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Epigenetic changes play a key role in development of chemo resistance in BCa

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At the 28th Annual EAU Congress currently ongoing in Milan until Tuesday, W. Tan and colleagues presented their study on neoadjuvant cisplatin-based chemotherapy which showed that epigenetic changes are potential key drivers in the development of chemo resistance in bladder cancer.

Neoadjuvant cisplatin-based chemotherapy is recommended for patients with muscle invasive bladder cancer. Cisplatin-based regimes have similar efficacy with complete response in 30% a survival advantage if 16% (HR, 0.84;CI 0.72 to 0.99), wrote Tan of the UCL, Dept. of Surgery and Interventional Science in London, the UK.

According to the researchers, the ability to identify a biomarker which is able to predict response to treatment would increase pathological complete response rates and spare nonresponders adverse events of chemotherapy. DNA hypermethylation has been implicated in chemotherapy resistance in cancers.

"We hypothesised that DNA methylation may not only represent the mechanisms for the acquisition of resistance, but may also be a potential biomarker to predict response to platinum based chemotherapy in bladder cancer," wrote Tan, lead author of the study titled "Epigenetic alterations associated with neo-adjuvant chemotherapy resistance in bladder cancer."

In the study, DNA was extracted from 48 muscular invasive bladder

tumours, taken prior to the patient to receiving a platinum based neo-adjuvant chemotherapy, all tumours had >80% tumour content. 1ug of DNA was bisulphite converted using the EZDNA Bisulfite Conversion Kit (Zymo Research). Genome-wide DNA methylation profiles were generated using the Infinium HumanMethylation 450K BeadChip (Illumina).

According to the researchers, the analysis suggests acquired resistance is associated with global hypermethylation in both primary tumours and paired cell lines. Singular value decomposition (SVD) analysis revealed the strongest methylation signature to be associated with chemotherapy response (p=