

EAU 2015 – Madrid highlights for NMIBC

Richard T Bryan April 2, 2015



As we have come to expect in the field of bladder cancer research, EAU Madrid did not present any revolutionary or paradigm-shifting data or papers; however, there were some very interesting updates and validations of previously presented novel data that may shift paradigms in the not too distant future. With a number of bladder cancer sessions overlapping I couldn't be everywhere, but these are my selected highlights, with an emphasis on my interests of NMIBC and translational research. Further scientific content can be found at the EAU Resource Centre: <http://remadrid2015.uroweb.org>

Non-invasive diagnosis

Genomic approaches to the analysis of urine for non-invasive disease diagnosis appear to be approaching the sensitivities and specificities required to be viable alternatives to flexible cystoscopy. Kim van Kessel (from Ellen Zwarthoff's group in Rotterdam) presented data on their approach (#837): utilising a combination of FGFR3, TERT and PIK3CA mutations with a number of methylation probes for OTX1 and ONECUT2, they were able to detect bladder cancer cases in haematuria patients (n=258, 175 BCs + 83 non-BCs) with a sensitivity of 93% and specificity of 89%. Although this case mix is very different to that which you would see in a UK haematuria clinic population (BC yield c.10%) and requires validation, their assays require very little DNA (only 50ng, such that over 95% of urine samples would yield adequate DNA) and are very cheap (total cost in the research laboratory of c.€20). Similarly, Maria Ribal (Barcelona) presented her data on a gene expression test for the non-invasive diagnosis of BC (#830): refining a 12-gene expression signature down to a 2-gene signature (IGF2, MAGEA3), they achieved an optimal sensitivity of 81% and specificity of 92% for diagnosing 216 BCs out of a total sample of 525. This case mix is more in line with a typical NMIBC surveillance cohort and the assay is cheap, although it relies upon more fragile RNA such that the yields from urine may not be as reliable as for DNA.

However, both studies show significant promise: based upon data from PDD and NBI studies, I often quote a sensitivity and specificity for conventional white light flexible cystoscopy of c.92% for the diagnosis of BC, and so these non-invasive urine-based biomarkers are getting close to clinical utility. They certainly appear more promising than the current generation of commercially available non-invasive urine tests, which, according to WHO/ICUD consensus, do not yet have any value for clinical decision-making (despite what the NICE Guidelines say...). Large multi-centre prospective studies in both the haematuria and surveillance settings are now needed to validate

accuracy and to assess reproducibility and commercial viability. Added to this mix, Chris Probert (Liverpool) captivated the NMIBC session (Thematic Session 6) with his electronic nose ('Odoreader') approach to non-invasive diagnosis, with preliminary data from controls and predominantly low-grade NMIBCs showing sensitivities and specificities for diagnosis of over 95%. Once again, larger studies in the appropriate populations are needed and this 'sniffing cancer' work is ongoing.

Highlighting the urgent need for cheap and accurate non-invasive diagnostics for BC, Sara Hall (Derby) presented local data on 2-week-wait referrals before and after the National Be Clear on Cancer 'blood in your pee' campaign commissioned by the UK Department of Health (#833): the number of 2ww referrals increased by 37% from 723 before the campaign to 988 after the campaign, yet significantly fewer patients referred after the campaign were diagnosed with a urological malignancy (13% versus 22%, $p < 0.001$). The campaign has therefore placed a large demand on local urology and radiology services without benefit. Jo Cresswell (Middlesbrough) commented from the audience that she and her colleagues had similar findings from the South Tees region. These data are obviously disappointing for the UK Department of Health and the UK urological community.

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