













EPICS

Conference Coverage: ESMO 2024 – Focus on Genitourinary (GU) Malignancies

September 24, 2024

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
September 24, 2024



**DISEASE-STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



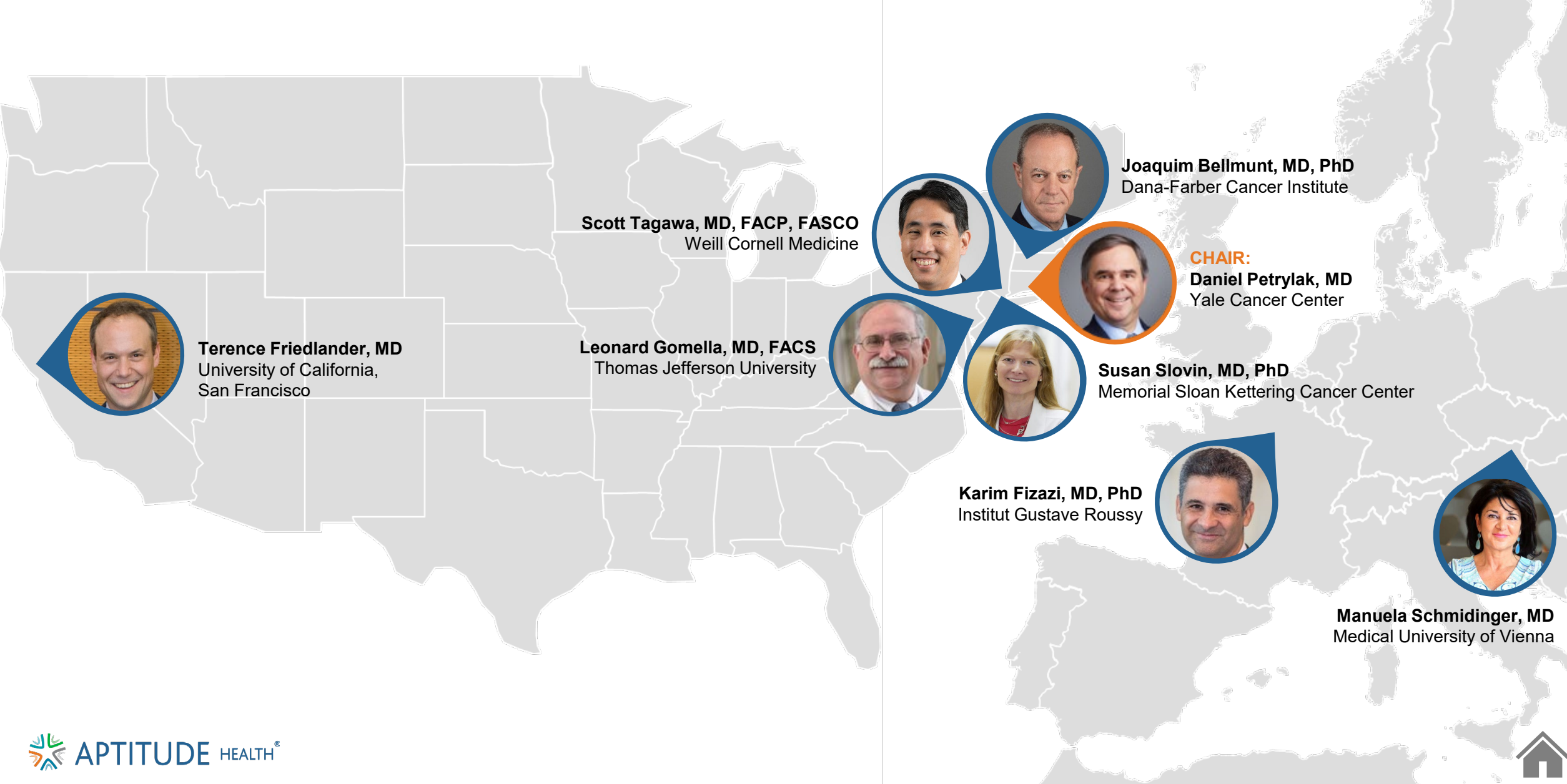
PANEL: Key experts in
GU malignancies

- > 6 from the US
- > 2 from Europe



**GU CANCER-SPECIFIC
DISCUSSIONS** on
therapeutic advances and
their application in clinical
decision-making

Panel Consisting of 6 US and 2 European GU Cancer Experts



Terence Friedlander, MD
University of California,
San Francisco

Scott Tagawa, MD, FACP, FASCO
Weill Cornell Medicine



Leonard Gomella, MD, FACS
Thomas Jefferson University



Joaquim Bellmunt, MD, PhD
Dana-Farber Cancer Institute



CHAIR:
Daniel Petrylak, MD
Yale Cancer Center



Susan Slovin, MD, PhD
Memorial Sloan Kettering Cancer Center



Karim Fizazi, MD, PhD
Institut Gustave Roussy



Manuela Schmidinger, MD
Medical University of Vienna



Meeting Agenda

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Time (EST)	Topic	Presenter
9.00 AM – 9.05 AM / 15.00 – 15.05	Welcome and Introductions	Daniel Petrylak, MD
9.05 AM – 9.15 AM / 15.05 – 15.15	Bladder Cancer Part 1 – NMIBC and MIBC	Leonard Gomella, MD, FACS; Terence Friedlander, MD
9.15 AM – 9.35 AM / 15.15 – 15.35	Discussion and Key Takeaways	Moderator: Daniel Petrylak, MD
9.35 AM – 9.45 AM / 15.35 – 15.45	Bladder Cancer Part 2 – Metastatic Urothelial Cancer	Joaquim Bellmunt, MD, PhD
9.45 AM – 10.05 AM / 15.45 – 16.05	Discussion and Key Takeaways	Moderator: Daniel Petrylak, MD
10.05 AM – 10.15 AM / 16.05 – 16.15	Renal Cell Carcinoma	Manuela Schmidinger, MD
10.15 AM – 10.35 AM / 16.15 – 16.35	Summary and Key Takeaways	Moderator: Daniel Petrylak, MD
10.35 AM – 10.40 AM / 16.35 – 16.40	BREAK	
10.40 AM – 10.50 AM / 16.40 – 16.50	Hormonal, Cytotoxic, and Targeted Therapies for Metastatic Castration-Resistant Prostate Cancer	Scott Tagawa, MD, FACP, FASCO
10.50 AM – 11.05 AM / 16.50 – 17.05	Discussion and Key Takeaways	Moderator: Daniel Petrylak, MD
11.05 AM – 11.15 AM / 17.05 – 17.15	Radioligand Therapies for Prostate Cancer	Karim Fizazi, MD, PhD
11.15 AM – 11.35 AM / 17.15 – 17.35	Discussion and Key Takeaways	Moderator: Daniel Petrylak, MD
11.35 AM – 11.45 AM / 17.35 – 17.45	Localized and Hormone-Sensitive Prostate Cancer	Susan Slovin, MD, PhD
11.45 AM – 12.00 PM / 17.45 – 18.00	Discussion and Key Takeaways	Moderator: Daniel Petrylak, MD
12.00 PM / 18.00	Summary and Closing Remarks	Daniel Petrylak, MD



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Conference Highlights

Bladder Cancer Part 1 – NMIBC and MIBC

TAR-200 + cetrelimab (CET) or CET alone as neoadjuvant therapy in patients with MIBC who are ineligible for or refuse Cis-based NAC: SunRISe-4

Necchi et al. ESMO 2024; LBA84

STUDY POPULATION AND METHODS

> Pts with cT2-T4a N0M0 MIBC were randomized to 12 wk of

EFFICACY BY TAR-200 DOSE EXPOSURE

STUDY POPULATION

1. 100 pts with cT2-T4a N0M0 MIBC were randomized to 12 wk of treatment with either TAR-200 + CET (n=50) or CET alone (n=50). The primary endpoint is overall survival (OS) at 12 weeks. Secondary endpoints include pathologic complete response (pCR), time to progression (TTP), and quality of life (QoL). The study is ongoing and will continue until 12 weeks of treatment have been completed.

RESULTS

1. OS at 12 weeks was significantly higher in the TAR-200 + CET group (n=50) compared to the CET alone group (n=50). The pCR rate was also higher in the TAR-200 + CET group.

CONCLUSIONS

Combining TAR-200 with CET as neoadjuvant therapy in patients with MIBC who are ineligible for or refuse Cis-based NAC significantly improved OS and pCR rates.

EFFICACY BY TAR-200 DOSE EXPOSURE



RESPONSE RATES BY TREATMENT GROUP AND TIME POINT



TAR-200 ± cetrelimab (CET) and CET alone in patients with BCG-unresponsive high-risk NMIBC: Updated results from SunRISe-1

Van der Heijden et al. ESMO 2024; LBA85

STUDY POPULATION AND METHODS

> Pts with BCG-unresponsive high-risk NMIBC were randomized to

DURABILITY OF RESPONSES



Nivolumab + chemoradiotherapy in patients with nmMIBC not undergoing cystectomy: Phase II, randomized study by the Hellenic GU Cancer Group

Kougioumtzopoulou et al. ESMO 2024; 1961O

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STUDY POPULATION AND METHODS

> 77 pts with nonmetastatic MIBC who were not candidates for

OVERALL SURVIVAL



JCOG1019: Phase III study comparing watchful waiting and intravesical BCG in high-grade pT1 bladder cancer with pT0 on the second TUR

Kitamura et al. ESMO 2024; 1963MO

STUDY POPULATION AND METHODS

> 263 pts with high-grade pT1 bladder cancer resected to PT0 on

RELAPSE-FREE SURVIVAL



Phase III trial of neoadjuvant durvalumab + chemotherapy followed by radical cystectomy and adjuvant durvalumab in MIBC (NIAGARA)

Powles et al. ESMO 2024; LBA5

STUDY POPULATION AND METHODS

> 1,063 pts with cisplatin-eligible MIBC were randomized to

OVERALL SURVIVAL



Alliance A031501: AMBASSADOR study of adjuvant pembrolizumab in MIUC vs observation – extended follow-up

Apolo et al. ESMO 2024; 1964MO

STUDY POPULATION AND METHODS

> 702 pts with MIBC (≥T2) were randomized to receive 1 yr of

DISEASE-FREE SURVIVAL

Figure 1: Disease-Free Survival (DFS) in the Intention-to-Treat Population (ITT)



Figure 2: Response Rates in the Intention-to-Treat Population (ITT)



Identification of patients with bladder cancer who could benefit from early post-cystectomy immunotherapy based on serial ctDNA testing: TOMBOLA

Jensen et al. ESMO 2024; 19600

STUDY POPULATION AND METHODS

> 190 pts with cT2-4a N0-1 M0 MIBC received NAC and underwent

RELAPSE FOLLOWING CYSTECTOMY

Early detection of relapse



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Key Insights

Bladder Cancer Part 1 – NMIBC and MIBC

Experts Considered the Implications of the NIAGARA Trial for the Management of MIBC

NIAGARA: PERIOPERATIVE DURVALUMAB

Key findings from the NIAGARA trial regarding the perioperative management of MIBC:

- 1. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.
- 2. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.
- 3. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.
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- 6. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.
- 7. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.
- 8. The combination of durvalumab, cisplatin, and gemtuzumab (CG) significantly improved overall survival compared to cisplatin and gemtuzumab (CG) in patients with MIBC.



Dr. [Name]
[Title]
[Institution]

Dr. [Name] is a leading expert in the field of MIBC. He has conducted numerous clinical trials, including the NIAGARA trial, and has published extensively on the management of MIBC. He is currently a member of the [Organization] and is actively involved in the development of new treatments for MIBC.

Experts Discussed Adjuvant Immunotherapy for MIBC, and the Potential for ctDNA-Guided Adjuvant Decision-Making

AMBASSADOR

Experts discussed the optimal sequencing of agents in the adjuvant setting for MIBC, and the potential for ctDNA-guided adjuvant decision-making.

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- The sequencing of agents in the adjuvant setting for MIBC is a complex decision, and experts discussed the potential for ctDNA-guided decision-making.
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Dr. [Name]
[Title]
[Affiliation]

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Experts Discussed Intravesical Therapies for Patients With NMIBC and MIBC

SunRISE-1

Key messages will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of the regimen of intravesical chemotherapy and intravesical BCG, followed by TURBT, particularly for most patients
- 2. Most experts are using intravesical chemotherapy therapy, but still practice the bladder-sparing approach for patients with evidence of local recurrence
- 3. The bladder-sparing approach may also be used in the neoadjuvant setting before TURBT for patients with documented local recurrence
 - 1. Preferred to avoid recurrence, experts are divided on whether they would currently use TURBT or intravesical chemotherapy
 - 2. Results of the ongoing SUNRISE-1 trial should help comparing intravesical chemotherapy or TURBT will help to clarify the optimal sequencing of these agents
- 4. Intravesical chemotherapy and the bladder-sparing approach may also be used earlier than starting a patient who was following treatment with intravesical chemotherapy and TURBT in the neoadjuvant setting, but this approach is used for a small fraction of patients
- 5. Future preferences can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus drug use in sequence)
- 6. The comparative efficacy of intravesical chemotherapy and the bladder-sparing approach have opened other options, such as intravesical chemotherapy combinations, vaccines, and immunotherapy, in the form of therapy



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Congress Highlights

**Bladder Cancer Part 2 – Metastatic
Urothelial Cancer**

BL-B01D1, an EGFR x HER3 bispecific antibody-drug conjugate, in patients with locally advanced or metastatic urothelial carcinoma

Ye et al. ESMO 2024; 19590

STUDY POPULATION AND METHODS

> 27 pts with previously treated mUC received treatment with BL-

DEPTH AND DURATION OF RESPONSE



HRQOL from the CheckMate 901 trial of nivolumab as first-line therapy for unresectable or metastatic urothelial carcinoma

Bedke et al. ESMO 2024; 19620

STUDY POPULATION AND METHODS

> 608 pts with previously untreated mUC were randomized to

LEAST SQUARES MEAN CHANGES: BASELINE–WK 16



Phase II study of futibatinib + pembrolizumab in patients with mUC: Final analysis

Koshkin et al. ESMO 2024; 1965MO

STUDY POPULATION AND METHODS

> Pts with previously untreated mUC received the FGFR inhibitor

ANTITUMOR ACTIVITY (COHORT A)



EV-302: Exploratory analysis of nectin-4 expression and response to 1L enfortumab vedotin (EV) + pembrolizumab in previously untreated Ia/mUC

Powles et al. ESMO 2024; 1966MO

STUDY POPULATION AND METHODS

> 886 pts with previously untreated Ia/mUC eligible for platinum-

OVERALL SURVIVAL



Efficacy and safety of disitamab vedotin (DV) with pembrolizumab in treatment-naive HER2-expressing Ia/mUC: RC48G001 Cohort C

Galsky et al. ESMO 2024; 1967MO

STUDY POPULATION AND METHODS

> Pts with HER2-expressing, previously untreated mUC received

ANTITUMOR ACTIVITY



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Key Insights

**Bladder Cancer Part 2 – Metastatic
Urothelial Cancer**

Experts Discussed Selecting Patients With mUC for Treatment With EV-Pembrolizumab

ENFORTUMAB VEDOTIN + PEMBROLIZUMAB

Experts discussed selecting patients for treatment with EV-Pembrolizumab and Enfortumab Vedotin (EV-Pembrolizumab + Enfortumab Vedotin) in patients with metastatic urothelial carcinoma (mUC).

- The experts discussed the importance of patient selection for treatment with EV-Pembrolizumab + Enfortumab Vedotin, including the use of PD-L1 testing and the presence of microsatellite instability (MSI) or mismatch repair deficiency (MMRD).
- The experts discussed the use of EV-Pembrolizumab + Enfortumab Vedotin in patients with mUC who have not received prior systemic therapy.
- The experts discussed the use of EV-Pembrolizumab + Enfortumab Vedotin in patients with mUC who have received prior systemic therapy.
- The experts discussed the use of EV-Pembrolizumab + Enfortumab Vedotin in patients with mUC who have received prior systemic therapy and are refractory to treatment.
- The experts discussed the use of EV-Pembrolizumab + Enfortumab Vedotin in patients with mUC who have received prior systemic therapy and are refractory to treatment.



Dr. [Name] is a leading expert in the field of mUC. He discussed the importance of patient selection for treatment with EV-Pembrolizumab + Enfortumab Vedotin, including the use of PD-L1 testing and the presence of MSI or MMRD. He also discussed the use of EV-Pembrolizumab + Enfortumab Vedotin in patients with mUC who have not received prior systemic therapy.

Experts Debated the Use of Sacituzumab Govitecan for mUC in the Wake of TROPiCS-04

SACITUZUMAB GOVITECAN

Following these data, experts debated the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of sacituzumab and pembrolizumab, followed by TROPiCS-04, for most patients.
- 2. Most experts are using sacituzumab pembrolizumab therapy, but will probably use the sacituzumab regimen for patients with evidence of local recurrence.
- 3. The sacituzumab regimen may also be used in the adjuvant setting, before TROPiCS-04, for patients with recurrent local recurrence.
 - 1. Provided a good performance, experts are divided on whether they would currently use TROPiCS-04 in combination with pembrolizumab.
 - 2. Results of the ongoing TROPiCS-04 trial comparing sacituzumab pembrolizumab vs TROPiCS-04 will help to clarify the optimal sequencing of these agents.
- 4. Sacituzumab pembrolizumab and the sacituzumab regimen may also be used earlier than pembrolizumab in patients who were following treatment with sacituzumab, pembrolizumab, and TROPiCS-04 in the adjuvant setting, but this represents a small fraction of patients.
- 5. Future publications can also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 1 drug).
- 6. The comparative efficacy of sacituzumab pembrolizumab and the sacituzumab regimen have opened other options, such as sacituzumab immunotherapy combinations, nivolumab, and immunotherapy in other lines of therapy.



Experts Considered Novel Investigational Therapies for mUC

CheckMate 901

The addition of nivolumab to first-line gem-cis did not have a detrimental effect on

- 1. Progression-free survival (PFS) in patients with metastatic mUC
- 2. Overall survival (OS) in patients with metastatic mUC
- 3. Quality of life (QoL) in patients with metastatic mUC
- 4. The overall safety profile in the overall population, including patients with metastatic mUC
- 5. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients
- 6. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients
- 7. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients
- 8. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients
- 9. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients
- 10. The overall safety profile in patients with metastatic mUC who were also receiving treatment with nivolumab, ipilimumab, and 5-FU in the maintenance setting, but this represents a small fraction of patients



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Congress Highlights

Renal Cell Carcinoma

NKT2152, a novel oral HIF-2 α inhibitor, in patients with previously treated accRCC: Preliminary results of a phase I/II study

Jonasch et al. ESMO 2024; 16900

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STUDY POPULATION AND METHODS

> 113 pts with heavily pretreated advanced ccRCC were treated

ADVERSE EVENTS

STUDY POPULATION

113 pts with heavily pretreated advanced ccRCC were treated. The study population included patients who had received ≥ 1 prior systemic anticancer therapy for advanced ccRCC. The median number of prior systemic anticancer therapies was 2 (range 1-7). The median time from diagnosis to study entry was 12.5 months (range 0.5-48.5). The median time from last prior systemic anticancer therapy to study entry was 12.5 months (range 0.5-48.5). The median time from study entry to treatment discontinuation was 12.5 months (range 0.5-48.5).

ADVERSE EVENTS

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Tivozanib ± nivolumab in patients with RCC following 1 or 2 prior therapies including an ICI: Results of the phase III TiNivo-2 study

Choueiri et al. ESMO 2024; LBA73

STUDY POPULATION AND METHODS

> 343 pts with advanced/metastatic ccRCC after progression on 1–2

TUMOR RESPONSE



Final analysis of the phase III LITESPARK-005 study of belzutifan vs everolimus in patients with previously treated advanced ccRCC

Rini et al. ESMO 2024; LBA74

STUDY POPULATION AND METHODS

> 746 pts with metastatic ccRCC previously treated with 1–3 lines of

PROGRESSION-FREE SURVIVAL



Randomized phase II trial of ipilimumab-nivolumab vs SOC in non-clear cell RCC: Results of the SUNNIFORECAST trial

Bergmann et al. ESMO 2024; LBA75

STUDY POPULATION AND METHODS

> 306 pts with advanced/metastatic non-clear cell RCC were

OVERALL SURVIVAL: CPS ≥1



Anlotinib + anti-PD-L1 antibody benmelstobart (TQB2450) vs sunitinib in first-line treatment of advanced RCC: Phase III study (ETER100)

Sheng et al. ESMO 2024; LBA76

STUDY POPULATION AND METHODS

> 531 pts with previously untreated advanced/metastatic ccRCC

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL IN THE INTENTION-TO-TREAT POPULATION



RESPONSE EVALUATION IN THE INTENTION-TO-TREAT POPULATION



Fecal microbiota transplantation (FMT) vs placebo in patients receiving pembrolizumab + axitinib for mRCC: Phase II TACITO trial

Ciccarese et al. ESMO 2024; LBA77

STUDY POPULATION AND METHODS

> 50 pts with RCC of any histology, initiating treatment with axitinib

12-MO PROGRESSION-FREE SURVIVAL



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Key Insights

Renal Cell Carcinoma

Experts Discussed Results From Investigational Agents and Strategies for Advanced/Metastatic ccRCC

ETER100

Keynote 100 will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of the agents, as well as combination and sequential therapy, followed by TDMT, according to their patients.
- 2. Most experts are using combination treatment, but all practice the limited data for patients with evidence of liver metastases.
- 3. The limited data may also be used in the retrospective setting, before TDMT, in patients with documented liver metastases.
 - 1. Preferred to use sequential agents are divided on whether they would actually use TDMT or combination treatment.
 - 2. Results of the ongoing IMmotion150 comparing combination treatment as TDMT will help to clarify the optimal sequencing of these agents.
- 4. Combination treatment and the limited data may also be used earlier than starting in patients who were following treatment with combination, sequential, and TDMT in the retrospective setting, but this represents a small fraction of patients.
- 5. Future preferences can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus drug-free or 2 drugs).
- 6. The comparative efficacy of combination treatment and the limited agents have opened other options, such as combination chemotherapy, combination, sequential, and combination, in the form of therapy.



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Experts Considered Treatment Options for Patients With Advanced/Metastatic Non-Clear Cell RCC

SUNNIFORECAST

Experts will discuss the optimal sequencing of agents in patients with advanced/metastatic non-clear cell renal cell carcinoma (RCC) and the role of immunotherapy, including TIGIT inhibitors, in these patients.

These experts are using immunotherapy, specifically nivolumab, but will address the limited data for patients with evidence of liver metastases.

The nivolumab study may also be used in the retrospective setting, before TIGIT, in patients with advanced non-clear cell RCC.

- Proposed to use immunotherapy, experts are divided on whether they would currently use TIGIT or immunotherapy, specifically nivolumab.
- Results of the ongoing IMbrave150 trial comparing nivolumab monotherapy to TIGIT will help to clarify the optimal sequencing of these agents.

Immunotherapy, specifically nivolumab, and the nivolumab study may also be used before than starting a patient who have following treatment with immunotherapy, specifically, and TIGIT in the retrospective setting, but this represents a small fraction of patients.

Future immunotherapy use may focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus drug use in sequence).

The comparative efficacy of immunotherapy, specifically nivolumab, and the nivolumab study have opened other options, such as immunotherapy, combination, nivolumab, and immunotherapy, in the use of therapy.



Dr. [Name]
[Title]
[Institution]

[Text]

Experts Discussed Sequencing Therapies for Metastatic ccRCC

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TiNivo-2

Results of the phase III TiNivo-2 study comparing tivozanib ± nivolumab in

- 1. Tivozanib and nivolumab are being compared in the sequenced setting of metastatic ccRCC. The primary endpoint is overall survival (OS) in the intent-to-treat population.
- 2. The study is a phase III, randomized, controlled trial comparing tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC. The study is designed to evaluate the efficacy and safety of tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC.
- 3. The study is designed to evaluate the efficacy and safety of tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC. The study is designed to evaluate the efficacy and safety of tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC.
- 4. The study is designed to evaluate the efficacy and safety of tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC. The study is designed to evaluate the efficacy and safety of tivozanib ± nivolumab in the sequenced setting of metastatic ccRCC.
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Dr. [Name]
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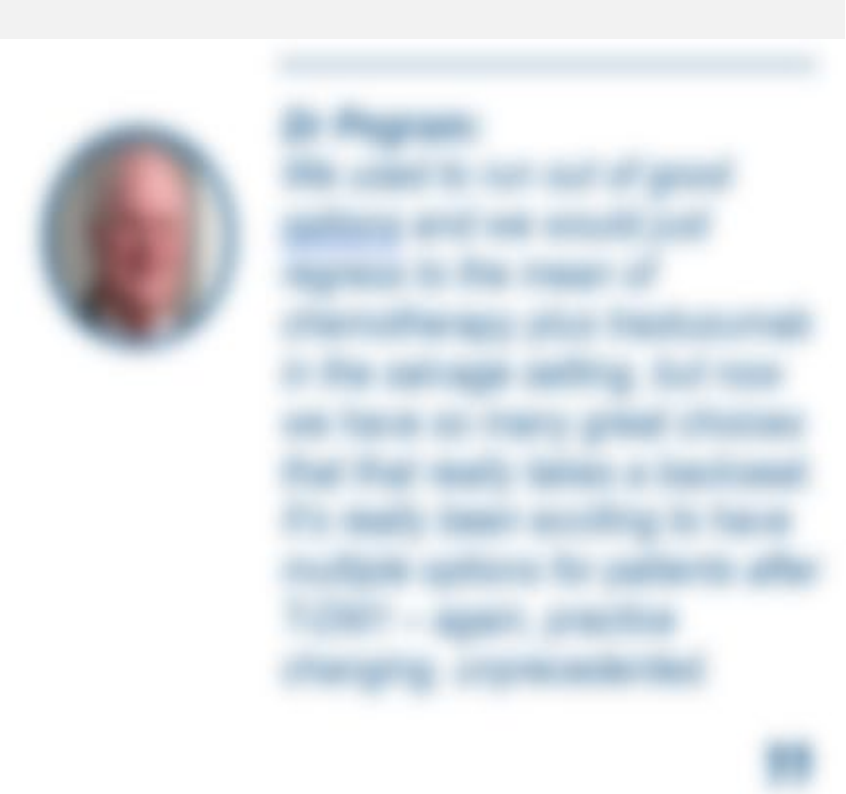
Experts Discussed Later-Line Trials for Metastatic ccRCC

LITESPARK-005

Longer follow-up of the LITESPARK-005 trial comparing belzutifan vs everolimus

Longer follow-up of the LITESPARK-005 trial comparing belzutifan vs everolimus

- 1. The primary aim of the study is to evaluate the overall survival of patients receiving everolimus compared with belzutifan in the second-line setting.
- 2. The secondary aim is to evaluate the overall survival of patients receiving everolimus compared with belzutifan in the first-line setting.
- 3. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the third-line setting.
- 4. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the fourth-line setting.
- 5. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the fifth-line setting.
- 6. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the sixth-line setting.
- 7. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the seventh-line setting.
- 8. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the eighth-line setting.
- 9. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the ninth-line setting.
- 10. The study will also evaluate the overall survival of patients receiving everolimus compared with belzutifan in the tenth-line setting.



EPICS

Congress Highlights

**Hormonal, Cytotoxic, and Targeted
Therapies for Metastatic Castration-
Resistant Prostate Cancer**

Clinical activity of BMS-986365 (CC-94676), a dual AR ligand-directed degrader and antagonist, in heavily pretreated mCRPC

Rathkopf et al. ESMO 2024; 1597MO

STUDY POPULATION AND METHODS

> 68 pts with mCRPC previously treated with at least 1 ARPI and a

PSA RESPONSE



Nivolumab 3 mg/kg and ipilimumab 1 mg/kg in molecularly selected patients with mCRPC

Mehra et al. ESMO 2024; LBA72

STUDY POPULATION AND METHODS

> 69 pts with previously treated, molecularly selected mCRPC

PROGRESSION-FREE SURVIVAL



Cabozantinib + atezolizumab vs second novel hormonal therapy (NHT) in mCRPC: Final OS results of the phase III CONTACT-02 study

Agarwal et al. ESMO 2024; LBA67

STUDY POPULATION AND METHODS

> 580 pts with mCRPC that had progressed on 1 prior ARPI

OVERALL SURVIVAL BY SUBGROUP



EPICS

Key Insights

**Hormonal, Cytotoxic, and Targeted
Therapies for Metastatic Castration-
Resistant Prostate Cancer**

Experts Considered Emerging AR-Targeted Agents for mCRPC

BMS-986365

BMS-986365 (CC-94676), a first-in-class dual AR ligand-directed degrader and

emerging AR-Targeted Agents for mCRPC

- Treatment of mCRPC with a first-in-class dual AR ligand-directed degrader and androgenesis inhibitor, BMS-986365, in mCRPC patients.
- BMS-986365 is a dual AR ligand-directed degrader and androgenesis inhibitor, but will provide the needed AR-Targeted Agent for patients with evidence of AR-Targeted Agent.
- The degrader may also be used in the androgenesis setting, either TAD or with androgenesis.
- Provided to mCRPC patients, agents are divided in whether they would provide AR-Targeted Agent.
- Results of the ongoing AR-Targeted Agent and androgenesis inhibitor BMS-986365 will help to define the optimal sequence of these AR-Targeted Agent and the needed AR-Targeted Agent may also be used with the degrader in patients who have received treatment with androgenesis inhibitor and TAD in the androgenesis setting, but this approach is a small number of patients.
- Patients with mCRPC may also benefit from the sequencing of these AR-Targeted Agent and TAD drug, which may lead to mCRPC.
- The sequencing efficacy of androgenesis inhibitor and the needed AR-Targeted Agent have shown other agents, such as androgenesis inhibitor, androgenesis inhibitor, and androgenesis inhibitor, in mCRPC patients.



Dr. [Name]
is a leading expert in the field of prostate cancer. He has published numerous articles and presented at international conferences. Dr. [Name] is currently a senior consultant at [Institution] and is also a member of the [Committee].

Experts Debated the Role of TKIs and Immunotherapies in mCRPC

CONTACT-02

Experts will debate the optimal sequencing of agents...

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- 8. Experts will debate the optimal sequencing of agents...



Dr. [Name]
[Title]
[Affiliation]

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EPICS

Congress Highlights

Radioligand Therapies for Prostate Cancer

Ra-223–docetaxel vs docetaxel–Ra-223 sequence in mCRPC with prospective biomarker evaluation (RAPSON study)

Conteduca et al. ESMO 2024; LBA71

STUDY POPULATION AND METHODS

> 70 pts with mCRPC and symptomatic bone-dominant metastases.

CHANGE IN HRQOL SCORES: BASELINE TO WK 12



First results of phase III EORTC-GUCCG 1333/PEACE-3: Enzalutamide ± Ra-223 in asymptomatic/mildly symptomatic bone-metastatic mCRPC

Gillessen et al. ESMO 2024; LBA1

STUDY POPULATION AND METHODS

> 446 pts with asymptomatic or mildly symptomatic mCRPC with

OVERALL SURVIVAL



UpFrontPSMA: A phase II study of sequential 177Lu-PSMA-617 and docetaxel vs docetaxel in mHSPC

Azad et al. ESMO 2024; LBA66

STUDY POPULATION AND METHODS

> 122 pts with mHSPC

PSA RESPONSE



Symptomatic skeletal events, HRQOL, and pain in PSMAfore: [177Lu]Lu-PSMA-617 in taxane-naive patients with PSMA-positive mCRPC

Fizazi et al. ESMO 2024; 1599P

STUDY POPULATION AND METHODS

> 468 pts with mCRPC (≥1 PSMA-positive metastatic lesion)

TIME TO WORSENING OF FACT-P TOTAL SCORE



Hematologic impact of [177Lu]Lu-PSMA-617 vs ARPI change in patients with mCRPC in PSMAfore

Chi et al. ESMO 2024; 1611P

STUDY POPULATION AND METHODS

> Adults with PSMA-positive mCRPC and 1 progression on prior

HEMATOLOGIC TEAEs BY NO. OF BONE METASTASES

HEMATOLOGIC TEAEs BY NO. OF BONE METASTASES



RESPONSE RATES BY NO. OF BONE METASTASES



Efficacy of ¹⁷⁷Lu-PNT2002 in PSMA-positive mCRPC following progression on an ARPI (SPLASH)

Sartor et al. ESMO 2024; LBA65

STUDY POPULATION AND METHODS

> 412 pts with mCRPC (PSMA-avid PET) that progressed after 1

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL IN THE INTENTION-TO-TREAT POPULATION



RESPONSE EVALUATION IN THE INTENTION-TO-TREAT POPULATION



Lutetium-177–Prostate-Specific Membrane Antigen (177Lu-PSMA) therapy in patients treated with prior Ra-223

Rahbar et al. ESMO 2024; 1629P

STUDY POPULATION AND METHODS

> 198 pts with heavily pretreated mCRPC, including prior Ra-223

SAFETY



EPICS

Key Insights

Radioligand Therapies for Prostate Cancer

Experts Considered New Data From Trials Evaluating Ra-223

PEACE-3

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Dr. [Name] is a... (text is blurred)

Experts Discussed Implications of Recent Trials Investigating 177Lu-PSMA in mPC

PSMAfore

Key points from the PSMAfore session include:

- 1. The PSMAfore session will focus on the clinical implications of recent trials.
- 2. The PSMAfore session will discuss the clinical implications of recent trials.
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Dr. [Name]
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Experts Assessed Novel PSMA-Targeted Radioligands

SPLASH

The SPLASH trial investigating ¹⁷⁷Lu-PNT2002 vs second ARPI in PSMA-positive

...investigating the optimal sequencing of agents

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EPICS

Congress Highlights

**Localized and Hormone-Sensitive
Prostate Cancer**

Decipher mRNA score for prediction of survival benefit from docetaxel at start of ADT for advanced PC: An ancillary study of the STAMPEDE trials

Grist et al. ESMO 2024; 15960

STUDY POPULATION AND METHODS

> Retrospective analysis of tissue samples from 895 pts enrolled in

IMPACT OF DECIPHER SCORE



Phenotypic and genomic characterization of de novo metastatic prostate cancer: An ancillary study of the PEACE-1 phase III trial

Pobel et al. ESMO 2024; 1595MO

STUDY POPULATION AND METHODS

> Samples from 350 pts enrolled in the PEACE-1 trial (abiraterone-

OVERALL SURVIVAL



Phase III evaluation of transdermal estradiol (tE2) vs LHRHa for androgen suppression in M0 prostate cancer

Langley et al. ESMO 2024; LBA69

STUDY POPULATION AND METHODS

> 1.360 pts with M0 PC were randomized to transdermal estradiol

METASTASIS-FREE SURVIVAL

Figure 1: Metastasis-Free Survival (MFS) in the Overall Population (N=1360)



Figure 2: Response Evaluation in the Overall Population (N=1360)



Efficacy and safety of darolutamide + ADT in patients with mHSPC from the phase III ARANOTE trial

Saad et al. ESMO 2024; LBA68

EPICS

STUDY POPULATION AND METHODS

> 669 pts with mHSPC were randomized 2:1 to ADT + darolutamide

SAFETY PROFILE

SAFETY PROFILE FROM STARTLINE TO THE LAST TREATMENT ASSESSMENT



RESPONSE EVALUATION AT FIRST ANALYSIS PERIOD



EPICS

Key Insights

**Localized and Hormone-Sensitive
Prostate Cancer**

Experts Discussed Hormonal Therapy Options for Patients With Advanced Prostate Cancer

ARANOTE

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Dr. [Name]
[Title]
[Institution]

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Experts Considered Potential Biomarkers for Guiding Treatment Decision-Making in Prostate Cancer

STAMPEDE


Stamper et al. will help clarify the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of docetaxel plus enzalutamide and apalutamide, however, TDMT is becoming the main option.
- 2. Most experts are using enzalutamide or apalutamide, but will prescribe the second agent for patients with evidence of prior resistance.
- 3. The second agent may also be used in the neoadjuvant setting before TDMT in patients with documented prior resistance.
 - 1. Preferred to used enzalutamide, experts are divided on whether they would currently use TDMT or enzalutamide.
 - 2. Results of the ongoing STAMPEDE trial comparing enzalutamide monotherapy as TDMT will help to clarify the optimal sequencing of these agents.
- 4. Enzalutamide and the second agent may also be used earlier than docetaxel in patients who were following treatment with enzalutamide, apalutamide, and TDMT in the neoadjuvant setting, but this represents a small fraction of patients.
- 5. Future guidelines can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus drug-free or 2 drugs).
- 6. The comparative efficacy of enzalutamide, apalutamide, and the second agent have opened other options, such as enzalutamide/abiraterone combinations, radium, and immunotherapy, in late lines of therapy.



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