

Prostate Cancer Molecular Medicine (PCMM)

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Research Areas



Tool Development



Biomarker Research

Diagnostic

At a Glance

- Status: **Completed Consortium**
- Year Launched: **2009**
- Initiating Organization: **Center for Translational Molecular Medicine (CTMM)**
- Initiator Type: **Government**
- Location: **Europe**

Abstract

Prostate Cancer Molecular Medicine (PCMM) was established by the Center for Translating Molecular Medicine (CTMM) to investigate biomarker screening and targeted imaging in prostate cancer diagnosis and therapy monitoring. A Dutch Biobank facilitated the biomarker and imaging studies in PCMM. Outcomes from biomarker and imaging studies were integrated into a clinical decision support system for prostate cancer.

Mission

PCMM will address two major clinical needs. First, the need to reduce over diagnosis and overtreatment of prostate cancer because of today's less than ideal screening tests (PSA tests). Second, the need for better therapy monitoring techniques for advanced disease.

To improve over diagnosis, the project will attempt to develop and validate novel biomarkers in blood, urine, and tissue that can be used to differentially diagnose and evaluate prognosis for individual patients, and that can also be applied for tailored treatment. To improve therapy monitoring for

metastatic tumors, PCMM will develop and test innovative imaging tools that can be used to visualize and evaluate early response to treatment, allowing therapy management at the level of the individual patient.

The biomarker and imaging studies in PCMM will be facilitated by a unique Dutch prospective biobank composed of biological specimens and imaging data from patients with various stages of prostate cancer. An information technology (IT) infrastructure will be designed that allows for the integration of clinical and research data in a central database.

Consortium History

January 2009: Consortium started

November 2014: Consortium ended

Financing

In response to the first call for project proposals in 2007, CTMM announced on April 1, 2008, that nine first-call projects would receive research funding totaling €150 million. On March 10, 2009, it announced that eight new project proposals, submitted in the fall of 2008 in response to the second call for proposals, would receive funding totaling almost €100 million. On August 4, 2009, it announced further funding of €15 million for this research project on prostate cancer.

Impact/Accomplishment

Progress in the third year of PCMM (2012):

PCMM has made go/no go decisions with respect to its marker and imaging programs in order to focus on the most promising products during the second half of the project. Because no promising protein or metabolite markers could be identified, the Proteomics and Metabolomics programs have been terminated. PCMM will now focus on the validation toward clinical implementation of a 13 genes panel and of a cAMP phosphodiesterase family-based marker, as well as on the early validation of candidate tissue markers. Next-generation sequencing will be implemented for a broad analysis of

genetic changes in prostate cancer as well as for the validation of the ribonucleic acid (RNA) and deoxyribonucleic (DNA) candidate markers.

In the Imaging program, a novel bombesin-targeted imaging ligand has been preclinically validated and will now be translated to the clinic. The preclinical validation of the anti-PSMA (prostate-specific membrane antigen) monoclonal antibody D2B has been completed, showing that D2B is suitable as an imaging ligand and confirming that tagged antibody-based imaging is feasible. A batch of a nanobody against PSMA was successfully radioactively labeled and will now be used for preclinical proof-of-principle studies. The development of nanobodies against a set of other prostate cancer-selective antigens is ongoing. The program on auto antibody-based imaging has been terminated because of unfavorable results. The regulatory dossier for the clinical trial on androgen receptor targeted imaging has been completed, and it is anticipated that the trial will start in the autumn of 2013.

The inclusion of patients with localized prostate cancer in the PCMM biobank, composed of biospecimens as well as magnetic resonance imaging (MRI) and ultrasound imaging data, is ongoing. Ethical approval has been obtained for the inclusion of men who are biopsied for prostate cancer. The biobank will be extended to patients participating in the clinical imaging trial. PCMM is closely collaborating with the CTMM TraIT project for data integration, and a collaboration has been set up with the Dutch String of Pearls for extending and safeguarding the PCMM biobank.

Progress in the second year of PCMM (2011):

Genomic profiling resulted in a number of differentially expressed genes that are now being validated in urine or tissue with the ultimate goal to deliver a validated assay. Fusion genes identified by whole-genome sequencing appeared to be typically patient-specific and as such are not useful as common markers. For the majority of serum candidate markers validated by multiple reaction monitoring, the marker potential could not be confirmed. Auto-antibody profiling has led to a set of candidates for which validation and assay development have been initiated. Profiling of transcriptional splice variants of cAMP pathway genes has delivered the protein marker PH-T1 with promising diagnostic and prognostic value. Evaluation of known metabolites has not confirmed marker potential. Metabolomics profiling is ongoing.

Various bombesin (BN) analogs to target the Gastrin Releasing Peptide Receptor have been studied. The tracer ^{99m}Tc-BN is now being studied in a Phase I trial, and the promising tracer ¹⁸F-TBN is being preclinically characterized. For tagged antibody-based imaging, PCMM focuses on PSMA targeting and auto-antibody antigens. Preclinical results on the anti-PSMA Mab D2B as imaging ligand

are favorable and further studies are being planned. Peptides from complementarity determining regions of antibodies were found that can discriminate between patients with PCa and controls, and are now being further explored as imaging ligands. Development of antibody-fragments such as svFv and nanobodies against various PCa-selective antigens for positron emission tomography/single, photon emission computed tomography imaging is ongoing. For the planned trial on AR targeted imaging, a clinical batch for the bench mark AR tracer 18F-DHT is in place. As an alternative, the imaging potential of a high affinity AR ligand is now being explored in in vitro and in vivo studies.

The infrastructure and protocols for the prospective PCMM biobank including multimodality MRI and CEUS-images have been installed in the four clinical centers. At the end of year 2, 40 percent inclusion for the first biobank group opened for inclusion in the beginning of 2011 was achieved. For the central database system, OpenClinica has been selected and implemented for the storage of clinical data, NBIA for imaging data, and caTissue for biobank data. PCMM expects support from the CTMM TraIT project for data integration.

Progress in the first year of PCMM:

In the first year of PCMM, candidate genomic and proteomic biomarkers have been identified in the biomarker program. These candidates will now be further evaluated for their diagnostic or prognostic value. The evaluation of novel imaging targets is ongoing, and preparations for the clinical testing of a bombesin-based imaging ligand targeting the Gastrin Releasing Peptide Receptor on prostate tumor cells are now entering a final stage. Standardized protocols for the collection of biomaterials involving blood, urine and prostate tissue, and imaging of the prostate by MRI and ultrasound have been developed for the PCMM biobank. Ethical approval has been obtained for the first phase of the PCMM biobank by all four clinical centers involved. The first group of patients, that is, men with localized prostate cancer who are scheduled for radical prostatectomy, is now open for inclusion. Furthermore, the IT infrastructure required to establish a central clinical database has been implemented.

Links/Social Media Feed

Homepage

<http://www.pcmmproject.org/>

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