P08 Combined metabolite and tissue expression profiling of TOP2A and EZH2 predicts biochemical recurrence in prostate cancer radiotherapy patients

Eur Urol Suppl 2019;18(8):e3070

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Introduction & Objectives: Biomarkers for prostate cancer (PCa) recurrence are urgently needed for better management and follow-up of radiotherapy patients. Low tissue levels of the metabolites citrate and the polyamine spermine have previously been associated with biochemical recurrence (BCR; PSA≥0.2 ng/ml) in radical prostatectomy (RP) patients[1]. Further, up-regulation of TOP2A and EZH2 have been connected to a more aggressive disease in RP patients[2]. The main aim of the present study was to investigate the potential of these MR tissue metabolites and immunohistochemistry markers as predictors of BCR in transrectal ultrasound-guided (TRUS) biopsies of PCa radiotherapy patients sampled prior to treatment. BCR for radiotherapy patients was defined as PSA levels ≥2ng/mL above nadir after radiotherapy.

[1] Braadland et al. 2017, Br J Cancer

[2] Labbè et al. 2017, Clin Cancer Res

Materials & Methods: One to two TRUS-guided biopsy samples were obtained from each of the 90 patients scheduled for radiotherapy (n=172). The cohort included 64 cancer-containing samples from 46 patients. Twenty-one of the cancer patients (n=31 samples) had received neoadjuvant hormonal treatment prior to sample collection. In total, 11 of the 46 patients with cancer-containing samples had BCR within four years (n=18). High-resolution magic angle spinning MR spectroscopy was performed to measure metabolites citrate and polyamines, and immunohistochemistry staining was subsequently performed on the same TRUS biopsy for assessment of TOP2A and EZH2 expression levels. Differences in rates of BCR were estimated with the Kaplan-Meier method and compared using the log-rank test.

Results: In all 64 cancer-containing samples, lower levels of citrate (p=0.0036) and polyamines (p=0.0056) were identified as predictors of BCR among PCa radiotherapy patients. In cancer-containing samples without hormone treatment, up-regulated TOP2A alone (p=0.045) and EZH2 alone (p=0.045) showed potential of predicting BCR in PCa patients scheduled for radiotherapy. When investigating the concurrent up-regulation of TOP2A and EZH2, a strong association to BCR was found (p=0.0079). Additionally, the combination of all four potential biomarkers (TOP2A and EZH2 in combination with lower levels of citrate and polyamines) was demonstrated as promising biomarkers for BCR among PCa radiotherapy patients (p=0.0058).

Conclusions: The combination citrate, polyamine, TOP2A and EZH2, are suggested as biomarkers for BCR in PCa radiotherapy patients not receiving neoadjuvant hormonal treatment measured in TRUS biopsies prior to treatment. This study offers a translational potential, as citrate and polyamine are detectable in *in vivo* MR spectroscopic imaging. However, this work should be validated in a larger cohort of radiotherapy patients.