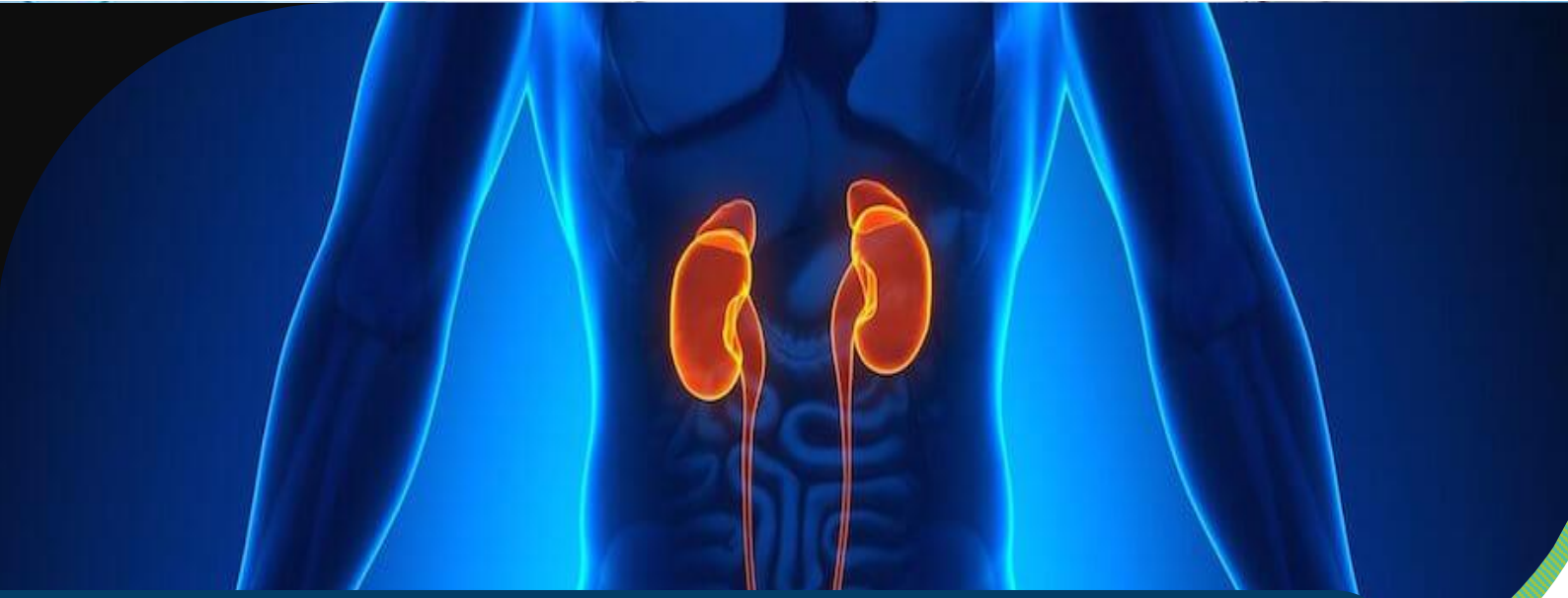

NU Rounds

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "**NU Rounds**" which contains latest and interesting news in the field of Urology.

Inside This Issue:

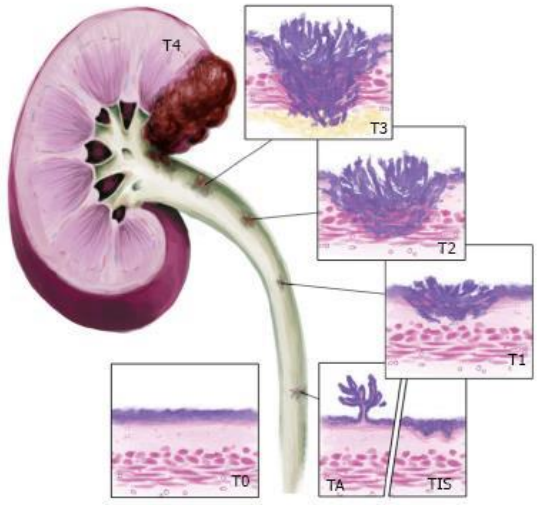
Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

Metastatic UTUC Has Low Chemosensitivity & Poor Prognosis



Upper urothelial carcinoma (UTUC) of the upper tract continues to metastasize and react poorly to chemotherapy, recent studies suggest.

In a case-series of 250 UTUC cases, 56 (22.4 percent) had stage IV illness. The most frequent metastatic locations involved lung (39.6%), remote lymph nodes (39.2%), bone (19.6%), liver (18.0%), and adrenal gland (7.2%). Just 1 in 10 patients reported recurrence in the surrounding region. 213 people were offered first-line chemotherapy for the procedure. Like gemcitabine plus cisplatin or cisplatin, gemcitabine, and paclitaxel or nab-paclitaxel, two-thirds obtained a cisplatin dependent treatment.

The average response rate was only 28.7 per cent, and the mean progression-free survival period was only 5.0 months, recorded in Urologic Oncology by Xinan Sheng, MD, Peking University Cancer Hospital & Institute, Beijing, China, and colleagues. Total time for survival was 18.0 months.

On multivariate analyses, a stage IV diagnosis, 3 or more sites of metastases, no response to chemotherapy, and 2 or fewer cycles of chemotherapy independently predicted poor overall survival.

According to Dr Sheng 's squad, UTUC is more prone to metastasize than recur locally, and is considered to have reduced chemosensitivity. They noted that these two characteristics should be taken into account in the care.

Source: Li X, Li S, Chi Z, et al. Clinicopathological characteristics, prognosis, and chemosensitivity in patients with metastatic upper tract urothelial carcinoma [published online ahead of print, 2020 Jul 9]. Urol Oncol. 2020;S1078-1439(20)30277-5.

Role of Enzalutamide on Survival in Non-metastatic, Castration-Resistant Prostate Cancer

INTRODUCTION

In 2018, the Food and Drug Administration approved enzalutamide, an oral androgen receptor inhibitor, in conjunction with androgen deprivation therapy for the diagnosis of non-metastatic, castration-resistant prostate cancer on the grounds of a slightly reduced probability of metastasis or mortality without radiographic worsening than with androgen deprivation therapy alone in the Phase 3 PROSPER study. Enzalutamide had a protection profile compatible with that seen in the prior Phase 3 tests. Enzalutamide was linked with better health-related quality of life and a slightly reduced likelihood of development of prostate-specific antigen (PSA), as well as greater duration of usage of concurrent antineoplastic treatment than androgen-deprivation treatment alone. Bone metastases was projected to grow in one third of non-metastatic, castration-resistant prostate cancer patients within 2 years of diagnosis. Since metastatic, castration-resistant prostate cancer is correlated with reduced average survival, declining quality of life, and elevated health-related expenses, a clinically important aim is to reduce time to metastasize. While there are positive improvements in preventing metastasis and preserving quality of life, sustained longevity has long been deemed a significant goal and the criterion for regulatory approval. Following 23 months of follow-up the results on total survival is incomplete at the primary study of the PROSPER experiment, with 165 fatalities during the experiment. For each diagnosis community the mean average survival was not met. Here the authors discuss results from the pre-specified third interim overall survival study.

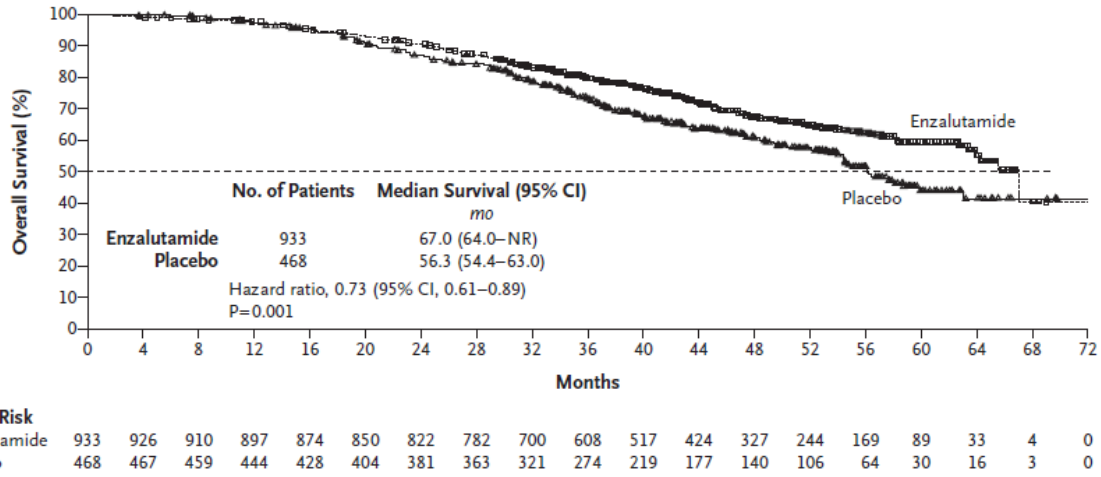
METHODS

In this double-blind, phase 3 trial, men with non-metastatic, castration-resistant prostate cancer (defined on the basis of conventional imaging and a PSA doubling time of ≤10 months) who were continuing to receive androgen-deprivation therapy were randomly assigned (in a 2:1 ratio) to receive enzalutamide at a dose of 160 mg or placebo once daily. Overall survival was assessed with a group sequential testing procedure and an O'Brien–Fleming–type alpha-spending function.

RESULTS

As of October 15, 2019, a total of 288 of 933 patients (31%) in the enzalutamide group and 178 of 468 (38%) in the placebo group had died. Median overall survival was 67.0 months (95% confidence interval [CI], 64.0 to not reached) in the enzalutamide group and 56.3 months (95% CI, 54.4 to 63.0) in the placebo group (hazard ratio for death, 0.73; 95% CI, 0.61 to 0.89; P = 0.001). The exposure-adjusted rate of adverse events of grade 3 or higher was 17 per 100 patient-years in the enzalutamide group and 20 per 100 patient-years in the placebo group.

Adverse events in the enzalutamide group were consistent with those previously reported for enzalutamide; the most frequently reported events were fatigue and musculoskeletal events.



No. at Risk																			
Enzalutamide	933	926	910	897	874	850	822	782	700	608	517	424	327	244	169	89	33	4	0
Placebo	468	467	459	444	428	404	381	363	321	274	219	177	140	106	64	30	16	3	0

CONCLUSIONS

Enzalutamide plus androgen-deprivation therapy resulted in longer average median survival than placebo plus androgen-deprivation therapy in men with nonmetastatic, castration-resistant prostate cancer and a steadily growing level of PSA. Enzalutamide-related chance of mortality was 27 per cent greater than placebo. Adverse effects coincided with the defined enzalutamide protection profile.

REFERENCE

Sternberg CN, Fizazi K, Saad F, et al. Enzalutamide and Survival in Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2020;382(23):2197-2206.

Guiding Opioid Administration by 3 Different Analgesia Nociception Monitoring Indices During General Anesthesia

INTRODUCTION

Apparently, optimum opioid titration during general anesthesia is also difficult, and the consequences of overdosing and underdosing with opioids are not well known. In recent years, numerous tracking systems have become available that measure the impact of analgesia during unconsciousness. Some tools produce an analgesic index dependent on physiological variables that are calculated by different techniques. Past findings have demonstrated that these tracking systems have been able to sense uniform unpleasant sensations and therefore display improvements in the equilibrium between nociception – antinocception between patients. Many reports have studied the efficacy of these tools in the clinical environment, but the impact of intraoperative analgesia driven by such tools has not been consistently measured at the same period. In this pilot research they examined mainly the theory that opioid titration utilizing specific analgesic tracking instruments or clinical sign instructions contributes to varying levels of opioid intake intraoperatively.

The investigators also tried to explore how this opioid instruction was associated with an altered release of stress hormones or discrepancies in the follow-up era. This study should hereby contribute to the question of whether the monitors are already optimized for routine use during general anesthesia for surgery. For this analysis, the investigators contrasted opioid instructions from the Surgical Pleth Index (SPI), obtained by photoplethysmography, the Pupillary Pain Index (PPI) calculated by visual pupillometry, the Nociception Level (NoL) multiparameter score, and a control group in which only clinical pain indicators were listed.

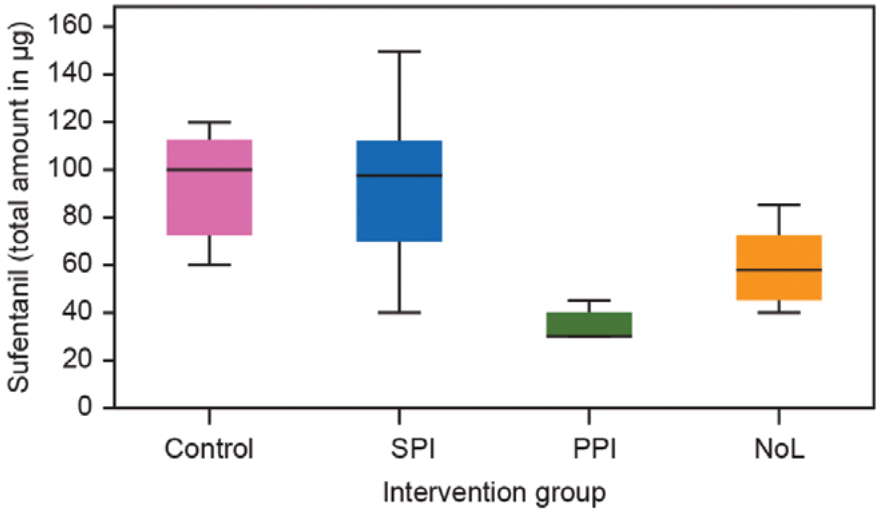
METHODS

Forty-eight patients undergoing radical retropubic prostatectomy with sevoflurane/ sufentanil anesthesia were randomly assigned into 4 groups and received sufentanil guided either by 1 of 3 analgesia monitoring devices (Surgical Pleth Index [SPI], Pupillary Pain Index [PPI], Nociception Level [NoL]) or by clinical judgment (control). The primary end point was intraoperative sufentanil consumption. Adrenocorticotropic hormone (ACTH) and cortisol were measured at 4 time points during the day of surgery. Data were analyzed by Kruskal–Wallis and Mann–Whitney U tests and by mixed model and area under the curve (AUC) analyses for group comparisons and time effects of stress hormones.

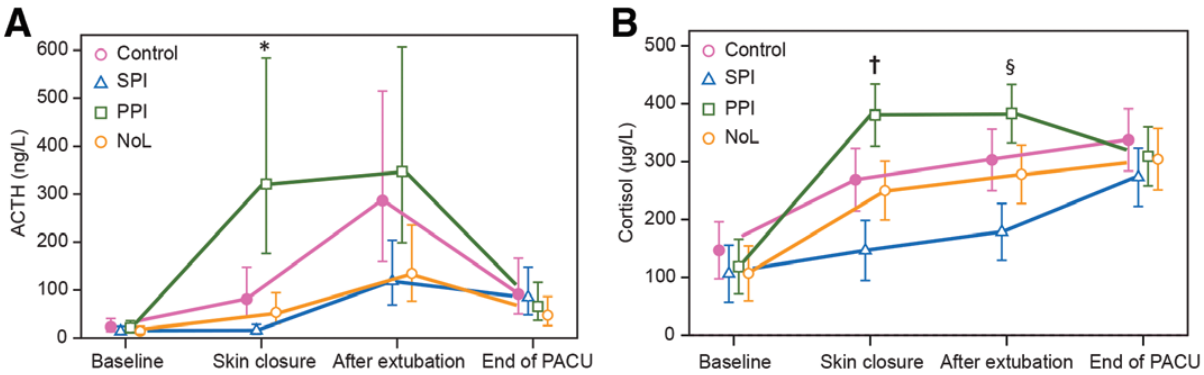
RESULTS

The total amount of sufentanil administration (μg · kg−1 · minute−1 · 10−3) differed between the groups (median [quartiles]: control = 5.6 [4.4–6.4], SPI = 7.2 [4.8–8.4], PPI = 2.0 [1.8–2.9], NoL = 3.8 [3.3–5.1]; PPI versus SPI, −5.1 [−6.6 to −1.3], P < .001; NoL versus SPI, −3.0 [−5.2 to 0.2], P = .024;

control versus SPI, −1.6 [−3.7 to 1.7], P = .128; NoL versus PPI, 1.7 [0.6–3.4], P < .001; control versus PPI, 3.4 [2.0–4.6], P < .001; control versus NoL, 1.6 [−0.2 to 3.3], P = .017) (Hodges–Lehmann estimator [99% confidence interval {CI}], P values). The AUC analysis indicated differences among groups in cumulative ACTH levels (ng · liter−1 · minute, natural logarithm (ln)-transformed data) of NoL versus PPI (−1.079 [−1.950 to −0.208], P = .001) and PPI versus SPI (1.192 [0.317–2.068], P = .001), as well as differences in cortisol levels (µg · liter−1 · minute) for PPI versus SPI (46,710 [21,145–72,274], P < .001), NoL versus SPI (27,645 [3163–52,126], P = .003), and control versus SPI (31,824 [6974–56,675], P = .001) (differences in means [99% CI], P value). Secondary end points (postoperative recovery, pain level, and analgesia medication) showed no differences



Sufentanil consumption.



Release of stress hormones. Plasma levels of (A) ACTH and (B) serum cortisol at 4 different time points during the day of surgery

CONCLUSION

The method of nociception control of analgesia influenced the overall volume of prescribed sufentanil. Lower doses of sufentanil have been linked with decreased endocrine stress response within the PPI population. SPI titration induced no decrease in opioid relative to regulation but was correlated with a decreased reaction to endocrine stress.

REFERENCE

Funcke S, Pinnschmidt HO, Wesseler S, et al. Guiding Opioid Administration by 3 Different Analgesia Nociception Monitoring Indices During General Anesthesia Alters Intraoperative Sufentanil Consumption and Stress Hormone Release: A Randomized Controlled Pilot Study. Anesth Analg. 2020;130(5):1264-1273.

MICRO KNOWLEDGE ACADEMY

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