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Conference Coverage: ASCO 2023 – Focus on Genitourinary (GU) Malignancies

Full Report

June 9, 2023

Report Contents

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Meeting Snapshot

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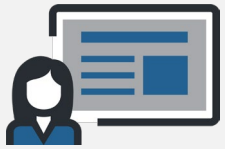
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
June 9, 2023



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GU malignancies
- > 7 from US
- > 2 from Europe

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

Panel Consisting of 7 US and 2 European GU Cancer Experts

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Oliver Sartor, MD, FACS
Mayo Clinic

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

Scott Tagawa, MD, FACP
Weill Cornell Medicine

Joaquim Bellmunt, MD, PhD
Harvard Medical School

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

CHAIR:
Daniel P. Petrylak, MD
Yale Cancer Center

Thomas Powles, MD, MRCP, MBBS
Barts Cancer Institute

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

Karim Fizazi, MD, PhD
Gustave Roussy

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Meeting Agenda

Time (EST)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	**Welcome and Introductions**	Daniel Petrylak, MD
10.05 AM – 10.15 AM	**Prostate Cancer Part 1 – Standard and Emerging Therapies**	Oliver Sartor, MD, FACS
10.15 AM – 10.30 AM	Discussion	All faculty
10.30 AM – 10.35 AM	Key Takeaways	
10.35 AM – 10.45 AM	**Prostate Cancer Part 2 – Targeting DNA Repair in mCRPC**	Karim Fizazi, MD, PhD; Susan Slovin, MD, PhD, FACP
10.45 AM – 11.00 AM	Discussion	All faculty
11.00 AM – 11.05 AM	Key Takeaways	
11.05 AM – 11.15 AM	**Bladder Cancer Part 1 – Immunotherapies**	Leonard Gomella, MD, FACS; Joaquim Bellmunt, MD, PhD
11.15 AM – 11.25 AM	Discussion	All faculty
11.25 AM – 11.30 AM	Key Takeaways	
11.30 AM – 11.40 AM	**Break**	
11.40 AM – 11.50 AM	**Bladder Cancer Part 2 – Targeted Therapies**	Scott Tagawa, MD, FACP
11.50 AM – 12.05 PM	Discussion	All faculty
12.05 PM – 12.10 PM	Key Takeaways	
12.10 PM – 12.20 PM	**Clear Cell Renal Cell Carcinoma**	Thomas Powles, MBBS, MRCP, MD
12.20 PM – 12.30 PM	Discussion	All faculty
12.30 PM – 12.35 PM	Key Takeaways	
12.35 PM – 12.40 PM	**Non-clear Cell Renal Cell Carcinoma**	Robert Dreicer, MD, MACP, FASCO
12.40 PM – 12.50 PM	Discussion	All faculty
12.50 PM – 12.55 PM	Key Takeaways	
12.55 PM – 1.00 PM	**Summary and Closing Remarks**	Daniel Petrylak, MD

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Congress Highlights

Prostate Cancer Part 1 – Standard and Emerging Therapies

Prostate irradiation in men with de novo, low-volume mCSPC: Results of PEACE-1, a phase 3 randomized trial with a 2x2 design

Bossi, et al. 2023, ASCO LBA5000

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STUDY POPULATION AND METHODS

> 1172 pts with de novo mCSPC were randomized to receive ADT-

RADIOGRAPHIC PROGRESSION-FREE SURVIVAL

STARTAR: A phase 2 trial of AR inhibition with ADT and apalutamide with RT followed by docetaxel in men with PSA recurrent PC after prostatectomy

Zhang, et al. 2023, ASCO 5016

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STUDY POPULATION AND METHODS

> 39 pts with high-risk PSA-recurrent PC post-prostatectomy

PSA PROGRESSION-FREE SURVIVAL

Phase I results of PSMA-targeted radionuclide therapy with alpha-radiolabeled antibody 225Ac-J591 and beta-radioligand 177Lu-PSMA

Tagawa, et al. 2023, ASCO 5018

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STUDY POPULATION AND METHODS

> 18 pts with progressive mCRPC, ≥1 prior AR signaling inhibitor

PSA RESPONSE

Phase I study of PSCA-targeted chimeric antigen receptor (CAR) T cells in patients with mCRPC

Dorff, et al. 2023, ASCO 5019

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STUDY POPULATION AND METHODS

> 14 pts with mCRPC previously treated with at least 1 ARSI

PSA RESPONSE

EMBARK: Phase 3 study of enzalutamide or placebo plus leuprolide and enzalutamide monotherapy in high-risk biochemically recurrent PC

Shore, et al. 2023, AUA LBA02-09

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STUDY POPULATION AND METHODS

> 1068 pts with PSA-recurrent PC post-prostatectomy and/or radiation

METASTASIS-FREE SURVIVAL

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Key Insights

Prostate Cancer Part 1 – Standard and Emerging Therapies

Experts Debated New Approaches for PSA-Recurrent PC Following Prostatectomy

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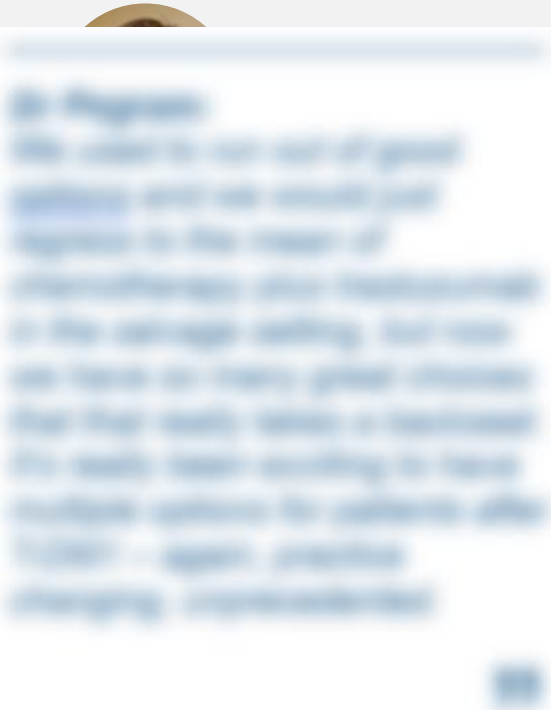
EMBARK

Experts expect the combination of ADT-enzalutamide for patients with rising PSA



Experts Debated the Role of Radiation in the Treatment of De Novo mCSPC

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PEACE-1

Analysis of the RT arms in the low-volume subset of patients with de novo

Experts Considered Novel Therapies for mCRPC

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RADIOLABELED PSMA-TARGETED THERAPIES

Efficacy and safety data from the phase I trial combining alpha- and beta-labeled

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Congress Highlights

Prostate Cancer Part 2 – Targeting DNA Repair in mCRPC

Presence of somatic/germline HRR mutations and outcomes in mCRPC pts receiving 1L treatment stratified by *BRCA* status

Olmos, et al. 2023, ASCO 5003

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STUDY POPULATION AND METHODS

- 729 pts with mCRPC were analyzed for the presence of HRR

OVERALL SURVIVAL

TALAPRO-2: Phase 3 of talazoparib + enzalutamide vs placebo + ENZA 1L treatment for mCRPC harboring HRR gene alterations

Fizazi, et al. 2023, ASCO 5004

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STUDY POPULATION AND METHODS

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

rPFS IN HRRm SUBGROUP

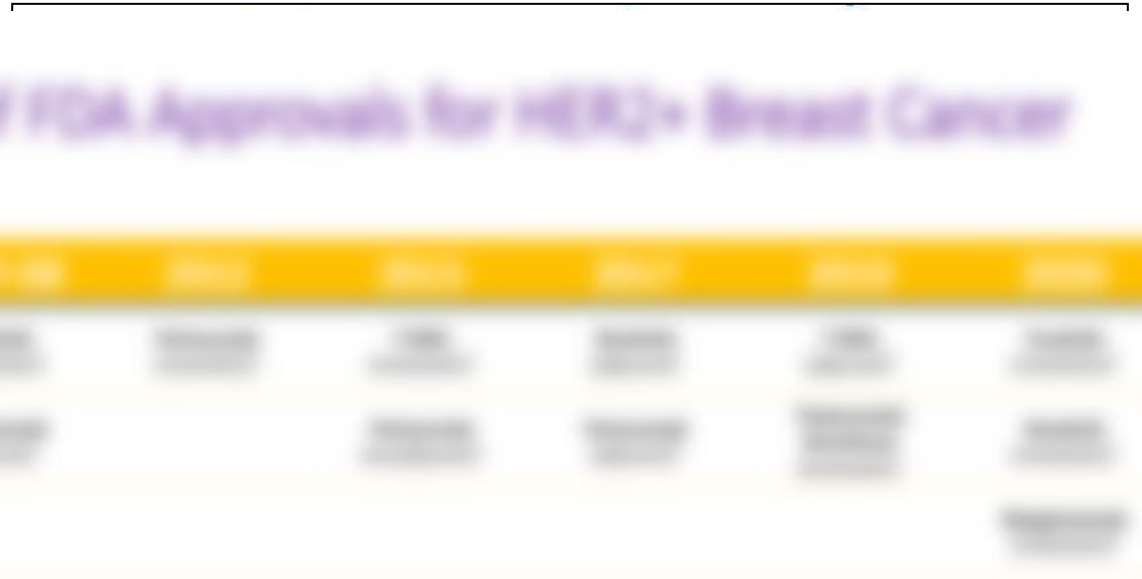
LuPARP: Phase 1 trial of 177Lu-PSMA-617 and olaparib in patients with mCRPC

Sandhu, et al. 2023, ASCO 5005

STUDY POPULATION AND METHODS

- 32 pts with mCRPC previously treated with an ARSI and

PSA RESPONSE BY COHORT



HRQoL and pain outcomes for pts with mCRPC who received abiraterone and olaparib vs abi and placebo in PROpel

Thiery-Vuillemin, et al. 2023, ASCO 5012

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STUDY POPULATION AND METHODS

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

FACT-P SCORES

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PROs among men receiving talazoparib + enzalutamide vs placebo + ENZA as 1L treatment for mCRPC: Results from TALAPRO-2

Agarwal, et al. 2023, ASCO 5013

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STUDY POPULATION AND METHODS

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

GLOBAL HEALTH/QUALITY OF LIFE

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Key Insights

Prostate Cancer Part 2 – Targeting DNA Repair in mCRPC

Experts Debated PARPi + ARSI Combinations for mCRPC

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TALAPRO-2

The magnitude of benefit observed in TALAPRO-2 with the addition of talazoparib

Dr Pegram

We used to run out of good options and we would just default to the mean of chemotherapy plus trastuzumab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DXd — again, practice changing, unprecedented.

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Experts Discussed Investigational PARPi + Radioligand Strategies

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LuPARP

Experts are enthusiastic about the phase I results from the LuPARP trial in

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Congress Highlights

Bladder Cancer Part 1 – Immunotherapies

SunRISe-1: Patients with BCG-unresponsive high-risk NMIBC receiving TAR-200 in combination with cetrelimab, TAR-200, or cetrelimab alone

Daneshmand, et al. 2023, AUA LBA02-03

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STUDY POPULATION AND METHODS

> 47 pts with BCG-refractory NMIBC

DURATION OF RESPONSE

CORE-001: Phase 2 study of CG0070 combined with pembrolizumab in patients with NMIBC unresponsive to BCG

Li, et al. 2023, AUA 23-5631

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STUDY POPULATION AND METHODS

> 35 pts with BCG-unresponsive CIS-containing NMIBC

DURATION OF RESPONSE

Long-term outcomes of pembro + gem and concurrent hypofractionated RT as bladder sparing treatment for MIUC: A phase 2 trial

Economides, et al. 2023, ASCO 4509

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STUDY POPULATION AND METHODS

> 54 pts with MIBC

2-YEAR EFFICACY OUTCOMES

OS by response to 1L induction treatment with atezolizumab + plt/gem vs placebo + plt/gem in mUC: Updated IMvigor130 OS final analysis

Grande, et al. 2023, ASCO 4503

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STUDY POPULATION AND METHODS

> Pts with mUC previously untreated for metastatic disease

POST-INDUCTION OS IN PATIENTS WITH NO PD

Impact of histology on the efficacy and safety of pembrolizumab for advanced UC in the phase 3 KEYNOTE-045 and KEYNOTE-361 trials

Giannatempo, et al. 2023, ASCO 4512

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STUDY POPULATION AND METHODS

> Pts with mUC treated with pembrolizumab monotherapy enrolled

OVERALL SURVIVAL

Long-term safety of avelumab 1L maintenance for advanced UC in the JAVELIN Bladder 100 trial

Bellmunt, et al. 2023, ASCO 4516

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STUDY POPULATION AND METHODS

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

irAEs OCCURRING AFTER 12 MONTHS OF THERAPY

Estimated net benefit of avelumab + BSC for aUC using a quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis

Powles, et al. 2023, ASCO 4515

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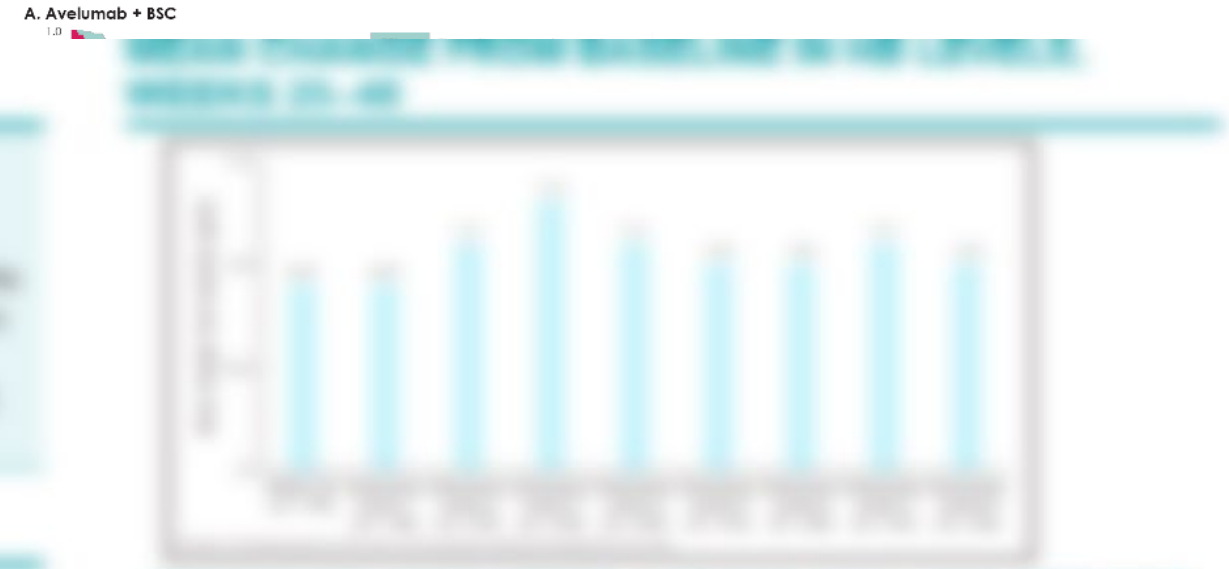
STUDY POPULATION AND METHODS

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

Q-TWiST ANALYSIS



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Key Insights

Bladder Cancer Part 1 – Immunotherapies

Experts Discussed the Development of New Therapies for Nonmuscle-Invasive Bladder Cancer

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INTRAVESICAL THERAPIES

There are a number of interesting agents currently in trials for BCG-

Experts Discussed Analyses of Previously Presented Trials in mUC

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JAVELIN BLADDER 100

The long-term safety analysis and the potential for irAEs with maintenance avelumab are considered important to discuss with patients who are on therapy

Experts Speculated on Future Treatment Practice Patterns

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EV-PEMBRO VS MAINTENANCE AVELUMAB

Experts speculated that a HR of 0.65–0.70 will be necessary for EV +

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Congress Highlights

Bladder Cancer Part 2 – Targeted Therapies

Phase 3 THOR study: Erdafitinib vs chemotherapy in advanced or metastatic urothelial cancer (mUC) with select *FGFR* alterations

Loriot, et al. 2023, ASCO LBA4619

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STUDY POPULATION AND METHODS

- 266 pts with advanced or mUC with select *FGFR3/2*alt

OVERALL SURVIVAL

Erdafitinib vs ERDA plus cetrelimab for mUC and FGFR alterations: Final results from the phase 2 Norse study

Siefker-Radtke, et al. 2023, ASCO 4504

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STUDY POPULATION AND METHODS

> 87 pts with previously untreated cis-ineligible mUC with

DURATION OF RESPONSE

EV-103 cohort A: Long-term outcome of enfortumab vedotin + pembro in 1L cisplatin-ineligible la/mUC with nearly 4 years of follow-up

Gupta, et al. 2023, ASCO 4505

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STUDY POPULATION AND METHODS

- 45 1L cisplatin-ineligible pts with la/mUC

DURATION OF RESPONSE

Safety analysis by *UGT1A1* status of TROPHY-U-01 cohort 1: sacituzumab govitecan (SG) in mUC after PT-based chemo and a CPI

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Tagawa, et al. 2023, ASCO 4514

STUDY POPULATION AND METHODS

- 113 pts with heavily pretreated mUC treated with SG

SAFETY

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Key Insights

Bladder Cancer Part 2 – Targeted Therapies

Experts Discussed the Treatment of *FGFR*-Altered mUC

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THOR

THOR phase III results support erdafitinib as SOC post-platinum and IO, and ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLEVPATH-like regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
- Most experts are using trastuzumab deruxtecan third-line, but will prioritize the tucatinib triplet for patients with evidence of brain metastases.
- The tucatinib triplet may also be used in the second-line setting, before T-DM1, for patients with documented brain metastases.
  - If tucatinib is used second-line, experts are divided on whether they would currently use T-DM1 or trastuzumab deruxtecan third-line.
    - Results of the ongoing DESTINY-Breast03 trial comparing trastuzumab deruxtecan vs T-DM1 will help to clarify the optimal sequence of these ADCs.
- Trastuzumab deruxtecan and the tucatinib triplet may also be used earlier than third-line in patients who recur following treatment with trastuzumab, pertuzumab, and T-DM1 in the (neo)adjuvant setting, but this represents a small fraction of patients.
- Patient preferences can also factor into the sequencing of these new agents (eg, 3 drugs vs 1 drug, concern about hair loss vs diarrhea).
- The impressive efficacy of trastuzumab deruxtecan and the tucatinib regimen have pushed other options, such as trastuzumab-chemotherapy combinations, neratinib, and margetuximab, to later lines of therapy.

Dr Pegram:
We used to run out of good options and we would just regress to the mean of chemotherapy plus trastuzumab in the salvage setting, but now we have so many great choices that that really takes a backseat. It's really been exciting to have multiple options for patients after T-DM1 — again, practice changing, unprecedented.

Experts Discussed the Use of ADCs in mUC

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ENFORTUMAB VEDOTIN + PEMBROLIZUMAB

Updated analysis of EV-103 showed excellent long-term PFS and OS with EV +

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Congress Highlights

Clear Cell Renal Cell Carcinoma

Atezolizumab plus cabozantinib vs cabozantinib alone after progression with prior ICI mRCC: Primary PFS analysis from CONTACT-03 study

Choueiri, et al. 2023, ASCO LBA4500

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STUDY POPULATION AND METHODS

> 522 pts with mRCC with radiographic progression on or after prior

PROGRESSION-FREE SURVIVAL

Adjuvant nivolumab plus ipilimumab vs placebo for localized RCC at high risk of relapse: Subgroup analyses CheckMate 914 (part A)

Motzer, et al. 2023, ASCO 4506

EPICS

STUDY POPULATION AND METHODS

- 816 pts with RCC at high risk of post-nephrectomy relapse

DFS SUBSET ANALYSIS

Pembrolizumab plus axitinib versus sunitinib as 1L therapy for advanced clear cell renal cell carcinoma: 5-year analysis of KEYNOTE-426

Rini, et al. 2023, ASCO LBA4501

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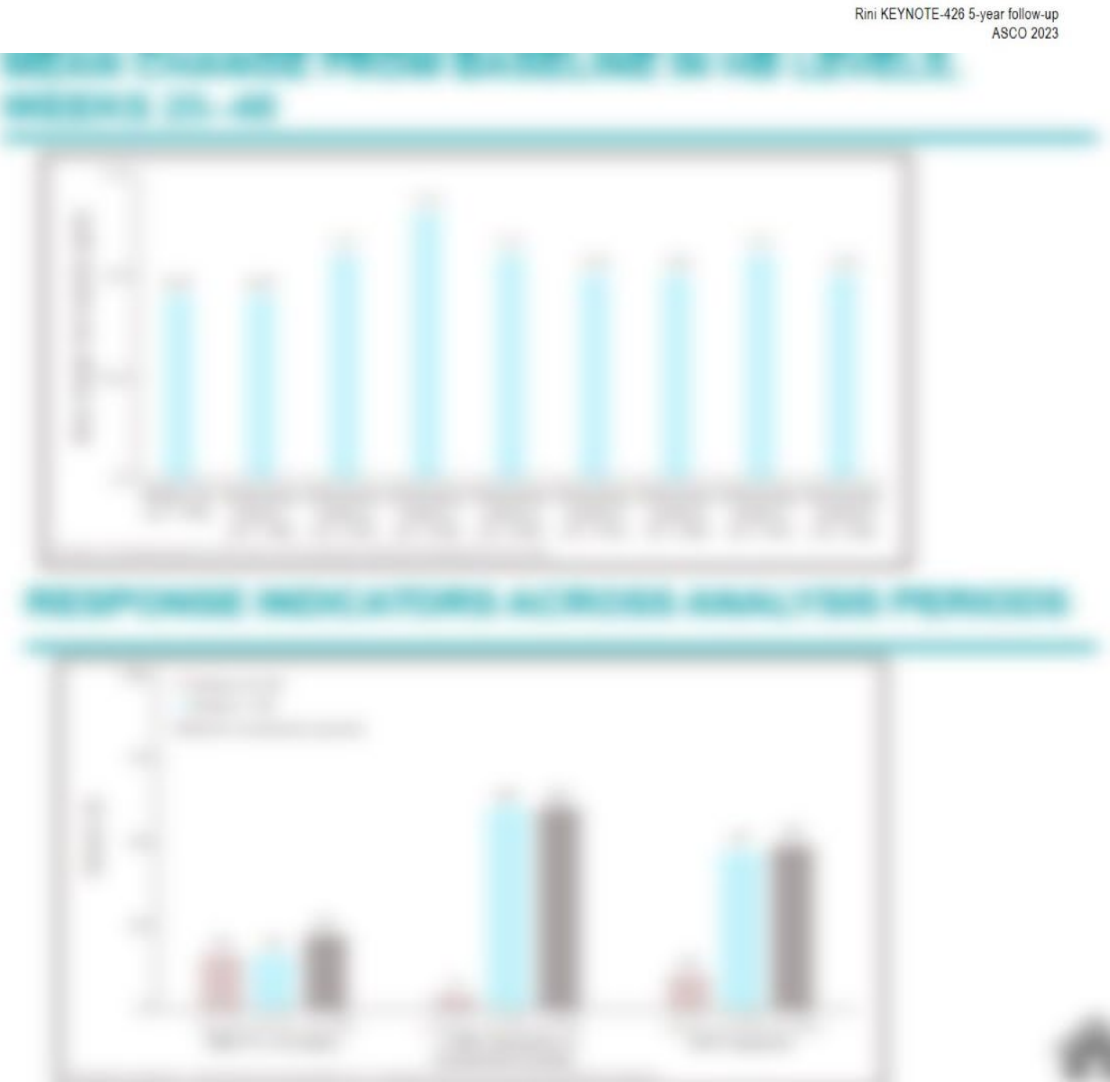
STUDY POPULATION AND METHODS

> 861 treatment-naive patients with advanced ccRCC were

OVERALL SURVIVAL



Final prespecified OS analysis of CLEAR: 4-year follow-up of lenvatinib plus pembrolizumab vs sunitinib in patients with aRCC

Motzer, et al. 2023, ASCO 4502

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STUDY POPULATION AND METHODS

> 1069 pts with treatment-naive advanced RCC randomized to

OVERALL SURVIVAL

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Key Insights

Clear Cell Renal Cell Carcinoma

Experts Discussed the Implications of Longer Follow-up of 1L IO-TKI Trials for mRCC

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KEYNOTE-426 AND CLEAR

Experts Discussed Rechallenging Patients With an ICI After Progression on an ICI-Containing Regimen

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CONTACT-03

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLEVPATEN-like regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
- Most experts are using trastuzumab deruxtecan third-line, but will prioritize the tucatinib triplet for patients with evidence of brain metastases.
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Experts Considered the Implications of the Subset Analyses of the Adjuvant CheckMate 914 Trial

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BIOMARKERS FOR IO THERAPY

Experts Debated the Comparative Efficacy of 1L IO-IO vs IO-TKI Regimens for mRCC

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Summary of 1st line renal cancer OS data at

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Congress Highlights

Non-clear Cell Renal Cell Carcinoma

First-line lenvatinib + pembrolizumab treatment across non-clear cell renal cell carcinomas: Results of the phase 2 KEYNOTE-B61 study

Lee, et al. 2023, ASCO 4518

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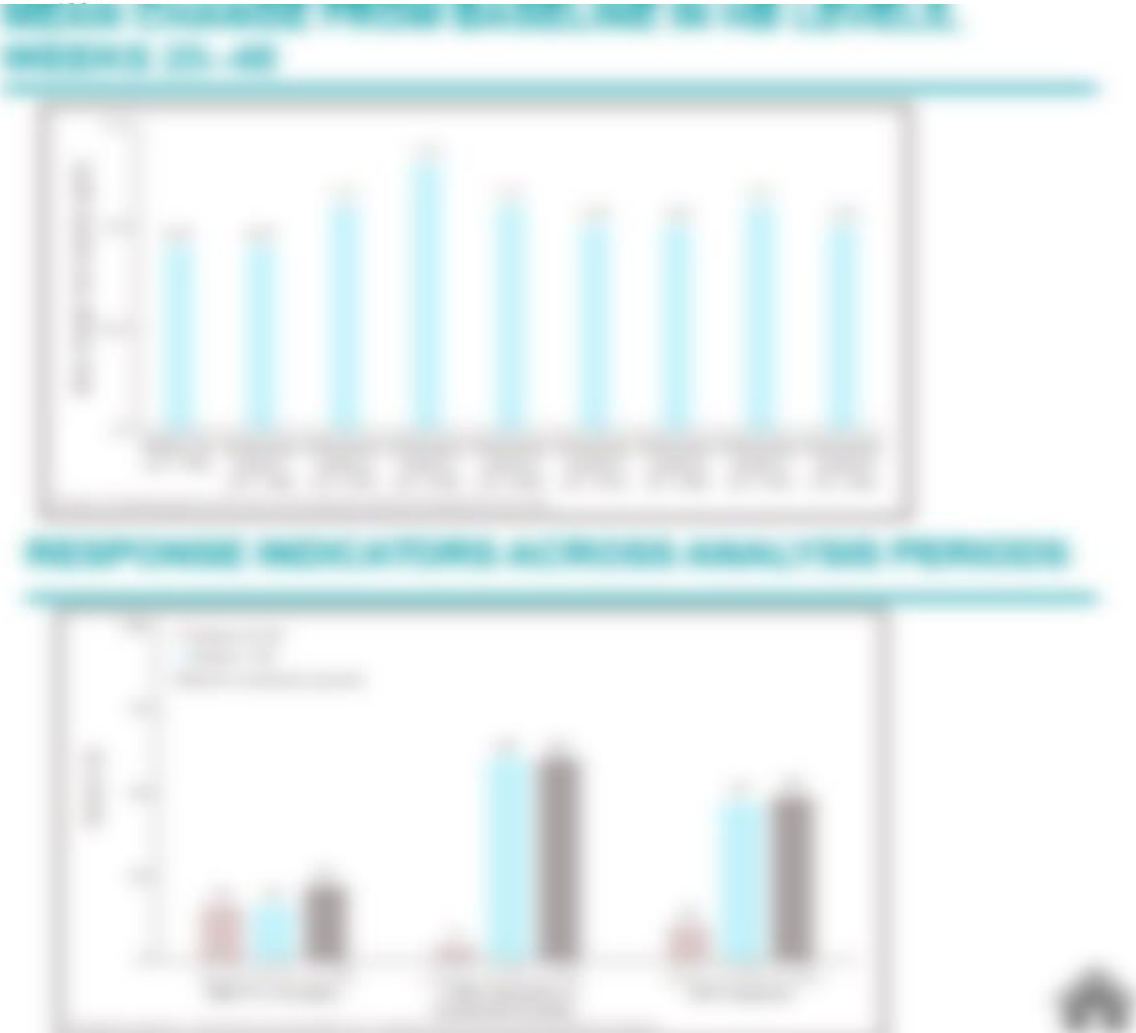
STUDY POPULATION AND METHODS

> 158 pts with previously treated advanced/metastatic nccRCC

OBJECTIVE RESPONSE BY HISTOLOGY



Efficacy of 1L IO-based regimens in patients with sarcomatoid and/or rhabdoid (S/R) metastatic nccRCC: Results from the IMDC

Labaki, et al. 2023, ASCO 4519

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STUDY POPULATION AND METHODS

> 103 pts with sarcomatoid/rhabdoid (S/R) nccRCC treated with

OUTCOMES IN S/R nccRCC – IO VS VEFG TKI

Phase II study of cabozantinib with nivolumab and ipilimumab in advanced renal cell carcinoma with variant histologies

McGregor, et al. 2023, ASCO 4520

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STUDY POPULATION AND METHODS

> 40 pts with RCC with variant histologies

TOXICITY

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Key Insights

Non-clear Cell Renal Cell Carcinoma

Experts Discussed Treatment Paradigms for Non-clear Cell RCC

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IMMUNOTHERAPY VS VEGFR TKIs

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a CLEAR/KEYNOTA-digo regimen (a lenvima plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
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[illegible] Progress

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