



Preface to “Management of advanced genitourinary malignancies”

There have been significant advances in the management of patients with advanced genitourinary malignancies in the last decade. These advances mostly affect prostate cancer, bladder cancer and renal cell carcinoma. For these patients, survival could be significantly improved by the introduction of new drugs including androgen-pathway targeting drugs for prostate cancer, immunotherapy and other targeted drugs (such as FGFR inhibitors and antibody drug conjugates) for urothelial carcinoma and immunotherapy combinations for renal cell carcinoma.

In the present series of *Translational Andrology and Urology* we have aimed to cover specific aspects of previous developments in the area of advanced GU malignancies.

For patients with prostate cancer, the use of new hormonal agents (NHA) such as Abiraterone, Enzalutamide and Apalutamide has led to a significant improvement of patients outcomes. Moreover, using Docetaxel upfront in combination with ADT has been shown to prolong overall survival. The availability of several options for treatment of mHSPC is associated with the challenge to find the optimal regimen for the individual patient. These aspects are covered by a review article from the PeterMac GU oncology team from Melbourne who have contributed significantly to this field in the last years.

The use of NHA and chemotherapy in the mHSPC setting also leads to challenges in the mCRPC setting as in the case of NHAs significant cross-resistances have been reported leading to unsatisfactory treatment responses in patients receiving NHA after failure of another NHA. Fortunately, recent advances in the understanding of genomic changes of PCa have led to the intense investigation of PARP inhibitors for patients with DNA Damage response gene defects. The current options for patients with mCRPC and the challenge of finding the optimal treatment sequence for these patients are covered by a review article from the British Columbia Cancer Agency GU group led by Kim Chi. A potential predictive marker for Docetaxel chemotherapy is the focus of an original work contributed by the group from Innsbruck, Austria.

Bone turnover markers in blood have been intensively investigated in the past but with the exception of alkaline phosphatase are not measured routinely in patients with advanced prostate cancer. The potential use of bone turnover markers is covered by two original works presented by the groups from Muenster and Tuebingen.

The importance of PSMA-guided imaging and therapy is constantly increasing. The potential of PSMA as diagnostic and therapeutic target is the focus of two articles in this *TAU* series. The group from Essen provides new insights into PSA radioguided surgery. In a contemporary review on PSMA radioligand therapy, the group from Munich covers an extremely hot topic in urology.

There is an increasing amount of evidence suggesting that the use of NHA is associated with an increased frequency of treatment emerging neuroendocrine prostate cancer. The group from Kyoto has contributed a comprehensive review on the various options for managing patients with this difficult to treat tumor type.

In contrast to other GU tumors covered in this series, immunotherapy has not become standard of care yet for the treatment of prostate cancer. The potential and pitfalls of immunotherapy in prostate cancer are covered by a review article from the group from Vancouver.

Similar to prostate cancer, the number of available options for the treatment of advanced urothelial carcinoma is constantly increasing. Immunotherapy has gained an important role in various lines of therapy and represents a well-established treatment option. The group from Peter Black in Vancouver discusses various options for combining immunotherapy in urothelial carcinoma patients in order to improve treatment outcomes. A collaborative review from Seattle and San Francisco provides an overview on the various options available for patients who have already been treated with immunotherapy.

Urothelial carcinoma of the lower urinary tract and upper tract UC have been shown to exhibit significant differences with regards to their molecular features. In a review from Bern, characteristics of UTUC in the context of bladder cancer are discussed. A review article from Vienna has focused on systemic treatment options for advanced UTUC.

In renal cell carcinoma, risk stratification has become an important part of the management of patients with advanced tumors. Major guidelines include prognostic scores (mostly the IMDC risk score) in their recommendations for systemic therapy. In an original work from Muenster, established prognostic scores for renal cell carcinoma have been compared with

physicians judgement in a cohort of mRCC patients.

The discovery of specific miRNAs as circulating biomarkers in patients with testicular cancer has drawn significant attention in the urologic community. The group from the British Columbia Cancer Agency (BCCA) who have significantly contributed to this field provides an overview on the development of new biomarkers for decision making in advanced testis cancer.

The topic of systemic therapy in patients with advanced penile cancer, which still represents an ongoing challenge with unsatisfactory results in daily clinical practice, is covered by a review from the group in Mainz, Germany.

Overall, the current series represents a valuable up-to-date summary of important developments in the field of Urooncology. I would like to thank all authors for their efforts and their excellent contributions.

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