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Genetic Factors and Prostate Cancer Conversion From Active Surveillance to Treatment HGG Advances

The aim of this study was to determine if there is an association between genetic factors and the conversion from active surveillance (AS) to active treatment for prostate cancer. Among the 5222 patients followed, all of whom initially elected for AS, 18 variants associated with conversion were detected, 15 of which were not previously associated with prostate cancer. The authors specifically found two genes associated with conversion (MAST3, P = 6,9x10-7 and GAB2, P = 2,0x10-6). A previously validated 269-variant genetic risk score for prostate cancer was also positively associated with conversion. These data suggest germline genetics may help guide the decision-making process regarding AS or active treatment for prostate cancer.

MV140 Vaccine May Prevent Recurrent Urinary Tract Infections

MV140, a sublingual vaccine of whole-cell inactivated bacteria, may prevent urinary tract infections (UTIs) in women with recurrent UTIs, according to new trial findings. The inactivated bacteria in the vaccine are O6:H49 V121 Escherichia coli, capsular type 3 V113 Klebsiella pneumoniae, V125 Enterococcus faecalis, and V127 Proteus vulgaris.



In the double-blind trial (ClinicalTrials.gov number, NCT02543827), investigators randomly assigned 240 women (aged 18-75 years) with at least 3 UTIs per year to 3 or 6 months of treatment with MV140 or placebo. The sublingual route was chosen for delivery of the MV140 vaccine because it has been shown to induce both systemic and mucosal immunity, including in the genitourinary tract.

FDA approves Pluvicto for metastatic castrationresistant prostate cancer FDA Approved Drugs

On March 23, 2022, the Food and Drug Administration approved Pluvicto (lutetium Lu 177 vipivotide tetraxetan, Advanced Accelerator Applications USA, Inc., a Novartis company) for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

On the same day, the FDA approved Locametz (gallium Ga 68 gozetotide), a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions, including selection of patients with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated. Locametz is the first radioactive diagnostic agent approved for patient selection in the use of a radioligand therapeutic agent. Patients with previously treated mCRPC should



be selected for treatment with Pluvicto using Locametz or another approved PSMA-11 imaging agent based on PSMA expression in tumors. PSMA-positive mCRPC was defined as having at least one tumor lesion with gallium Ga 68 gozetotide uptake greater than normal liver. Patients were excluded from enrollment if any lesions exceeding certain size criteria in the short axis had uptake less than or equal to uptake in normal liver efficacy was evaluated in VISION (NCT03511664), a randomized (2:1), multicenter, open-label trial that evaluated Pluvicto plus best standard of care (BSoC) (n=551) or BSoC alone (n=280) in men with progressive, PSMApositive mCRPC. All patients received a GnRH analog or had prior bilateral orchiectomy. Patients were required to have received at least one AR pathway inhibitor, and 1 or 2 prior taxane-based chemotherapy regimens. Patients received Pluvicto 7.4 GBg (200 mCi) every) weeks for up to a total of 6 doses plus BSoC or BSoC alone.

The trial demonstrated a statistically significant improvement in the primary endpoints of overall survival (OS) and radiographic progression-free survival (rPFS). Hazard ratio (HR) for OS was 0,62 (95% CI: 0,52, 0,74; p<0,001) for the comparison of Pluvicto plus BSoC versus BSoC. Median OS was 15,3 months (95% CI: 14,2, 16,9) in the Pluvicto plus BSoC arm and 11.3 months (95% CI: 9.8, 13.5) in the BSoC arm, respectively.

Interpretation of the magnitude of the rPFS effect was limited due to a high degree of censoring from early drop out in the control arm. The most common adverse reactions (>20%) occurring at a higher incidence in patients



receiving Pluvicto were fatigue, dry mouth, nausea, anemia, decreased appetite, and constipation.

The most common laboratory abnormalities that worsened from baseline in >30% of patients receiving Pluvicto were decreased lymphocytes, decreased hemoglobin, decreased leukocytes, decreased platelets, decreased calcium, and decreased sodium. Treatment with Pluvicto may result in risk from radiation exposure, myelosuppression, and renal toxicity. The safety follow-up duration in VISION was not su,cient to capture late radiationassociated toxicities. The recommended Pluvicto dose is 7.4 GBq (200 mCi) intravenously every) weeks for up to) doses, or until disease progression or unacceptable toxicity.

Choosing the Most Elcacious and Safe Oral Treatment for Idiopathic OAB European Urology Focus

This systematic review and meta-analysis aimed to evaluate which oral therapies are most efficacious and safe for the treatment of overactive bladder (OAB). A total of 54 studies met inclusion criteria — all randomized controlled trials in idiopathic OAB with oral antimuscarinics or beta-3 agonists. Oxybutynin 5 mg immediaterelease 3 times daily was the most effective agent at reducing incontinence episodes per 24 hours relative to placebo followed by solifenacin 10 mg extended-release. Imidafenacin 0,5 mg/day and solifenacin 5 mg and 10 mg extendedrelease were most efficacious for decrease in micturition



episodes, and fesoterodine and solifenacin most efficacious for reducing urgency episodes. The highest rate of dry mouth was associated with oxybutynin 5 mg immediate-release and lowest with beta-! agonists, which were similar to placebo. Constipation was common to all OAB medications (except for vibegron 100 mg). Mirabegron 25 mg had the highest rates of diarrhea and tolterodine 4 mg the highest rates of blurred vision.

Overall, efficacy across symptom relief were similar for antimuscarinics and beta-3 agonists with somewhat variable rates of adverse events.

Risk of Cognitive Effects in Comorbid Patients With Prostate Cancer Treated With Androgen Receptor Inhibitors

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Prostate cancer (PC) is primarily a disease of older men. As the risk of neurocognitive decline increases as people age, cognitive dysfunction is a potential complication in men with PC, imposing detrimental effects on functional independence and quality of life. Importantly, risk of cognitive decline may increase with exposure to androgen deprivation therapy and other hormonal therapies. Particular consideration should be given to patients with castrationresistant PC (CRPC), many of whom require continuous, long-term androgen deprivation therapy combined with a second-generation androgen receptor inhibitor. Non-comparative evidence from interventional trials of androgen



receptor inhibitors in men with non-metastatic CRPC suggests differential effects on cognitive function and central nervous system-related adverse events within this drug class. Drugdrug interactions with concomitant medications for chronic, non-malignant comorbidities differ among ARIs and thus may contribute further to cognitive impairment. Hence, establishing baseline cognitive function is a prerequisite to identifying subsequent clinical decline associated with androgen receptor-targeted therapies. Although brief, sensitive screening tools for cancer-related cognitive dysfunction are lacking, mental status can be ascertained from the initial medical history and neurocognitive examination, progressing to more in-depth evaluation when impairment is suspected. On-treatment neurocognitive monitoring should be integrated into regular clinical follow-up to preserve cognitive function and guality of life throughout disease management. This review summarizes the multiple factors that may contribute to cognitive decline in men with CRPC, awareness of which will assist clinicians to optimize individual treatment. Practical, clinic-based strategies for managing the risks for and symptoms of cognitive dysfunction are also discussed.

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