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Authors
Cooperberg, MR
Hinotsu, S
Chancellor, MB
et al.

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Meeting Report

Fourth Joint Meeting of the American Urological Association and the Japanese Urological Association Specialty Society Program at the 104th Annual Meeting of the American Urological Association at Chicago 2009

Matthew R Cooperberg, Shiro Hinotsu, Michael B Chancellor, Yukio Homma, Peter S Nelson, Hideyasu Matsuyama, Mani Menon, Omer Kucuk, Isao Hara, Shin Egawa, Robert G Uzzo, Hiro-omi Kanayama*, Akihiko Okuyama and Hideyuki Akaza

Preface: We are heartily grateful for the warm support of all of the people concerned, including the moderators and panelists of both societies for giving us the opportunity to hold the 4th American Urological Association/Japanese Urological Association (AUA/JUA) Joint Meeting, held once again at the 104th Annual Meeting of the American Urological Association (25–30 April 2009, Chicago, Illinois, USA).

2009 is a memorable year, being the start of new collaborations between AUA and JUA. The JUA in collaboration with AUA is promoting an academic exchange program whereby outstanding and promising Japanese and American junior faculty members will be given the opportunity to work in the USA and Japan for one month. The program not only allows the sharing of knowledge and experience, but is designed to foster a closer alliance between the AUA and JUA, and assists in identifying future leaders within both organizations.

The JUA will have an exhibit booth at the AUA annual meeting, promoting our new joint activities. The Journal of Urology and International Journal of Urology will share reviewers. The JUA will participate in developing AUA guidelines. With all of these activities, the JUA hopes it will provide greater opportunities to young Japanese urologists to participate in educational projects in the US.

We would like to thank Professor Robert C. Flanigan, the Secretary General of AUA, Professor Glenn M. Preminger, the Chairman of the AUA Office of Education and the staff of AUA and JUA for supporting our program. We hope to keep holding the joint meeting and have plenty of ideas on themes and forums. We believe that this international program helps to establish a closer relationship between JUA and AUA in the scientific field.

Akihiko Okuyama MD, President of JUA
Hideyuki Akaza MD, Chairman of the International Committee of JUA

Program

2:00 pm..............WELCOME AND INTRODUCTION
Robert C Flanigan
Secretary of AUA

2:00 pm...................ANDROGEN DEPLETION THERAPY ON PROSTATE CANCER FROM CAPSURE AND J-CAP
Moderators: Peter R Carroll
Professor and Chairman, University of California, San Francisco
Hideyuki Akaza
Professor and Chairman, University of Tsukuba

Panelists:
Matthew R Cooperberg
University of California, San Francisco
Shiro Hinotsu
Associate Professor, Kyoto University

2:40 pm...................VOIDING DYSFUNCTION
Moderators: Kenneth M Peters
Chairman, William Beaumont Hospital
Satoru Takahashi
Professor and Chairman, Nihon University

Panelists:
Michael B Chancellor
University of California, San Francisco
Yukio Homma

3:20 pm...................Break

3:35 pm...................PROSTATE CANCER: BASIC STUDY
Moderators: Robert H Getzenberg
Professor and Director, James Buchanan Brady Urological Research Institute
Tomohiko Ichikawa
Professor and Chairman, Chiba University

Panelists:
Peter S Nelson
Fred Hutchinson Cancer Research Center
Hideyasu Matsuyama
Professor and Chairman, Yamaguchi University

4:15 pm...................PROSTATE CANCER: CASE STUDY
Moderators: Fray F Marshall
Professor and Chairman, Emory University
Yoshiyuki Kakehi
Professor and Chairman, Kagawa University

Panelists:
Mani Menon
Chairman and Director, Henry Ford Hospital
Omer Kucuk
Professor, Emory University
Isao Hara
Professor, Wakayama Medical University
Shin Egawa
Professor and Chairman, The Jikei University School of Medicine

*Authors are listed in order of the Program.
Androgen Depletion Therapy on Prostate Cancer from CaPSURE and J-CaP

Moderators
Peter R Carroll MD
Professor and Chairman
Department of Urology
University of California
San Francisco

Hideyuki Akaza MD
Professor and Chairman
Department of Urology
University of Tsukuba

Primary androgen deprivation for prostate cancer: perspective from CaPSURE

Panelist
Matthew R Cooperberg MD MPH
Department of Urology
University of California
San Francisco

In the United States primary androgen deprivation therapy (PADT) is the mainstay of treatment for men with metastatic prostate cancer. The role of PADT in the setting of localized disease, however, is not well defined given a lack of controlled trials comparing PADT outcomes to those following active surveillance, surgery, and radiation therapy. We have conducted a series of analyses on PADT utilization and outcomes based on CaPSURE, a national disease registry of over 13,000 prostate cancer patients managed at 40 practice sites across the US.

Overall, approximately 15% of prostate cancer patients in CaPSURE are managed with PADT. Use of PADT increases steadily and rapidly with increasing disease risk. Over time, PADT use has fallen among low-risk patients, and has risen among intermediate- and high-risk patients. Other patient characteristics predicting PADT use include older age, higher comorbidity burden, and lower education and socioeconomic status. Substantial regional and local variation in use of PADT exists, moreover, which is not explained by clinical risk or other patient factors. Other investigators have noted similar findings in analyses of Medicare and Surveillance, Epidemiology, and End Results (SEER) data. Higher risk patients are more likely to receive combined androgen blockade (CAB); use of CAB has fallen slightly over the past decade, and use of orchietomy has become very uncommon.

With longer-term follow up becoming available in CaPSURE, we have started to conduct analyses of risk-adjusted cancer-specific and overall survival. Compared with patients with similar disease risk undergoing radical prostatectomy and external-beam radiation therapy, PADT patients have higher likelihood of both cancer-specific and overall mortality; the survival differences tend to increase at higher levels of disease risk. The hazard ratio (HR) for cancer-specific mortality relative to prostatectomy is 3.3 (95% confidence interval [CI] 2.3–4.7), and relative to external-beam radiation therapy is 1.7 (95% CI 1.2–2.3). The HR for all-cause mortality was 2.3 (95% CI 1.9–2.7) for PADT relative to prostatectomy, and 1.5 (95% CI 1.3–1.7) relative to radiation therapy. Previous CaPSURE studies have found increased cardiac mortality among PADT patients, though other analyses of large prospective cohorts have not substantiated this association.

Overall, analyses from CaPSURE find that PADT is commonly used among men with localized prostate cancer, but do not support this treatment approach based on higher cancer-specific and overall mortality compared with men managed initially with local therapy.

Androgen Depletion Therapy on Prostate Cancer from the Japan Study Group of Prostate Cancer database

Panelist
Shiro Hinotsu MD
Associate Professor
Pharmacoepidemiology
Kyoto University

In 2001, the Japan Study Group of Prostate Cancer (J-CaP Study Group) was organized to gather information about the hormone therapy given to Japanese prostate cancer patients and to evaluate the trends and outcome of the hormone therapy. J-CaP surveillance is a nationwide longitudinal observational study of the patients newly starting hormone therapy for prostate cancer after January 2001 to December 2003.

Institutions participating in this program registered individual cases, with entry of information pertaining to endocrine therapy via secure server over the Internet. After registration, information on the prognosis of individual registered cases and changes in treatment, if any, were entered periodically.

A total of 26,272 cases were registered from 395 institutions in the J-CaP server. Of these cases, 26,170 cases were diagnosed by biopsy as having prostate cancer and began to receive treatment between 1 January 2001 and 31 December 2003. Among these cases, the number of cases who initially received primary androgen depletion therapy (PADT) after diagnosis of prostate cancer and on whom detailed information on the endocrine therapy given was available was 19,409. The present analysis was carried out about these 19,409 cases. The initial hormone therapy was divided into eight categories by its features. Patients who received maximum androgen blockade (MAB) accounted for 59.0% of all patients. MAB tends to be more often selected for patients who are rated as being at high risk on the basis of high Gleason score or prostate-specific antigen level upon diagnosis in each clinical stage of the disease.
Investigations on the outcome and adverse events, especially cardiovascular events from cause of death data, would make clear the significant usefulness of PADT for prostate cancer in Japan.

**Voiding Dysfunction**

**Moderators**
Kenneth M Peters MD  Satoru Takahashi MD
Chairman  Professor and Chairman
Department of Urology  Department of Urology
William Beaumont Hospital  Nihon University

**Urine Inflammatory Biomarkers for the Diagnosis of Overactive bladder**

**Panelist**
Michael B Chancellor MD
Director
Neuro-Urology Program
William Beaumont Hospital

Overactive bladder (OAB) symptoms are characterized by lower urinary tract symptoms of urgency, frequency and/or urgency incontinence. These symptoms also overlap with symptoms of interstitial cystitis/painful bladder syndrome (IC/PBS) and there is an absence of diagnostic tools for objective classification.

Histological studies on tissue biopsy of IC/PBS patients from clinics all across the world have consistently reported signs of inflammation as evident from degranulated mast cells, infiltration of mast cells, macrophages and neutrophils. Recent biopsy studies on OAB patients have also reported signs of inflammation. Since inflammation is associated with most diseases of chronic nature, the definition of inflammation is plural in nature and the disease in question generally defines the associated inflammation. The cellular events involved in inflammation may be common, but phenotype and mechanism of inflammation associated with OAB and IC/PBS is different due to differences in chemokines, lipids and genetic influences. Different inflammatory pathways activated due to different pathology of OAB and IC/PBS provides an opportunity for objective detection of OAB.

Basic research has demonstrated that cardinal signs of inflammation such as infiltration of mononuclear cells, activation of mast cells and neovascularization (angiogenesis) are orchestrated by chemokines, cytokines and growth factors. The secretion of these diffusible growth factors and chemokines by resident bladder cells and further amplified by immune cells leads to their release into the urine. It has been demonstrated that expression of chemokines by tissues temporally precedes the inflammatory cell infiltration noted in biopsy findings and preliminary data described in this proposal report a selective elevation of specific chemokines in the urine of OAB relative to IC/PBS patients. Herein we propose that chemokines may contribute to alter sensory processing in bladder, because of their role in the sensitization of afferents. In addition, basal levels of chemokines are involved in the paracrine signaling within the bladder and tissue levels of these chemokines are dramatically increased in inflammation, we hypothesize that the differential in the urinary chemokine repertoire associated with OAB and IC/PBS will indicate subtle mechanistic differences in the inflammatory pathways associated with OAB and IC/PBS. I will present recent data on target proteomics of urine biomarkers that correlate bladder inflammation with OAB and IC/PBS.

Considering these clinical results in light of the published biology of these chemokines led us to hypothesize that increased production of these chemokines may contribute to alter sensory processing in bladder, because of their role in the sensitization of afferents. In addition, basal levels of chemokines are involved in the paracrine signaling within the bladder and tissue levels of these chemokines are dramatically increased in inflammation, we hypothesize that the differential in the urinary chemokine repertoire associated with OAB and IC/PBS will indicate subtle mechanistic differences in the inflammatory pathways associated with OAB and IC/PBS. I will present recent data on target proteomics of urine biomarkers that correlate bladder inflammation with OAB and IC/PBS.

**New tool for assessment of important lower urinary tract symptoms: Core Lower Urinary Tract Symptom Score**

**Panelist**
Yukio Homma MD
Professor
Department of Urology
The University of Tokyo

Lower urinary tract symptoms (LUTS) are important clinical indicators for many urological diseases. Commonly they are assessed by asking the patients to complete valid questionnaires that are to be specifically applied to the disorders. Use of such questionnaires in the clinical setting is associated with various difficulties, however. First, the correct diagnosis may not be obvious initially. Applying a disease-specific questionnaire based on the physician’s presumed diagnosis may lead to overlooking other important symptoms that are not included in the questionnaire. Second, patients often have more than one disease. How are the overall symptoms to be evaluated for such patients by a disease-specific tool only? Third, a new disease/condition may develop incidentally or as an adverse event related to therapy, but assessment using a questionnaire designed for the original disease may be unable to capture the overall impact of treatment. The International Consultation on Incontinence Modular Questionnaire (ICIQ) comprises multiple questionnaires that cover a wide range of LUTS. The ICIQ-MLUTS and ICIQ-FLUTS were designed to assess a variety of LUTS in a non-disease-specific manner for men and women, respectively. However, these questionnaires may be too extensive and partly inconsistent with terminology defined by the International Continence Society (ICS) standardization committee.2

Recently we have developed a symptom questionnaire named Core Lower Urinary Tract Symptom Score (CLSS), which comprises 10 core symptoms chosen from 25 symptoms of the ICS terminology report1 by examining 1000 adults complaining of LUTS and 360 not complaining (controls) (Table 1). Symptoms were defined as ‘highly relevant (or

<table>
<thead>
<tr>
<th><strong>Table 1</strong> Core Lower urinary tract Symptom Score (CLSS) Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please circle the number that applies best to your urinary condition during the last week.</td>
</tr>
<tr>
<td>Q1: How many times do you typically urinate from waking in the morning until sleeping at night?</td>
</tr>
<tr>
<td>Q2: How many times do you typically urinate from sleeping at night until waking in the morning?</td>
</tr>
</tbody>
</table>

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core symptom) when indicated by at least 25% of symptomatic patients with nine common diseases/conditions as one of the three symptoms that had a significant impact on their daily life. The selected symptoms are daytime frequency, nocturia, urgency, urgency incontinence, stress incontinence, slow urinary stream, straining, feeling of incomplete emptying, bladder pain, and urethral pain. Core symptom showed significantly higher scores in the symptomatic patients than controls and they were not correlated with other more prevalent symptoms (r < 0.5).

The CLSS, providing an overall assessment of relevant symptoms without significant omissions, may be useful at multiple clinical settings; for example, when evaluating LUTS for new patients, those with multiple diseases, and those without a definite diagnosis, as well as before and after interventions that may cause other symptoms.

### Table 1 (to be continued)

<table>
<thead>
<tr>
<th>How often do you have the following symptoms?</th>
<th>no</th>
<th>rarely</th>
<th>sometimes</th>
<th>often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q3: A sudden strong desire to urinate, which is difficult to postpone</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q4: Leaking of urine because you cannot hold it</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q5: Leaking of urine, when you cough, sneeze, or strain</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q6: Slow urinary stream</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q7: Need to strain when urinating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q8: Feeling of incomplete emptying of the bladder after urination</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q9: Pain in the bladder</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Q10: Pain in the urethra</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

CLSS (Sum of scores of Q1–10)___________

Which symptoms have negative impact on your daily life?

Choose 3 or fewer symptoms with negative impact.

<table>
<thead>
<tr>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>Q6</th>
<th>Q7</th>
<th>Q8</th>
<th>Q9</th>
<th>Q10</th>
</tr>
</thead>
</table>

Choose only 1 symptom with the most negative impact.

<table>
<thead>
<tr>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>Q6</th>
<th>Q7</th>
<th>Q8</th>
<th>Q9</th>
<th>Q10</th>
</tr>
</thead>
</table>

If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?

<table>
<thead>
<tr>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly satisfied</th>
<th>Mixed about equally satisfied and dissatisfied</th>
<th>Mostly dissatisfied</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Major advances have been achieved using pharmacological approaches for the treatment of advanced prostate cancer. Prostate cancer prevention has also arguably been improved using drug therapy. However, although suppression of the androgen axis and cytotoxic therapies clearly prolong survival in advanced disease, ultimate resistance to these treatments is almost universal. Understanding the tumor and host mechanisms contributing to therapy resistance could provide new targets for circumventing resistance pathways. To achieve this goal, basic scientific principles testing cause-effect hypotheses must be applied. This presentation will describe the application of this concept using examples designed to understand in vivo mechanisms underlying resistance to taxane and hormonal therapies.

### Prostate Cancer: Basic Study

**Moderators**

Robert H Getzenberg PhD  
Professor and Director  
The James Buchanan Brady Urological Research Institute

Tomohiko Ichikawa MD PhD  
Professor and Chairman  
Department of Urology  
Chiba University

**Applying Basic Science to Clinical Problems: Defining and Exploiting Mechanisms of Therapy Resistance in Localized and Advanced Prostate Cancer**

**Panelist**

Peter S Nelson MD  
Fred Hutchinson Cancer Research Center

Hideyasu Matsuyama MD PhD  
Professor and Chairman  
Department of Urology  
Yamaguchi University

**Is there any difference of somatic genetic alterations between different ethnics in prostate cancer?**

**Panelist**

Hideyasu Matsuyama,1 Peter Ekman2 and Jan Fichtner3

1Department of Urology, Yamaguchi University Graduate School of Medicine, Ube, Japan, 2Karolinska University Hospital, Stockholm, Sweden, and 3Johanniter Krankenhaus, Oberhausen, Germany

**Objective:** The difference of genetic background between different ethnicities, and its impact (if any) on prevalence or patient outcome
remain unclear in prostate cancer (PCa). The aim of this study is to identify the difference of somatic genetic alterations between Japanese and Caucasian patients with PCa.

Methods: Totally 168 PCa patients were investigated by two studies consisting of (A) deletion study of the short arm 22 region of chromosome 8 (8p22), the most frequently deleted region in PCa patients in the literature, by fluorescence in situ hybridization (FISH) technique in 97 PCa patients (41 Japanese and 56 Swedish); and (B) allelic imbalance (AI) of the long arm of chromosome 13 (13q) using eight microsatellite markers by polymerase chain reaction technique in 71 PCa patients (32 Japanese and 39 German). No significant difference was observed in terms of age, pathological stage, Gleason score (or tumor grade) between different ethnicities in both studies. Fifty-seven patients were followed with a median follow up of 59 months in study A.

Results: Deletion of 8p22 was significantly increased in proportion to advancing pathological stage (P < 0.05), and tumor grade (P < 0.01), while no significant difference was observed in the frequency of 8p22 between Japanese and Swedish patients. Multivariate analysis proved deletion of 8p22 to be an independent prognostic factor predicting disease progression in both ethnicities (odds ratio [OR]: 5.75 95% confidence interval [CI]: 2.31-17.63, P = 0.0001), and haploinsufficiency (gene dosage) of 8p22 to be a sole independent factor for cancer-specific death (OR: 1.10, 95% CI: 1.03-1.19, P = 0.0031) in Japanese PCa. In contrast, frequency of AI was significantly higher in Japanese than in German PCa in two loci of 13q (13q14; 53% vs. 11%, P = 0.0128, 13q14.3-21.2; 42% vs. 4%, P = 0.0078, respectively). AI of 13q14, locating RB1 gene, was significantly associated with higher Gleason score (P = 0.0478).

Conclusion: Two studies suggest that 8p22 deletion may be a common somatic genetic alteration affecting patient outcome regardless of different ethnicity, and that 13q14 may be a unique genetic alteration in Japanese PCa, which may explain the tendency towards higher Gleason scores in Japanese PCa patients.

Prostate Cancer: Case Study

Moderators
Fray F Marshall MD
Professor and Chairman
Department of Urology
Emory University

Yoshiyuki Kakehi MD
Professor and Chairman
Department of Urology
Kagawa University

Panelists
Mani Menon MD
Chairman and Director
Vattikuti Urology Institute
Henry Ford Hospital

Isao Hara MD
Professor
Department of Urology
Wakayama Medical University

Omer Kucuk MD
Professor
Winship Cancer Institute
Emory University

Shin Egawa MD PhD
Professor and Chairman
Department of Urology
The Jikei University School of Medicine

Both the incidence and the mortality rates of prostate cancer continue to increase in Japan while the mortality rate is declining in the USA. It is, however, no doubt that the trend toward early stage shifting is common to both countries. Prostate cancer is a heterogeneous disease; some patients are destined to die shortly after diagnosis while others live as long as healthy individuals of similar age. Treatment strategy is decided based upon accumulated evidence as well as the patient’s condition and preference. Treatment options, however, are usually multiple for each individual case. Physicians are often confronted with this dilemma at diagnosis and treatment intervention. Many factors, including curability, toxicity profile and cost efficiency, should be taken into consideration.

The first case in this case discussion session was a 71-year-old man with T1c cancer who chose active surveillance (AS). Six years later, his serum prostate-specific antigen rose from 8.6 to 16 ng/mL and a hard nodule was palpable in the right apex. His performance status was zero, even though he had undergone bilateral cranial artery bypass due to cerebral infarction 1 year previously. The pros and cons of several treatment options including radical prostatectomy (RP), seed implantation, external beam radiotherapy, androgen deprivation therapy, and AS were discussed. In the next case, the indication and timing of adjuvant (or salvage) radiotherapy for sexually active men who underwent nerve-sparing RP were considered. Most of the panelists were in favor of early radiotherapy against margin-positive or capsular penetration cases. Then, focal therapy with high-intensity focused ultrasound or additional seed implantation for tumor lesions visualized by magnetic resonance imaging was debated. Finally, the treatment strategy for relatively young patients who showed chemotherapy-naïve hormone-refractory prostate cancer (HRPC) following RP was discussed. Docetaxel has been introduced as the first-line chemotherapy for HRPC but its survival benefit is still minimal. Panelists made reference to the possibility of new compounds including a selective inhibitor of CYP17, abiraterone acetate.

In summary, despite racial and socio-economic differences in clinical decision-making for prostate cancers between the two countries, the present participants and moderators confirmed the strong possibility of overcoming the clinical dilemmas common to both Japan and the USA.

Molecular Targeted Therapy for Renal Cell Carcinoma in Japan and the US: Lecture and Case Discussion

Moderators
W Marston Linehan MD
Branch Chief
National Cancer Institute

Seiji Naito MD
Professor and Chairman
Department of Urology
Kyushu University

Commentator
Yoshikoto Tomita MD PhD
Professor and Chairman
Department of Urology
Yamagata University

Molecular Targeted Therapy for Renal Cell Carcinoma in the US

Panelist
Robert G Uzzo MD FACS
Chairman
Department of Surgery
Fox Chase Cancer Center
Temple University

Surgical monotherapy as part of a multimodal approach remains the standard of care for most cases of renal cell carcinoma (RCC). Radical
or partial nephrectomy is associated with a 5-year cancer specific survival (CSS) of 85–97% for pT1 tumors. Data regarding laparoscopic partial nephrectomy are favorable, with more limited follow up. Minimally invasive ablative technologies are emerging as potential treatment options for localized RCC with excellent early outcomes.

Unfortunately, 20% of patients have either locally advanced or node positive (N+) RCC, while another 22% have metastatic RCC (mRCC) at presentation. Unlike the outcomes in early localized disease, survival rates for N+ patients are poor and patients with mRCC are rarely cured despite aggressive multimodal therapy. Classic cytotoxic chemotherapy has repeatedly been shown to have little effect and only 5–20% of patients with mRCC respond to immunologic agents such as interferon and/or interleukin. Cytoreductive nephrectomy with systemic immunotherapy is associated with few cures with median survival of 12–24 months. A recent meta-analysis of 53 published randomized clinical trials that stratified 6117 patients with advanced RCC to an immunotherapeutic agent in at least one arm demonstrated an overall chance of partial or complete response to immunotherapies of only 12.9%, compared with 4.3% in the placebo arm with a median survival of 13 months.

Recent advances in our understanding of the molecular origins and pathways of RCC have led to the development of more effective targeted therapies. This lecture will review the use of molecular targeted therapies in the United States focusing on the implications for the practicing urologist.

Molecular targeted therapy and present status of treatment of stage IV renal cell carcinoma patients in Japan

Panelist
Hiro-omi Kanayama MD
Professor and Chairman
Department of Urology
The University of Tokushima

In Japan, the patients with renal cell carcinomas (RCCs) including advanced cases have been and are managed by urologists. Japanese urologists diagnose, and perform surgery, minimal invasive therapy such as radiofrequency ablation, and also medical therapy. Under the circumstances, RCC patients with metastasis (mRCC) are subjected to radical nephrectomy, immediately followed by metastatectomy. As for Sorafenib, almost all patients revealed AEs, but grade 3 or 4 were limited in 61%. In 2008, the Japanese Ministry of Health, Labor and Welfare approved Sorafenib and Sunitinib as drugs to patients with unresectable or metastatic RCC. After approval of Sorafenib and Sunitinib, many advanced cases have been treated; Sorafenib was given in over 2000 and Sunitinib in 600 advanced RCC cases so far (February, 2009). However, other molecular targeted drugs including bevacizumab, everolimus or temsirolimus have not been approved, yet.

The treatment strategy of mRCC is being changed in Japan after introducing Sorafenib and Sunitinib. Sunitinib is recommended as first line therapy for mRCC based on firm clinical evidence, but it is not necessarily applied to Japanese patients in that way. Detailed consideration of Japanese RCC patients with metastasis seems to be still encouraging cytokine therapy, IFN-α with or without low dose IL-2, as a first line therapy for subgroups of patients; namely, those with clear cell carcinoma and lung metastases only. The response rates of cytokine therapy to these selected cases are relatively high, and complete response (CR) cases are included in responders. Moreover, the responders (CR/partial response (PR)) may frequently be long survivors. On the other hand, patients with non-clear cell carcinoma or with extra-pulmonary metastases are usually treated with molecular targeted drugs, Sunitinib or Sorafenib. Cytokine-refractory cases are also treated by molecular targeted drugs. Because AEs of Sorafenib are not so severe, as mentioned above, Sorafenib tends to be chosen at first in older patients and those with comorbidities or poor performance status.

More updated issues will be presented and discussed.

References