COMMENTARY

BCG for high grade NMIBC - Lessons learned over 40 years

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This is an excellent review of the scientific discoveries which led to the use of intravesical BCG for the treatment of carcinoma in situ (CIS) of the bladder and its role as an adjuvant post TUR of HG Ta and T1 urothelial carcinoma of the lower urinary tract. Morales's important contribution exemplifies the benefit of being in the right place, i.e. National Cancer Institute, at the right time, i.e. Zbar's investigations with BCG and melanoma, and his realization that it makes sense to place BCG into the bladder where it would be in contact with malignant cells.[1] He details the 14 year process from initial clinical observations to FDA approval. A must read for all those who prescribe BCG.

I was fortunate to spend 2 years at the NCI and observed some of the early clinical work with intralesion BCG in a variety of malignancies. I completed my urology residency in 1975 and have closely followed the "BCG story" over the last 40 years. I have a few observations.

Like other anti cancer medical treatments, e.g. cisplatin in bladder cancer, intravesical BCG for CIS/HG Ta/T1 produces either a dramatic positive response or has little impact on CIS or the recurrence pattern of HG Ta/T1 bladder cancer (BC). In my experience there are few "partial responses". Unfortunately, we are not yet able to predict which patients will be responders and which will not benefit. I have confidence that with the emphasis on finding markers for response and personalized medicine, scientists will be able to determine which patients should receive this form of immunotherapy and which should move directly to another approach. Since the patient population has a potentially lethal BC, time is not on the side of the patient. A retrospective analysis of patients who received BCG for NMIBC and subsequently underwent a radical cystectomy indicates urologists often wait too long with the bladder preservation approach, i.e. BCG, and too many patients with initial < T2 BC die of BC.[2,3]

I would like to also expand on the correct statement made by Morales that according to the EAU guidelines BCG is not indicated for adjuvant therapy following resection of low grade bladder tumors. Indeed patients with LG Ta tumors rarely progress or die of BC.[4] He states that it is indicated for intermediate and high risk NMIBC ideally as an adjuvant following a complete TUR BT for HG Ta/T1 (reTUR BT for T1) and for CIS. The AUA/SUO guidelines, however, state that the only tumors listed under low risk are primary, low grade, papillary tumors less than 3 cm. All other low grade tumors are intermediate risk. This includes any low grade tumor which recurs within 1 year regardless of size or number, any patient with multifocal LG Ta, or any tumor > 3 cm. In my view this would subject many patients with LG Ta tumors to BCG.[5] The reasoning for not using BCG for LG tumors is the higher side effect profile of BCG compared to intravesical chemotherapy and the relative lack of efficacy of BCG for LG bladder tumors. □

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