1. There is little detail in this request about the exact nature of the research proposed or the methods to be used. The requestor points out the difference between China and the US in the stage at which prostate cancer presents, and attributes this to screening in the US, while at the same time proposing the possibility of genomic differences. There is mention of a parallel study in which "Differences in genomic alteration between Asian and Western men with de novo metastatic prostate cancer will be performed in two separate cohorts." I am not clear as to how this relates to the request for data in the LATTITUDE trial.

2. The hypothesis to be tested is that "PSA screen may be associated with a more aggressive phenotype and genotype of de novo metastatic prostate cancer. The heterogeneity may refine our understanding of de novo metastatic prostate cancer and subsequently improve individualized treatment approach." There is no description of a logical process by which this can be addressed by using data from LATTITUDE and if relevant data on screening history and genomic tumor analysis are necessary for their analysis.

3. The investigators describe using genomic data from Fudan for the patients in China. This will be linked to the requested trial data? Where might they obtain this genetic data for the "western" patients in the trial?

Reply:
We thank the reviewers for their comments about the logic and design of our proposal. PSA screen actually finds a composite of prostate cancer with different biology and growth rates (Figure).
Therefore, we hypothesized that the clinical outcome as well as biology background of metastatic prostate cancer may varied according to PSA screen status. In order to test the hypothesis, we will analyze oncological outcome from the international LATITUDE trial with patients from different PSA screen policies (Asia vs. Europe). Furthermore, we also will compare the genomic features between Chinese men and Caucasian counterparts from western countries. Our center has set up the Chinese Prostate Cancer Genomic (CPCG) project with more than 1000 prospectively enrolled patients. We will compare the genomic features of metastatic patients from CPCG to the western patients from public available database (for example, cBioportal). Better understanding the outcome and genomic features according to regions with different PSA screen background may provide further information for better clinical decision.

We summarized the study design in the following flowchart.