Current status of the focused series "Urothelial Carcinoma"

Urothelial cancer (UC) is the second most common cancer of the urinary tract with approximately 81,400 new diagnosed cases and 17,980 deaths each year (1). UC involves various sections of the urinary tract, has different tumor stages and grades, and mostly occurs in the bladder or involves the upper urinary tract (2). Various complex treatment methods for UC include endoscopic surgery, open and minimally invasive surgery, intravesical therapy, chemotherapy, radiation therapy, and immunotherapy (2). It is very important to understand the nature of these UC and to classify the risks that determine the appropriate stage and type of treatment required. In this context, the diagnostics section includes topics on the histologic variant, one of the many issues of UC, the implications of treatment and prognosis for the recently highlighted molecular biomarker, and the recently developed and noninvasive urinary biomarkers. One of the many features of UC is its diverse morphological appearance due to molecular heterogeneity as can be seen in patients with UC with various histologic variants (3). The association between histologic variants and the clinical prognosis is being identified increasingly, with some types showing distinct molecular variations, helping in targeted therapy (3). In addition, recent reports have suggested methods classifying molecular subtypes based on RNA expression profiles to be related to prognosis (4). In UC diagnosis and monitoring, periodic invasive cystoscopy has been traditionally performed as well as urine tests, computed tomography, and magnetic resonance imaging (MRI). While these methods are reliable, they might be very uncomfortable and painful for the patient. Recently, there have been several studies on testing methods that are noninvasive. Although these methods lack formal indications, noninvasive urine biomarkers are available and potential factors are present (5). The treatment section covers novel systemic therapeutic agents used in metastatic UC in the era of immune checkpoint inhibitors. It also includes high-risk NMIBC and immunotherapy for MIBC in the setting of unresponsive Bacillus Calmette-Guérin (BCG), a recent subject of active clinical trials. Systemic cytotoxic chemotherapy has been the standard treatment for metastatic UC for decades (6). However, after the first platinum-based chemotherapy, the survival period of patients with relapse was mostly less than 2 years, and new treatments were needed. It has been used in patients with NMIBC who were at high risk for decades after BCG treatment in the 1970s (7). There have been no breakthrough immune drugs that considered the immune sensitivity of bladder cancer. Recently, immune-checkpoint inhibitors targeting programmed death 1/programmed death-ligand 1 (PD-1/PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) pathways have demonstrated significant long-term antitumor activity (8), as well as safety. Following atezolizumab, which was approved in May 2016, nivolumab, avelumab, durvalumab, and pembrolizumab were approved and used for metastatic UC (8). Recently, pembrolizumab has also been approved by the Food and Drug Administration and used in the treatment of patients with BCG unresponsive NMIBC (9). It also introduces various topics such as the role of steroid hormone receptor signaling pathways in UC and neoadjuvant chemotherapy and nephron-sparing approaches in upper tract UC. The editors wanted to introduce an interesting and varied topic of UC and would like to thank prominent researchers of bladder cancer around the world who participated in this topic.

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