> a significant overall reduction in penile curvature of 31.2° … was observed

penile length (mean 1.8 cm; $P = 0.03$) and PDQ psychosexual symptom (from 12.3 to 7.8; $P < 0.001$) and symptom bother (from 3.8 to 7.2; $P < 0.001$) domains, and a nonsignificant improvement in International Index of Erectile Function scores (from 23.6 to 26.1; $P < 0.23$), compared with baseline (and the non-intervention group).

Regarding safety, mild adverse events — mainly local discomfort and glans numbness — occurred in 43% of patients in the PTD group and were well tolerated.

The findings suggest that PTDs are useful noninvasive modalities that should be offered to patients with PD, either as part of a combination therapy regimen or before corrective surgery.

Conor A. Bradley

ORIGINAL ARTICLE Moncada, I. et al. Penile traction therapy with the new device 'Penimaster PRO' is effective and safe in the stable phase of Peyronie's disease: a controlled multicenter study. *BJU Int.* https://doi.org/10.1111/bju.14602 (2018)
FURTHER READING Tsambarlis, P. et al. Nonsurgical management of Peyronie's disease. *Nat. Rev. Urol.* https://doi.org/10.1038/s41585-018-0117-7 (2018)

> With its interdisciplinary synthesis of recent data and insights, EMUC18 set a high bar

successor, POUT2. James N'Dow also promoted PIONEER, an ambitious big data project aiming to inform prostate cancer diagnosis, treatment and outcomes research.

A short but informative plenary session on new developments in prostate cancer evaluation was highlighted by a lecture by Jonathan Epstein, who addressed controversial and under-recognized issues in pathology that impact management.

The final plenary tackled current dilemmas in metastatic prostate cancer management. Ganesh Palapattu discussed how to effectively treat oligometastases, which was followed by a debate on metastasis-directed therapy for oligometastatic recurrence, with Piet Ost arguing that the first evidence is promising, and Philip Cornford cautioning that no consensus exists on the definition of oligometastasis.

With its interdisciplinary synthesis of recent data and insights, EMUC18 set a high bar — we eagerly anticipate EMUC19 next year in Vienna, Austria.

Conor A. Bradley

BLADDER CANCER

ERCC2 mutations drive cisplatin sensitivity

Despite its survival benefits, responses to DNA-damaging cisplatin-based chemotherapy are variable in muscle-invasive bladder cancer (MIBC) and predictive biomarkers are sought. A new study using genomic and functional approaches now establishes a role for mutations in the nucleotide excision repair (NER) gene *ERCC2* in driving cisplatin sensitivity in MIBC.

Although *ERCC2* missense mutations have been associated with improved cisplatin response, Li et al. found that the mutational landscape is broad, identifying 37 *ERCC2* mutations at 23 amino acid positions across 3 MIBC cohorts. As the functional influence of individual *ERCC2* variants on NER capacity, and therefore cisplatin sensitivity, is unknown, a novel microscopy-based assay was developed to measure the NER capacity of *ERCC2* mutations observed across cohorts.

Overall, 23 of 26 clinically observed *ERCC2* mutations conferred loss of NER function and increased cisplatin sensitivity, consistent with the role of ERCC2 in repair of cisplatin-induced DNA adducts. Additionally, most *ERCC2* mutations were located within or adjacent to helicase domains (which couple ATP hydrolysis with DNA duplex unwinding).

> the findings support a role for *ERCC2* mutational status as a predictive biomarker

Next, the relationship between ERCC2 functional status, inferred using the NER assay, and clinical outcomes was assessed. *ERCC2* mutational frequency was significantly divergent between cisplatin responders and nonresponders (38% versus 6%; $P < 0.0001$), and each cisplatin-responsive *ERCC2*-mutant tumour harboured a functionally deleterious helicase domain mutation.

Following the finding that most *ERCC2* mutations confer NER deficiency and cisplatin sensitivity, the investigators directly measured the effect of an *ERCC2* mutation on cisplatin sensitivity in preclinical models. The CRISPR–Cas9-mediated introduction of an *ERCC2* mutation into a high-grade bladder transitional cell carcinoma cell line markedly increased cisplatin sensitivity, which was rescued upon re-expression of wild-type *ERCC2*. Furthermore, in an orthotopic tumour xenograft model in immunodeficient mice, *ERCC2*-mutant tumours were markedly more sensitive to cisplatin than *ERCC2*-wild-type tumours, confirming that ERCC2 loss is sufficient to drive cisplatin sensitivity.

Overall, the findings support a role for *ERCC2* mutational status as a predictive biomarker to guide precision oncology in MIBC. Indeed, ongoing trials (NCT03609216, NCT02710734 and NCT03558087) are incorporating DNA damage response gene alterations, including *ERCC2* mutational status, as prospective biomarkers.

Conor A. Bradley

ORIGINAL ARTICLE Li, Q. et al. *ERCC2* helicase domain mutations confer nucleotide excision repair deficiency and drive cisplatin sensitivity in muscle-invasive bladder cancer. *Clin. Cancer Res.* https://doi.org/10.1158/1078-0432.CCR-18-1001 (2018)