways active in the prostate cancer cell, pathways that implicate many factors, some of which could potentially be targetable with existing drugs.

(4) To further define the AR cistrome in actual tissue, High Impact Principal Investigator Matthew Freedman (Dana-Farber Cancer Institute), with his coworkers, developed a working method to perform AR chromatin immunoprecipiation (ChIP) in human prostate tissue. Given the likely importance of enhancer binding sites, Dr. Freedman and his team reasoned that obtaining data outside of cell lines would be important to: (a) compare the AR cistrome in cell lines versus human tissue; and (b) provide a more comprehensive catalog of the AR sites across multiple individuals (as opposed to in only a few cell lines). Thus far, their data reveals that there are tens of thousands of AR sites that exist in human tissue that are not present in the LNCaP cell line.

(5) Investigator Glenn Liu (University of Wisconsin) reported a

strong clinical effort to determine, by PET ICT imaging, the total burden of cancer in patients with metastatic prostate cancer. Early results demonstrate a concordance of imaging results at multiple centers. A multicenter protocol has been developed to validate this imaging modality as a biomarker for response to therapies for metastatic prostate cancer. If successful, this imaging biomarker will greatly reduce the complexity of clinical trials that are dependent on the endpoint of overall survival and will shorten the time and cost for determining the efficacy of new treatments.

(6) Investigator William Nelson (Johns Hopkins Medicine) is conducting an epigenetics study of chemical modification of DNA that control the expression of genes. His research has demonstrated that blocking certain epigenetic alterations with an FDA 12 approved medication such as Vidaza sensitizes treatment-resistant prostate cancer cells to a variety of therapies. Clinical trials in advanced prostate cancer patients are planned based on these findings and will be funded by resources that leverage this Mazzone-PCF Challenge Award.

(7) Principal Investigator Martin Pomper (Johns Hopkins Medicine), with others, successfully created a gene therapy approach that causes the expression of a new receptor on the surface of prostate cancer cells. Infusion of a binding partner to this receptor combined with either a

lethal radioactive payload or a molecular imaging tracer allows simultaneous detection and killing of metastatic prostate cancer. This approach has created what is termed a theranostic, enabling simultaneous detection and killing of prostate cancer.

(8) Bert O'Malley (Baylor College of Medicine) is examining the engine of prostate cancer - the androgen receptor molecule. AR combines with a complex set of proteins that ultimately bind specific regions of the cancer cell genome and drive the progression and survival of the disease. Dr. O'Malley reports that his group is exploring experimental medicines that will disrupt the AR regulatory complex, possibly leading to a new treatment modality for metastatic prostate cancer.

CONCLUSION

The court appreciates the thoroughness of the Report submitted by Dr. Kantoff and Dr. Simons and congratulates the Mazzone research award recipients for their ongoing achievements. The court looks forward to the receipt of Annual Report #6 on or before March 30, 2014.

/s/ Hon. Richard G. Steams

United States District Judge