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Conference Coverage: ASCO GU 2023 Highlights

February 24, 2023

1.00 PM – 4.00 PM EST

Report Contents

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Meeting Snapshot

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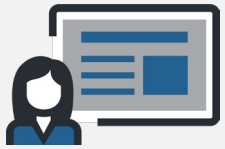
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
February 24, 2023



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GU malignancies
- > 5 from US
- > 2 from Europe

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

Panel Consisting of 5 US and 2 European GU Cancer Experts

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

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

CHAIR:
Daniel P. Petrylak, MD
Yale Cancer Center

Joaquim Bellmunt, MD, PhD
Harvard Medical School

Thomas Powles, MD, MRCP, MBBS
Barts Cancer Institute

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

Karim Fizazi, MD, PhD
Gustave Roussy Institute

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Meeting Agenda

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Time (EDT)	Topic	Speaker/Moderator
1.00 PM – 1.05 PM	Welcome, Introductions, and Meeting Objectives	Daniel Petrylak, MD
1.05 PM – 1.15 PM	Prostate Cancer Part 1 – Localized and Castrate-Sensitive Prostate Cancers	Susan Slovin, MD, PhD
1.15 PM – 1.30 PM	Discussion	Daniel Petrylak, MD
1.30 PM – 1.35 PM	Key Takeaways	Susan Slovin, MD, PhD
1.35 PM – 1.50 PM	Prostate Cancer Part 2 – Metastatic Castration-Resistant Prostate Cancer	Karim Fizazi, MD, PhD; Robert Dreicer, MD, MACP, FASCO
1.50 PM – 2.05 PM	Discussion	Daniel Petrylak, MD
2.05 PM – 2.10 PM	Key Takeaways	Karim Fizazi, MD, PhD; Robert Dreicer, MD, MACP, FASCO
2.10 PM – 2.20 PM	Bladder Cancer Part 1 – NMIBC and MIBC	Leonard Gomella, MD, FACS
2.20 PM – 2.30 PM	Discussion	Daniel Petrylak, MD
2.30 PM – 2.35 PM	Key Takeaways	Leonard Gomella, MD, FACS
2.35 PM – 2.45 PM	*Break*	
2.45 PM – 2.55 PM	Bladder Cancer Part 2 – Metastatic Urothelial Cancer	Joaquim Bellmunt, MD, PhD
2.55 PM – 3.10 PM	Discussion	Daniel Petrylak, MD
3.10 PM – 3.15 PM	Key Takeaways	Joaquim Bellmunt, MD, PhD
3.15 PM – 3.30 PM	Renal Cell Carcinoma	Thomas Powles, MBBS, MRCP, MD
3.30 PM – 3.50 PM	Discussion	Daniel Petrylak, MD
3.50 PM – 3.55 PM	Key Takeaways	Thomas Powles, MBBS, MRCP, MD
3.55 PM – 4.00 PM	Summary and Closing Remarks	Daniel Petrylak, MD

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Congress Highlights

Prostate Cancer Part 1 – Localized and Castrate-Sensitive Prostate Cancers

FORMULA-509: Salvage radiotherapy and 6 months of GnRH agonist ± abiraterone and apalutamide post-radical prostatectomy

Nguyen et al. 2023, ASCO GU 303

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STUDY POPULATION AND METHODS

- 345 pts with recurrent prostate cancer following prostatectomy

METASTASIS-FREE SURVIVAL

Darolutamide in combination with ADT and docetaxel by disease volume and disease risk in the phase 3 ARASENS study

Hussain et al. 2023, ASCO GU 15

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STUDY POPULATION AND METHODS

> 1306 pts with mHSPC were randomized to darolutamide or

OVERALL SURVIVAL

Abiraterone and ADT ± docetaxel in older patients (≥70 years) with de novo mCSPC compared to younger patients: The PEACE-1 trial

Mourey et al. 2023, ASCO GU 20

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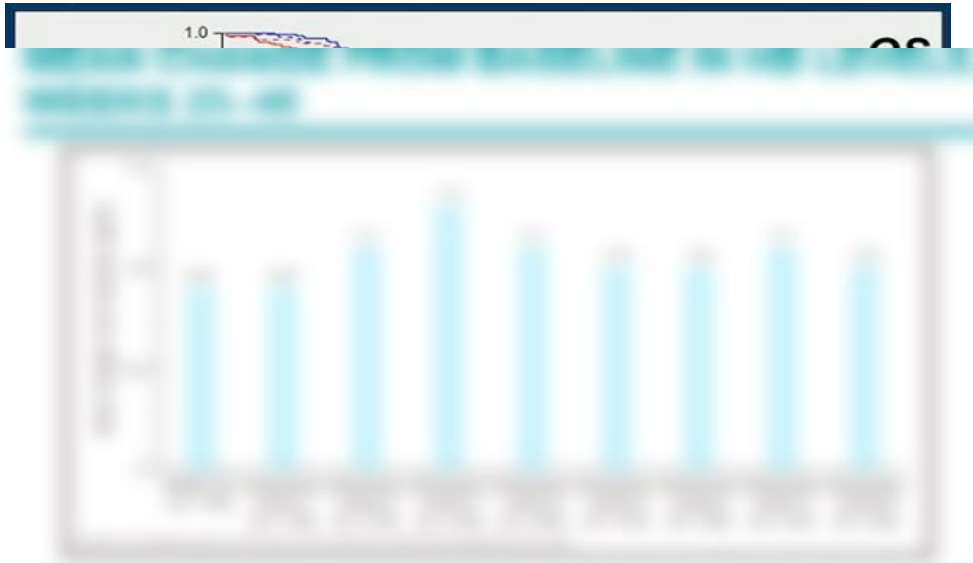
STUDY POPULATION AND METHODS

> Pts with de novo mCSPC were randomized to receive ADT-

OVERALL SURVIVAL



Randomized phase II study of ketoconazole, hydrocortisone, and anti-PSMA antibody J591 labeled with ^{177}Lu or ^{111}In in nonmetastatic CRPC

Tagawa et al. 2023, ASCO GU LBA21

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STUDY POPULATION AND METHODS

- 55 pts with high-risk nmCRPC with biochemical progression with

METASTASIS-FREE SURVIVAL

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Key Insights

Prostate Cancer Part 1 – Localized and Castrate-Sensitive Prostate Cancers

Experts Debated the Role of Treatment Intensification for Biochemically Recurrent PC Following Prostatectomy

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FORMULA-509

Experts consider the FORMULA-509 trial to be a good proof-of-concept study, although

Experts Considered Areas for Future Investigation in Nonmetastatic Prostate Cancer

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RADIOLABELED ANTI-PSMA ANTIBODIES

Radiolabeled PSMA-directed mAbs are moving into earlier stages of disease, but it remains

Experts Discussed Treatment Intensification for mCSPC

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PEACE-1 AND ARASENS

Results from ARASENS and PEACE-1 are consistent, showing an OS benefit for triplet

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Congress Highlights

Prostate Cancer Part 2 – Metastatic Castration-Resistant Prostate Cancer

Rucaparib for mCRPC: TRITON3 interim OS and efficacy of rucaparib vs docetaxel or second-generation androgen pathway inhibitor therapy

Bryce et al. 2023, ASCO GU 18

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STUDY POPULATION AND METHODS

> 405 pts with chemotherapy-naive mCRPC previously treated with

PROGRESSION-FREE SURVIVAL

Niraparib + abiraterone in mCRPC and homologous recombination repair (HRR) gene alterations: Second interim analysis of MAGNITUDE

Efstathiou et al. 2023, ASCO GU 170

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STUDY POPULATION AND METHODS

> 423 pts with mCRPC eligible for first-line therapy (≤4 mo prior

PROGRESSION-FREE SURVIVAL

Final OS in PROpel: Abiraterone ± olaparib as first-line therapy for mCRPC

Clarke et al. 2023, ASCO GU LBA16

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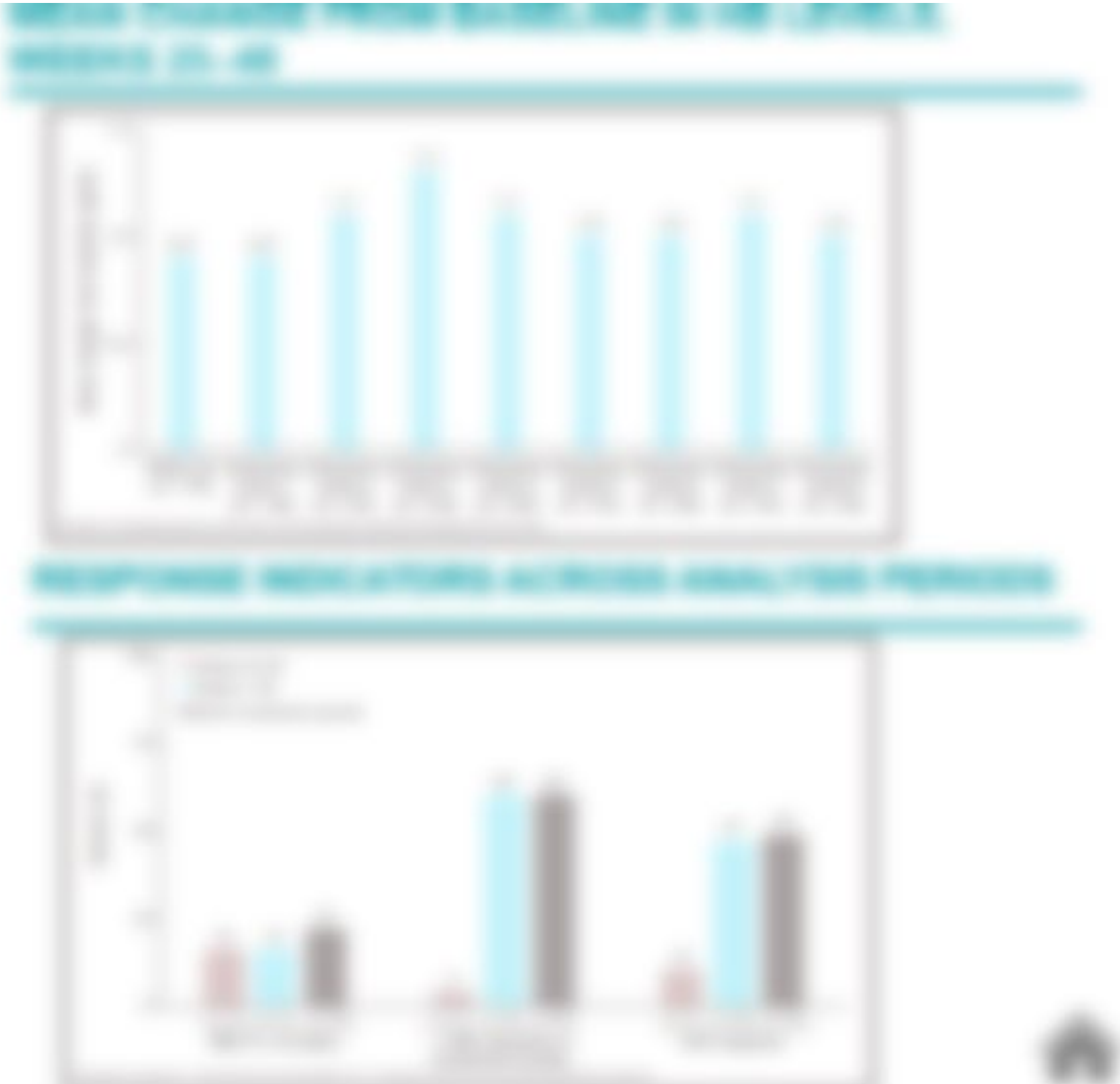
STUDY POPULATION AND METHODS

> 398 pts with mCRPC, no prior chemotherapy or next-generation

OVERALL SURVIVAL



TALAPRO-2: Phase 3 study of enzalutamide ± talazoparib as first-line treatment for mCRPC

Agarwal et al. 2023, ASCO GU LBA17

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STUDY POPULATION AND METHODS

> 805 pts with mCRPC (prior abiraterone and docetaxel allowed in

PROGRESSION-FREE SURVIVAL

Phase 1/2 study of co-stimulatory bispecific PSMAxCD28 antibody REGN5678 in patients with mCRPC

Stein et al. 2023, ASCO GU 154

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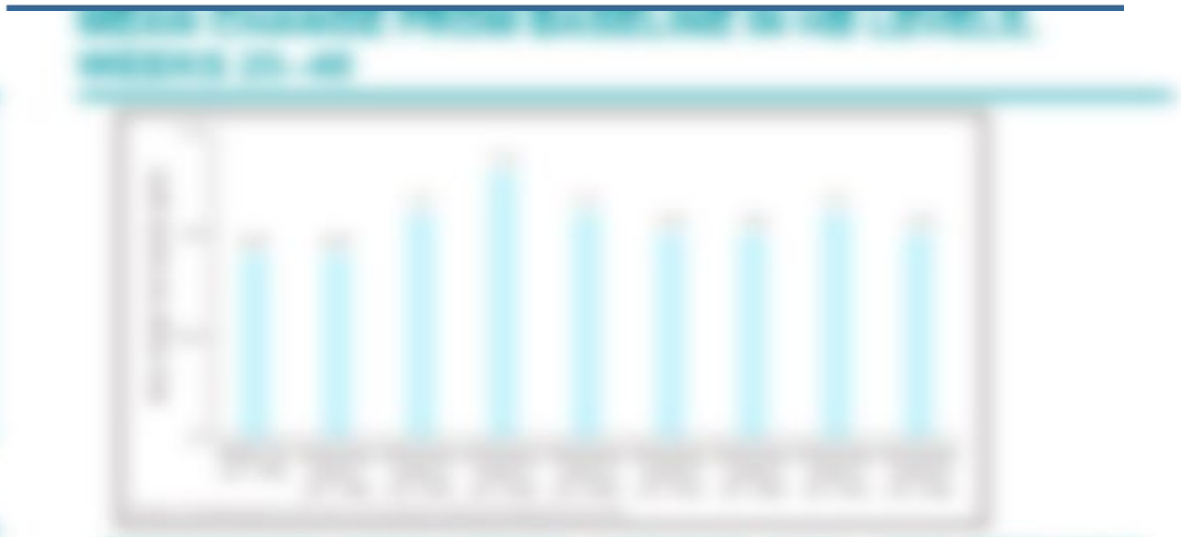
STUDY POPULATION AND METHODS

> 35 pts with mCRPC with ≥2 lines of systemic therapy, including ≥1

MECHANISM OF ACTION



Early dose escalation of LAVA-1207, a novel PSMA-targeted bispecific gamma-delta T-cell engager (Gammabody), in patients with mCRPC

Mehra et al. 2023, ASCO GU 153

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STUDY POPULATION AND METHODS

> 16 pts with refractory mCRPC received treatment with escalating

PSA RESPONSE

A phase 2 expansion study of ARV-766, a PROTAC androgen receptor degrader, in mCRPC

Petrylak et al. 2023, ASCO GU TPS290

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BACKGROUND

> ARV-766 is a novel, potent, orally bioavailable proteolysis

STUDY DESIGN

> 2 doses of ARV-766 (100 mg and 300 mg administered orally once

Oral innate immune activator BXCL701 + pembrolizumab in patients with mCRPC of small cell neuroendocrine phenotype: Phase 2a final results

Aggarwal et al. 2023, ASCO GU 176

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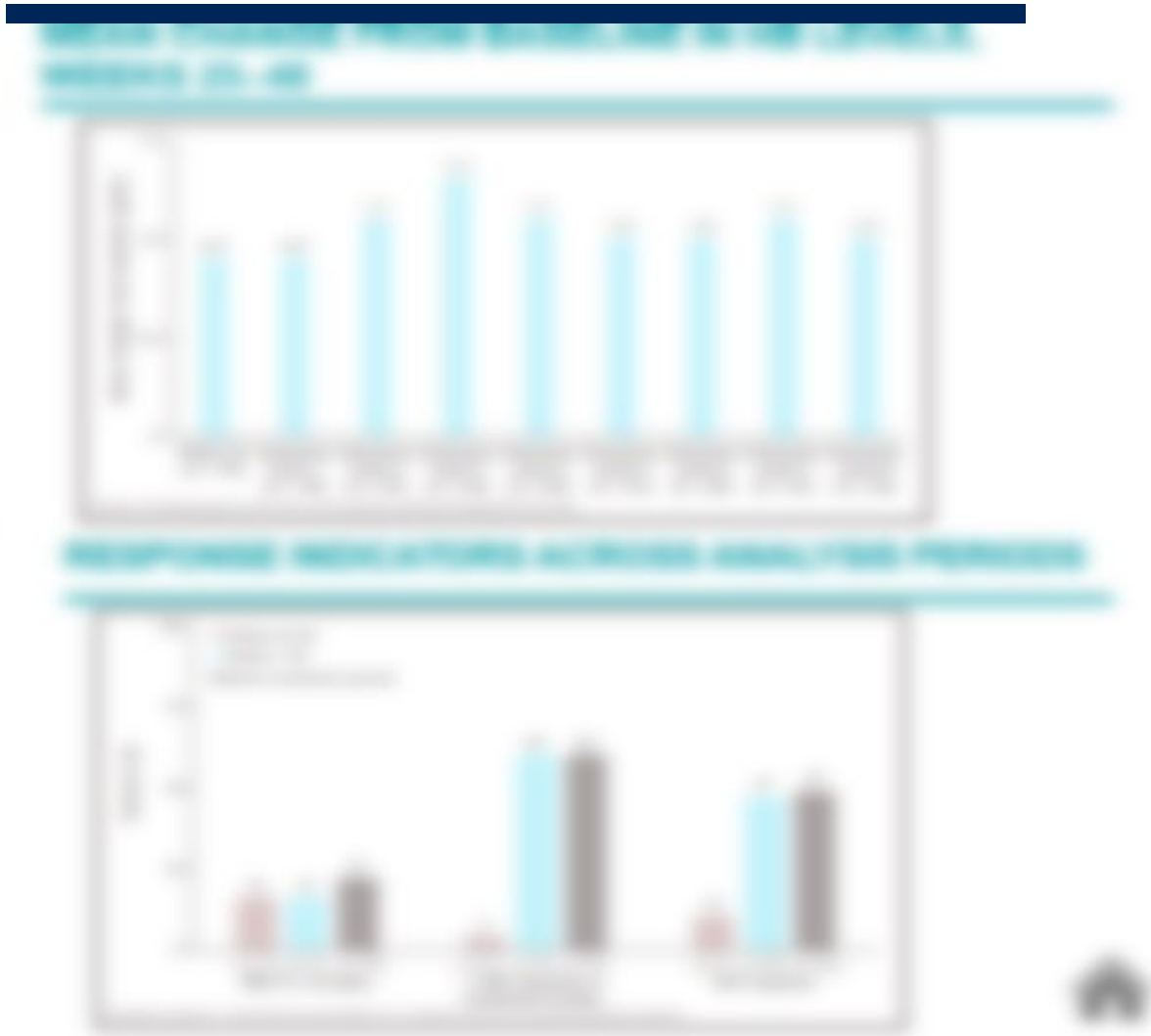
STUDY POPULATION AND METHODS

> 32 pts with mCRPC with the small cell neuroendocrine phenotype

MECHANISM OF ACTION



Pembrolizumab + docetaxel for mCRPC: Randomized, double-blind, phase 3 KEYNOTE-921 study

Petrylak et al. 2023, ASCO GU 19

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STUDY POPULATION AND METHODS

> 1030 pts with mCRPC that progressed on ADT, and who had

OVERALL SURVIVAL

Nivolumab + ipilimumab for post-chemotherapy mCRPC: Additional results from the randomized phase 2 CheckMate 650 trial

Sharma et al. 2023, ASCO GU 22

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STUDY POPULATION AND METHODS

> 259 pts with mCRPC previously treated with docetaxel

STUDY SCHEMA

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Key Insights

Prostate Cancer Part 2 – Metastatic Castration-Resistant Prostate Cancer

Experts Discussed the Role for PARP Inhibitors in *BRCA*-Mutated mCRPC

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TRITON-3 AND PROFOUND

Cumulative data from TRITON-3 and PROFOUND strongly support using a single-agent

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Experts Debated the Potential Role for PARP Inhibitors in *BRCA*-Nonmutated mCRPC

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PROpel AND TALAPRO

Both PROpel and TALAPRO showed a modest rPFS benefit for PARPi + ARSI combinations

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Experts Reviewed Investigational Agents for the Treatment of mCRPC

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IMMUNE CHECKPOINT INHIBITORS

Negative results from KEYNOTE-921 and CheckMate 650 further confirm that ICIs rarely

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Congress Highlights

Bladder Cancer Part 1 – NMIBC and MIBC

Pembrolizumab monotherapy for high-risk NMIBC unresponsive to BCG: Results from Cohort B of the phase 2 KEYNOTE-057 trial

Necchi et al. 2023, ASCO GU LBA442

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STUDY POPULATION AND METHODS

> Pts with BCG-unresponsive, high-risk NMIBC

OVERALL SURVIVAL

HCRN GU 16-257: Phase 2 trial of gemcitabine, cisplatin, + nivolumab with selective bladder sparing in patients with MIBC

Galsky et al. 2023, ASCO GU 447

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STUDY POPULATION AND METHODS

> 76 pts with cisplatin-eligible with cT2-T4aN0M0 bladder cancer

OVERALL SURVIVAL

HCRN GU14-188: Phase Ib/II study of neoadjuvant pembrolizumab and chemotherapy for T2-4aN0M0 urothelial cancer

Brown et al. 2023, ASCO GU 448

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STUDY POPULATION AND METHODS

> Pts were surgical candidates with clinical stage T2-4aN0M0 UC,

RELAPSE-FREE AND OVERALL SURVIVAL

Extended follow-up results from the CheckMate 274 trial

Galsky et al. 2023, ASCO GU LBA443

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STUDY POPULATION AND METHODS

> 353 pts with high-risk MIBC after radical resection

DISEASE-FREE SURVIVAL

Quality of life in QUILT 3.032 study: Patients with BCG-unresponsive NMIBC receiving IL-15RαFc superagonist N-803 + BCG

Chamie et al. 2023, ASCO GU 495

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STUDY POPULATION AND METHODS

> Pts with BCG-unresponsive NMIBC

QUALITY-OF-LIFE MEASURES

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Key Insights

Bladder Cancer Part 1 – NMIBC and MIBC

Experts Discussed the Management of NMIBC

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QUILT 3.032

Experts had positive perceptions of the intravesical IL-15 superagonist N-803 on the basis

Experts Considered Results From Trials for MIBC

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CheckMate 274

An updated analysis of CheckMate 274 showed that the DFS and DMFS advantages

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Congress Highlights

Bladder Cancer Part 2 – Metastatic Urothelial Cancer

TROPHY-U-01 cohort 2, a phase 2 study of sacituzumab govitecan in platinum-ineligible mUC that progressed after prior CPI therapy

Petrylak et al. 2023, ASCO GU 520

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STUDY POPULATION AND METHODS

- 38 pts with platinum-ineligible mUC that progressed after prior ICI

OVERALL SURVIVAL

Platinum/gemcitabine ± atezolizumab as first-line treatment of locally advanced or mUC: Final OS from phase 3 IMvigor130 study

Galsky et al. 2023, ASCO GU LBA440

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STUDY POPULATION AND METHODS

> Pts with mUC previously untreated for metastatic disease

OVERALL SURVIVAL

Final OS analysis of atezolizumab monotherapy vs chemotherapy in untreated locally advanced or mUC from the phase 3 IMvigor130 study

Bamias et al. 2023, ASCO GU LBA441

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STUDY POPULATION AND METHODS

> Pts with mUC previously untreated for metastatic disease

OVERALL SURVIVAL

PROs in cisplatin-ineligible mUC with enfortumab vedotin alone or with pembrolizumab in the phase 1b/2 EV-103 Cohort K study

Milowsky et al. 2023, ASCO GU 439

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STUDY POPULATION AND METHODS

> Cisplatin-ineligible pts with previously untreated la/mUC

QUALITY OF LIFE

Biomarkers of response to enfortumab vedotin in patients with advanced urothelial carcinoma: Analysis of the UNITE study

Jindal et al. 2023, ASCO GU 450

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STUDY POPULATION AND METHODS

> 170 pts with mUC from 16 sites treated with EV and registered in

OVERALL SURVIVAL

Avelumab maintenance: Long-term follow-up from JAVELIN Bladder 100 in subgroups

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Sridhar et al. 2023, ASCO GU 508

STUDY POPULATION AND METHODS

> Pts with advanced UC that had not progressed with 4–6 cycles of

OVERALL SURVIVAL FROM START OF FIRST-LINE THERAPY

BT8009-100: A phase I/II study of novel bicyclic peptide and MMAE conjugate BT8009 in advanced malignancies associated with nectin-4

Baldini et al. 2023, ASCO GU 498

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STUDY POPULATION AND METHODS

- 24 pts with heavily pretreated mUC (median 3 prior lines of

RESPONSE

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Key Insights

Bladder Cancer Part 2 – Metastatic Urothelial Cancer

Experts Discussed the Cytotoxic Drug Conjugates for mUC

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SACITUZUMAB GOVITECAN

Experts consider SG to be an active agent, but a head-to-head trial with EV would be

Experts Debated the Timing of Immune Checkpoint Inhibitors for mUC

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JAVELIN Bladder 100

JAVELIN Bladder 100 long-term follow-up showed that OS benefits associated with

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Congress Highlights

Renal Cell Carcinoma

HCRN GU16-260-Cohort A: Treatment-free survival with nivolumab and salvage nivolumab + ipilimumab in advanced ccRCC

Atkins et al. 2023, ASCO GU 604

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STUDY POPULATION AND METHODS

- 128 pts with advanced ccRCC

TUMOR RESPONSE

Nivolumab plus cabozantinib vs sunitinib for first-line treatment of advanced RCC: 3-year follow-up from the phase 3 CheckMate 9ER trial

Burotto et al. 2023, ASCO GU 603

EPICS

STUDY POPULATION AND METHODS

> Pts with previously untreated mRCC were randomized to

OVERALL SURVIVAL BY IMDC RISK

Biomarker analysis from the phase 3 CheckMate 9ER trial of nivolumab + cabozantinib vs sunitinib for advanced renal cell carcinoma (aRCC)

Choueiri et al. 2023, ASCO GU 608

EPICS

STUDY POPULATION AND METHODS

> Pts with previously untreated mRCC were randomized to

PFS OUTCOMES BY PD-L1 STATUS

COSMIC-313 phase 3 trial evaluating cabozantinib + nivolumab and ipilimumab in first-line advanced intermediate- or poor-risk RCC

Powles et al. 2023, ASCO GU 605

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STUDY POPULATION AND METHODS

> 855 pts with advanced ccRCC of IMDC intermediate or poor risk

PROGRESSION-FREE SURVIVAL

CaboPoint: Phase 2 study of cabozantinib after checkpoint inhibitor therapy in patients with advanced RCC

Albiges et al. 2023, ASCO GU 606

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STUDY POPULATION AND METHODS

> 88 pts with advanced RCC progressing after first-line ICI-based

RESPONSE RATES ACROSS SUBGROUPS

OS and efficacy of second-line treatment in patients with mRCC treated in the randomized phase II BIONIKK trial

Vano et al. 2023, ASCO GU 607

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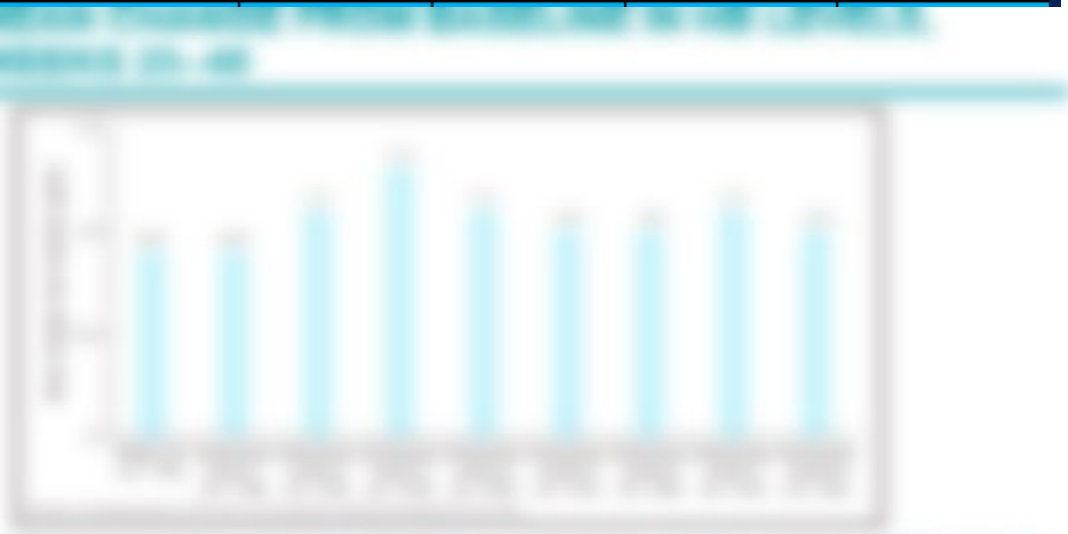
STUDY POPULATION AND METHODS

> 199 pts with previously untreated mRCC

UPDATED ORR AND PFS



Results from phase 3 study of ^{89}Zr-DFO-girentuximab for PET/CT imaging of clear cell renal cell carcinoma (ZIRCON)

Shuch et al. 2023, ASCO GU LBA602

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STUDY POPULATION AND METHODS

> 300 pts with an indeterminate renal mass (≤7 cm; tumor stage

RATIONALE FOR RADIOTRACER TARGET

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Key Insights

Renal Cell Carcinoma

Experts Discussed First-Line ICI-TKI Combinations for mRCC

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CheckMate 9ER

The 44-month follow-up of CheckMate 9ER comparing cabozantinib-nivolumab vs sunitinib

Experts Debated the Implications of Investigational First-Line Strategies

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HCRN GU16-260

The HCRN GU16-260 study in treatment-naive mRCC reported that adding

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Experts Discussed Later-Line Therapy and Biomarker-Driven Approaches for mRCC

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TKIs FOLLOWING PROGRESSION ON AN ICI

The phase II CaboPoint trial reported ORRs of ~30% with single-agent cabozantinib in

Experts Speculated on Diagnostic Imaging for ccRCC

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^{89}Zr-DFO-GIRENTUXIMAB PET IMAGING

Data with the new CAIX-targeted PET tracer are promising, and will likely play an expanded

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