

Development and prospective evaluation of a 20-gene model for molecular nodal staging of bladder cancer

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Background: Neoadjuvant chemotherapy prior to cystectomy confers a small yet significant survival benefit in bladder cancer. Yet, it has not been widely adopted, since most patients do not benefit and we are currently unable to predict those that do. We propose that tools identifying patients with advanced disease prior to surgical management would be useful in selecting patients for neoadjuvant chemotherapy.

Methods: We developed a gene expression model (GEM) predictive of pathological node status for use on primary tumor tissue from clinically node negative (cN0) patients. From a subset of transcripts, we developed both the GEM and cutoffs identifying patient strata with elevated and decreased risk of nodal involvement using two separate training cohorts (N=90 and N=66). We then independently evaluated the GEM and cutoffs to predict node positive disease in tissues from a Phase III trial cohort (AUO-AB-05/95, N=185).

Findings: A 20-gene GEM was developed and the stratification schema from it identified subjects with high (RR 1.74, [1.03-2.93]) and low (RR 0.70, [0.51-0.96]) relative risk of node positive disease. Multivariate logistic regression demonstrated the GEM predictor was independent of age, gender, pathologic stage, and lymphovascular space invasion (P=0.019).

Interpretations: This study proves the principle that molecular staging before surgery can be faithfully achieved and could change the way we view urothelial cancer management and practice. Selecting patients for neoadjuvant chemotherapy based on the risk of node positive disease has the potential to benefit high-risk patients while sparing others toxicity and delay to cystectomy.

Biography

Alexander Baras is a young investigator with interests in surgical pathology, personalized medicine, and computational biology. He completed his combined M.D. & Ph.D at the age of 29 in 2011 from the University of Virginia under the Medical Scientist Training Program. He has published 18 manuscripts in various journals and he has recently started reviewing manuscripts for BMC Biochemistry and Cancer. He has served as a bioinformatics consultant for Novartis in the past and is currently a resident physician in the department of Pathology at Johns Hopkins University.