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Re: Defining Progression in Nonmuscle Invasive Bladder Cancer: It is Time for a New, Standard Definition: D. Lamm, R. Persad, M. Brausi, R. Buckley, J. A. Witjes, J. Palou, A. Böhle, A. M. Kamat, M. Colombel and M. Soloway J Urol 2014;191:20-27

Bryan, R T; Cheng, K K; James, N D; Zeegers, M P; Wallace, D M A

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1 **RE: DEFINING PROGRESSION IN NON-MUSCLE-INVASIVE BLADDER CANCER:** 2 IT IS TIME FOR A NEW, STANDARD DEFINITION RT Bryan^a, ND James^b, MP Zeegers^c, KK Cheng^d, DMA Wallace^e 3 4 5 ^a School of Cancer Sciences, University of Birmingham, UK. 6 ^b University of Warwick, UK. ^c Department of Complex Genetics, Cluster of Genetics and Cell Biology, NUTRIM School for 7 8 Nutrition, Toxicology and Metabolism, Maastricht University Medical Centre, Maastricht, The 9 Netherlands. ^d School of Health and Population Sciences, University of Birmingham, UK 10 11 ^e University of Western Australia, Fremantle Hospital, Fremantle, Perth, Western Australia. 12 13 Word count: 236 14 Correspondence to: Mr. RT Bryan, School of Cancer Sciences, University of Birmingham, Edgbaston, 15 16 Birmingham B15 2TT, UK. E: r.t.bryan@bham.ac.uk. T: +44 7785 396958. 17

We write in agreement with Lamm et al in proposing a new standard definition for progression in non-muscle-invasive bladder cancer (NMIBC)¹. We too recognised that defining a state of progression before the development of muscle-invasion would be a useful tool for clinical trials in NMIBC. Consequently, in 2005 we went through a very similar process to Lamm et al when writing the protocol for the West Midlands' (UK) Bladder Cancer Prognosis Programme (BCPP, incorporating the SELENIB clinical trial), defining progression as "a recurrence with an increase in tumour grade from 1/2 to grade 3, or an increase in TNM stage, or the new occurrence of carcinoma in situ (CIS) in a bladder previously free from such lesions, or the new occurrence of multiple tumours following resection of a solitary tumour, or the need for a cystectomy because of refractory disease"3. Clearly, there are many similarities between our definition of progression for the purposes of BCPP/SELENIB and that proposed by Lamm et al, and we support their rationale and endeavour¹. As we have observed with the change in terminology from "superficial bladder cancer" to "NMIBC" over the last ten years or more^{4,5}, the key to adoption is utilising a term which is universally applicable and acceptable. In BCPP/SELENIB we have always qualified our definition of progression by describing it as "biological progression". Perhaps "biological progression" could be the term that best describes Lamm et al's new definition?

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