

Round up

DAROLUTAMIDE VERSUS ENZALUTAMIDE IN MEN WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER: PATIENT PREFERENCE AND COGNITIVE FUNCTION IN ODENZA TRAIL – A RANDOMIZED CONTROLLED TRIAL

The ODENZA trial, a prospective, randomized, multicenter, crossover, phase 2 study, aimed to assess patient preference based on cognitive deterioration between darolutamide and enzalutamide in asymptomatic or mildly symptomatic metastatic castrate-resistant prostate cancer.^[1] In preclinical studies, darolutamide demonstrated lower blood–brain barrier penetration than enzalutamide, with brain–plasma drug ratios of 2%–3% for darolutamide, compared with 27% for enzalutamide.^[2] Patient preference was the primary endpoint which was determined by a preference questionnaire. Of the 200 patients evaluated, 49% chose darolutamide, 40% chose enzalutamide, and 12% had no preference. Darolutamide demonstrated a clinically meaningful benefit in episodic memory, with less fatigue and better quality of life compared to enzalutamide.

IMPROVED OUTCOMES WITH ENZALUTAMIDE ALONE IN BIOCHEMICALLY RECURRENT PROSTATE CANCER AFTER RADICAL PROSTATECTOMY OR RADICAL RADIOTHERAPY

The EMBARK trial, a phase 3 trial, investigated the efficacy and safety of enzalutamide in combination with leuprolide or as monotherapy compared to leuprolide alone in patients with biochemical recurrence after radical prostatectomy/radical radiotherapy (RP/RT).^[3] Patients with adenocarcinoma and high-risk disease (defined as a PSA doubling time of ≤ 9 months and a PSA level of ≥ 2 ng/ml above nadir after RT or ≥ 1 ng/ml after RP \pm postoperative RT) were randomized, in a 1:1:1 ratio, to receive enzalutamide (160 mg) daily plus leuprolide every 12 weeks (combination group = 355), placebo plus leuprolide (leuprolide-alone group = 358), or enzalutamide monotherapy (monotherapy group = 355).

Over a median follow-up of 60.7 months, the 5-year metastasis-free survival rates were 87.3%, 71.4%, and 80.0% for various groups, respectively. Enzalutamide plus leuprolide exhibited superiority over leuprolide

alone (hazard ratio [HR] 0.42). Enzalutamide monotherapy also surpassed leuprolide alone (HR 0.63). Enzalutamide plus leuprolide and enzalutamide monotherapy both resulted in significantly longer metastasis-free survival and a longer time to PSA progression than leuprolide alone while maintaining overall quality of life. The results demonstrated that enzalutamide only had clinical benefits in patients with high-risk biochemical recurrence after definitive treatment without new safety signals.

NEPHRECTOMY FOR KIDNEY TUMOR INCREASES THE RISK OF *DE NOVO* ARTERIAL HYPERTENSION UNLIKE PARANEOPLASTIC HYPERTENSION WHICH IMPROVES AFTER NEPHRECTOMY

The VAPANCR trial^[4] was a prospective multicenter study involving 200 patients who underwent radical/partial nephrectomy (RN/PN) between 2018 and 2020. The effects of surgical excision on blood pressure (BP) were assessed. All patients had localized cancer and did not have preexisting hypertension (HTN) (BP $< 140/90$). BP was measured preoperatively at 1 month and 6 months postoperatively using home BP monitoring. Plasma renin levels were also measured before and after surgery. HTN was defined as systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or *de novo* use of antihypertensive medications.

De novo HTN was observed at 1 month and 6 months in 23 (14.3%) and 31 patients (19.2%). Seven patients (4.3%) required antihypertensive treatment. Significant increases in BP were seen in 17 (10.3%) and 43 patients (26.3%) at 1 and 6 months, respectively. The type of surgery (PN vs. RN) did not influence the risk of HTN (21.7% PN vs. 15.7% RN; $P = 0.59$). Plasma renin levels showed no significant difference before and after surgery. Multivariable analysis identified age and body mass index (BMI) as predictors of *de novo* HTN. In the case of PN, arterial clamping was not associated with an increased risk of HTN. Renin secretion was decreased after RN and increased after PN. RN/PN leads to notable BP changes, with nearly 20% developing *de novo* HTN, unaffected by the surgical approach.

MONOPOLAR VERSUS BIPOLAR VERSUS THULIUM LASER FOR EN BLOC RESECTION OF BLADDER TUMOR

The study^[5] analyzed different energy sources in *en bloc* transurethral resection of bladder tumors (ERBT) for pathological, surgical, and postoperative outcomes. Participants were randomized into monopolar (M-ERBT, $n = 45$), bipolar (B-ERBT, $n = 45$), or thulium laser (T-ERBT,

$n = 46$) groups. The presence of detrusor muscle was not significantly different across energy types or lesion locations. However, obturator nerve reflex (ONR) occurrences were reduced in the T-ERBT group (0%) versus M-ERBT (10.2%) and B-ERBT (22.2%) groups. Lesions in the anterior wall/dome/neck were more likely to require conversion to conventional TURBT, irrespective of the energy used. Notably, higher artifact presence in pathological specimens was observed in the posterior wall and trigone lesions. Staging feasibility did not substantially differ among energy sources. Laser energy showed potential benefits in averting ONR, particularly in lateral wall lesions. The authors recommended electrocautery for anterior wall lesions to minimize material waste and conversion to conventional TURBT.

PREDICTORS OF TIME-TO-NADIR SERUM CREATININE AFTER DRAINAGE OF BILATERALLY OBSTRUCTED KIDNEYS DUE TO BLADDER CANCER

This prospective, nonrandomized study investigated the efficacy of unilateral/bilateral percutaneous nephrostomy (PCN) in draining bilaterally obstructed kidneys (BOKs) caused by bladder cancer (BC) and identified the predictors influencing the time-to-nadir (TTN) of serum creatinine (SCr) levels post drainage.^[6] It included adult patients with SCr > 2 mg/dL and BOKs of grades 1–3 hydronephrosis. The laterality of drainage was decided considering factors such as the general condition or performance status, anticipated effect on quality of life after patient counseling, and clinical and laboratory findings.

Among 55 patients (U/L-PCN = 23, B/L PCN = 32), 58.2% achieved normal nadir SCr while 41.8% exhibited elevated levels within 21 days after PCN. Elevated nadir SCr correlated with higher age and lower BMI. Patients with normal nadir SCr had a significantly shorter TTN and increased SCr trajectory during TTN. Multivariate analysis revealed that predrainage low urine output and high BMI were associated with prolonged TTN. Notably, parenchymal thickness and drainage laterality had no significant impact on TTN and SCr normalization rates. Despite PCNs, over 41% (U/L-PCN = 15, B/L-PCN = 8) of patients failed to attain normal nadir SCr, highlighting the need for personalized considerations in BC-related BOK drainage.

THE IMPACT OF DIABETES AND HYPERTENSION ON RENAL ALLOGRAFT SURVIVAL – A SINGLE-CENTER STUDY

This retrospective analysis included 1685 adult first kidney-only transplant recipients (84% deceased donors) from 1966 to 2013. The prevalence of pretransplant DM (ptDM) and HT 1-year posttransplant was 6.5% ($n = 107/1625$) and

53.6% ($n = 503/1072$), respectively.^[7] For those with ptDM, graft survival at 1 year for was 67.5%. The risk of graft loss was significantly higher in those with ptDM (HR, 1.26; 95% confidence interval [CI], 1.011.58). In recipients with HT present at 1-year posttransplant, the overall graft survival analysis at 5 and 10 years was 75.4% (95% CI, 72.4%–78.1%) and 52.6% (95% CI, 49%–56%), respectively. Adjusted survival analysis revealed that both ptDM (HR 1.26, 95% CI 1.01–1.58, $P = 0.043$) and posttransplant HT (HR 1.63, 95% CI 1.37–1.94, $P < 0.0001$) were the significant risk factors for renal allograft loss.

THE DEPTH OF ENDOSCOPIC PERFORATION SCALE TO ASSESS INTRAOPERATIVE PERFORATIONS DURING TRANSURETHRAL RESECTION OF BLADDER TUMOR: SUBGROUP ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL

This study was a subanalysis of a prospective randomized trial involving 248 patients undergoing transurethral resection of bladder tumors from March 2018 to June 2021.^[8] The Depth of Endoscopic Perforation (DEEP) Scale, ranged from 0 to 3, “0” visible muscular layer with no perivesical fat; “1” visible muscle fibers with spotted perivesical fat; “2” exposition of perivesical fat; and “3” intraperitoneal perforation, respectively.

The results revealed that 146 (58.9%), 56 (22.6%), 41 (16.5%), and 5 (2.0%) patients presented with DEEP grades 0, 1, 2, and 3, respectively. Female gender, tumor location, and obturator nerve reflex were identified as the independent predictors of high-grade perforations (DEEP 2–3). The DEEP scale independently predicted major complications ($P = 0.026$), absence of post-operative intravesical chemotherapy ($P = 0.001$), longer irrigation time ($P < 0.001$), and extended hospital stay ($P = 0.003$). The DEEP scale is a valuable visual tool for standardizing complication reporting and guiding postoperative management in TURBT.

THE BRAIN AT WORK: HOW YOUR JOB'S PHYSICAL DEMANDS SHAPE YOUR COGNITIVE DESTINY

The relationship between physical activity (PA) and cognitive health is complex. As indicated by several studies, occupational PA has been associated with a higher risk of cognitive impairment, while leisure-time PA appears to have a more protective effect.^[9,10] These contrasting effects between leisure time and occupational PA on cognitive health have been termed the “PA paradox.”

A study involving 7005 participants examined the impact of occupational PA trajectories from ages 33 to 65 on the risk of dementia and mild cognitive impairment (MCI) at ages 70 and older.^[11] Four distinct PA trajectories were identified:

stable low, increasing then decreasing, stable intermediate, and stable high. Participants with stable high PA trajectories had a 34% higher risk of dementia and an 80% higher risk of MCI compared to those with stable low PA trajectories, after adjusting for other factors. Stable intermediate PA trajectories were associated with a 36% higher risk of MCI but not dementia. Interestingly, participants with increasing then decreasing PA had a 24% lower risk of dementia and an 18% higher risk of MCI compared to the stable low PA group, although these differences were not statistically significant. These findings suggest that prolonged exposure to physically demanding occupations may increase the risk of cognitive impairment, emphasizing the need for preventive strategies in such occupations.

Swarnendu Mandal*

Department of Urology, AIIMS, Bhubaneswar, Odisha, India

*E-mail: urol_swarnendu@aiimsbhubaneswar.edu.in


REFERENCES

- Colomba E, Jonas SF, Eymard JC, Delva R, Brachet PE, Neuzillet Y, *et al.* A randomized, open-label, cross-over phase 2 trial of darolutamide and enzalutamide in men with asymptomatic or mildly symptomatic metastatic castrate-resistant prostate cancer: Patient preference and cognitive function in ODENZA. *Eur Urol* 2023;S0302-2.
- Moilanen AM, Riikonen R, Oksala R, Ravanti L, Aho E, Wohlfahrt G, *et al.* Discovery of ODM-201, a new-generation androgen receptor inhibitor targeting resistance mechanisms to androgen signaling-directed prostate cancer therapies. *Sci Rep* 2015;5:12007.
- Freedland SJ, de Almeida Luz M, De Giorgi U, Gleave M, Gotto GT, Pieczonka CM, *et al.* Improved outcomes with enzalutamide in biochemically recurrent prostate cancer. *N Engl J Med* 2023;389:1453-65.4.
- Bigot P, Bernhard JC, Khene ZE, Dariane C, Lebdaï S, Doumerc N, *et al.* Nephrectomy for kidney tumour increases the risk of *de novo* arterial hypertension. *BJU Int* 2023;132:575-80.
- Diana P, Gallioli A, Fontana M, Territo A, Bravo A, Piana A, *et al.* Energy source comparison in en-bloc resection of bladder tumors: Subanalysis of a single-center prospective randomized study. *World J Urol* 2023;41:2591-7.
- Gadelkareem RA, Abdelraouf AM, Ahmed AI, El-Taher AM, Behnsawy HM. Predictors of time-to-nadir serum creatinine after drainage of bilaterally obstructed kidneys due to bladder cancer. *Curr Urol* 2023;17:246-50.
- Padayachee S, Adam A, Fabian J. The impact of diabetes and hypertension on renal allograft survival- a single center study. *Curr Urol* 2023;17:286-91.
- Breda A, Gallioli A, Diana P, Fontana M, Territo A, Gaya JM, *et al.* The DEpth of endoscopic perforation scale to assess intraoperative perforations during transurethral resection of bladder tumor: Subgroup analysis of a randomized controlled trial. *World J Urol* 2023;41:2583-9.
- Ogino E, Manly JJ, Schupf N, Mayeux R, Gu Y. Current and past leisure time physical activity in relation to risk of Alzheimer's disease in older adults. *Alzheimers Dement* 2019;15:1603-11.
- Tolppanen AM, Solomon A, Kulmala J, Kåreholt I, Ngandu T, Rusanen M, *et al.* Leisure-time physical activity from mid- to late life, body mass index, and risk of dementia. *Alzheimers Dement* 2015;11:434-43.e6.
- Zotcheva E, Bratsberg B, Strand BH, Jugessur A, Engdahl BL, Bowen C, *et al.* Trajectories of occupational physical activity and risk of later-life mild cognitive impairment and dementia: The HUNT4 70+ study. *Lancet Reg Health Europe* 2023;34:100721.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/iju.iju_472_23

How to cite this article: Mandal S. Round up. *Indian J Urol* 2024;40:3-5.