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HIGHLIGHTS OF THE

5th Belgian Multidisciplinary Meeting on Urological Cancers (BMUC)

BMUC

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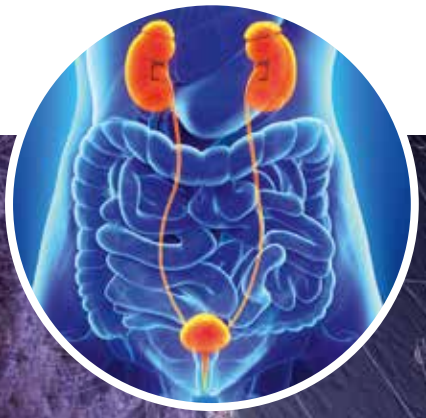

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COLOPHON

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Special editions are distributed amongst medical specialists in Belgium, such as oncologists, surgeons and radiotherapists.

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5th Belgian Multidisciplinary Meeting on Urological Cancers (BMUC)

Interview with Professor Sylvie Rottey
(BMUC President)

2018 Marked the 5th edition of the Belgian Multidisciplinary Meeting on Urological Cancers (BMUC). This meeting is a collaboration between the BSMO, BVU/SBU, and BVRO/ABRO and took place on 9 and 10 March 2018. We invited Prof. Sylvie Rottey *(BMUC President)* to share her thoughts on the achievements of BMUC and of the future plans with the organization.

FOR THOSE NOT FAMILIAR WITH HOW THE SOCIETY WAS FOUNDED, CAN YOU SHARE THE INSPIRATION FOR AND FOUNDING OF THE SOCIETY?

About 5 years ago the idea was raised at the BSMO to organise a meeting bringing together urologists, radiation oncologists and medical oncologists involved in the management of urological cancers. All these specialties are very much involved in the care for urological cancer patients, especially in prostate cancer. We set up a scientific committee consisting of 3 medical oncologists, 3 urologists and 3 radiation oncologists coming from the three established organisations/societies in their field of expertise. We had some meetings to discuss the content and formula of such a meeting and that's how we started.

The main goal of BMUC was to combine the different multidisciplinary specialties. This multidisciplinarity is key for BMUC as we strive to have a platform allowing for in depth discussions and brainstorms on new data and emerging clinical insights in the field of urological cancer.

WHAT IS THE ADDED VALUE OF MULTIDISCIPLINARITY IN MANAGING UROLOGICAL CANCERS?

Especially for patients with prostate cancer, but also for patients with other urological cancers, there are often different treatment options, all supported by level 1 evidence. In these cases it is important to discuss the patient file and the patient comorbidities with the entire medical team. If there are different options, the patient has the right to hear the

Active surveillance in prostate cancer

Presented by: A. de la Taille
(CHU Henri Mondor, assistance publique des hôpitaux de Paris, Paris, France)

Data regarding the natural history of prostate cancer (PCa) disease confirm the clinical insignificance of low-grade prostate cancer, which is associated with scant or no metastatic dissemination. Active surveillance (AS) is a conservative management approach, conducted for patients with "low-" or "favorable-risk" disease, which avoids long-term adverse effects on the patient's quality of life. In a lecture during BMUC 2018, **Prof. de la Taille** explained why he thinks that AS is an option that we need to consider and why we should discuss this with the patient before the biopsy is taken.

INTRODUCTION

Prospective trials evaluating the effect of prostate-specific-antigen (PSA) screening indicate that this approach decreases the incidence of metastatic disease with 41% and reduces the mortality rate by 20%. However, the number needed to treat to prevent 1 PCa death is 48. This indicates that there is a significant over diagnosis with this PSA approach.[1] The vast majority of men diagnosed with localized PCa in the US opt for active treatment, indicating the significant over-treatment in PCa. This is not surprising as it is not always easy to convince your patients to opt for AS if something abnormal is seen on his biopsy. Therefore it is important for physicians to come up with strong arguments in support of AS. The main objective of AS is reducing the overtreatment of clinically insignificant disease and reserve treatment for patients whose disease is reclassified as higher risk after a period of observation within the window of curability. This raises three main questions:

1) Can we determine who has insignificant disease?
2) What constitutes reclassification and need for intervention?
3) How do we avoid that the window of curability is missed?

WHO HAS INSIGNIFICANT DISEASE?

To determine who has insignificant disease we must first take a closer look at the inclusion and exclusion criteria of the clinical trials evaluating AS in PCa. A systematic review of these studies indicates that the inclusion criteria differ between the trials. There are differences in the maximum Gleason score (up to 6, or 7), the maximum number of positive cores (2 to 3), the PSA level (ranges from below 10 to below 20), the percentage of cancer involvement per core, etc...[2] Based on the different studies, nine criteria for AS eligibility were established:

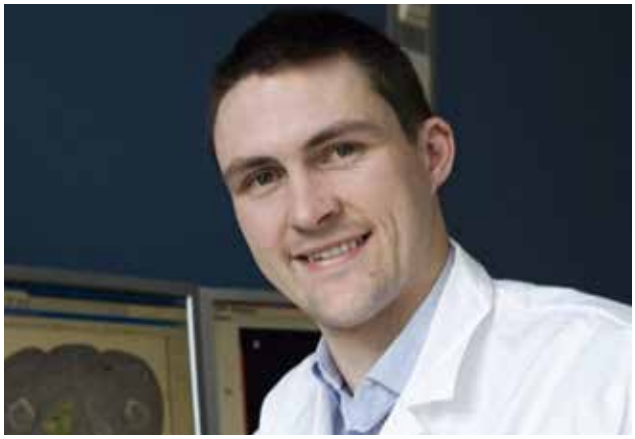
1. Histologically proven adenocarcinoma of the prostate
2. Men should be fit for curative treatment
3. PSA level at diagnosis ≤ 10 ng/mL
4. PSA density less than 0.2
5. Clinical stage T1C or T2
6. Adequate biopsy sampling
7. Gleason score 3+3= 6
8. <2 positive biopsy cores
9. Participants must be willing to attend the follow-up visits

With respect to pathology, the following exclusion criteria for AS were set: predominant ductal carcinoma (including pure intraductal carcinoma), sarcomatoïd carcinoma, small cell carcinoma, EPE or LVI in needle biopsy and perineural invasion.

What about follow-up? The different studies included in the systematic review of *Thomson et al.* have a median

What about oligometastatic therapy in prostate cancer?

Presented by: Prof. P. Ost, MD, PhD *(University Hospital Ghent)* and Prof. B. Tombal, MD, PhD *(Cliniques Universitaires St-Luc, Brussels)*



In a pro and con debate, **Prof. Piet Ost** and **Prof. Betrand Tombal** discussed the potential of metastasis-directed therapy for patients with oligorecurrent prostate cancer.

CASE PRESENTATION

To set the scene for the discussion, *Prof. Ost* started with the presentation of a typical clinical case. A 61 year old male presents with a PSA of 5.3 ng/ml. An MRI and biopsy reveal a Gleason 3+4=7 in 6/21 cores. The patient underwent a robot-assisted radical prostatectomy (RARP) with negative margins and the tumor was staged as pT3a 4+3=7, N0. Unfortunately, the patient relapses and receives salvage radiotherapy, but after some time his PSA starts to rise again. This is what happens in about 30% of all localized prostate cancer patients. What we used to do in these patients was conventional imaging. However, if the PSA is below 10 and you perform a bone scan, you will most likely end up with a negative result. The question now is: *"How do you treat this guy?"*. The majority of the BMUC attendees deemed it best to 'wait and see' in this patient (observation and ADT at time of progression). Nowadays, conventional imaging has largely been replaced by more modern imaging tools, like PET PSMA. This patient also underwent PSMA imaging and he turned out to have a solitary nodal lesion. When asked how to treat this patient now, a shift was seen in the audience. In fact, 66% of the audience indicated that local, metastasis-directed therapy (MDT) would be the best option in this case. *Prof. Ost* build further on the case and asked if the treatment would change if the patient had a solitary bone metastasis instead of a single node lesion? In this scenario, 60% of attendees still opted for MDT.

> The current EAU guidelines state that it is not recommended to routinely offer ADT to asymptomatic prostate cancer patients with a biochemical recurrence.

CLINICAL DATA IN SUPPORT OF MDT

The current EAU guidelines state that it is not recommended to routinely offer an androgen-deprivation therapy (ADT) to asymptomatic prostate cancer patients with a biochemical recurrence. They also argue against the use of ADT in patients with a PSA doubling time above 12 months.[1] These 'wait and see' recommendations are backed by the results of a recent Australian trial (TOAD) demonstrating that there is no advantage of immediate ADT over delayed ADT in prostate cancer patients with biochemical recurrence.[2]

Therapeutic sequencing in prostate cancer

Presented by: A. de la Taille
(CHU Henri Mondor, assistance publique des hôpitaux de Paris, Paris, France)

Over the last 10 years we have witnessed a revolution in the treatment of metastatic castration-resistant prostate cancer (mCRPC). The introduction of several new therapeutic modalities had a significant impact on the overall survival (OS) of these patients. Whereas the median OS for patients with mCRPC was only 24.2 months back in 1997, this has increased to 39.4 months in a patient cohort from 2007 to 2013. This represents an increase in the median OS with 1.5 years.[1] Currently, patients with mCRPC have 6 different drugs at their disposal. The question now is: "how to best sequence these different options?"

mCRPC: FIRST-LINE CHOICES

A first question that needs to be answered in the light of first-line therapy for mCRPC is *"when to start therapy?"* Is it best to wait with the treatment, or do patients benefit from early treatment? Blood prostatic-specific antigen (PSA) testing allows the identification of CRPC before clinical metastases or symptoms occur, providing a long diagnostic lead time in many patients. Several hormonal manipulations are directed towards lowering the PSA in patients. For example, adding bicalutamide was shown to be associated with a PSA response in 20% of patients, but did not impact the overall survival (OS). Also, the PSA decrease obtained with this approach is usually short lived.[2] Changing the LHRH agonist can also lead to a PSA response, but also has no impact on progression-free survival (PFS) or OS. A recent study looking into early treatment initiation of mCRPC is of the TERRAIN trial. In this study, 375 asymptomatic or mildly symptomatic mCRPC patients who did not receive prior chemotherapy were randomized to receive either enzalutamide, or bicalutamide.[4] In this study, enzalutamide was associated with a 10 month improvement in PFS compared to bicalutamide (median PFS 15.7 *vs.* 5.8 months; HR[95CI]: 0.44 [0.34-0.57]; p< 0.0001).[5] Similar results were obtained in the phase II STRIVE trial, where enzalutamide significantly reduced the risk of prostate cancer progression or death compared with bicalutamide in patients with non-metastatic or metastatic CRPC.[5] Now what do the guidelines say? The French national guidelines state that there is level 1 evidence that hormonal manipulations are not recommended. Second, it is advised to stop anti-androgen if prescribed and not to wait for potential withdrawal syndrome before changing therapy (go directly for newer agents).[6] The EAU guidelines recommend a similar approach in this setting.[7]

> The introduction of several new therapeutic modalities had a significant impact on the OS of mCRPC patients.

A second question that was raised is *"do we need to use chemotherapy, or prefer novel hormonal therapy?"* The 2018 EAU guidelines for mCRPC indicate that the first parameter to assess is the ECOG performance status

Congress highlights 2018

Presented by: Dr. D. De Maeseneer *(University Hospital Ghent)*, Dr. F-X. Otte *(Institut Jules Bordet, ULB Brussels)* and Dr. S. Albisinni *(Hôpital Erasme, ULB Brussels)*

ASCO GU represents one of the yearly highlights in the field of genitourinary cancer. During BMUC 2018 the key data presented at this meeting were summarized.

THE UROLOGIST

Dr. Simone Albisinni gave an overview of the ASCO GU highlights from an urologist point of view. He selected three studies: POUT, SPARTAN and PROSPER.[1-3]

The POUT study enrolled 26,261 patients with histologically confirmed stage pT2–T4, N0–N3 upper tract urothelial cancer following radical nephroureterectomy and removal of any obvious nodal disease and with a negative postoperative CT scan. Within 90 days postsurgery, patients were randomized (1:1) to receive 4 cycles of gemcitabine-based chemotherapy or surveillance. The choice of chemotherapy partner (cisplatin or carboplatin) depended on glomerular filtration rate alone: patients with a glomerular filtration rate >50 mL/min were given cisplatin, and if the glomerular filtration rate was 30 to 49 mL/min, they were given carboplatin. Patients who were deemed unfit for cisplatin based on other comorbidities were not allowed to enter the trial. All patients received supportive care. In total, 261 patients were recruited in the trial with a mean age of 69 years. Twenty-nine percent of patients had pT2 disease, 71% had pT3-4 disease and 91% was N0. Two thirds of patients were eligible for cisplatin and the remaining third was treated with carboplatin.

The two blockbuster studies presented at ASCO GU 2018 were SPARTAN and PROSPER.

Overall, 64% received the four planned chemotherapy doses.

For the primary endpoint of 3-year disease-free survival (DFS), chemotherapy had a strong benefit: 71% in the chemotherapy group *vs.* 54% in the surveillance group (HR[95%CI]: 0.49[0.31-0.76]; p= 0.001). Chemotherapy was significantly superior to surveillance in subgroups of nodal involvement, planned type of chemotherapy, microscopic margin, and disease stage (with a similar hazard ratio for benefit seen across all subgroups). The Metastasis-free survival at 2 years also favored adjuvant chemotherapy (74% *vs.* 60%; p< 0.001). With respect to overall survival (OS), a trend towards superiority of chemotherapy was seen (HR: 0.55), but these data were still immature. Grade 3 or higher toxicities were reported in 53.2% of the chemotherapy recipients and in 13.5% in the surveillance group. The most frequent grade 3/4 toxicities with chemotherapy were neutropenia (24.3% with gemcitabine/cisplatin and 37.3% with gemcitabine/carboplatin); nausea (2.9% and 7.8%, respectively); vomiting (1.4% and 9.8%); and febrile neutropenia in 5.7% and 7.8%.[1]

The two blockbuster studies presented at ASCO GU 2018 were PROSPER and SPARTAN. The SPARTAN study enrolled 1,207 men with non-metastatic castration-resistant prostate cancer (CRPC) who stopped responding to androgen-deprivation therapy and were at high risk of metastasis, with a PSA doubling time of 10 months or less, and randomized them in a 2:1 ratio to receive oral apalutamide *vs* placebo added to ongoing

A new treatment paradigm in metastatic bladder cancer: chemotherapy and immune checkpoint inhibition in 2018

Presented by: Ronald de Wit; MD, PhD
(Erasmus MC Cancer Institute; Rotterdam, The Netherlands)

The positive outcome of several randomized clinical trials evaluating immune checkpoint inhibitors in patients with metastatic bladder cancer dramatically changed the treatment paradigm in this setting. In his presentation, **Prof. de Wit** summarized the clinical data generated with PD-1/PD-L1 inhibitors in this setting, but he kicked off by summarizing the historical results obtained with chemotherapy in patients with metastatic urothelial cancer.

CHEMOTHERAPY IN METASTATIC UROTHELIAL CANCER

Cisplatin-based combination chemotherapy has long been the standard of care for patients with metastatic bladder cancer. The landmark of systemic chemotherapy in advanced urothelial cancer was the development of the combination of methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) at the Memorial Sloan-Kettering Cancer Center (MSKCC) in 1983.[1] Its activity against urothelial cancer has been considerable with response rates of >50%, 3-year survival of 20-25% and a median survival of >1 year.[1-3] Furthermore, MVAC was shown to be superior to single-agent cisplatin in a randomized trial establishing the role of combination chemotherapy in advanced bladder cancer.[4] In 2000, *von der Maase et al*. established gemcitabine-cisplatin as an alternative for MVAC, yielding a comparable overall survival (OS) with a more favorable safety profile.[5] Several studies have evaluated the substitution of cisplatin by carboplatin, but carboplatin-based chemotherapy has generally produced inferior results (both in RR and median OS) to cisplatin-containing combinations. Two randomized phase II studies showed inferior RR with carboplatin as opposed to cisplatin-based chemotherapy indicating the inferiority of carboplatin-based chemotherapy.[6,7] In the EORTC 30986 study, gemcitabine-cisplatin was compared to M-CAVI. In this trial, both regimens were effective, but it became clear that for both regimens the response rate dropped with rising toxicity in patients with more adverse factors (e.g. visceral metastasis, poor performance status, renal impairment, etc.).[8] This finding set the treatment paradigm for cisplatin-unfit urothelial cancer patients. For elderly patients that are basically healthy, gemcitabine-cisplatin was the preferred option. In unfit patients (comorbidities, GFR rate 30-60 ml/min, unfit performance status [PS]), gemcitabine-carboplatin was the treatment of choice. The third group consists of unfit patients with additional adverse prognostic factors. For them, it is unlikely that chemotherapy will have any benefit.[8]

The clinical efficacy of chemotherapy in the second-line therapy of metastatic bladder cancer is limited (overall response rate [ORR] of only 12%). In the US the use of docetaxel in second-line is widespread, while in the EU vinflunine is used in some countries.

IMMUNE CHECKPOINT INHIBITION IN METASTATIC UROTHELIAL CARCINOMA

Keynote-045 is an open-label, international, phase 3 trial including 542 patients with advanced urothelial cancer with an ECOG PS of 0-2, that had recurred

Biomarkers in the era of immunotherapy: lessons learned from lung, bladder and kidney cancer

Presented by: M. Kockx, MD, PhD *(HistoGeneX)*

Immune checkpoint inhibition has rapidly changed the treatment paradigm of several cancer types, including non-small cell lung cancer (NSCLC), melanoma, urothelial cancer and renal cell carcinoma (RCC). Lots of research is currently focused on the search for biomarkers that can predict whether a patients will respond to immunotherapy or not. During his lecture at BMUC 2018, **Dr. Mark Kockx**, pathologist and founder of HistoGeneX shared his views on this matter.

WHAT CAN PATHOLOGY TELL US?

Tumors are developing ecosystems with clinical interactions between cancer cells and the microenvironment. When looking at tumor samples as a pathologist you notice that some tumors have inflamed characteristics, while in other tumors, there is hardly any inflammation in the stroma. A good way to visualize this is a dual staining for pancytokeratin (staining a marker for epithelial differentiation) and CD8. In doing so you can see whether the immune cells have penetrated the tumor or not. If this is the case you have an indication that the immune system is still capable to move into the tumor strands and attack the tumor cells. The presence of these CD8+ cytotoxic T cells in the tumor is essential given their central role in the anti-tumor immune response. In many cancers, this CD8 infiltration is suboptimal. What is the reason for this? Let us go back to basics: the tumor microenvironment is a pathologically active niche that shapes tumor evolution. The immune system naturally identifies and eliminates cancerous cells. However, the tumor exploits a number of molecular pathways to proliferate and evade the immune system. Chen and Mellman brought all this information together in a rational map of the cancer-immunology interface. The result of this effort was a seminal article that continues to provide an intellectual framework for cancer immunotherapy research around the world.[1]

> The presence of CD8-positive cytotoxic T-cells in the tumor is essential given their central role in the anti-tumor immune response.

Chen and Mellman demonstrated that the generation of an anti-cancer immune response is a cyclic process that can be self-propagating, leading to an accumulation of immune-stimulatory factors that in principle should amplify and broaden T cell responses.[1] First, neo-antigens created by oncogenesis are released and captured by antigen presenting cells (APCs) for processing (*step 1*). For this step to yield an anticancer T cell response, it must be accompanied by immunogenic signals (e.g. pro-inflammatory cytokines, factors released by dying tumor cells). In the second step, APCs present the tumor-associated antigens to T-cells via MHC molecules (*step 2*). When a T cell encounters an antigen-presenting cell to which it can bind, it will initiate an activation program (*step 3*, priming and activation). This activation requires three sets of signals: a cascade generated by the T-Cell Receptor (TCR), a cascade generated through the costimulatory molecules (B7:CD28) and cytokines. This T-cell activation is regulated by immune checkpoints: costimulatory and inhibitory interactions that protect against auto-immunity and exces-

What do we still need to know about the treatment of RCC?

Presented by: L. Albiges, MD, PhD
(Institut Gustave Roussy, Paris, France)

The introduction of immune checkpoint inhibitors dramatically changed the treatment paradigm of patients with advanced RCC. In her lecture, **Dr. Laurence Albiges** gave an overview of real-life data with nivolumab and gave her insights on how the first-line treatment landscape of patients with advanced RCC will evolve in the years to come.

MAKING THE MOST OF THE AVAILABLE OPTIONS

The real-world GETUG-AFU 26 NIVOREN study evaluates the performance of nivolumab in daily clinical practice. In this prospective, single arm, French multicenter study, 729 metastatic clear-cell RCC patients were treated with 3 mg/kg Q2W. All patients in the study failed at least 1 line of VEGF inhibition. The primary endpoint of the study was the incidence of high-grade (3-5) adverse events, but the study also evaluated overall survival (OS), progression-free survival (PFS) and overall response rate (ORR) as secondary objectives. The presented analysis is based on the data from the first 528 patients enrolled in the study (median follow-up 12 months).[1] In total, 15% of these patients had an ECOG PS 2 and 26.5% had poor IMDC prognosis features. About half of patients received one prior line of treatment, but 25% of patients received nivolumab in 4th line, or beyond. Furthermore, 14% had brain metastases, one quarter received prior everolimus and one third had a GFR of less than 60 ml/min. After a median follow-up of 13.3 months, 71.2% of patients had discontinued treatment: 50.4% due to progression, 9.7% due to toxicity and 6.6% due to death. The median duration of therapy was 4.2 months (median of about 10 infusions). Treatment-related grade 3-4 adverse events were seen in 14.6% of patients and 4 patients had a (suspected) treatment-related death. The confirmed ORR was 18.5% (18.1% partial responses), but 47.2% of patients had upfront progressive disease. The median PFS was 4.0 months, while the median OS was 18.6 months. After 1 year, two thirds of patients were still alive (66.3%). Looking at specific subgroups, it is not surprising to see that PS 2 patients do worse with a median OS of 10.8 months *vs.* 18.6 months in PS 0/1 patients ($p < 0.0001$). More surprisingly, the number of previous therapy lines did not seem to have an impact on the OS with nivolumab: median OS in patients with 2 or less previous treatment lines 18.6 months *vs.* 16.2 months for patients with more than 2 previous treatment lines. In patients who previously received everolimus, the outcome on nivolumab was worse than on patients who did not (median OS 15.9 *vs.* 18.6 months; $p = 0.0442$). Importantly, patients with a poor kidney function derived the same benefit of nivolumab than patients with an adequate renal function ($p = 0.8560$). In *Table 1*. The results of this real-world study are compared to the results obtained in the pivotal Checkmate 025 study.[1,2] This comparison shows that in real-life, a shorter OS is obtained, with a lower response rate and a higher risk of upfront disease progression. Of note, about 40% of patients in the real-life study received nivolumab beyond progression, indicating that they also received some degree of benefit from the treatment.

> Real-life data with nivolumab in RCC show a shorter OS than in clinical trials, with a lower response rate and a higher risk of upfront disease progression.

Several open questions on the routine use of nivolumab remain to be answered. First of all, when should we use nivolumab? Is it best to use it in second-line, or third line? To address this question, the GETUG AFU

The continuously evolving treatment landscape in renal cell carcinoma

Presented by: Viktor Grünwald, MD, PhD
(Hannover medical School, Hannover, Germany)

As a result of intensive fundamental and clinical research the treatment of localized and advanced renal cell carcinoma is constantly changing and improving. At the 2018 annual BMUC meeting, **Prof. Viktor Grünwald** gave an overview of the recent findings in clinical research and of the approaches that are expected to change the management of renal cell carcinoma (RCC) in the future.

ADJUVANT THERAPY FOR RCC

A number of clinical studies recently evaluated whether adjuvant therapy could improve the treatment of patients with locoregional RCC. This includes three randomized phase 3 studies on adjuvant treatment with tyrosine kinase inhibitors (TKIs) in patients with resected high-risk RCC (ASSURE, PROTECT, S-TRAC).[1-4] Unfortunately, only S-TRAC had a positive outcome in terms of its primary endpoint of disease-free survival (DFS; HR[95%CI]: 0.76[0.59-0.98]; p= 0.03).[1] Moreover, since S-TRAC failed to show an overall survival (OS) benefit of its investigational drug sunitinib versus placebo (HR[95%CI]: 1.01[0.72-1.44]) one can argue about the added value of adjuvant TKIs in mRCC. As a result, the Committee for Medicinal Products for Human Use of the European Medicines Agency refused to recommend sunitinib as adjuvant treatment in high-risk RCC.

> It seems unlikely that one fixed TKI dose accomodates the needs of all RCC patients. Individual dosing according to the tolerability of the patients rather seems the key to success.

Adjuvant treatment with immune checkpoint inhibitors has shown positive results in melanoma, where the outcome of these inhibitors has been investigated for more than a decade.[5] Currently, adjuvant immunotherapy is also being tested in RCC. For instance, the randomized phase 3 CheckMate 914-study compares the efficacy and safety of CTLA-4 inhibitor ipilimumab plus PD-1 inhibitor nivolumab with placebo in patients with resected high-risk, localized RCC. The primary outcome of the study is DFS, and secondary outcomes include OS and toxicity. A second example is the randomized phase 3 IMmotion 010-study evaluating the outcome of adjuvant treatment with PD-L1-inhibitor atezolizumab or placebo.

MULTIPLE OPTIONS FOR THE TREATMENT OF METASTATIC RCC

The availability of TKIs has clearly improved the survival of RCC patients. Grünwald: *"However, it took us a long time to realize that the outcome of many TKIs is similar. For instance, the efficacy of sunitinib and pazopanib has been shown to be virtually equal.[6] Furthermore, in my view we have been reluctant to learn how to optimally use TKIs. For instance, it seems unlikely that one fixed dose of TKIs accommodates the needs of all patients. Individual dosing according to the tolerability of the patient rather seems to be the key to success."*[7]

At present, over ten different drugs are available for the treatment of metastatic RCC (mRCC). This includes first, second and third generation TKIs, as well as the PD-1 inhibitor nivolumab, the VEGF inhibitor bevaci-

Penile cancer

Presented by: M. Albersen, MD, PhD
(University hospital Leuven, Belgium)

It has become of yearly tradition of BMUC to put a tumor type in the spotlight that is often overlooked at (inter)national symposia. This year, **Prof. Maarten Albersen** gave an overview of the current treatment landscape of penile cancer.

INTRODUCTION

Penile cancer is a rare cancer type that is associated with considerable patient morbidity. It represents less than 1% of all male cancers and most commonly has a squamous histology. Known risk factors for the development of penile cancer include no childhood circumcision, HPV and HIV infections, smoking and a low socio-economic status.[1] Overall, the incidence of penile cancer is 8/million/year, corresponding to 45 new cases of penile cancer per year in Belgium. With approximately 500 physicians licensed in urology, this would mean that, on average, an urologist sees one case of penile cancer per 5.6 years. This low patient number, in combination with the specialized and complex management that these patients need, make a strong case for a centralized care of penile cancer. Data from the cancer registry indicate that between 2001 and 2010, 406 cases of penile cancer were diagnosed in Flanders, with a 5-year overall survival (OS) rate of 69.8%.[2]

TREATMENT OF THE PRIMARY TUMOR

Recently the TNM staging for penile cancer was updated. This was necessary, as the previous TNM classification had several shortcomings in terms of usability in clinical staging and prognostic value. In *Table 1*, an overview of the current TNM staging is provided.[3]
When there is a suspicion for a penile carcinoma in situ (PeIN), it is important to always take a biopsy. In fact, about 20% of these cases actually turn out to have

TABLE 1. 2017 TNM staging for penile cancer.[3]

Stage	Criteria
pTis	Carcinoma in situ (PeIN)
pTa	Non-invasive localized squamous cell carcinoma
pT1	Invades lamina propria
pT1a	No lymphovascular or perineural invasion, or G3 tumor
pT1b	With lymphovascular and/or perineural invasion, and/or G3 tumor
pT2	Invades corpus spongiosum with/without urethra invasion
pT3	Invades corpora cavernosa (including tunica albuginea) with/without urethra invasion
pT4	Invades into adjacent structures (scrotum, bone, prostate)