

 EPICS An abstract graphic consisting of several thick, curved lines in various colors (teal, green, orange, grey, light blue) arranged in a circular pattern, resembling a stylized sunburst or a cluster of paths.

# GENITOURINARY (GU) MALIGNANCIES IN 2021 AND BEYOND

December 7 and 8, 2021

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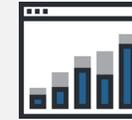
## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
December 7 and 8, 2021



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



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations



**PANEL:** Key experts in  
GU cancers  
> 9 from US



**GENITOURINARY CANCER-  
SPECIFIC DISCUSSIONS** on  
therapeutic advances and  
their application into clinical  
decision-making

# Panel Consisting of 9 US GU Cancer Experts

EPICS

Susan F. Slovin, MD, PhD  
Memorial Sloan Kettering  
Cancer Center



David M. Nanus, MD  
Weill Cornell Medicine



Scott Tagawa, MD, FACP  
Weill Cornell Medicine



Leonard G. Gomella, MD, FACS  
Sidney Kimmel Cancer Center



Bernard H. Bochner, MD  
Memorial Sloan Kettering  
Cancer Center



**CHAIR:**  
Daniel P. Petrylak, MD  
Yale Cancer Center

David Quinn, MBBS, PhD,  
FRACP, FACP  
University of Southern California



Robert Dreicer, MD, MS,  
MACP, FASCO  
University of Virginia  
Cancer Center



Oliver Sartor, MD  
Tulane Cancer Center



# Agenda (Day 1)

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Time	Topic	Speaker/Moderator
4.00 PM – 4.05 PM	<b>Welcome and Introductions</b>	Daniel Petrylak, MD
4.05 PM – 4.15 PM	<b>Advances in Imaging Technologies for GU Cancers</b>	Leonard G. Gomella, MD, FACS
4.15 PM – 4.35 PM	<b><i>Key Questions and Topics for Discussion</i></b>	All
4.35 PM – 4.40 PM	<b>Summary and Key Takeaways</b>	
4.40 PM – 4.50 PM	<b>Diagnosing and Managing Localized/Locally Advanced Prostate Cancer</b>	Susan Slovin, MD, PhD
4.50 PM – 5.10 PM	<b><i>Key Questions and Topics for Discussion</i></b>	
5.10 PM – 5.15 PM	<b>Summary and Key Takeaways</b>	
5.15 PM – 5.30 PM	<b>Treatment Paradigms for Advanced Prostate Cancer</b>	Oliver Sartor, MD
5.30 PM – 6.05 PM	<b><i>Key Questions and Topics for Discussion</i></b>	All
6.05 PM – 6.10 PM	<b>Summary and Key Takeaways</b>	
6.10 PM – 6.20 PM	<b>BREAK</b>	
6.20 PM – 6.35 PM	<b>Investigational Therapies for Metastatic CRPC</b>	Scott Tagawa, MD, MS, FACP
6.35 PM – 7.05 PM	<b><i>Key Questions and Topics for Discussion</i></b>	All
7.05 PM – 7.10 PM	<b>Summary and Key Takeaways</b>	
7.10 PM – 7.25 PM	<b>Early Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC)</b>	Bernard Bochner, MD, FACS
7.25 PM – 7.50 PM	<b><i>Key Questions and Topics for Discussion</i></b>	All
7.50 PM – 7.55 PM	<b>Summary and Key Takeaways</b>	
7.55 PM – 8.00 PM	<b>Conclusions and Wrap-up</b>	Daniel Petrylak, MD



# Agenda (Day 2)

EPICS

Time	Topic	Speaker/Moderator
4.00 PM – 4.05 PM	<b>Welcome and Introductions</b>	Daniel Petrylak, MD
4.05 PM – 4.20 PM	<b>Current Paradigms and Future Directions in Metastatic Bladder Cancer</b>	Robert Dreicer, MD, MS, MACP, FASCO
4.20 PM – 5.05 PM	<i>Key Questions and Topics for Discussion</i>	
5.05 PM – 5.10 PM	<b>Summary and Key Takeaways</b>	
5.10 PM – 5.25 PM	<b>Evolving Paradigms for Metastatic RCC</b>	David Nanus, MD
5.25 PM – 6.10 PM	<i>Key Questions and Topics for Discussion</i>	All
6.10 PM – 6.15 PM	<b>Summary and Key Takeaways</b>	
6.15 PM – 6.25 PM	<b>BREAK</b>	
6.25 PM – 6.40 PM	<b>Neo/Adjuvant Treatment of RCC</b>	David Quinn, MBBS, PhD, FRACP, FACP
6.40 PM – 7.05 PM	<i>Key Questions and Topics for Discussion</i>	
7.05 PM – 7.10 PM	<b>Summary and Key Takeaways</b>	
7.10 PM – 7.20 PM	<b>Current and Future Management of Non-clear Cell RCC</b>	David Quinn, MBBS, PhD, FRACP, FACP
7.20 PM – 7.45 PM	<i>Key Questions and Topics for Discussion</i>	All
7.45 PM – 7.50 PM	<b>Summary and Key Takeaways</b>	
7.50 PM – 8.00 PM	<b>Wrap-up and Adjourn</b>	Daniel Petrylak, MD



**EPICS**

**Summary of Faculty  
Presentations and Key  
Insights**

**EPICS**

# Advances in Imaging Technologies for GU Cancers





# Advances in Imaging Technologies for GU Cancers (2/2)

Presented by Leonard G. Gomella, MD, FACS

## PSMA-TARGETED PET IMAGING

### STUDY POPULATION

1. 1000 patients with prostate cancer, 500 with PSA > 10 ng/mL and Gleason score > 7, and 500 with PSA < 10 ng/mL and Gleason score < 7. All patients were treated with androgen deprivation therapy (ADT) and received either PSMA-targeted PET imaging or conventional imaging (CT, MRI, and bone scan). The study was designed to evaluate the impact of PSMA-targeted PET imaging on treatment decisions and patient outcomes.

### RESULTS

2. 500 patients received PSMA-targeted PET imaging, and 500 received conventional imaging. The study found that PSMA-targeted PET imaging identified more metastatic disease compared to conventional imaging, leading to more aggressive treatment in the PSMA group.

### KEY TAKEAWAYS

3. PSMA-targeted PET imaging provides more accurate staging of prostate cancer, leading to improved patient outcomes and reduced healthcare costs.

## RESEARCH AND FUTURE DIRECTIONS

### PSMA-TARGETED PET IMAGING IN THE CLINICAL SETTING



### RESPONSE EVALUATION USING PSMA-TARGETED PET IMAGING



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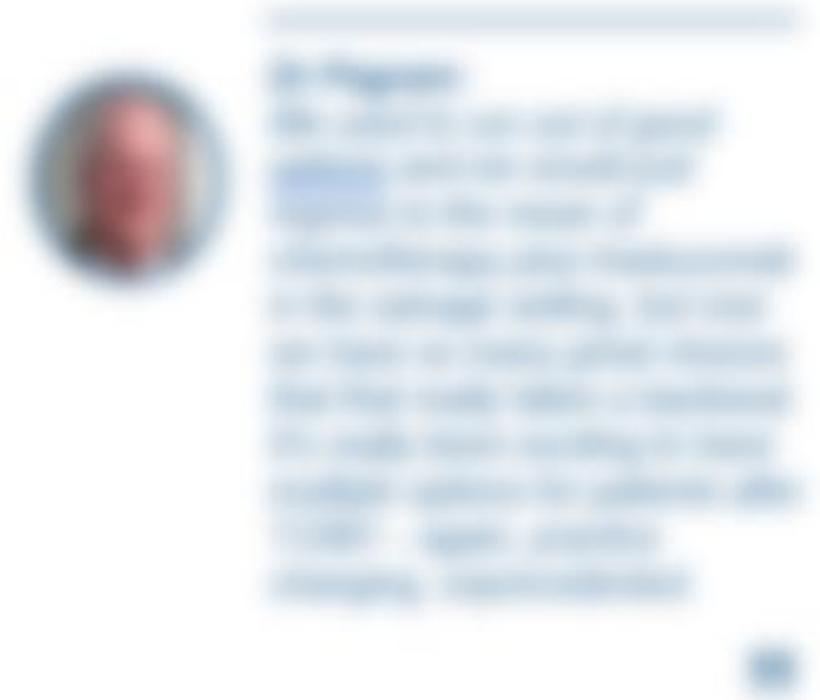
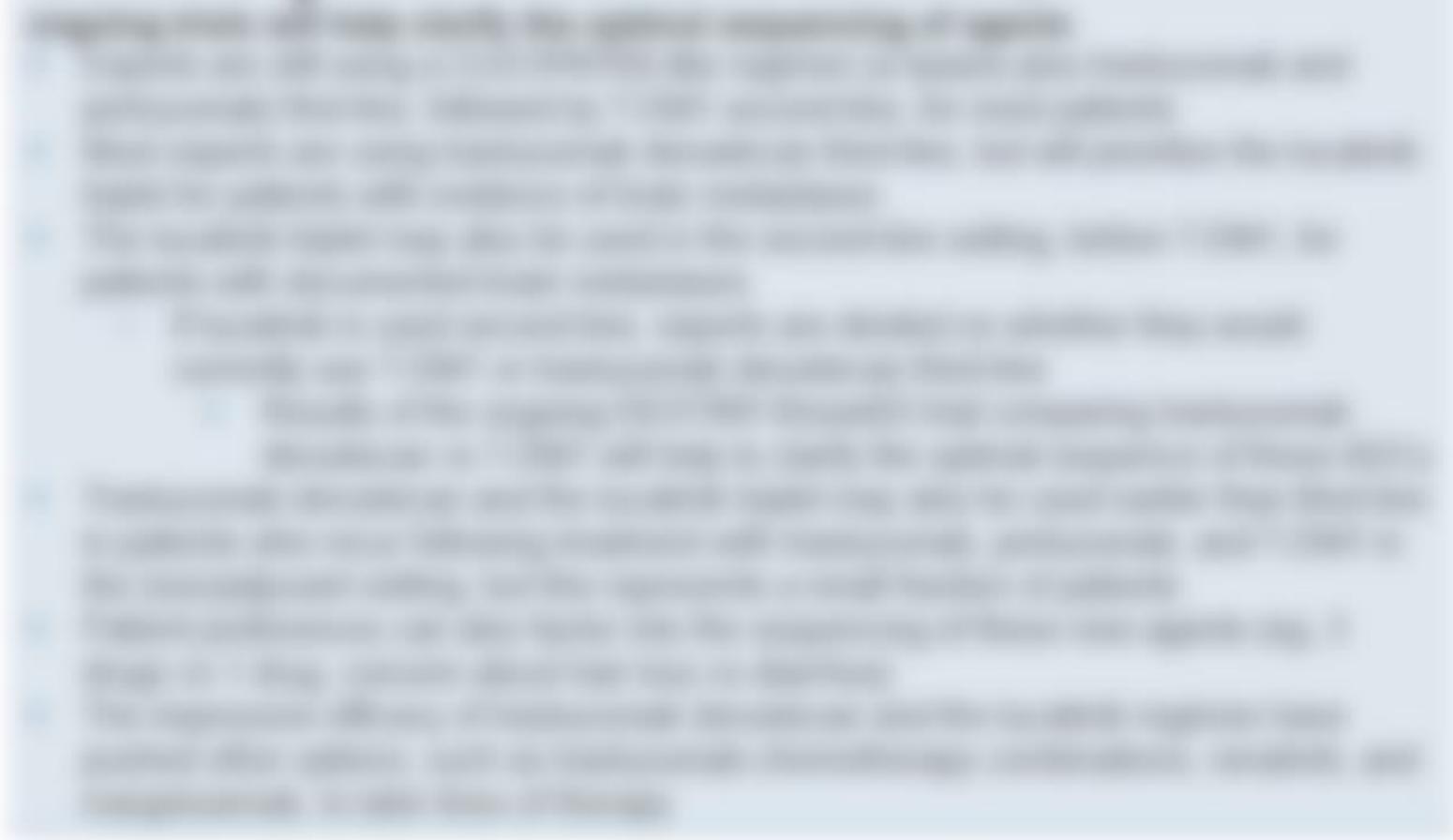
## Key Insights

Imaging Technologies for GU Cancers

# Experts Debated the Evolving Role for PSMA PET Scans in Prostate Cancer

## POTENTIAL USES FOR PSMA PET SCANS

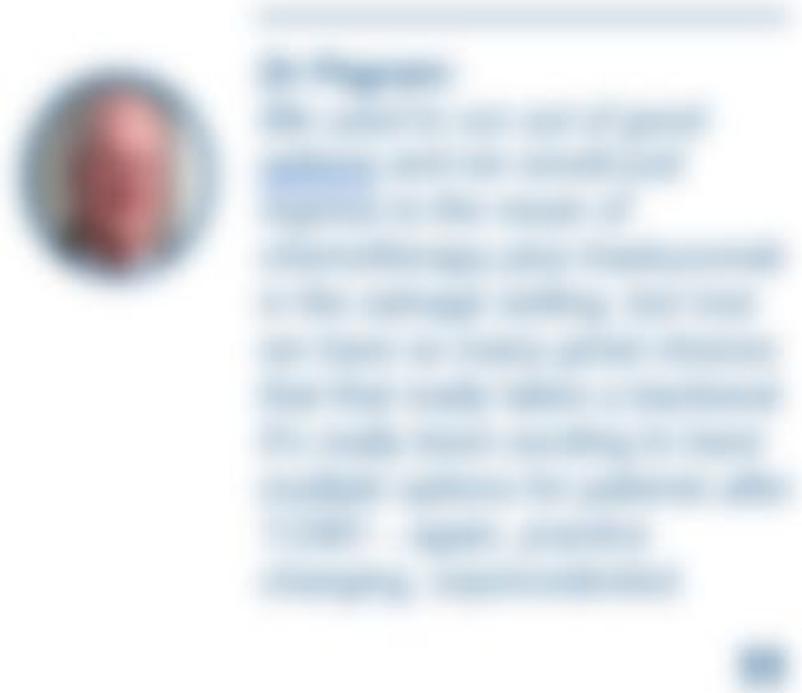
The clinical utility of PSMA PET scans is evolving and will be better defined over



# Experts Discussed Other Considerations Regarding Imaging Modalities in Patients With Prostate Cancer

## PSMA PET SCANS

> Several experts noted they are having difficulty getting PSMA PET scans reimbursed by



**EPICS**

# Diagnosing and Managing Localized/Locally Advanced Prostate Cancer



# Diagnosing and Managing Localized/Locally Advanced Prostate Cancer (1/2)

Presented by Susan Slovin, MD, PhD

## SELECTING PATIENTS FOR ACTIVE SURVEILLANCE

Active surveillance is a management strategy for prostate cancer that involves monitoring the cancer closely with regular PSA tests, digital rectal exams, and repeat biopsies. The goal is to detect any progression early so that treatment can be initiated if needed. Active surveillance is not a "wait and see" approach, but rather a proactive management strategy that allows for early intervention if the cancer shows signs of progression.

- Active surveillance is appropriate for patients with low-risk prostate cancer (PSA < 10, Gleason score < 7, and clinical stage T1-T2a).
- Active surveillance is also appropriate for patients with intermediate-risk prostate cancer (PSA 10-20, Gleason score 7-8, and clinical stage T2b-T2c).
- Active surveillance is not appropriate for patients with high-risk prostate cancer (PSA > 20, Gleason score > 8, and clinical stage T3-T4).





# Diagnosing and Managing Localized/Locally Advanced Prostate Cancer (2/2)

Presented by Susan Slovin, MD, PhD

## TRANSITIONING FROM ACTIVE SURVEILLANCE TO TREATMENT

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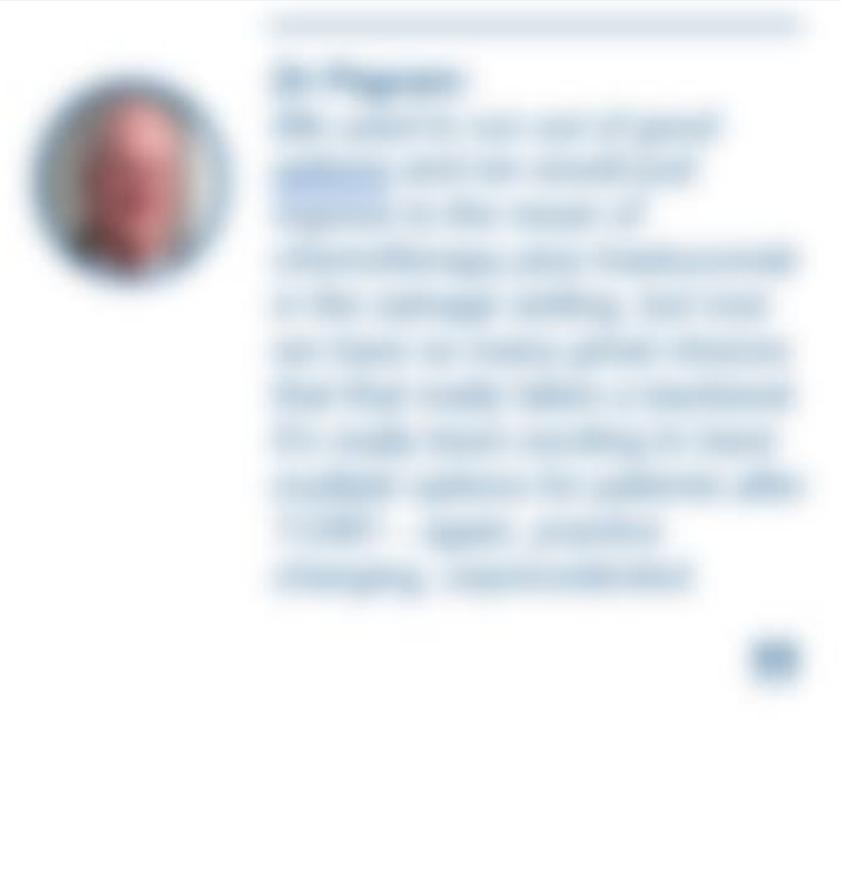
## Key Insights

Localized/Locally Advanced Prostate Cancer

# Experts Discussed Factors Impacting Patient Selection for Active Surveillance

## CLINICAL AND MOLECULAR CONSIDERATIONS

Active surveillance remains an area of uncertainty and debate focused on 2 key questions: who are the ideal candidates for active surveillance?



# Experts Discussed Evolving Treatment Options for Patients With Localized Prostate Cancer

## ANTIANDROGEN THERAPY

Several experts indicated they are comfortable adding abiraterone to ADT for patients with high-risk localized CSPC, on the basis of

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# Treatment Paradigms for Advanced Prostate Cancer



# Treatment Paradigms for Advanced Prostate Cancer (1/3)

Presented by Oliver Sartor, MD

## STUDY POPULATION

Approximately 1000 patients with advanced prostate cancer... (text is blurred)

## RESULTS

Median overall survival... (text is blurred)

## KEY TAKEAWAYS

Continuing treatment beyond week 25 provides clinical benefit... (text is blurred)

## PROSTATE-SPECIFIC ANTIGEN (PSA) RESPONSE



## RESPONSE RATE AT 24 WEEKS AND 48 WEEKS





# Treatment Paradigms for Advanced Prostate Cancer (2/3)

Presented by Oliver Sartor, MD

## STUDY POPULATION

1000 patients with advanced prostate cancer, randomized to either docetaxel or placebo. The study population was defined as patients with a PSA level of  $\geq 10$  ng/mL, a Gleason score of  $\geq 7$ , and a clinical stage of  $\geq T2c$ . The median age was 73 years. The median time from diagnosis to randomization was 1.5 years. The median PSA at randomization was 15.5 ng/mL. The median time to death was 15.5 months. The median time to death was 15.5 months.

## RESULTS

1000 patients with advanced prostate cancer, randomized to either docetaxel or placebo. The study population was defined as patients with a PSA level of  $\geq 10$  ng/mL, a Gleason score of  $\geq 7$ , and a clinical stage of  $\geq T2c$ . The median age was 73 years. The median time from diagnosis to randomization was 1.5 years. The median PSA at randomization was 15.5 ng/mL. The median time to death was 15.5 months. The median time to death was 15.5 months.

## KEY CONCLUSIONS

Docetaxel treatment improved overall survival compared to placebo and decreased the proportion of patients with advanced disease.

## RESPONSE RATE AND TOXICITY



## RESPONSE RATE AND TOXICITY





# Treatment Paradigms for Advanced Prostate Cancer (3/3)

Presented by Oliver Sartor, MD

## STUDY POPULATION

Approximately 1000 patients with advanced prostate cancer... (text is blurred)

## RESULTS

Median overall survival... (text is blurred)

## KEY TAKEAWAYS

Continuing testosterone treatment beyond week 25 provides clinical benefit... (text is blurred)

## PROSTATE-SPECIFIC ANTIGEN (PSA) LEVELS



## RESPONSE RATE AT 24 WEEKS AND 48 WEEKS



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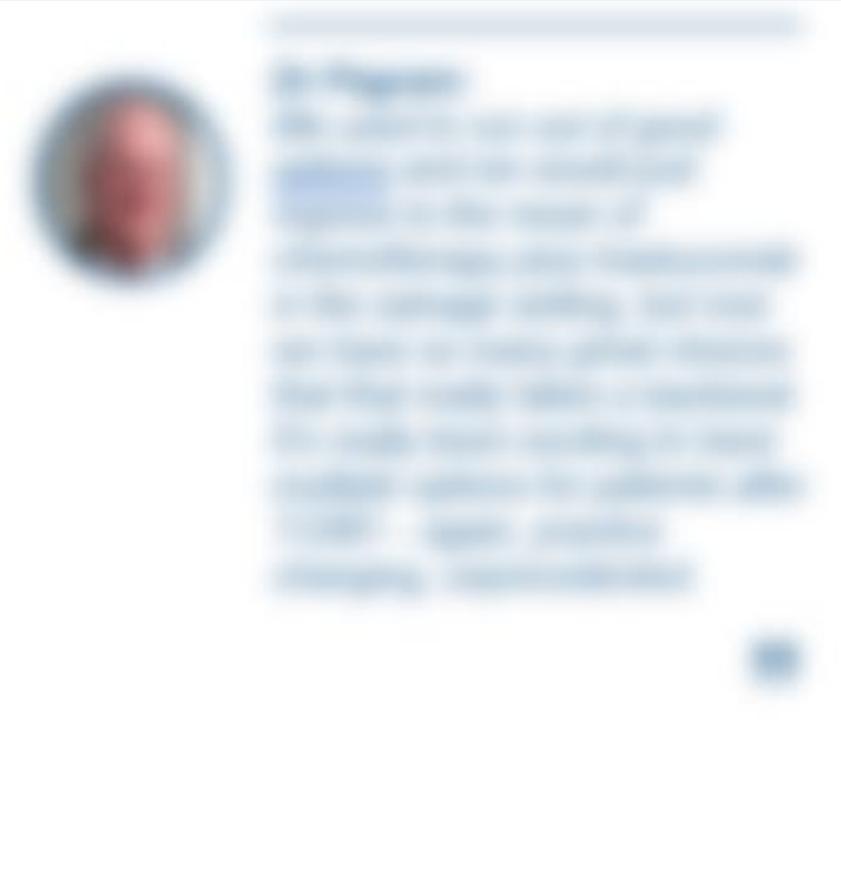
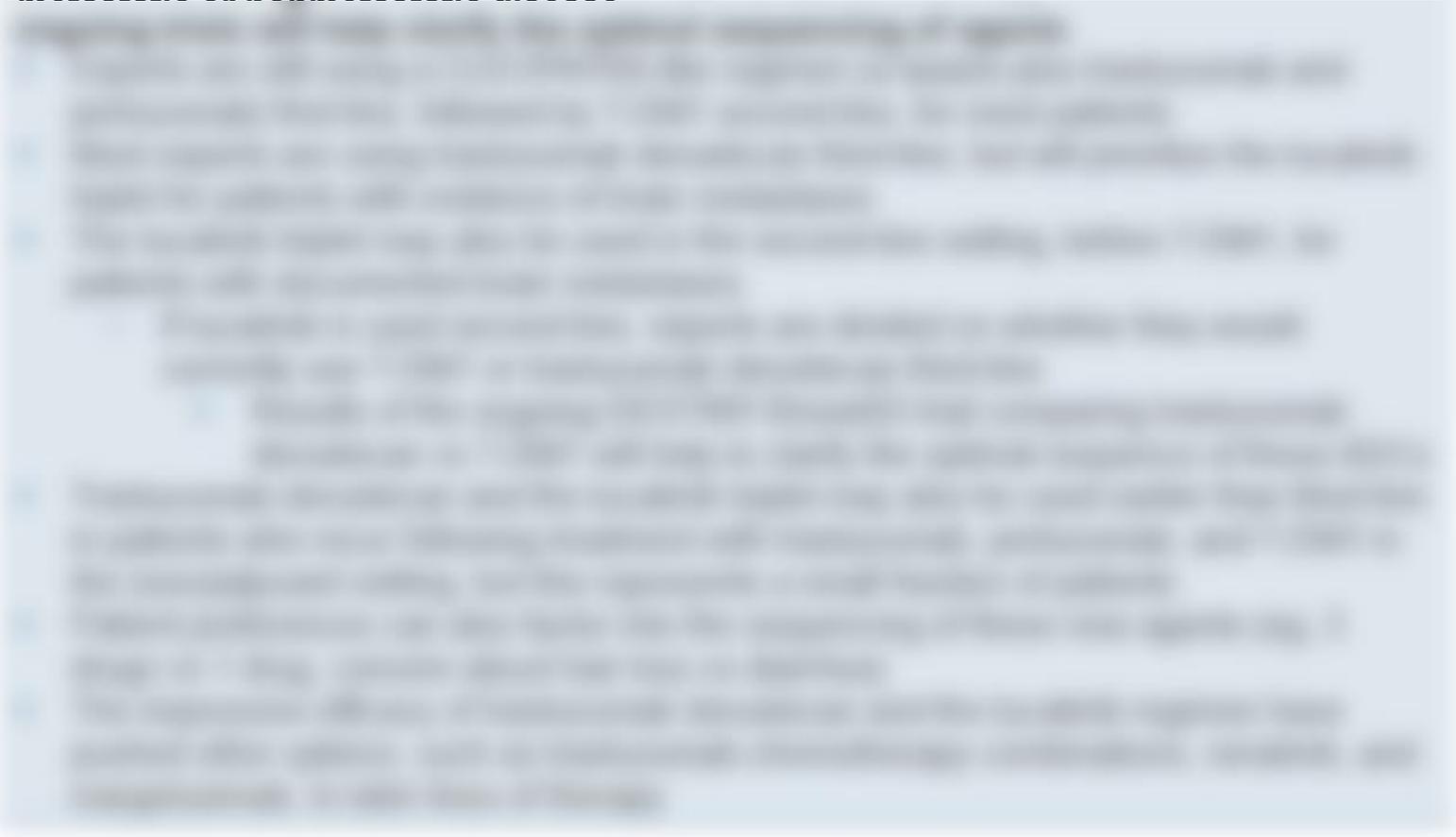
## Key Insights

Advanced Prostate Cancer

# Experts Debated Management Options for Nonmetastatic CRPC

## IMAGING

Several experts are now using more-sensitive imaging modalities such as PSMA PET to determine if patients with CRPC have metastatic or nonmetastatic disease

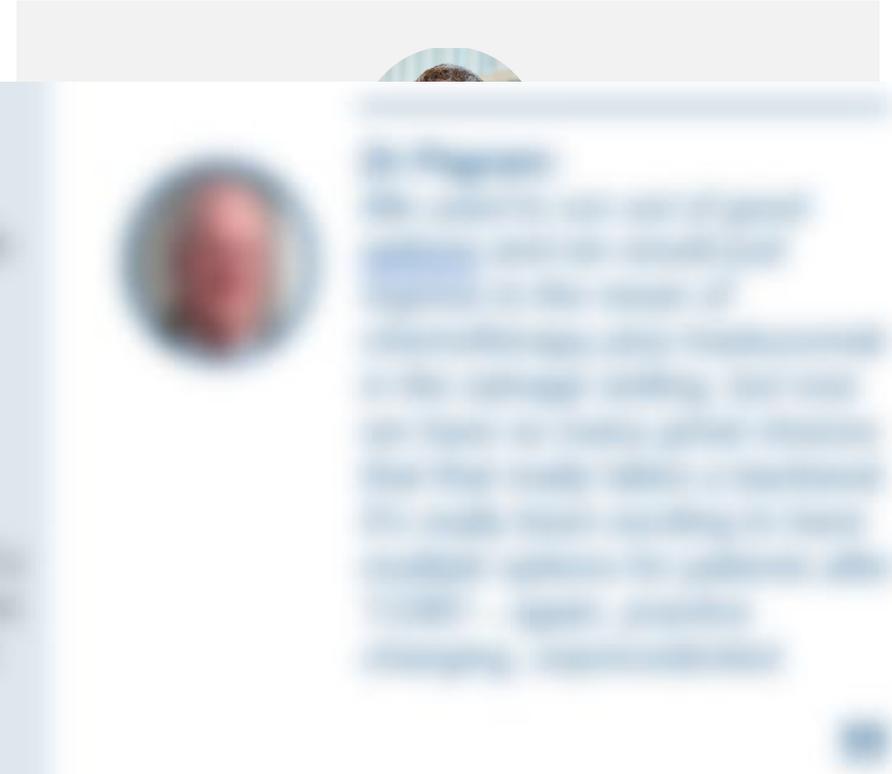
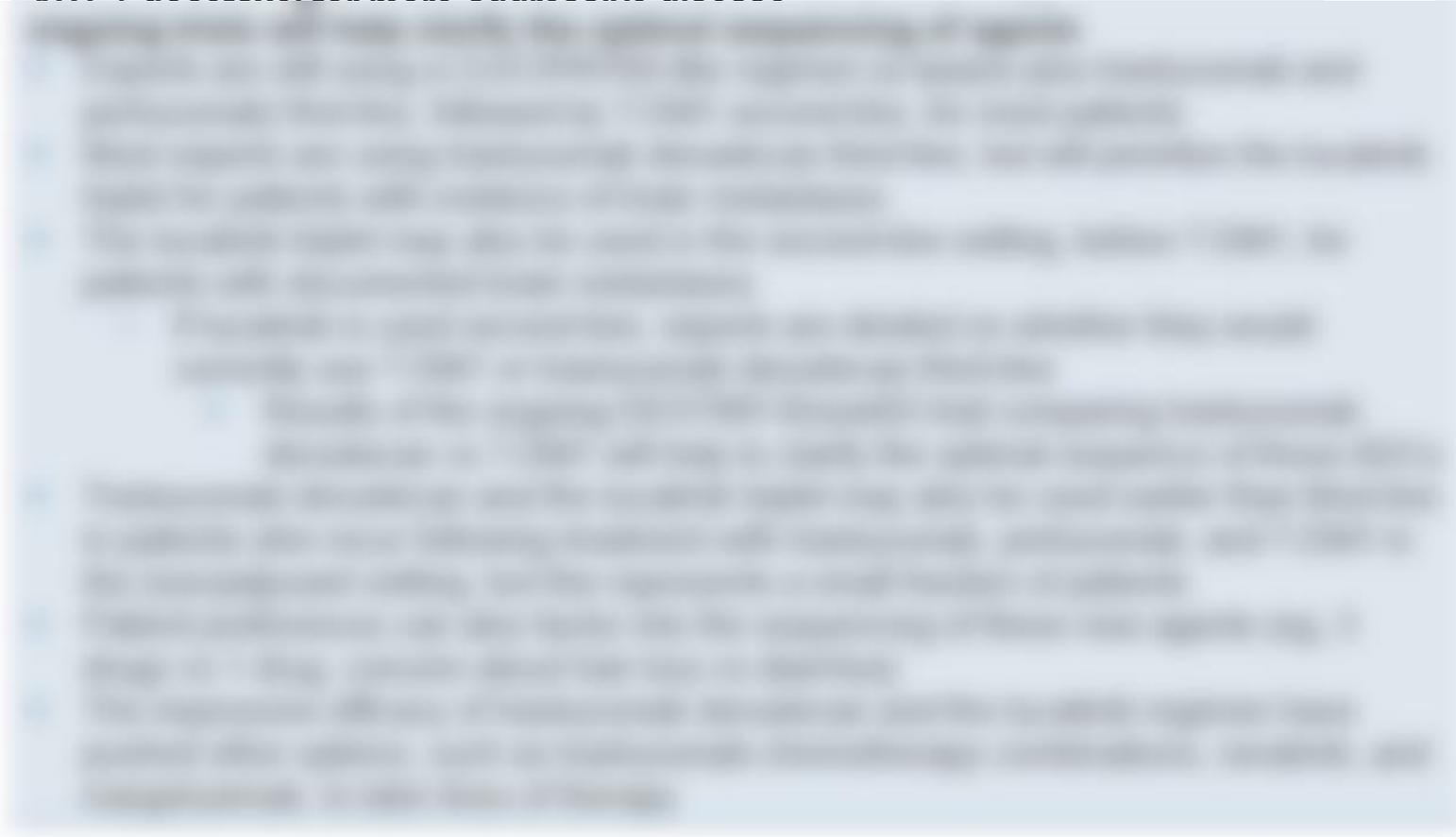


# Experts Discussed Treatment Options for Patients With Metastatic Castration-Sensitive PC

## CURRENT AND EVOLVING PARADIGMS

ADT + an antiandrogen is typically used for most patients with mCSPC, or

ADT + docetaxel for more symptomatic disease



# Experts Reviewed Sequencing Considerations for Patients With mCRPC

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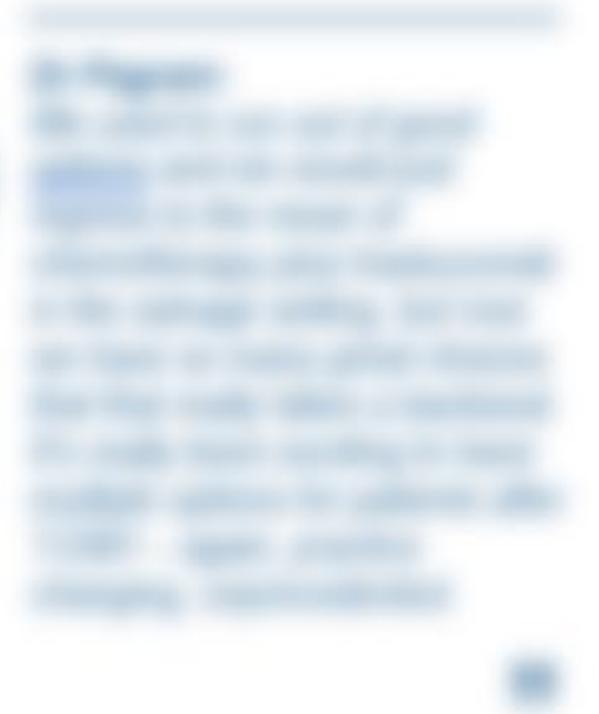


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# Experts Reviewed Approved and Investigational Targeted Therapies for mCRPC

## PARP INHIBITORS

> All of the experts test their patients with metastatic PC for germline mutations, but expressed concern that community practitioners are not



## IDENTIFICATION

> Neuroendocrine-emergent mCRPC may be suspected in patients with visceral disease and low PSA  
Several comments commented that the neuroendocrine variant is a common cause of low PSA results, especially in patients with visceral disease. The decision to treat

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# Investigational Therapies for Metastatic CRPC



# Investigational Therapies for Metastatic CRPC (1/2)

Presented by Scott Tagawa, MD, MS, FACP

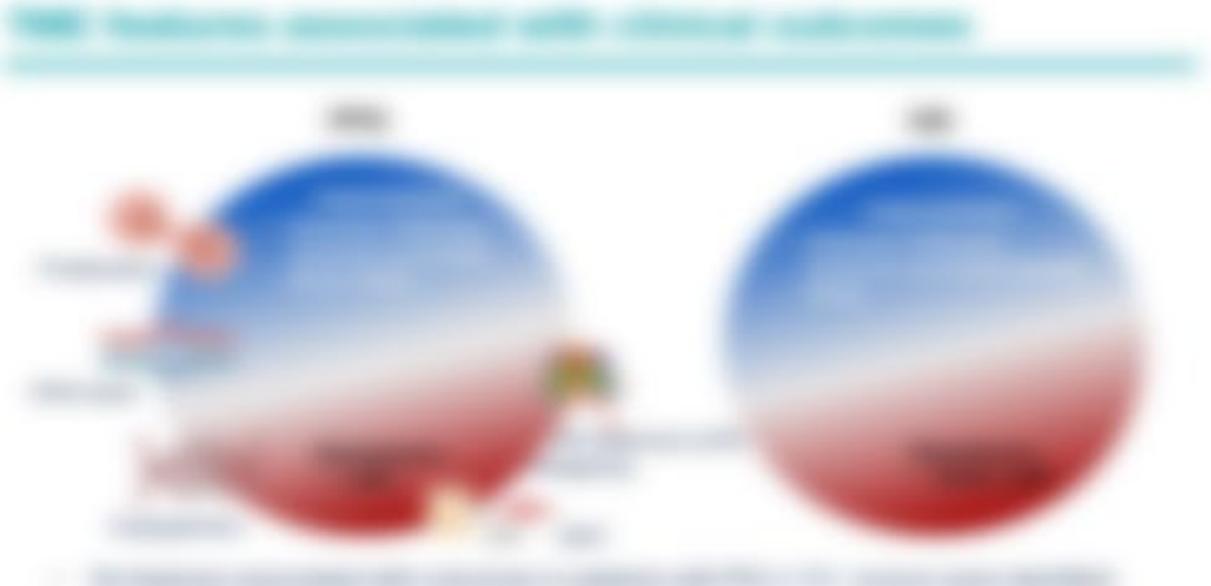
## PSMA-TARGETED AGENTS

**PSMA-TARGETED AGENTS**

PSMA-targeted agents are a class of investigational therapies for metastatic CRPC. They consist of a PSMA-targeting antibody or ligand conjugated to a cytotoxic payload or a radionuclide. These agents are designed to bind to PSMA on the surface of prostate cancer cells, leading to cell death through various mechanisms such as antibody-dependent cellular cytotoxicity (ADCC) or internalization and release of cytotoxic agents.

Key examples include:

- PSMA-703 (Pluvicto):** A PSMA-targeting antibody conjugated to Lutetium-177 (177Lu), used for radioligand therapy (RLT).
- PSMA-750 (BMS-986207):** A PSMA-targeting antibody conjugated to a cytotoxic payload, used in phase I trials.
- PSMA-750 (BMS-986207):** A PSMA-targeting antibody conjugated to a cytotoxic payload, used in phase I trials.





# Investigational Therapies for Metastatic CRPC (2/2)

Presented by Scott Tagawa, MD, MS, FACP

## INVESTIGATIONAL DIRECTIONS – AVAILABLE AGENTS

**Investigational Agents**

Agents currently in clinical trials for metastatic CRPC, including:

- Enzalutamide
- Abiraterone
- Apalutamide
- Radix-100
- MDV3100
- MDM200
- MDM201
- MDM202
- MDM203
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- MDM250

## NOVEL TARGETED AGENTS

**Novel Targeted Agents**

Agents targeting novel pathways in metastatic CRPC, including:

- MDM200
- MDM201
- MDM202
- MDM203
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- MDM250



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## Key Insights

Investigational Therapies for Metastatic CRPC

# Experts Discussed the Potential of Novel Agents in Development for Prostate Cancer

## PSMA-TARGETED THERAPIES

**Keynote Address: PSMA-Targeted Therapies in Prostate Cancer**

The keynote address focused on the potential of novel PSMA-targeted therapies in the treatment of prostate cancer. The speaker discussed the current landscape of PSMA-targeted therapies, including the use of PSMA-targeted radioligand therapy (RLT) and the development of novel PSMA-targeted agents. The speaker highlighted the importance of understanding the biology of PSMA and the potential for personalized medicine in the treatment of prostate cancer.

**Panel Discussion: PSMA-Targeted Therapies in Prostate Cancer**

The panel discussion featured four experts who discussed the potential of novel PSMA-targeted therapies in the treatment of prostate cancer. The panelists discussed the current landscape of PSMA-targeted therapies, including the use of PSMA-targeted radioligand therapy (RLT) and the development of novel PSMA-targeted agents. The panelists highlighted the importance of understanding the biology of PSMA and the potential for personalized medicine in the treatment of prostate cancer.



**Speaker:** [Name]

[Blurred text describing the speaker's role and the content of their presentation.]

# Experts Discussed Early Phase Investigational Agents and Shifting Paradigms

**KEY TAKEAWAYS**

- 1. The industry is seeing a shift in early phase investigational agents, with a focus on novel targets and mechanisms of action.
- 2. Shifting paradigms in drug development are leading to a re-evaluation of traditional trial designs and endpoints.
- 3. Collaboration between academia and industry is essential for advancing novel therapies through the pipeline.

**CHALLENGES AND OPPORTUNITIES**

- 1. Navigating the regulatory landscape for novel agents and trial designs remains a significant challenge.
- 2. Limited patient access to novel therapies in early phase trials is a major barrier to development.
- 3. The high cost of drug development necessitates innovative financing models and risk-sharing strategies.

**CONCLUSION**

The future of early phase drug development lies in embracing novel paradigms, fostering collaboration, and addressing the challenges of patient access and cost. By doing so, the industry can accelerate the delivery of novel, transformative therapies to patients in need.



# Experts Discussed Challenges and Opportunities for New Drug Development in mCRPC

## OPPORTUNITIES AND CHALLENGES IN NEW THERAPY DEVELOPMENT

**OPPORTUNITIES AND CHALLENGES IN NEW THERAPY DEVELOPMENT**

The oncology landscape is rapidly evolving, and the development of new therapies for metastatic castration-resistant prostate cancer (mCRPC) is a complex and challenging endeavor. This session explored the key challenges and opportunities in this space.

**Challenges:**

- Limited target discovery and validation in mCRPC.
- High attrition rates in clinical trials due to lack of efficacy or toxicity.
- Limited patient access to novel therapies.
- High cost of drug development.

**Opportunities:**

- Advances in genomics and biomarker discovery.
- Novel drug classes and combination therapies.
- Improved patient stratification and personalized medicine.
- Streamlined regulatory pathways.

**Key Takeaways:**

While the challenges are significant, the opportunities for new therapy development in mCRPC are substantial. Collaboration between academia, industry, and regulatory agencies is essential to overcome these challenges and bring novel therapies to patients.

**Next Steps:**

- Focus on target discovery and validation.
- Optimize clinical trial design and execution.
- Improve patient access and affordability.
- Foster collaboration and knowledge sharing.



**Speaker:**

[Name of speaker]

[Biography of speaker]

**EPICS**

**Early Stage Bladder Cancer  
(BCG-Resistant NMIBC;  
MIBC)**



# Early Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC) (1/4)

Presented by Bernard Bochner, MD, FACS



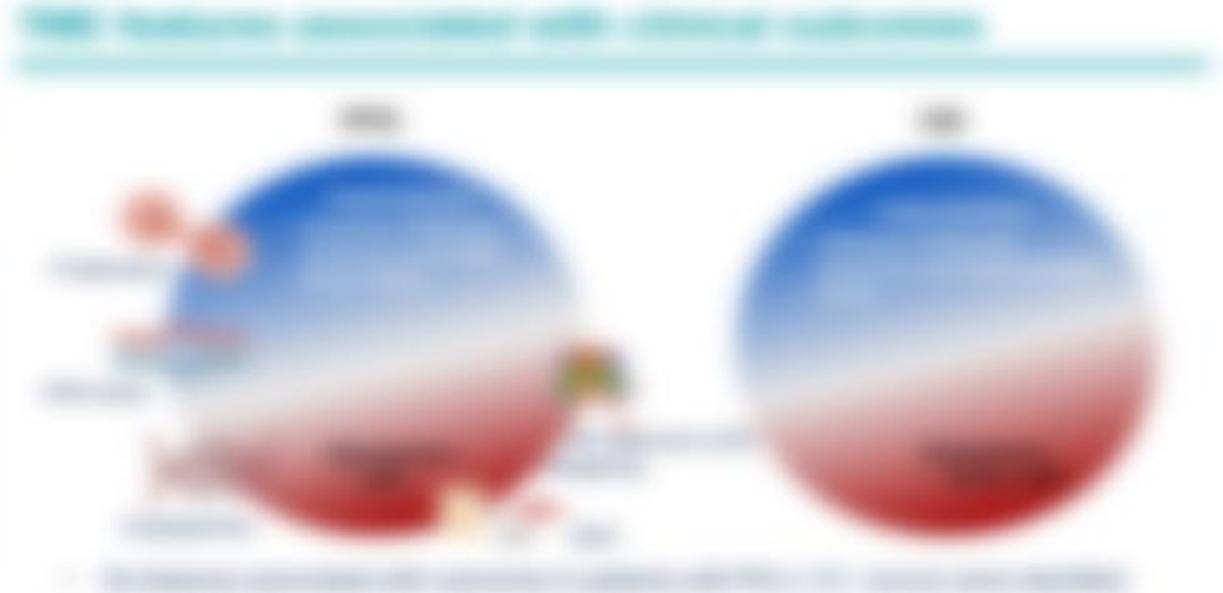
## NON-MUSCLE-INVASIVE BLADDER CANCER – CONVENTIONAL APPROACHES

**CONVENTIONAL APPROACHES**

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# Early Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC) (2/4)

Presented by Bernard Bochner, MD, FACS

## IMMUNE CHECKPOINT INHIBITORS – NMIBC

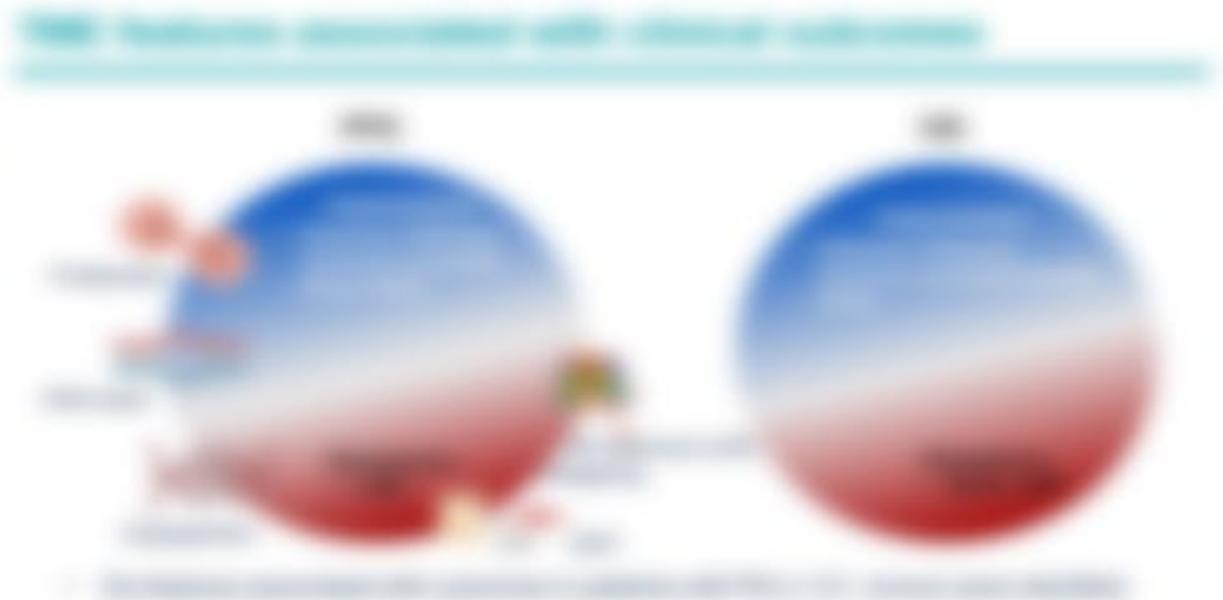
## INVESTIGATIONAL AGENTS – NMIBC

**Background**

Immune checkpoint inhibitors (ICIs) have shown promising results in various cancer types, including bladder cancer. In NMIBC, ICIs aim to enhance the immune system's ability to recognize and destroy cancer cells.

**Key Findings**

- ICIs, such as pembrolizumab and nivolumab, have been evaluated in clinical trials for NMIBC.
- These treatments have shown potential for improving survival and delaying recurrence in BCG-resistant NMIBC.
- Side effects, including immune-related adverse events, are closely monitored during treatment.





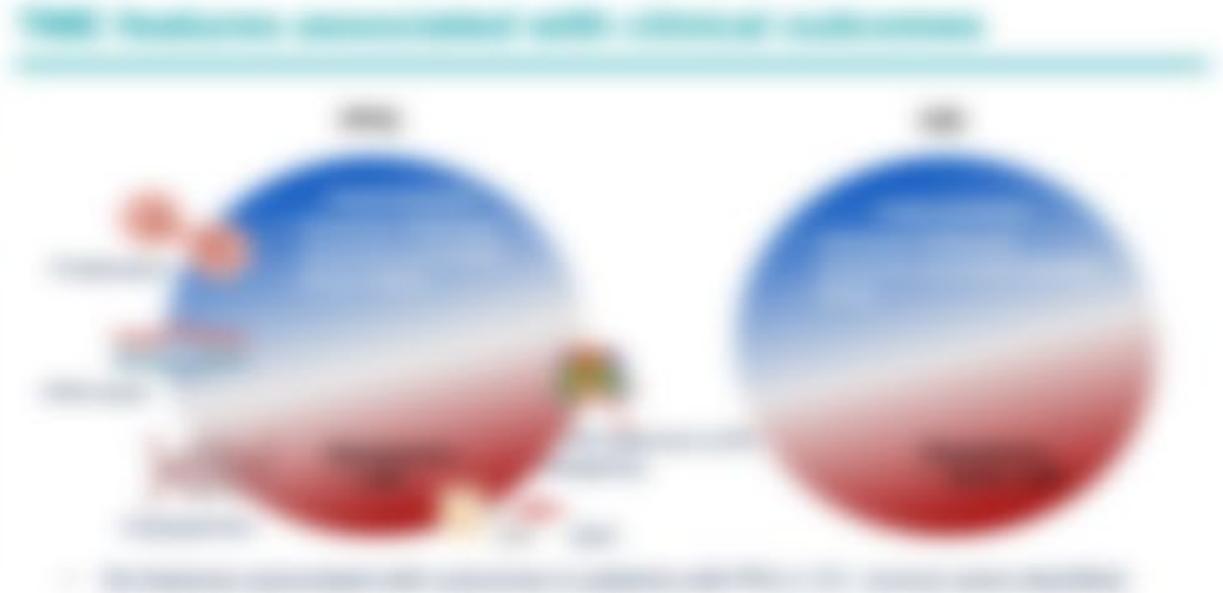
# Early Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC) (3/4)

Presented by Bernard Bochner, MD, FACS

## MUSCLE-INVASIVE BLADDER CANCER – CONVENTIONAL APPROACHES

**CONVENTIONAL APPROACHES**

Radical cystectomy (RC) with pelvic lymph node dissection (PLND) and urinary diversion (UD) is the standard of care for muscle-invasive bladder cancer (MIBC). The goal of RC is to achieve a pathologic complete response (pCR) and to prevent local recurrence and distant relapse. The extent of PLND and the type of UD are still subjects of debate. The most common approach is a total cystectomy with a continent urinary diversion, such as an ileal conduit or an orthotopic neobladder. The most common type of UD is an ileal conduit, which is a segment of ileum that is used to create a new urinary reservoir. The most common type of orthotopic neobladder is a continent neobladder, which is a segment of ileum that is used to create a new urinary reservoir that is connected to the ureters. The most common type of continent neobladder is a Mitrofanoff reservoir, which is a segment of ileum that is used to create a new urinary reservoir that is connected to the ureters and has a continent valve. The most common type of continent neobladder is a Mitrofanoff reservoir, which is a segment of ileum that is used to create a new urinary reservoir that is connected to the ureters and has a continent valve.





# Early Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC) (4/4)

Presented by Bernard Bochner, MD, FACS

## NEOADJUVANT ICI – MIBC

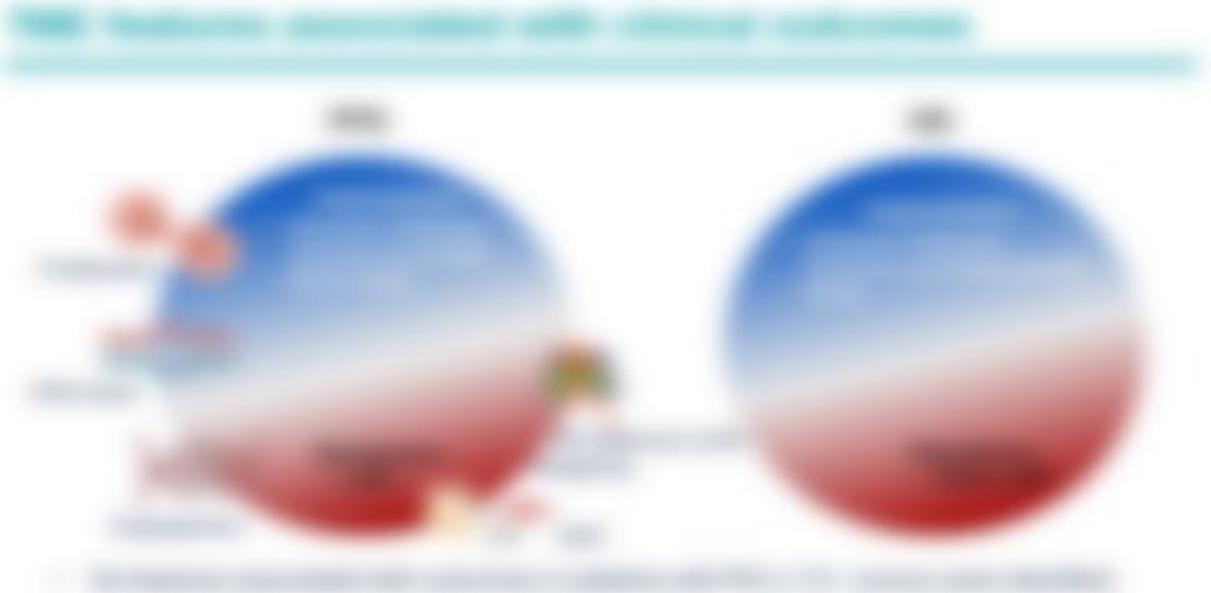
**Background**

Neoadjuvant immunotherapy (ICI) in muscle-invasive bladder cancer (MIBC) aims to improve outcomes by targeting the immune system before surgery. Key trials include the phase III CheckMate 277 trial, which compared nivolumab (an anti-PD-1 ICI) to placebo in combination with cisplatin and enfortumab vedotin (an antibody-drug conjugate). The trial showed that the combination of nivolumab, cisplatin, and enfortumab vedotin significantly improved overall survival compared to cisplatin and enfortumab vedotin alone.

**CheckMate 277**

This phase III trial evaluated the efficacy and safety of nivolumab (anti-PD-1 ICI) in combination with cisplatin and enfortumab vedotin (antibody-drug conjugate) compared to cisplatin and enfortumab vedotin alone in patients with MIBC. The primary endpoint was overall survival (OS). The combination of nivolumab, cisplatin, and enfortumab vedotin significantly improved OS compared to cisplatin and enfortumab vedotin alone.

## ADJUVANT ICI – MIBC



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## Key Insights

Early Stage Bladder Cancer (BCG-Resistant  
NMIBC; MIBC)

# Experts Reviewed Current and Emerging Options for BCG-Unresponsive NMIBC

## SURGERY

**KEY TAKEAWAYS**

The experts reviewed the current and emerging options for BCG-unresponsive NMIBC. The experts discussed the challenges of BCG-unresponsive NMIBC and the need for novel treatment options. The experts reviewed the current and emerging options for BCG-unresponsive NMIBC, including surgery, systemic therapy, and immunotherapy. The experts discussed the challenges of BCG-unresponsive NMIBC and the need for novel treatment options.

**KEY TAKEAWAYS**

Although the experts reviewed the current and emerging options for BCG-unresponsive NMIBC, the experts discussed the challenges of BCG-unresponsive NMIBC and the need for novel treatment options. The experts reviewed the current and emerging options for BCG-unresponsive NMIBC, including surgery, systemic therapy, and immunotherapy. The experts discussed the challenges of BCG-unresponsive NMIBC and the need for novel treatment options.



Text block containing a blurred portrait of a person and associated text.

- FGFR-targeted agents are perceived to be particularly challenging

# Experts Discussed Neoadjuvant and Adjuvant Approaches for MIBC

## NEOADJUVANT THERAPY

**NEOADJUVANT THERAPY**

The neoadjuvant setting is a critical time to address the patient's needs and to establish a multidisciplinary approach to care. The goal is to achieve the best possible outcome for the patient, while minimizing toxicity and maximizing quality of life. This approach involves a combination of systemic therapy, surgery, and radiation therapy, tailored to the individual patient's needs.

**KEY TAKEAWAYS**

While the standard of care for MIBC is still evolving, the use of neoadjuvant therapy is becoming increasingly common. This approach involves the use of systemic therapy, such as chemotherapy and immunotherapy, before surgery. The goal is to shrink the tumor and improve the chances of a successful surgical outcome. This approach is particularly beneficial for patients with high-risk disease, as it can improve their overall survival and quality of life.



**KEY TAKEAWAYS**

The use of neoadjuvant therapy is becoming increasingly common in the treatment of MIBC. This approach involves the use of systemic therapy, such as chemotherapy and immunotherapy, before surgery. The goal is to shrink the tumor and improve the chances of a successful surgical outcome. This approach is particularly beneficial for patients with high-risk disease, as it can improve their overall survival and quality of life.

# Experts Discussed Challenges to Clinical Development for Early Stage Bladder Cancer

## PATIENT AVAILABILITY

**CHALLENGES TO CLINICAL DEVELOPMENT**

The challenges to clinical development for early stage bladder cancer are significant. The limited number of patients available for clinical trials is a major barrier. This is due to the low incidence of early stage bladder cancer and the difficulty of identifying patients who are eligible for clinical trials. Additionally, the high cost of clinical trials and the long time to recruit patients are also major challenges.

**KEY TAKEAWAYS**

Despite the challenges, there are several strategies that can be used to improve patient availability for clinical trials. These include: 1) expanding the geographic reach of clinical trials, 2) using social media and other digital marketing strategies to reach potential patients, and 3) partnering with patient advocacy groups to help identify and recruit patients.



**CONCLUSION**

The challenges to clinical development for early stage bladder cancer are significant, but there are strategies that can be used to improve patient availability. By expanding the geographic reach of clinical trials, using digital marketing strategies, and partnering with patient advocacy groups, it is possible to increase the number of patients available for clinical trials and improve the chances of successful clinical development.

EPICS

# Current Paradigms and Future Directions in Metastatic Bladder Cancer



# Current Paradigms and Future Directions in Metastatic Bladder Cancer (1/2)

Presented by Robert Dreicer, MD, MS, MACP, FASCO

## TREATMENT ALGORITHM FOR mUC

*(This section contains a blurred treatment algorithm for metastatic urothelial carcinoma (mUC).)*





EPICS

## Key Insights

Metastatic Bladder Cancer

## EVOLVING FIRST-LINE STANDARDS

**KEY TAKEAWAYS**

- 1. The standard of care for mUC is evolving, with a focus on personalized medicine and improved patient outcomes.
- 2. The use of immunotherapy and targeted therapies is increasing, offering new options for patients.
- 3. Clinical trials are essential for advancing the field and identifying the most effective treatments.

**CLINICAL RESEARCH**

While the standard of care for mUC is evolving, clinical research remains a critical component of advancing the field. Key areas of focus include:

- 1. Identifying biomarkers to predict treatment response and personalize therapy.
- 2. Evaluating the efficacy and safety of novel immunotherapies and targeted agents.
- 3. Exploring combination therapies to improve outcomes for patients.



**CONCLUSION**

The landscape of first-line treatment for mUC is rapidly changing. As clinical research continues to uncover new therapeutic options, personalized medicine will play an increasingly important role in improving patient outcomes.

# Experts Discussed Sequencing Treatments for mUC in the Second Line and Beyond

## ENFORTUMAB VEDOTIN

**ENFORTUMAB VEDOTIN** is a monoclonal antibody that targets the CD3 protein on T cells. It is used to treat moderate to severe ulcerative colitis (UC) in patients who have not responded to other treatments. The drug is administered intravenously and is known for its potential to reduce inflammation and improve symptoms.

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EPICS

# Evolving Paradigms for Metastatic RCC



# Evolving Paradigms for Metastatic RCC (1/3)

Presented by David Nanus, MD

## FIRST-LINE LANDSCAPE

**Standard of Care**

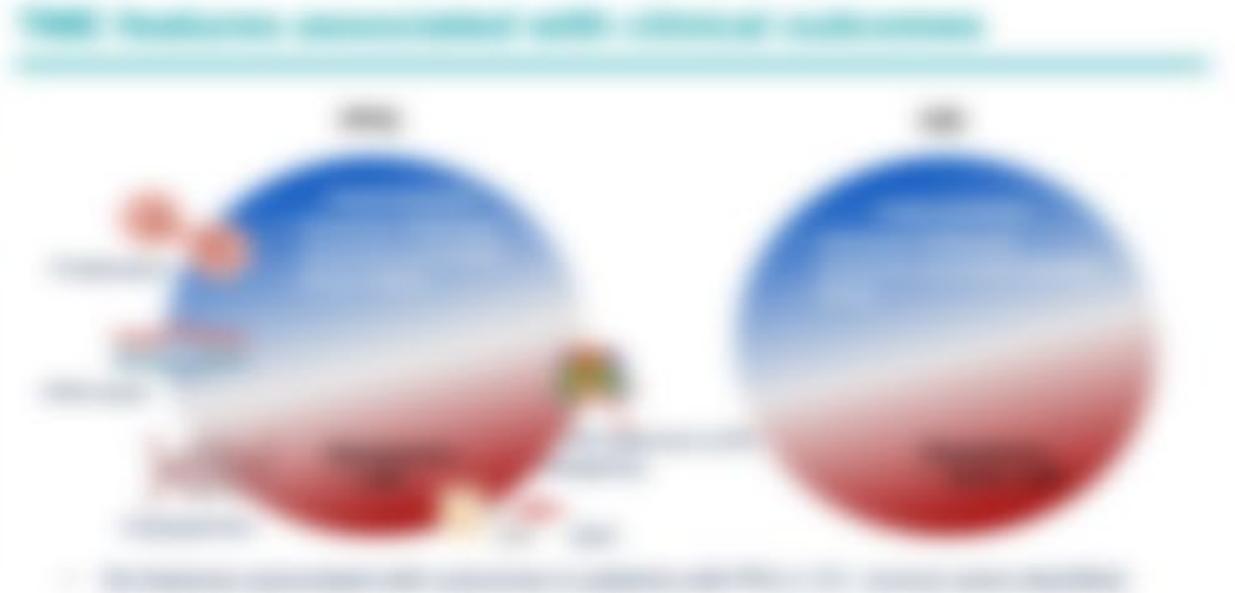
First-line treatment for metastatic RCC includes sunitinib, pazopanib, and cabometyx. These are tyrosine kinase inhibitors that target multiple growth factors.

**Emerging Therapies**

Immune checkpoint inhibitors (ICIs) such as nivolumab and ipilimumab are being evaluated in combination with sunitinib or pazopanib. These combinations aim to improve overall survival and response rates.

**Targeted Therapies**

Next-generation tyrosine kinase inhibitors (TKIs) like cabometyx (nivolumab + ipilimumab) are showing promising results in clinical trials, potentially offering a more effective first-line option.





# Evolving Paradigms for Metastatic RCC (2/3)

Presented by David Nanus, MD

## FIRST-LINE THERAPY – UNMET NEEDS AND AREAS OF INVESTIGATION

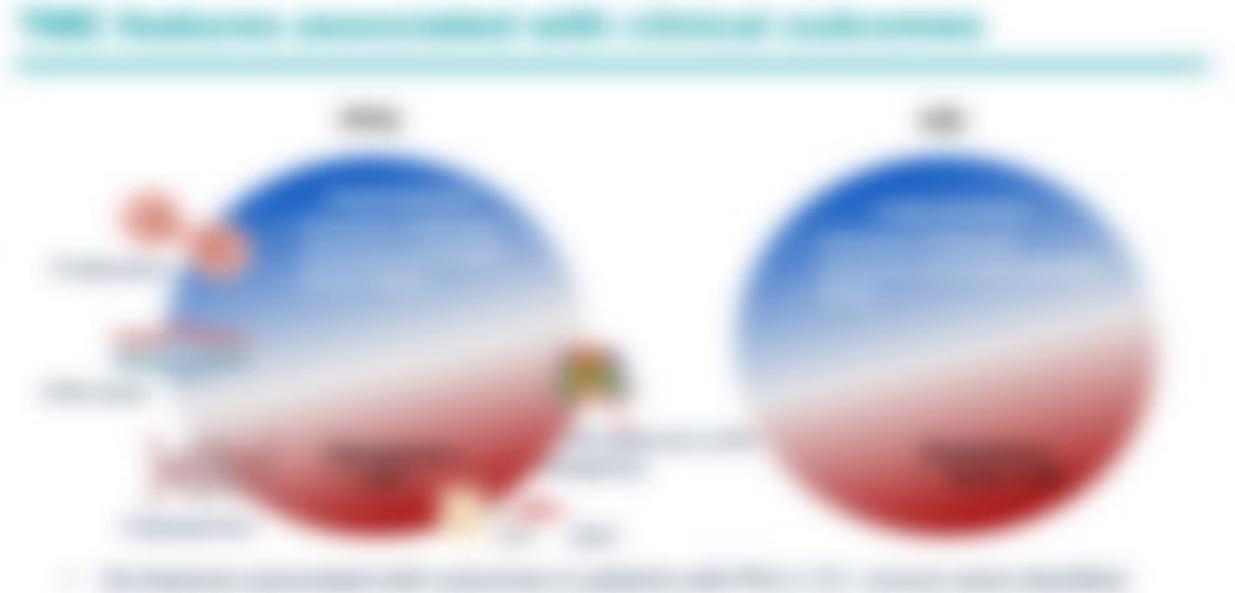
**Current Standard of Care**

First-line systemic therapy for metastatic RCC includes combination of an mTOR inhibitor (everolimus or temsirolimus) with an anti-angiogenic agent (axitinib, pazopanib, or sunitinib). The combination of everolimus and axitinib is the most commonly used regimen.

**Unmet Needs**

Despite the use of combination therapy, the median overall survival (OS) remains limited, typically around 18-24 months. There is a clear need for novel agents and combination strategies that can improve OS and quality of life. Areas of investigation include:

- Novel immunotherapies (e.g., immune checkpoint inhibitors, adoptive cell transfer)
- Targeted therapies (e.g., VEGFR tyrosine kinase inhibitors, mTOR inhibitors, HIF-2α inhibitors)
- Combination strategies (e.g., immunotherapy + anti-angiogenics, immunotherapy + mTOR inhibitors)
- Personalized medicine approaches based on genetic and molecular profiling





# Evolving Paradigms for Metastatic RCC (3/3)

Presented by David Nanus, MD

## SECOND LINE AND BEYOND

**KEY TAKEAWAYS**

- [Blurred text]
- [Blurred text]
- [Blurred text]

**CONCLUSIONS**

- [Blurred text]
- [Blurred text]
- [Blurred text]

## INVESTIGATIONAL THERAPIES

**KEY TAKEAWAYS**

**CONCLUSIONS**

- [Blurred text]
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- [Blurred text]



EPICS

## Key Insights

Metastatic RCC



# Experts Discussed Second-Line-and-Later Options and the Impact of Toxicities

## CONSIDERATIONS BEYOND FIRST-LINE THERAPY

**KEY TAKEAWAYS**

- The importance of understanding the impact of toxicities on quality of life and patient outcomes.
- The role of supportive care in managing toxicities and improving patient outcomes.
- The importance of patient education and shared decision-making in selecting second-line and later options.

**KEY TAKEAWAYS**

Although the overall goal of cancer therapy is to improve survival, the impact of toxicities on quality of life and patient outcomes is increasingly being recognized. Supportive care plays a critical role in managing toxicities and improving patient outcomes. Patient education and shared decision-making are essential in selecting second-line and later options.



**KEY TAKEAWAYS**

The importance of understanding the impact of toxicities on quality of life and patient outcomes.

**EPICS**

# Neo/Adjuvant Treatment of RCC



# Neo/Adjuvant Treatment of RCC (1/2)

Presented by David Quinn, MBBS, PhD, FRACP, FACP

## PREOPERATIVE AND SURGICAL MANAGEMENT

**Preoperative Management**

1. **Immunohistochemistry (IHC)**

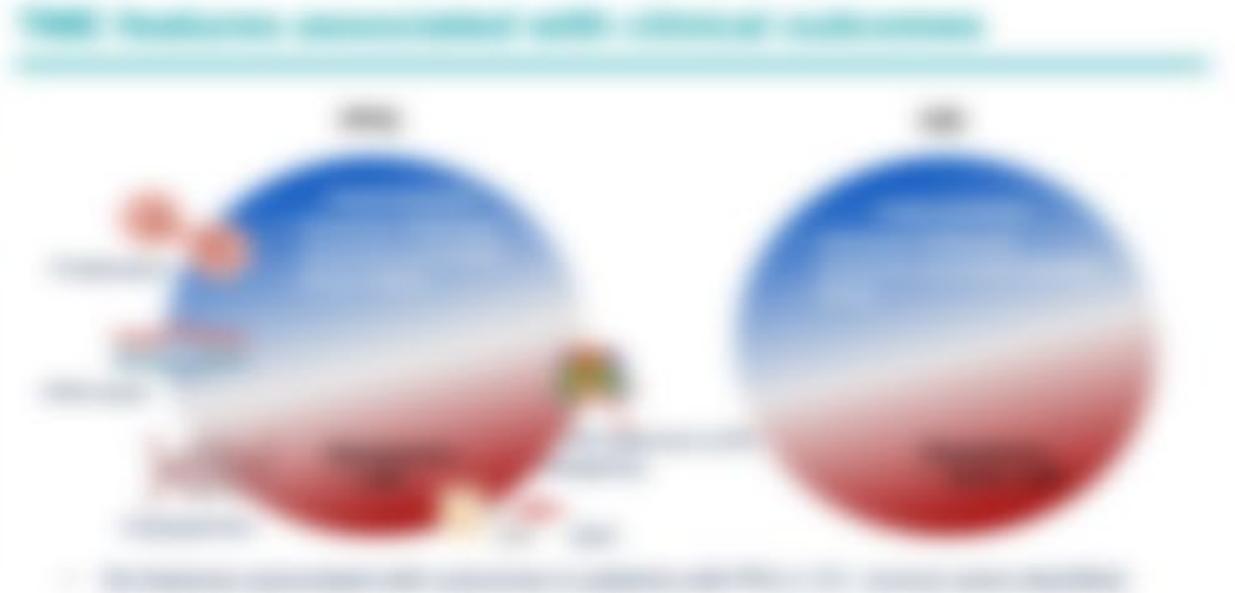
2. **Genetic Testing**

3. **Staging**

4. **Performance of Surgery**

5. **Pathologic Complete Response (pCR)**

6. **Adjuvant Therapy**





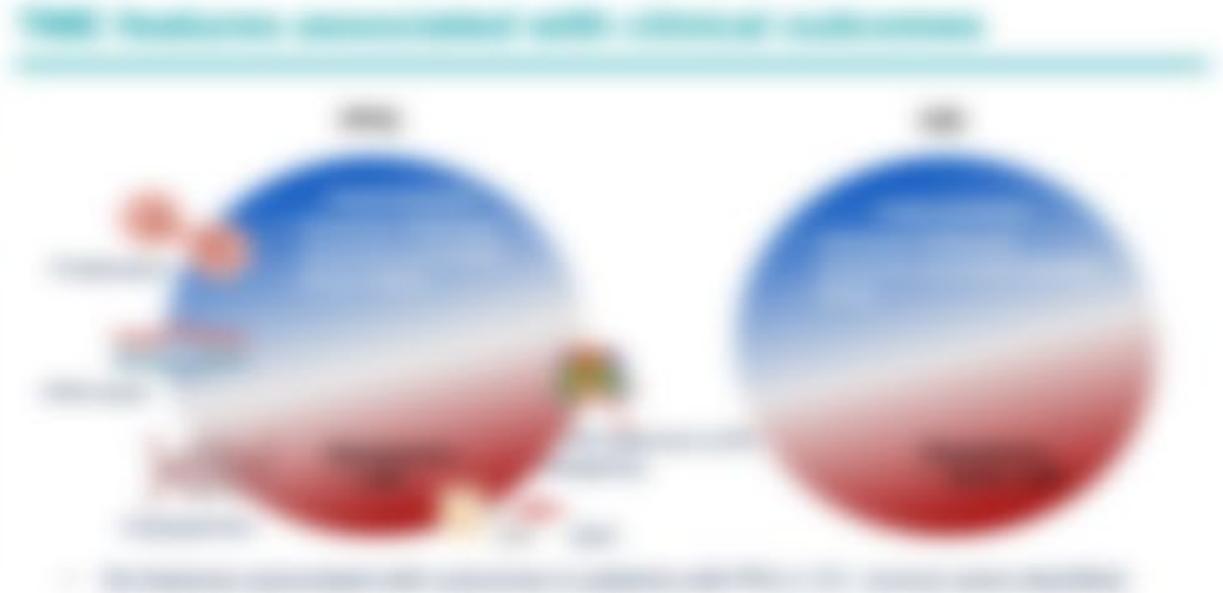
# Neo/Adjuvant Treatment of RCC (2/2)

Presented by David Quinn, MBBS, PhD, FRACP, FACP

## ADJUVANT THERAPY

**ADJUVANT THERAPY**

...with ...



**EPICS**

## **Key Insights**

Neo/Adjuvant Treatment of RCC

# Experts Discussed the Impact of KEYNOTE-564 on the Management of Early Stage RCC

## ADJUVANT PEMBROLIZUMAB

**KEYNOTE-564: ADJUVANT PEMBROLIZUMAB IN EARLY-STAGE RENAL CELL CARCINOMA**

The KEYNOTE-564 trial is a phase III, randomized, controlled trial that evaluated the efficacy and safety of adjuvant pembrolizumab in early-stage renal cell carcinoma (RCC). The trial compared pembrolizumab plus standard of care (SOC) to SOC alone in patients with early-stage RCC. The primary endpoint was overall survival (OS). The trial is ongoing, and results are expected to be published in the near future.

**ADJUVANT THERAPY IN EARLY-STAGE RCC**

Adjuvant therapy in early-stage RCC is a topic of ongoing research. The goal of adjuvant therapy is to improve outcomes in patients with early-stage RCC. Pembrolizumab is a promising agent in this setting, and the results of the KEYNOTE-564 trial will help to determine its role in the management of early-stage RCC.



# Experts Discussed Research Directions, Unmet Needs, and Evolving Standards of Care in ccRCC

## CLINICAL TRIAL CONSIDERATIONS

**CLINICAL TRIAL CONSIDERATIONS**

The clinical trial landscape for ccRCC is rapidly evolving, with a focus on identifying novel therapeutic targets and combination therapies. Key considerations include patient selection, biomarker-driven trials, and the integration of immunotherapy with targeted agents. The challenge remains to identify biomarkers that predict response to these complex regimens and to optimize the timing and sequence of treatments.

**CLINICAL TRIAL CONSIDERATIONS**

Despite the progress in immunotherapy, there is a clear need for improved biomarkers to identify patients who will benefit most from these treatments. Additionally, the development of novel immunomodulators and combination therapies offers promising avenues for further research. Clinical trial design must be tailored to address these challenges, incorporating rigorous biomarker validation and adaptive trial strategies to maximize the chances of identifying effective treatments for ccRCC.



**CLINICAL TRIAL CONSIDERATIONS**

The integration of immunotherapy with targeted agents represents a significant shift in the treatment paradigm for ccRCC. However, the complexity of these combination therapies necessitates a deep understanding of the underlying mechanisms of action and the potential for synergistic effects. Clinical trials must carefully monitor for both efficacy and toxicity, ensuring that the benefits of these novel regimens outweigh the risks.

**EPICS**

# **Current and Future Management of Non-clear Cell RCC**



# Current and Future Management of Non-clear Cell RCC (1/1)

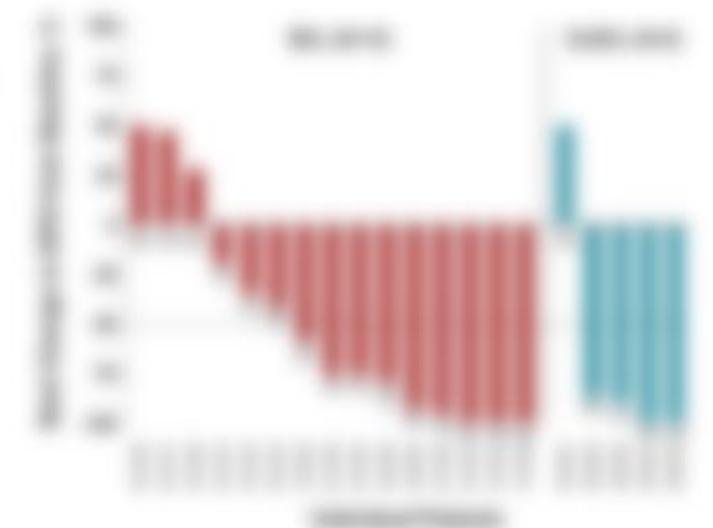
Presented by David Quinn, MBBS, PhD, FRACP, FACP

## Background

- Phase 1 dose-toxicity study of VEGF-TKI, a VEGFR-inhibiting TKI, in patients with locally advanced RCC and CRCC.
- Primary objective was to define maximum tolerated dose and recommended dosing regimen.

## Results

- 22 patients were enrolled, including 10 patients with RCC.
- 16/22 were CR-metastases and 10/22 were CR.
- CR-metastases occurred in 20% of patients, 10/22 successfully completed treatment.
- In study overall CR-metastases occurred in 9% of patients, no CR-metastases observed.
- CRCC was 47% (2/4), 47% (2/4) for RCC cohort and 50% (2/4), 27% (1/4) for CRCC cohort.
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks.



**Key takeaway:** VEGF-TKI demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced RCC and CRCC. Experts mentioned neuropathy as a potential concern and the need to identify the best treatment in which to test this agent.

EPICS

## Key Insights

Non-clear Cell RCC

# Experts Reviewed Current Treatment Paradigms for Non-clear Cell mRCC Subtypes

## PAPILLARY mRCC

**KEY TAKEAWAYS**

The experts reviewed the current treatment paradigms for papillary mRCC and discussed the challenges associated with this subtype. They highlighted the need for more targeted therapies and the importance of clinical trials in advancing the field.

- Papillary mRCC is a distinct subtype of renal cell carcinoma with unique molecular and histological features.
- Current treatment paradigms for papillary mRCC are largely based on the experience with clear cell mRCC, which may not be optimal for this subtype.
- The experts discussed the challenges of identifying novel therapeutic targets and developing effective clinical trial designs for papillary mRCC.

**CLINICAL IMPLICATIONS**

Understanding the unique biology of papillary mRCC is crucial for developing more effective treatments. The experts emphasized the need for a multidisciplinary approach involving basic science, clinical oncology, and patient advocacy to address the unmet needs of patients with this subtype.

- Further research is needed to elucidate the molecular mechanisms underlying papillary mRCC and to identify potential therapeutic targets.
- Clinical trials should be designed to evaluate novel therapies specifically for papillary mRCC, taking into account its unique characteristics.
- Patient education and awareness are essential for increasing participation in clinical trials and improving outcomes for patients with papillary mRCC.



**CONCLUSION**

The experts' review highlights the need for more targeted and effective treatments for papillary mRCC. Continued research and collaboration are essential to improve the outcomes for patients with this subtype.