THE IMPACT OF THE DERIVED NEUTROPHIL TO LYMPHOCYTE RATIO AND DURATION OF INITIAL ANDROGEN DEPRIVATION THERAPY (ADT) ON SURVIVAL OF MEN WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) RECEIVING FIRST-LINE CHEMOTHERAPY: DATA FROM TWO RANDOMIZED PHASE III TRIALS

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Aim: Since 2004 docetaxel has been the standard first-line chemotherapy for men with mCRPC. The neutrophil to lymphocyte ratio (NLR), a marker of host inflammation has been associated with worse outcomes in several solid tumors. Here, we investigated the impact of the derived NLR (dNLR) and the duration of initial ADT on survival of men with mCRPC receiving first-line chemotherapy.

Methods: Data from the multinational randomized phase III studies VENICE and TAX327 were used as training and independent validation sets respectively. The dNLR was calculated as the absolute neutrophil count divided by (absolute white cell count minus the absolute count of neutrophils). The duration of initial ADT was defined as the time from start of first-line hormonal therapy to the start of subsequent treatment. Median overall survival (OS) was estimated using the Kaplan Meier method. The impact of dNLR and duration of initial ADT on OS was evaluated by multivariable Cox regression analysis stratified for performance status and treatment arm. The final model was then tested in the validation set. Subsequently we investigated the treatment effect of docetaxel on OS in subgroups according to dNLR and duration of initial ADT.

Results: In the training set both dNLR ≥ 2 (median) and a duration of ADT < 15 months (median) were associated with an increased risk of death (HR = 1.29; 95%CI: 1.11-1.50, P < 0.001 and HR = 1.41; 95%CI: 1.21-1.64, P < 0.001, respectively) after adjustment for age, alkaline phosphatase, hemoglobin, and pain at baseline. In the validation set, dNLR remained an independent prognostic factor for OS (HR = 1.43; 95%CI: 1.20-1.70, P < 0.001), whereas duration of ADT was not independently associated with OS (HR = 1.16; 95%CI: 0.97-1.37, P = 0.10). In subgroup analysis of the TAX327 study, docetaxel improved OS in all patient subgroups defined by dNLR and the duration of initial ADT.

Conclusions: In this study we identified and externally validated the dNLR as a new prognostic biomarker in men with mCRPC receiving first-line chemotherapy.

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