APTITUDE HEALTH®

EPICS

EPICS Global Perspectives: GU Malignancies in 2022 and Beyond

Tuesday, December 13, 2022

Friday, December 16, 2022

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Report Contents

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Meeting Snapshot

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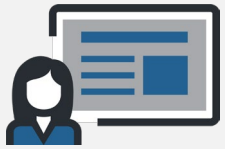
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
December 13 and 16, 2022



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GU malignancies
- > 8 from US
- > 4 from Europe

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

Panel Consisting of 8 US and 4 European GU Cancer Experts

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

Scott Tagawa, MD, FACP
Weill Cornell Medicine

Joaquim Bellmunt, MD, PhD
Harvard Medical School

Thomas Powles, MD, MRCP, MBBS
Barts Cancer Institute

Mitchell Benson, MD
Columbia University, Irving Medical Center

CHAIR:
Daniel P. Petrylak, MD
Yale Cancer Center

Manuela Schmidinger, MD
Medical University of Vienna

E. David Crawford, MD
University of California, San Diego

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

Karim Fizazi, MD, PhD
Gustave Roussy Institute

Oliver Sartor, MD
Tulane University School of Medicine

José Pablo Maroto Rey, MD, PhD
Hospital de la Santa Creu i Sant Pau

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Meeting Agenda – Day 1

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Time (ET)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	Welcome and Introductions	Daniel Petrylak, MD
10.05 AM – 10.15 AM	**Early-Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC)**	Mitchell Benson, MD
10.15 AM – 10.35 AM	Key Questions and Topics for Discussion	All
10.35 AM – 10.40 AM	Summary and Key Takeaways	
10.40 AM – 10.50 AM	**Current Paradigms and Future Directions in Metastatic Bladder Cancer**	Joaquim Bellmunt, MD, PhD
10.50 AM – 11.20 AM	Key Questions and Topics for Discussion	All
11.20 AM – 11.25 AM	Summary and Key Takeaways	
11.25 AM – 11.35 AM	BREAK	
11.35 AM – 11.45 AM	**Evolving Paradigms for Metastatic RCC**	Manuela Schmidinger, MD
11.45 AM – 12.15 PM	Key Questions and Topics for Discussion	All
12.15 PM – 12.20 PM	Summary and Key Takeaways	
12.20 PM – 12.30 PM	**Neo/Adjuvant Treatment of RCC**	Pablo Maroto Rey, MD, PhD
12.30 PM – 12.50 PM	Key Questions and Topics for Discussion	All
12.50 PM – 12.55 PM	Summary and Key Takeaways	
12.55 PM – 1.00 PM	Conclusions and Wrap-up	Daniel Petrylak, MD

Meeting Agenda – Day 2

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Time (ET)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	Welcome and Introductions	Daniel Petrylak, MD
10.05 AM – 10.15 AM	**Current and Future Management of Non-clear Cell RCC**	Thomas Powles, MD, MRCP, MBBS
10.15 AM – 10.25 AM	Key Questions and Topics for Discussion	All
10.25 AM – 10.30 AM	Summary and Key Takeaways	
10.30 AM – 10.40 AM	**Diagnosing and Managing Localized/Locally Advanced Prostate Cancer**	E. David Crawford, MD
10.40 AM – 10.55 AM	Key Questions and Topics for Discussion	All
10.55 AM – 11.00 AM	Summary and Key Takeaways	
11.00 AM – 11.10 AM	**Treatment Paradigms for Advanced Prostate Cancer**	Oliver Sartor, MD
11.10 AM – 11.25 AM	Key Questions and Topics for Discussion	All
11.25 AM – 11.30 AM	Summary and Key Takeaways	
11.30 AM – 11.40 AM	BREAK	
11.40 AM – 11.55 AM	**Investigational Therapies for Metastatic CRPC**	Susan Slovin, MD, PhD
11.55 AM – 12.20 PM	Key Questions and Topics for Discussion	All
12.20 PM – 12.25 PM	Summary and Key Takeaways	
12.25 PM – 12.35 PM	**Advances in Imaging Technologies for Genitourinary Cancers**	Scott Tagawa, MD, FACP
12.35 PM – 12.55 PM	Key Questions and Topics for Discussion	All
12.55 PM – 1.00 PM	Summary and Key Takeaways	
1.00 PM	Conclusions and Wrap-up	Daniel Petrylak, MD

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

Early-Stage Bladder Cancer (BCG-Resistant NMIBC; MIBC) (1/2)

Presented by Mitchell Benson, MD

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CURRENT TREATMENT OPTIONS FOR BCG-UNRESPONSIVE NMIBC

> A number of chemotherapy drugs have been utilized in the

CGC Outcomes

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

Presented by Mitchell Benson, MD

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CYSTECTOMY FOR BCG-UNRESPONSIVE NMIBC

> Cystectomy still has a role in the management of BCG-

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Key Insights

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

Experts Debated the Role of Systemic Therapy for BCG-Resistant NMIBC

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PEMBROLIZUMAB FOR BCG-RESISTANT NMIBC

Experts perceive that pembrolizumab is rarely used in the community, and those patients with NMIBC who are referred for systemic

[redacted]

Experts Discussed Emerging Therapies for NMIBC and the Ongoing Role for Cystectomy

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Experts Discussed Preoperative Therapy for Patients With MIBC

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Experts Discussed Adjuvant Therapy and Patient Selection for MIBC

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Current Paradigms and Future Directions in Metastatic Bladder Cancer

Current Paradigms and Future Directions in Metastatic Bladder Cancer (1/3)

Presented by Joaquim Bellmunt, MD, PhD

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TREATMENT ALGORITHMS FOR mUC

- Current algorithms for the treatment of metastatic urothelial cancer (mUC) differ

US Algorithm

Current Paradigms and Future Directions in Metastatic Bladder Cancer (2/3)

Presented by Joaquim Bellmunt, MD, PhD

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FIRST-LINE INVESTIGATIONAL APPROACHES FOR mUC

- To date, trials evaluating first-line chemotherapy +

Current Paradigms and Future Directions in Metastatic Bladder Cancer (3/3)

Presented by Joaquim Bellmunt, MD, PhD

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NOVEL INVESTIGATIONAL AGENTS

> An important area of investigation is therapies for

HER2-TARGETED THERAPIES

> Several ADCs targeting HER2 are in development in mUC

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Key Insights

Current Paradigms and Future Directions in Metastatic Bladder Cancer

Experts Discussed Current Algorithms for Managing mUC

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FIRST-LINE PLATINUM FOLLOWED BY MAINTENANCE

Platinum-based chemotherapy followed by maintenance avelumab currently remains the

Experts Debated the Potential Implications of the EV-302 Trial

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FIRST-LINE EV + PEMBROLIZUMAB

Results of the EV-302 trial evaluating first-line therapy with EV + pembrolizumab are

Experts Considered Available and Investigational ADCs for mUC

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ANTIBODY-DRUG CONJUGATES

The targets, payloads, and toxicity profiles of EV and sacituzumab govitecan are non-

Experts Discussed the Future of FGFR Inhibitors in mUC

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FGFR INHIBITORS

> The percentage of patients with *FGFR*-altered mUC is perceived to be much lower in

Experts Discussed Other Research Considerations in Therapeutic Development for mUC

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NEW THERAPIES and SEQUENCING

The mUC field is becoming more complex – as agents move into earlier lines of therapy,

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Evolving Paradigms for Metastatic RCC

Evolving Paradigms for Metastatic RCC (1/3)

Presented by Manuela Schmidinger, MD

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CURRENT TREATMENT ALGORITHMS FOR CLEAR CELL mRCC

Evolving Paradigms for Metastatic RCC (2/3)

Presented by Manuela Schmidinger, MD

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FACTORS IN FIRST-LINE TREATMENT SELECTION

- [illegible]
- [illegible]
  - [illegible]
  - [illegible]
  - [illegible]

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Evolving Paradigms for Metastatic RCC (3/3)

Presented by Manuela Schmidinger, MD

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TARGETING HIF1α

> The HIF1α inhibitor belzutifan is emerging as an important new

INVESTIGATIONAL FIRST-LINE TRIPLETS

> Triplet combinations (IO-IO-TKI) are also being investigated for

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Key Insights

Evolving Paradigms for Metastatic RCC

Experts Debated First-Line Treatment Options for Clear Cell mRCC (1/2)

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FAVORABLE-RISK mRCC

IO-TKI doublets are preferred for favorable-risk mRCC, particularly when there is a high

Experts Debated First-Line Treatment Options for Clear Cell mRCC (2/2)

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INTERMEDIATE/POOR-RISK mRCC

An IO-IO doublet is generally preferred for fit patients with intermediate/poor-risk mRCC

Experts Considered Treatment Holidays and Other Treatment Options for mRCC

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TREATMENT HOLIDAYS AND LATER-LINE OPTIONS

Drug holidays tend to be used in Europe, particularly in academic centers, but less so in

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Neo/Adjuvant Treatment of RCC

Neo/Adjuvant Treatment of RCC (1/3)

Presented by José Pablo Maroto Rey, MD, PhD

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ADJUVANT THERAPY for ccRCC: TKIs

Neo/Adjuvant Treatment of RCC (2/3)

Presented by José Pablo Maroto Rey, MD, PhD

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ADJUVANT THERAPY for ccRCC: IMMUNE CHECKPOINT INHIBITORS

Neo/Adjuvant Treatment of RCC (3/3)

Presented by José Pablo Maroto Rey, MD, PhD

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BIOMARKERS

> Biomarkers to select patients and predict benefit for adjuvant

CYTOREDUCTIVE NEPHRECTOMY

> The use of cytoreductive nephrectomy (CN) for mRCC appears to

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Key Insights

Neo/Adjuvant Treatment of RCC

Experts Debated Adjuvant Therapy for High-Risk RCC and Future Directions for Research

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ADJUVANT ICI TRIALS

KEYNOTE-564 showed a clear DFS benefit for adjuvant pembrolizumab; OS is immature

Experts Discussed Cytoreductive Nephrectomy and Individualization of Therapy

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CYTOREDUCTIVE NEPHRECTOMY

Overall, use of CN for patients with mRCC is decreasing

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Current and Future Management of Non-clear Cell RCC

Current and Future Management of Non-clear Cell RCC (1/2)

Presented by Thomas Powles, MD, MRCP, MBBS

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CURRENT AND EMERGING OPTIONS FOR PAPILLARY mRCC

> Papillary RCC remains an area of pressing unmet needs,

PAPMET Randomized Phase II Study

Current and Future Management of Non-clear Cell RCC (2/2)

Presented by Thomas Powles, MD, MRCP, MBBS

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MET-DRIVEN PAPILLARY RCC

> Approximately 30% of patients with papillary

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Key Insights

Current and Future Management of Non-clear Cell RCC

Experts Discussed Evolving Treatment Paradigms for Papillary mRCC

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CURRENT TREATMENT OPTIONS

Cabozantinib is the preferred first-line option, on the basis of results of the PAPMET trial

Experts Considered Therapeutic Options for Other Rare Subtypes of RCC

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CHROMOPHOBE RCC

There is no clear standard treatment, and this is an area of clear unmet need

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Diagnosing and Managing Localized/Locally Advanced Prostate Cancer

Diagnosing and Managing Localized/Locally Advanced Prostate Cancer (1/3)

Presented by E. David Crawford, MD

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INITIAL MANAGEMENT OF LOCALIZED PROSTATE CANCER

- The goal of early detection should be to find

Diagnosing and Managing Localized/Locally Advanced Prostate Cancer (2/3)

Presented by E. David Crawford, MD

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ACTIVE SURVEILLANCE

> For patients on active surveillance, there are variations in follow-

FOCAL THERAPY

> Interest in focal therapy for localized prostate cancer has

Diagnosing and Managing Localized/Locally Advanced Prostate Cancer (3/3)

Presented by E. David Crawford, MD

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ADT + RADIATION

> For patients with high-risk disease, ADT

Prognostic and ***Predictive*** Biomarkers Can Both Inform

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Key Insights

Diagnosing and Managing Localized/Locally Advanced Prostate Cancer

Experts Discussed the Initial Diagnosis and Management of Men With Localized Prostate Cancer

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DIAGNOSTIC TOOLS

PSA is considered a good initial screening method, although it is influenced by the size

Experts Debated Treatments Options and Related Considerations for Localized Prostate Cancer

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HORMONAL THERAPY

Some experts have added a next-gen AR inhibitor to ADT-RT for patients with nodal

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Treatment Paradigms for Advanced Prostate Cancer

Treatment Paradigms for Advanced Prostate Cancer (1/3)

Presented by Oliver Sartor, MD

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mHSPC

> For patients with overt metastases that remain castration sensitive, treatment options include ADT + docetaxel or

ARASENS OS (primary endpoint)

Smith MR, et al. *N Engl J Med*. 2022;386:1132-1142

Treatment Paradigms for Advanced Prostate Cancer (2/3)

Presented by Oliver Sartor, MD

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OLIGOMETASTATIC PROSTATE CANCER

> There is interest in exploring de-intensified treatment options for patients with

Radiation/Surgery for PSMA PET-Detected Oligorecurrent

Treatment Paradigms for Advanced Prostate Cancer (3/3)

Presented by Oliver Sartor, MD

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NONMETASTATIC CRPC

- PSMA PET imaging is redefining this subset of disease
  - 98% of patients with nmCRPC will have PSMA

mCRPC

- The major recent breakthrough for mCRPC was the introduction of 177Lu-PSMA-617, on the basis of the VISION trial demonstrating rPFS and OS

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Key Insights

Treatment Paradigms for Advanced Prostate Cancer

Experts Discussed Evolving Treatment Paradigms for Nonmetastatic CRPC

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NEXT-GENERATION AR INHIBITORS

Darolutamide is perceived to be the best tolerated of the next-gen AR inhibitors, but

Experts Debated Dose-Intensification for Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)

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PEACE-1 AND ARASENS

PEACE-1 and ARASENS are clearly positive trials, showing benefit for adding a next-

Experts Discussed the Role of Radioisotopes for mCRPC

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177-Lu-PSMA-617

> The current shortage of 177-Lu-PSMA-617 is a critical issue in the clinic

Experts Considered Current Biomarkers for mCRPC

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STANDARD BIOMARKER TESTING

Experts indicated they typically test for DNA repair gene mutations and MSI/TMB status

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Investigational Therapies for Metastatic CRPC

Investigational Therapies for Metastatic CRPC (1/3)

Presented by Susan Slovin, MD, PhD

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BiTEs

> Bispecific T-cell engagers (BiTEs) are molecules that bind to an immune effector cell (typically T cells) and

Response to Anti-PSMA BiTE Pasotuxizumab

Investigational Therapies for Metastatic CRPC (2/3)

Presented by Susan Slovin, MD, PhD

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CAR T CELLS

> Preliminary results with prostate stem cell antigen (PSCA) directed CAR T cells

Investigational Therapies for Metastatic CRPC (3/3)

Presented by Susan Slovin, MD, PhD

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PROTACs

> PROTACs (proteolysis targeting chimeras) are

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Key Insights

Investigational Therapies for Metastatic CRPC

Experts Considered the Development of BiTEs and CAR T Cells in mCRPC

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BiTEs

BiTEs can be short-lived, and the challenge is maintaining a sustained effect

Experts Discussed ICIs and PROTACs for mCRPC

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IMMUNE CHECKPOINT INHIBITORS

Immune checkpoint inhibitors (ICIs) in unselected patients with mCRPC are unlikely to

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Advances in Imaging Technologies for Genitourinary Cancers

Advances in Imaging Technologies for GU Cancers (1/2)

Presented by Scott Tagawa, MD, FACP

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PSMA-DIRECTED RADIOISOTOPE TRACERS FOR PROSTATE CANCER

> Currently there are 2 PSMA-targeted radioisotope

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

Presented by Scott Tagawa, MD, FACP

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OTHER RADIOLABELED TRACERS IN DEVELOPMENT

> Another class of radioisotope tracers targets the CAIX

^{18}F-FDG TLX250-CDx

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Key Insights

Advances in Imaging Technologies for Genitourinary Cancers

Experts Discussed Practical Considerations Regarding PSMA PET Scans

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PRACTICAL CONSIDERATIONS – PET SCANS

PSMA PET imaging is perceived to be superior to

Experts Debated the Implications of PSMA PET Scans for Managing Patients With Prostate Cancer

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PATIENT MANAGEMENT CONSIDERATIONS WITH PSMA PET

The availability of highly sensitive PSMA PET imaging has complicated patient

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