Circulating tumor cell (CTC) analysis of biomarkers and outcomes in Japanese metastatic castration-resistant prostate cancer (mCRPC) patients treated with abiraterone acetate plus prednisone

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Background
Biomarkers are essential for predicting efficacy and resistance of abiraterone acetate plus prednisone. We conducted an exploratory analysis of CTC biomarker associations with outcomes in 2 phase 2 trials of Japanese mCRPC patients treated with abiraterone acetate plus prednisone.

Methods
Patients with (n = 47) or without (n = 48) prior docetaxel treatment were included. Select CTC biomarkers were evaluated at baseline and end of treatment (EOT; n = 26 and n = 38 patients with and without prior docetaxel, respectively) using androgen receptor (AR) nuclear protein staining and mRNA expression analyses. Treatment effect and biomarker associations with clinical end points were assessed by Cox proportional hazard models, with number of CTCs as a covariate. Clinical end points included prostate-specific antigen (PSA) response (≥ 50% decline) by 12 weeks (primary), overall survival (OS), PSA progression-free survival (PFS), and radiographic PFS (rPFS).

Results
PSMA expression was higher at EOT versus baseline (69% vs 48%; p = 0.003). *ARv1* and *ARv7* expression were higher at EOT (40% vs 10% and 48% vs 26%, respectively; p < 0.01). Normalized expression of *IFIH1* and *CDH1* markers decreased in docetaxel-resistant tumors and was lower at EOT versus baseline and in samples with ≥ 5 CTCs at baseline and EOT. Higher frequency of baseline *PSMA* was associated with shorter OS, rPFS, and PFS (HR = 4.9, 2.3, and 3.2, respectively; p < 0.05), and positive EOT *PSMA* was associated with lower PSA response rate (31% in *PSMA*+ vs 75% in *PSMA*–; p = 0.01) and shorter PFS (HR = 3.1; p = 0.04). BL *ARv7* showed no association with PSA response, OS, PFS, or rPFS (p > 0.05). 44% of patients with baseline *ARv7* expression had a PSA response versus 47% without baseline *ARv7* expression. Baseline *AR* full length *(AR FL)* was associated with PFS (HR = 2.5; p = 0.004), with no evidence of association between EOT *AR FL* and outcomes. EOT expression of *NPY* (neuropeptide), *UBE2C* (proliferation marker), and *ACADL* (androgen-related dehydrogenase) was associated with worse outcomes.

Conclusions
This study is the first to find an association between higher frequency of baseline or EOT *PSMA* and resistance to abiraterone acetate plus prednisone. Baseline *ARv7* did not show an association with outcomes. These findings require validation in large-scale prospective studies.

Conflict of Interest:

W Li and D Ricci have been employed by Janssen Research & Development and have owned stock or held an ownership interest with Johnson & Johnson.

T Satoh has received honoraria from Daiichi Sankyo, AstraZeneca, Janssen Pharmaceutics, and Astellas Pharma.

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