Phase II study of the Prednisone to Dexamethasone switch in mCRPC patients on Abiraterone plus Prednisone (SWITCH study).

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Background: Despite most mCRPC patients may benefit from abiraterone acetate plus prednisone 5mg bid (AA+P) resistance will eventually occur, partly related to prednisone. Switching the concomitant steroid may reverse this resistance.

Objective: To evaluate the antitumour activity of abiraterone acetate plus dexamethasone 0.5mg daily (AA+D) in mCRPC patients progressing to AA+P.

Design, setting and participants: SWITCH was a multicentre, single arm, open label, single-stage, phase II study. Clinically stable mCRPC patients who had PSA and/or limited radiographic progression after at least 12-weeks on AA+P, switched to AA+D. Archival tissue and plasma samples were collected.

Outcome measurements and statistical analysis: The primary endpoint was PSA30 >6-weeks response rate. Secondary endpoints included: PSA50 >12-weeks response rate, biochemical and radiological progression, overall survival, safety profile evaluation, subsequent treatment lines activity, and exploration of biomarkers of response (AR copy-number, TMPRSS2-ERG status and PTEN expression).

Results and limitations: Twenty-six patients were enrolled. PSA30 >6-weeks and PSA50 >12-weeks were 46.2% and 34.6%, respectively. Median time to biochemical and radiological progression were 5.3 and 11.8 months, respectively. Two radiological responses were observed. Median overall survival was 20.9 months. Patients with AR amplification detected in plasma ctDNA did not responded to switch. No significant toxicities were observed and PSA50 response rate to subsequent taxane was 50%. Our study is limited by the lack of comparator-arms that demonstrated the long-term benefits of AA+D switch over maintaining AA+P or single-agent dexamethasone.

Conclusions: In selected clinical stable mCRPC patients with limited disease progression, the prednisone to dexamethasone switch concomitant to Abiraterone Acetate could be an active option in selected patients.

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Conflict of interest
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