













EPICS

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

Full Report

June 9, 2023

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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



**Thomas Powles, MD,
MRCP, MBBS**
Barts Cancer Institute

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



CHAIR:
Daniel P. Petrylak, MD
Yale Cancer Center

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



Karim Fizazi, MD, PhD
Gustave Roussy



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

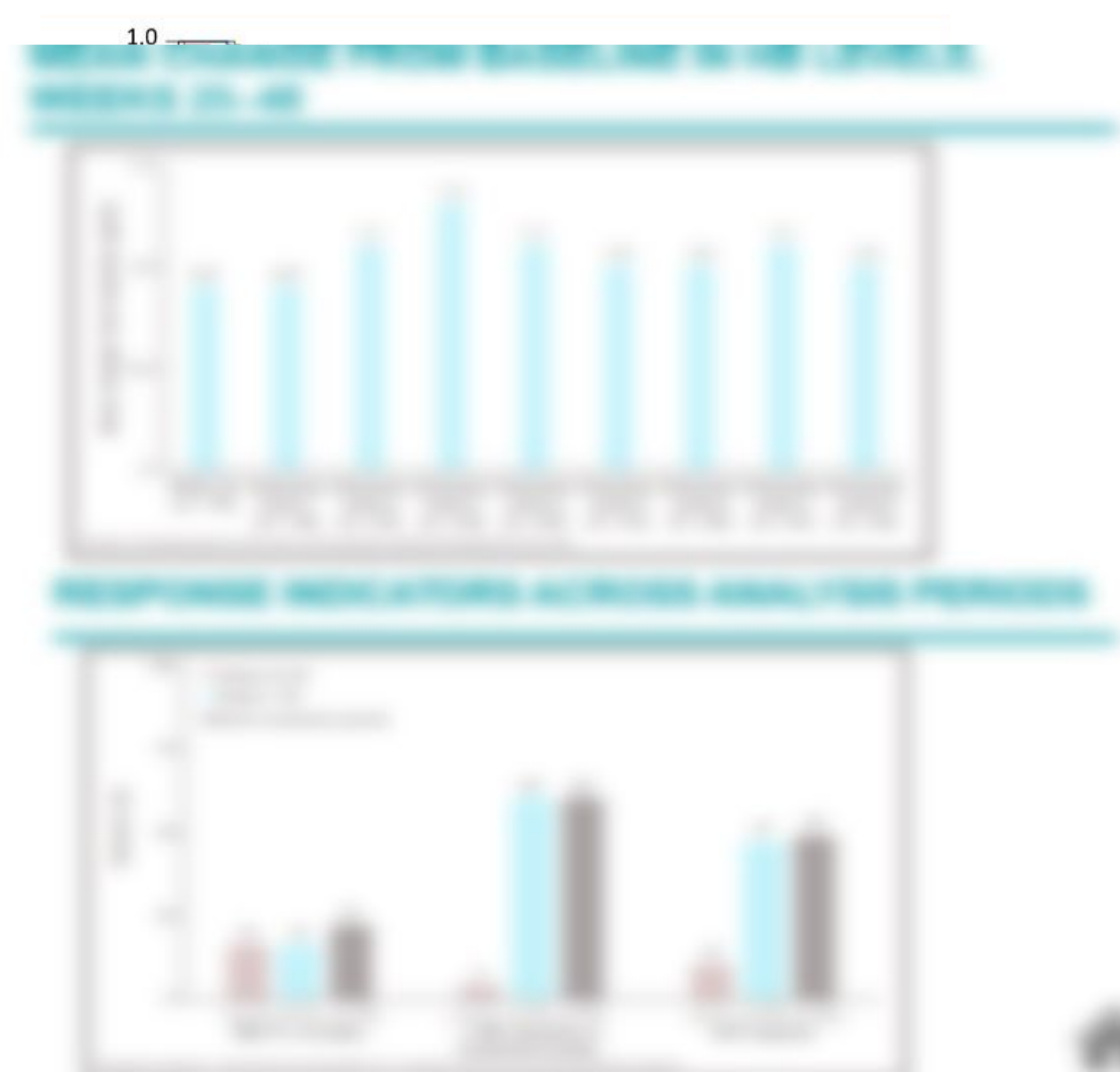
Prostate irradiation in men with de novo, low-volume mCSPC: Results of PEACE-1, a phase 3 randomized trial with a 2x2 design

Bossi, et al. 2023, ASCO LBA5000

STUDY POPULATION AND METHODS

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

RADIOGRAPHIC PROGRESSION-FREE SURVIVAL



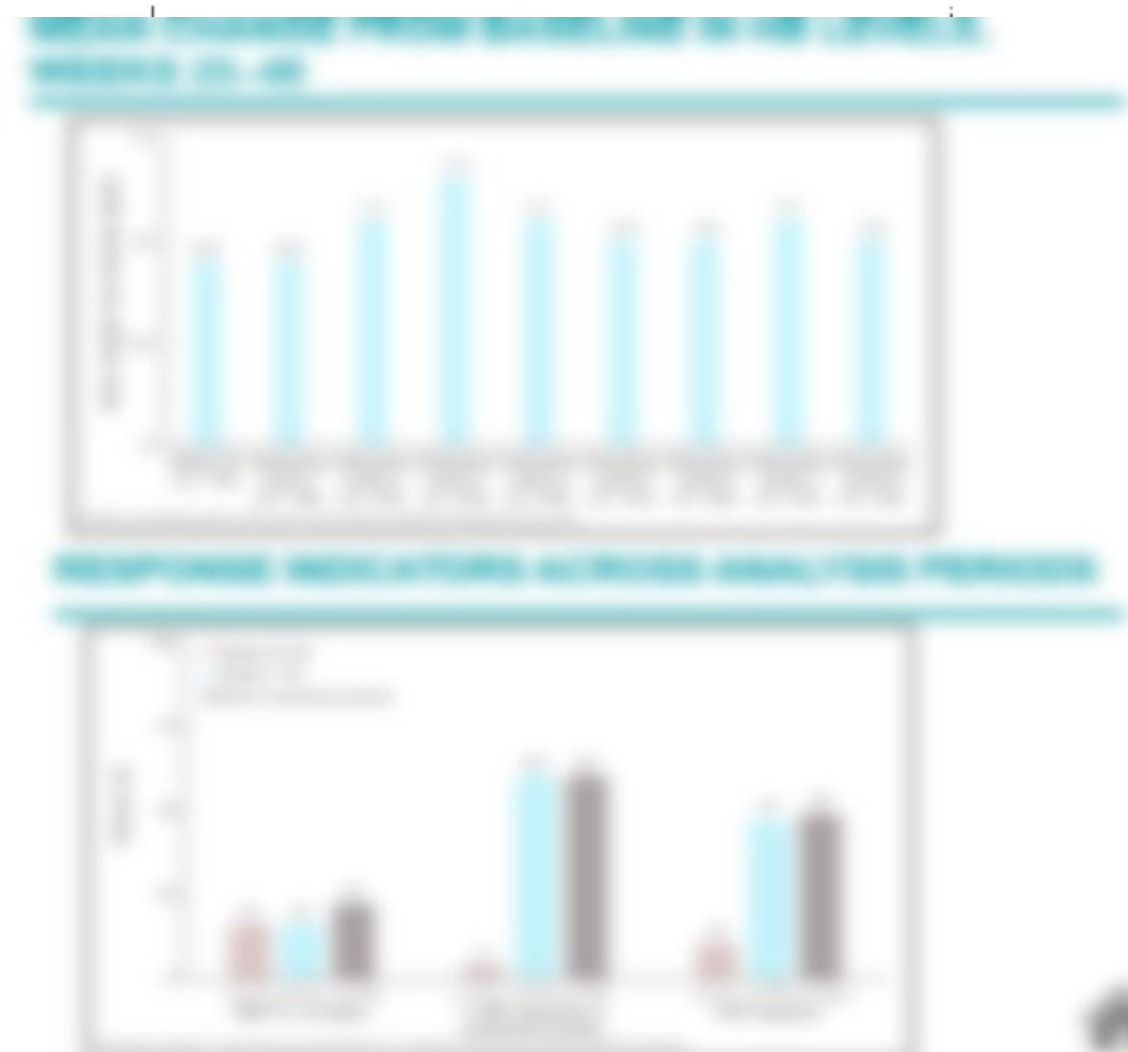
STARTAR: A phase 2 trial of AR inhibition with ADT and apalutamide with RT followed by docetaxel in men with PSA recurrent PC after prostatectomy

Zhang, et al. 2023, ASCO 5016

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 ^{225}Ac -J591 and beta-radioligand ^{177}Lu -PSMA

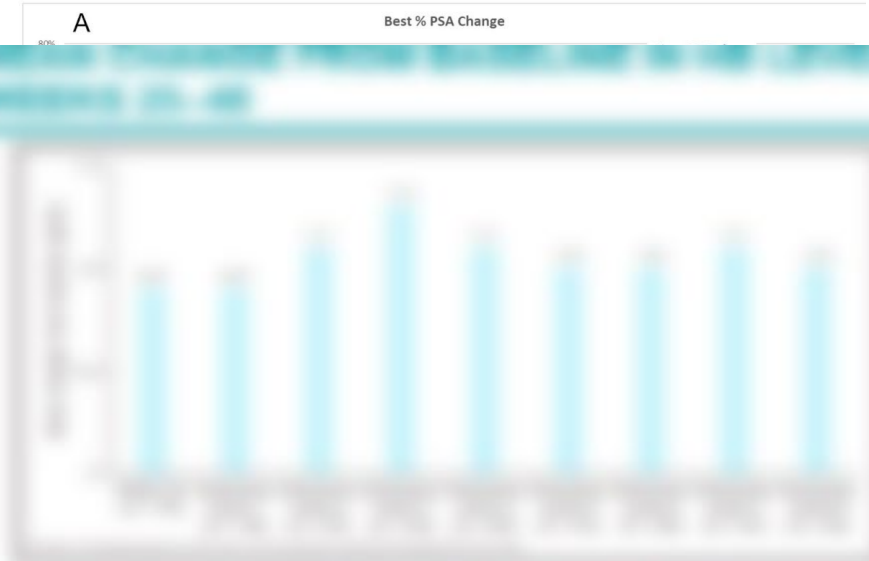
Tagawa, et al. 2023, ASCO 5018

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STUDY POPULATION AND METHODS

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

PSA RESPONSE



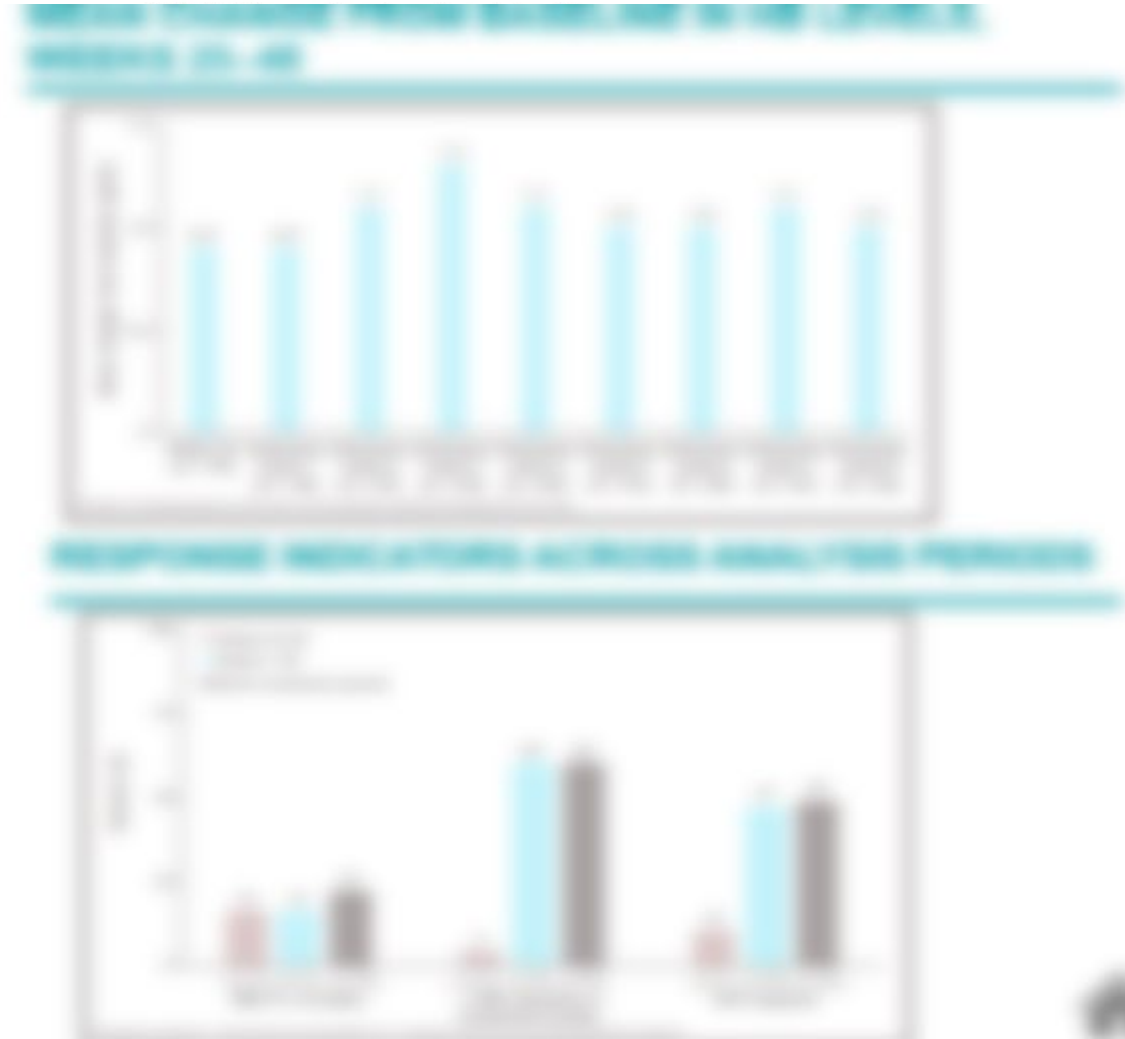
Phase I study of PSCA-targeted chimeric antigen receptor (CAR) T cells in patients with mCRPC

Dorff, et al. 2023, ASCO 5019

STUDY POPULATION AND METHODS

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

PSA RESPONSE



EMBARC: 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

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

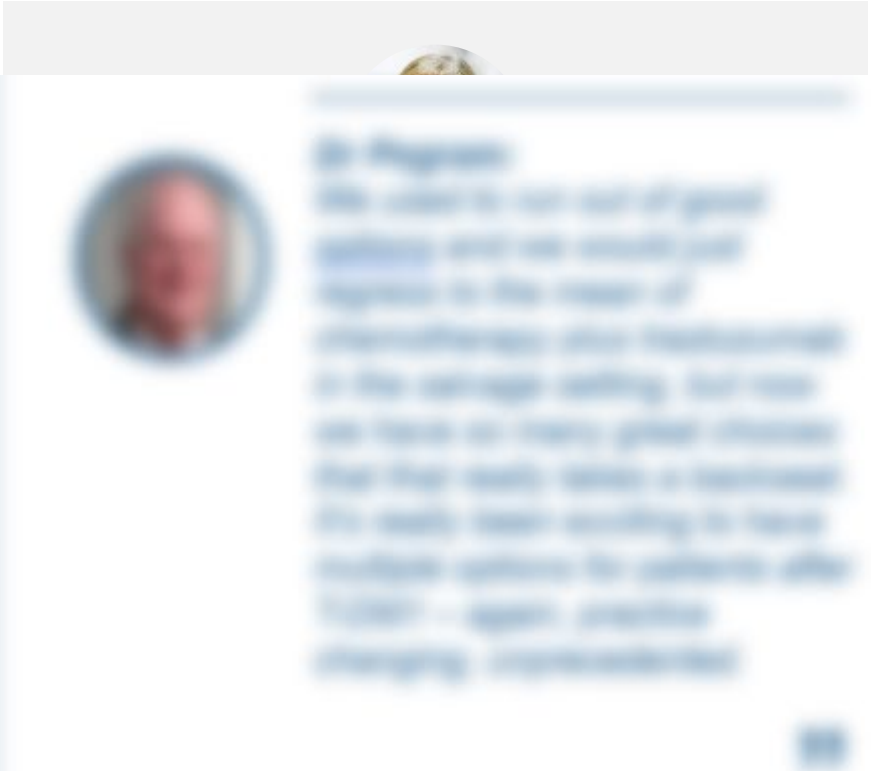
Experts Debated the Role of Radiation in the Treatment of De Novo mCSPC

PEACE-1

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

Supporting results will help clarify the optimal sequencing of agents.

- 1. Treatment arms will include a combination of docetaxel, prednisone, and radiotherapy, followed by TDM1 maintenance, for most patients.
- 2. Other regimens will include docetaxel, prednisone, docetaxel, but will provide the treatment option for patients with evidence of local progression.
- 3. The treatment option may also be used in the maintenance setting, before TDM1, for patients with documented local progression.
 - 1. Provided a local progression, experts are divided on whether they would normally use TDM1 or docetaxel, prednisone, docetaxel.
 - 2. Results of the ongoing 2017/18 PROSPER trial comparing docetaxel, prednisone or TDM1 will help to clarify the optimal sequencing of these agents.
- 4. Docetaxel, prednisone and the treatment option may also be used within the treatment of patients who have following treatment with docetaxel, prednisone, and TDM1 in the maintenance setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, concern about hair loss or diarrhea).
- 6. The comparative efficacy of docetaxel, prednisone and the treatment option have varied over options, such as docetaxel, chemotherapy, combination, steroids, and combination, in other trials of therapy.



Experts Considered Novel Therapies for mCRPC

RADIOLABELED PSMA-TARGETED THERAPIES

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

Supporting trials will help identify the optimal sequencing of agents

- 1. Treatment will start with a 10-day course of the alpha- and beta-labeled PSMA-targeted and PSMA-targeted therapies, followed by TDM1 administration, to most patients
- 2. Most patients will receive PSMA-targeted therapies, but will provide the second cycle for patients with evidence of local progression
- 3. The second cycle may also be used in the second-line setting, before TDM1, for patients with documented local progression
 - 1. Provided to most participants, experts are divided on whether they would normally use TDM1 in metastatic disease setting
 - 1. Results of the ongoing 2017 trial showed that combining PSMA-targeted therapies with TDM1 will help to identify the optimal sequencing of these agents
- 4. PSMA-targeted therapies and the second cycle may also be used earlier than starting a patient who have following treatment with docetaxel, enzalutamide, and TDM1 in the metastatic setting, but this represents a small fraction of patients
- 5. Future studies will also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug versus drug-free vs 2 drugs)
- 6. The impressive efficacy of PSMA-targeted therapies and the second-line setting have opened other options, such as PSMA-targeted chemotherapy combinations, vaccines, and immunotherapy, to new lines of therapy



Dr. [Name]
[Blurred text describing the expert's role and the trial details]

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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

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

STUDY POPULATION AND METHODS

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

rPFS IN HRRm SUBGROUP

Timeline of FDA Approvals for HER2+ Breast Cancer



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

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2018	2019	2020	2021	2022	2023	2024
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							
HER2+ Breast Cancer							



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

STUDY POPULATION AND METHODS

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

FACT-P SCORES

Timeline of FDA Approvals for HER2+ Breast Cancer

A horizontal timeline chart showing FDA approvals for HER2+ breast cancer treatments from 2000 to 2020. The timeline is represented by a yellow bar with vertical lines indicating approval years. The years shown are 2000, 2005, 2010, 2015, 2020, 2025, and 2030. There are several vertical lines indicating approvals, with some lines having small text labels next to them, though they are too small to read. The timeline shows a steady progression of approvals over the period.

Year	Year	Year	Year	Year	Year	Year
2000	2005	2010	2015	2020	2025	2030



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

Agarwal, et al. 2023, ASCO 5013

STUDY POPULATION AND METHODS

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

GLOBAL HEALTH/QUALITY OF LIFE

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	Year	Year	Year	Year	Year	Year
2000	2005	2010	2015	2020	2025	2030



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Key Insights

Prostate Cancer Part 2 – Targeting DNA Repair in mCRPC

Experts Debated PARPi + ARSI Combinations for mCRPC

TALAPRO-2

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

Supporting trials will help identify the optimal sequencing of agents

- 1. Talazoparib was used in a 100 mg daily regimen in the regimen of docetaxel plus metformin and talazoparib, followed by TDM1 maintenance, in most patients
- 2. Most patients are using metformin + docetaxel + talazoparib, but will probably be treated with docetaxel with evidence of liver metastases
- 3. The standard of care may also be used in the maintenance setting, before TDM1, in patients with documented liver metastases
 - 1. Provided to most participants, experts are divided on whether they would actually use TDM1 in maintenance docetaxel therapy
 - 1. Results of the ongoing TDM1 docetaxel plus docetaxel maintenance docetaxel vs TDM1 will help to clarify the optimal sequencing of these drugs
- 4. Docetaxel + metformin and the standard of care may also be used earlier than docetaxel in patients who were following treatment with metformin, docetaxel, and TDM1 in the maintenance setting, but this represents a small fraction of patients
- 5. Future comparisons will also focus on the sequencing of these two agents (eg, 1 drug vs 1 drug versus drug-free vs 2 drugs)
- 6. The impressive efficacy of metformin + docetaxel and the standard regimen have opened other options, such as metformin + chemotherapy combinations, metformin and talazoparib, or other types of therapy



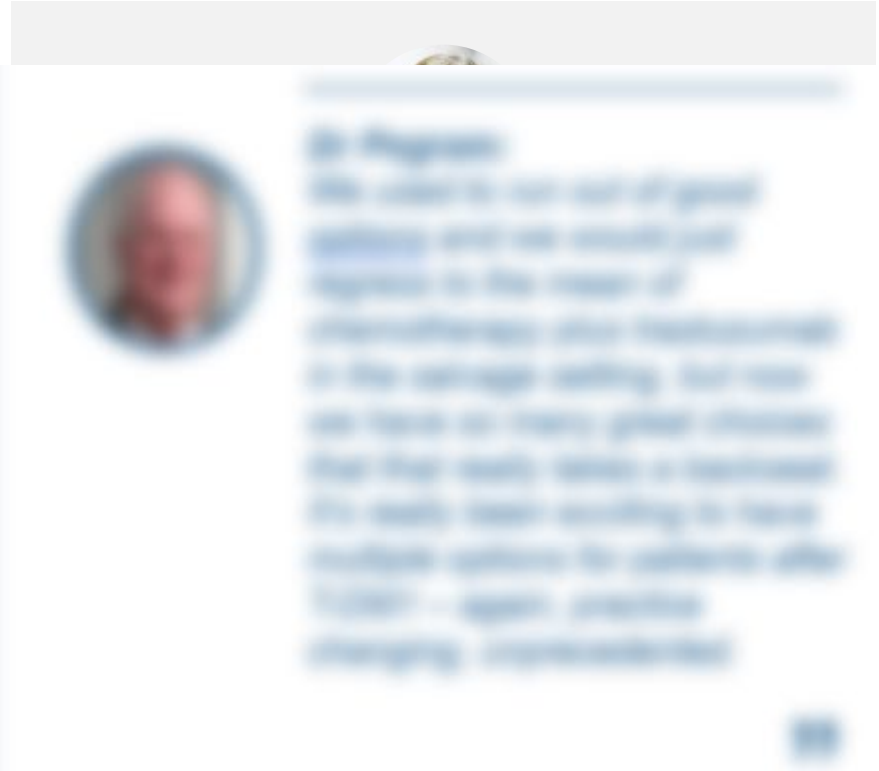
Dr. [Name]
[Faded text describing the expert's perspective on the clinical trial results and treatment sequencing.]

Experts Discussed Investigational PARPi + Radioligand Strategies

LuPARP

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

... (blurred text) ...



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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

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

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

STUDY POPULATION AND METHODS

> 54 pts with MIBC

2-YEAR EFFICACY OUTCOMES

BLADDER Sparing Treatment Outcome in the Overall Population (n=54)



RESPONSE, REPLICATION, AND BLADDER SAVING PERIODS



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

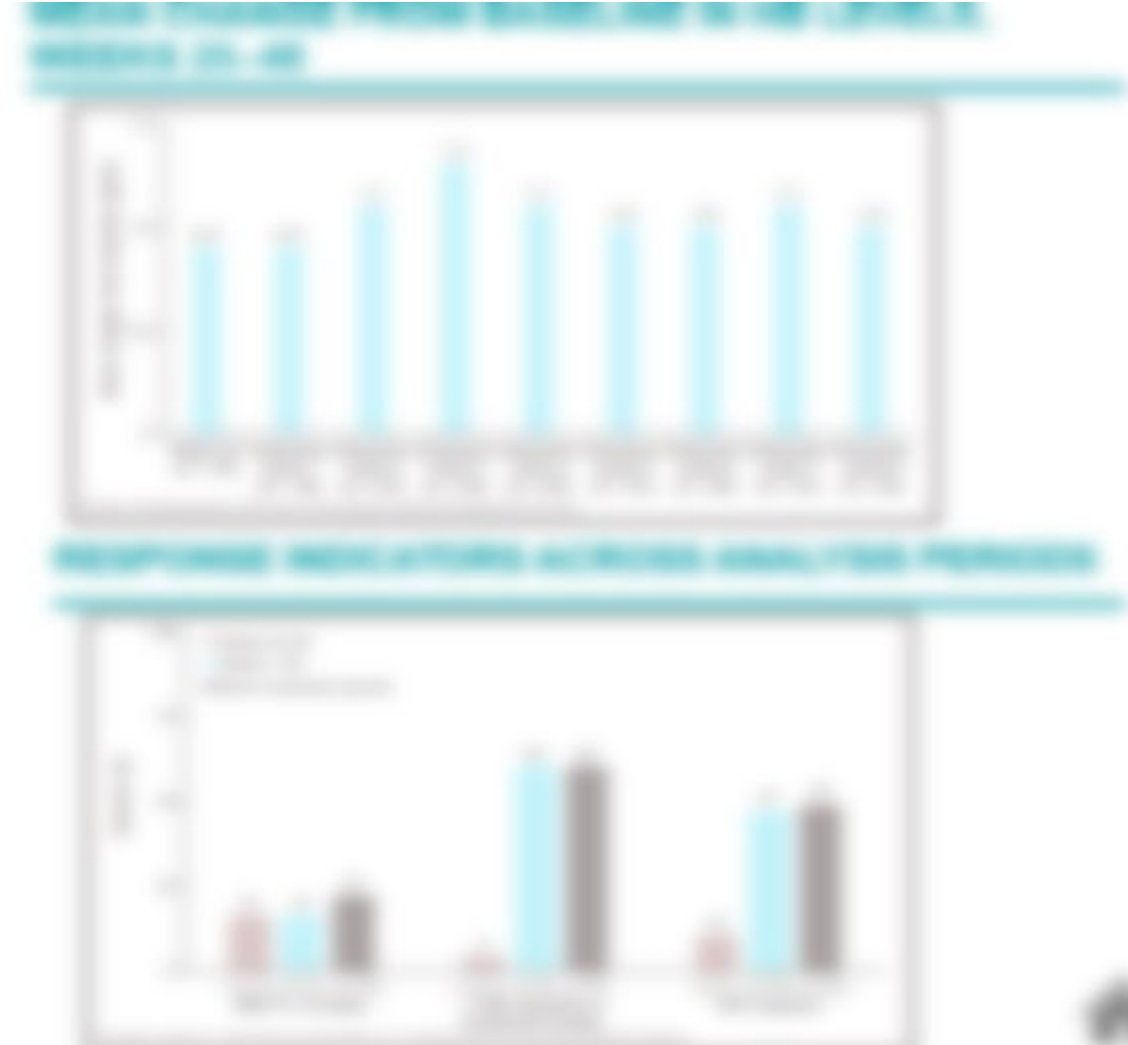
Grande, et al. 2023, ASCO 4503

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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

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

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

STUDY POPULATION AND METHODS

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

Q-TWiST ANALYSIS

A. Avelumab + BSC

Figure 1. Quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis for avelumab + best supportive care (BSC) versus BSC alone in advanced urothelial carcinoma (aUC). The y-axis represents Q-TWiST (months), and the x-axis represents the number of cycles (4, 5, 6). Error bars represent 95% confidence intervals.



Figure 2. Q-TWiST analysis for avelumab + BSC versus BSC alone in advanced urothelial carcinoma (aUC) using a quality-adjusted time without cancer symptoms or toxicity (Q-TWiST) analysis. The y-axis represents Q-TWiST (months), and the x-axis represents the number of cycles (4, 5, 6). Error bars represent 95% confidence intervals.



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Key Insights

Bladder Cancer Part 1 – Immunotherapies

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

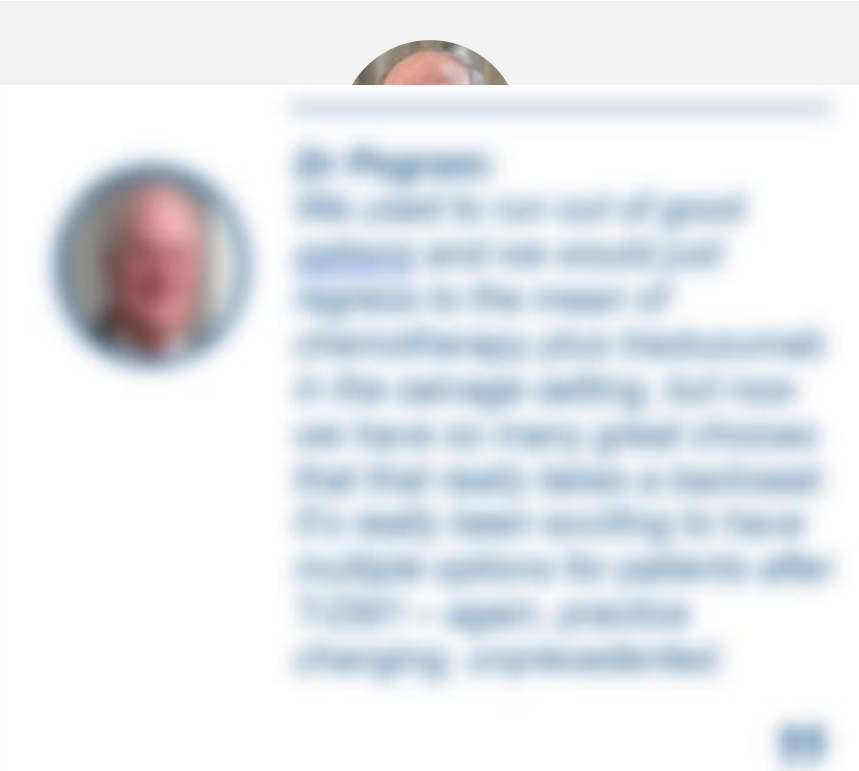
INTRAVESICAL THERAPIES

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

nonmuscle-invasive NMIBC

...discussing trials will help clarify the optimal sequencing of agents ...

- ...
- ...
- ...
- ...
- ...
- ...
- ...
- ...



Experts Discussed Analyses of Previously Presented Trials in mUC

JAVELIN BLADDER 100

The long-term safety analysis and the potential for irAEs with maintenance

analyses are considered important to discuss with patients who are on the

... of the long-term safety analysis and the potential for irAEs with maintenance analyses are considered important to discuss with patients who are on the ...



... of the long-term safety analysis and the potential for irAEs with maintenance analyses are considered important to discuss with patients who are on the ...

Experts Speculated on Future Treatment Practice Patterns

EV-PEMBRO VS MAINTENANCE AVELUMAB

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

Supporting points will likely include the optimal sequencing of agents

- 1. Treatment will likely be a combination of the regimen of pembrolizumab and nivolumab followed by TDM1 maintenance, for most patients
- 2. Most experts are using nivolumab maintenance therapy, but will probably be looking for patients with evidence of local progression
- 3. The nivolumab regimen will be used in the maintenance setting, unless TDM1 is preferred in some circumstances, experts are divided on whether they would consider use of TDM1 in combination maintenance
 - 1. Results of the ongoing IMpower133 trial comparing nivolumab monotherapy to TDM1 will help to clarify the optimal sequencing of these drugs
- 4. Pembrolizumab monotherapy and the nivolumab regimen may also be used earlier than starting a patient who was following treatment with pembrolizumab, nivolumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients
- 5. Future preferences will also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug regimen) about how best to sequence
- 6. The comparative efficacy of pembrolizumab monotherapy and the nivolumab regimen have not been fully explored, such as pembrolizumab monotherapy combination, nivolumab, and nivolumab, in any form of therapy



Dr. [Name]
The combination of pembrolizumab and nivolumab followed by TDM1 is the most likely to be used in the maintenance setting, but we will see some patients getting pembrolizumab monotherapy or the nivolumab regimen earlier than starting a patient who was following treatment with pembrolizumab, nivolumab, and TDM1 in the maintenance setting. This represents a small fraction of patients.

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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 *FGFR3/2alt*

OVERALL SURVIVAL

STUDY POPULATION

266 pts with advanced or mUC with select *FGFR3/2alt* (100 pts with *FGFR3* alterations, 166 pts with *FGFR2alt* alterations). Median age 70 years (range 55-85). 100 pts (37.6%) had *FGFR3* alterations, 166 pts (62.4%) had *FGFR2alt* alterations. 100 pts (37.6%) had *FGFR3* alterations, 166 pts (62.4%) had *FGFR2alt* alterations. 100 pts (37.6%) had *FGFR3* alterations, 166 pts (62.4%) had *FGFR2alt* alterations.

DESIGN

Phase 3, randomized, controlled, open-label, parallel-group study comparing erdafitinib (150 mg qd) to chemotherapy (cisplatin 50 mg/m² q3w + gemtuzumab 100 mg q3w or cisplatin 50 mg/m² q3w + paclitaxel 175 mg/m² q3w) in patients with advanced or mUC with select *FGFR3/2alt*.

KEY RESULTS

Median OS was significantly longer in the erdafitinib group compared with the chemotherapy group (12.1 months vs 9.1 months, *P* = 0.0001).



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

STUDY POPULATION AND METHODS

- > 87 pts with previously untreated cis-ineligible mUC with FGFR alterations

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

STUDY POPULATION AND METHODS

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

DURATION OF RESPONSE

STUDY POPULATION

45 patients with 1L cisplatin-ineligible la/mUC, ECOG PS 0-1, no prior systemic anticancer therapy, and no prior treatment with immune-checkpoint inhibitors. The median age was 67 years (range 50-82). The majority of patients (38/45, 84%) had metastatic disease. The median time from diagnosis to enrollment was 1.7 years. The median time from enrollment to random assignment was 1.1 days. All patients received enfortumab vedotin + pembrolizumab through week 48.

RESULTS

45 patients were randomized to enfortumab vedotin + pembrolizumab (n=22) or enfortumab vedotin + placebo (n=23). The median overall survival was 18.1 months (95% CI, 15.1-21.1) in the enfortumab vedotin + pembrolizumab group and 14.1 months (95% CI, 11.1-17.1) in the enfortumab vedotin + placebo group.

CONCLUSIONS

Enfortumab vedotin + pembrolizumab significantly improved overall survival compared to enfortumab vedotin + placebo in patients with 1L cisplatin-ineligible la/mUC.



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

STUDY POPULATION

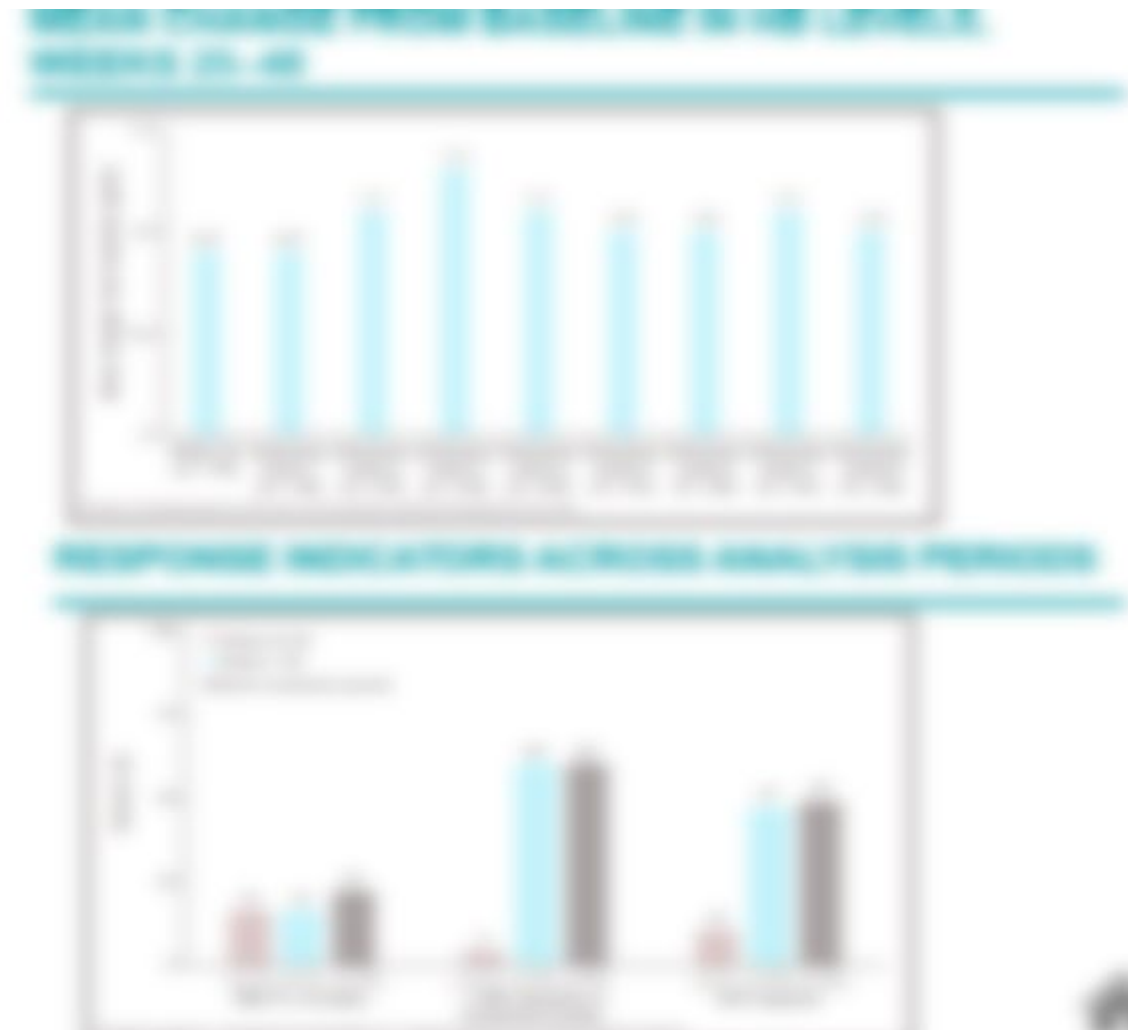
113 pts with heavily pretreated mUC treated with SG

SAFETY

113 pts with heavily pretreated mUC treated with SG

KEY POINT CONCLUSIONS

SG was well tolerated in heavily pretreated mUC patients. The most common adverse events were diarrhea, nausea, and vomiting. The majority of adverse events were grade 1 or 2.



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Key Insights

Bladder Cancer Part 2 – Targeted Therapies

Experts Discussed the Treatment of *FGFR*-Altered mUC

THOR

THOR phase III results support erdafitinib as SOC post-platinum and IO, and

supporting these will help clarify the optimal sequencing of agents

- 1. Treatment will start with a combination of platinum-based chemotherapy and immunotherapy, followed by TIGIT inhibitors, for most patients
- 2. Most patients will receive immunotherapy monotherapy, but will provide the needed data for patients with evidence of local progression
- 3. The overall study may also be used in the retrospective setting, before TIGIT, for patients with documented local progression
 - Provided to local investigators, experts are divided on whether they would actually use TIGIT in combination monotherapy
 - Results of the ongoing TIGIT trials themselves are supporting combination monotherapy as TIGIT will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy monotherapy and the overall study may also be used earlier than starting in patients who were following treatment with immunotherapy, platinum, and TIGIT in the retrospective setting, but this represents a small fraction of patients
- 5. Future combination use may focus on the sequencing of these two agents day 1 through 7 drug versus drug day 1 in therapy
- 6. The impressive efficacy of immunotherapy monotherapy and the overall regimen have opened other options, such as immunotherapy chemotherapy combinations, vaccines, and combination, in late lines of therapy



Dr. [Name]
The study is an example of great science and we are excited to support it in the name of immunotherapy and combination in the overall setting, but we do have to really great things that they will bring a paradigm to really help clarify in late stage options for patients with TIGIT – again, exciting things, combination

Experts Discussed the Use of ADCs in mUC

ENFORTUMAB VEDOTIN + PEMBROLIZUMAB

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

Supporting results will help identify the optimal sequencing of agents

- 1. Treatment with EV + pembrolizumab (EV+) showed superior overall survival (OS) compared to pembrolizumab monotherapy, followed by TDM1 monotherapy, in most patients.
- 2. EV+ patients also showed superior progression-free survival (PFS), but not overall response rate (ORR) or quality of life (QoL) compared to pembrolizumab monotherapy.
- 3. The overall results may also be used in the adjuvant setting, before TDM1, in patients with unresectable liver metastases.
 - Provided a clear recommendation, experts are divided on whether they would currently use TDM1 + pembrolizumab monotherapy.
 - Results of the ongoing EV-103 trial (EV+ vs pembrolizumab monotherapy vs TDM1) will help to clarify the optimal sequencing of these agents.
- 4. Pembrolizumab monotherapy and the overall results may also be used earlier than starting a patient who have following treatment with pembrolizumab, pembrolizumab + TDM1 in the maintenance setting, but this represents a small fraction of patients.
- 5. Future pembrolizumab use also hinges on the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 1 drug).
- 6. The impressive efficacy of pembrolizumab monotherapy and the overall results have opened other options, such as pembrolizumab immunotherapy combinations, readouts, and sequencing, in late lines of therapy.



Dr. [Name]
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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

STUDY POPULATION AND METHODS

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

PROGRESSION-FREE SURVIVAL

PROGRESSION-FREE SURVIVAL IN THE CONTACT-03 STUDY



RESPONSE RATES IN THE CONTACT-03 STUDY



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

STUDY POPULATION AND METHODS

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

DFS SUBSET ANALYSIS

NIVO+IPI Placebo

Figure 1: DFS Subset Analysis



Figure 2: Response Evaluation in Disease Analysis (RESOLVE)



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

STUDY POPULATION AND METHODS

> 861 treatment-naive patients with advanced ccRCC were

OVERALL SURVIVAL

Rini KEYNOTE-426 5-year follow-up
ASCO 2023

Overall Survival (OS) at 5 Years



Response Rate (RR) at 5 Years



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

STUDY POPULATION AND METHODS

> 1069 pts with treatment-naive advanced RCC randomized to

OVERALL SURVIVAL

STUDY POPULATION

1069 pts with treatment-naive advanced RCC randomized to lenvatinib plus pembrolizumab (LP) or sunitinib (S). LP group: 534 pts (50% male, 50% female), median age 65 years, median time to treatment initiation 1.1 years. S group: 535 pts (50% male, 50% female), median age 65 years, median time to treatment initiation 1.1 years. The primary endpoint was overall survival (OS) at 4 years. OS was defined as the time from randomization to death from any cause. All patients were followed up through week 48.

RESULTS

At 4 years, OS was significantly higher in the LP group compared with the S group (hazard ratio [HR], 0.67; 95% CI, 0.53-0.85; P < .001). The median OS was 48.1 months in the LP group and 36.1 months in the S group.

CONCLUSIONS

At 4 years, OS was significantly higher in the LP group compared with the S group. These findings support the use of LP as a first-line treatment for advanced RCC.

OS AT 4 YEARS



OS AT 4 YEARS BY SUBGROUP



EPICS

Key Insights

Clear Cell Renal Cell Carcinoma

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

KEYNOTE-426 AND CLEAR

Supporting trials will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of the regimen of nivolumab plus ipilimumab and ipilimumab monotherapy, followed by TKI as maintenance, for most patients
- 2. Most experts are using combination immunotherapy, but will probably be looking again for patients with evidence of local progression
- 3. The standard of care may also be used in the maintenance setting, before TKI, for patients with documented local progression
 - 1. Preferred to avoid immunotherapy, experts are divided on whether they would consider use TKI in combination immunotherapy
 - 1. Results of the ongoing IMpower010 trial comparing combination immunotherapy to TKI will help to clarify the optimal sequencing of these drugs
- 4. Combination immunotherapy and the standard of care may also be used earlier than starting a patient who was following treatment with combination immunotherapy and TKI in the maintenance setting, but this represents a small fraction of patients
- 5. Future preferences will also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus drug-free or best)
- 6. The impressive efficacy of combination immunotherapy and the standard regimen have opened other options, such as combination chemotherapy, combination, nivolumab, and ipilimumab, in the first line of therapy



Dr. [Name]
[Blurred text describing the speaker's role and the content of their presentation, including mentions of clinical trials and treatment options.]

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

CONTACT-03

Supporting these will help clarify the optimal sequencing of agents.

- 1. Experts are still using a combination of the regimen of nivolumab plus ipilimumab and pembrolizumab, followed by TDM1, according to most patients.
- 2. Most experts are using pembrolizumab monotherapy, but will consider the second-line option for patients with evidence of local progression.
- 3. The second-line option may also be used in the metastatic setting, before TDM1, for patients with documented local progression.
 - 1. Provided to most practitioners, experts are divided on whether they would consider use TDM1 in metastatic disease setting.
 - 1. Results of the ongoing IMPOWER010 trial comparing pembrolizumab monotherapy to TDM1 will help to clarify the optimal sequencing of these drugs.
- 4. Pembrolizumab monotherapy and the second-line option may also be used earlier than starting a patient who have following treatment with pembrolizumab, ipilimumab, and TDM1 in the metastatic setting, but this represents a small fraction of patients.
- 5. Future practitioners can also learn on the sequencing of these two agents (eg, 1 drug vs 1 drug versus dual use in therapy).
- 6. The comparative efficacy of pembrolizumab monotherapy and the second-line regimen have varied after patients, such as pembrolizumab monotherapy, combination, nivolumab, and ipilimumab, in the first-line setting.



...the overall goal is to improve patient outcomes and quality of life. The experts discussed the importance of patient-centered care and the need for ongoing research to better understand the optimal sequencing of immunotherapy agents. They also discussed the role of biomarkers in patient selection and the importance of clinical trial design in evaluating new treatment strategies. The experts emphasized the need for a multidisciplinary approach to cancer care, involving oncologists, radiologists, pathologists, and other healthcare professionals. They also discussed the importance of patient education and shared decision-making in the management of cancer. The experts concluded by stating that the goal is to provide the best possible care for each patient, based on their individual characteristics and preferences.

Experts Considered the Implications of the Subset Analyses of the Adjuvant CheckMate 914 Trial

BIOMARKERS FOR IO THERAPY

Supporting these findings will help identify the optimal sequencing of agents.

- 1. Treatment arms will receive a 1:1 randomization to the regimen of nivolumab plus ipilimumab and ipilimumab monotherapy, followed by T1DM monotherapy, for most patients.
- 2. Most patients will receive nivolumab plus ipilimumab monotherapy, but will proceed to the second cycle for patients with evidence of tumor progression.
- 3. The second cycle may also be used in the maintenance setting, before T1DM, for patients with documented tumor progression.
 - 1. Provided to your organization, experts are divided on whether they would consider use of T1DM in combination with nivolumab plus ipilimumab.
 - 2. Results of the ongoing 2017 trial described may complicate combination treatment as T1DM will help to verify the optimal sequencing of these agents.
- 4. Nivolumab plus ipilimumab and the second cycle may also be used earlier than starting a patient who was following treatment with nivolumab plus ipilimumab and T1DM in the maintenance setting, but this represents a small fraction of patients.
- 5. Future preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug, versus drug-free vs 1 drug).
- 6. The impressive efficacy of nivolumab plus ipilimumab and the second regimen have opened other options, such as nivolumab plus ipilimumab combination, nivolumab, and ipilimumab, in other lines of therapy.



Dr. [Name]
[Blurred text]

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

Summary of 1st line renal cancer OS data at

The Urologist



Dr. [Name]
The debate is not one of good vs bad, but one of what is best for the patient in the context of their overall health and quality of life. In the average setting, we see that the 1L IO-IO combination is the standard of care. However, in the setting of a patient who is frail or has comorbidities, the IO-TKI combination may be a better option. It's important to consider the patient's overall health and quality of life when making these decisions.

...regimen will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of the regimen of nivolumab plus ipilimumab and pembrolizumab, followed by 1L IO-TKI combination, in most settings.
- 2. Most experts are using nivolumab plus pembrolizumab, but will consider the standard of care for patients with evidence of liver metastases.
- 3. The standard of care may also be used in the metastatic setting, before 1L IO-TKI, in patients with documented liver metastases.
 - 1. Provided a good performance, experts are divided on whether they would consider use 1L IO-TKI in metastatic disease setting.
 - 1. Results of the ongoing IMmotion150 comparing nivolumab plus pembrolizumab to 1L IO-TKI will help to clarify the optimal sequencing of these agents.
- 4. Nivolumab plus pembrolizumab and the standard of care may also be used earlier than starting a patient who was following treatment with nivolumab plus pembrolizumab and 1L IO-TKI in the metastatic setting, but this represents a small fraction of patients.
- 5. Future performance will also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug versus dual drug vs 2 drugs).
- 6. The comparative efficacy of nivolumab plus pembrolizumab and the standard regimen have varied other options, such as nivolumab plus pembrolizumab combination, nivolumab, and pembrolizumab, in the first line of therapy.



EPICS

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

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

STUDY POPULATION AND METHODS

> 103 pts with sarcomatoid/rhabdoid (S/R) nccRCC treated with 1L IO-based regimens (IO-IO, IO-VEFG TKI), 41 VEGF TKI

OUTCOMES IN S/R nccRCC – IO VS VEGF TKI

STUDY POPULATION

103 pts with sarcomatoid/rhabdoid (S/R) nccRCC treated with 1L IO-based regimens (IO-IO, IO-VEFG TKI), 41 VEGF TKI

RESULTS

103 pts with sarcomatoid/rhabdoid (S/R) nccRCC treated with 1L IO-based regimens (IO-IO, IO-VEFG TKI), 41 VEGF TKI

CONCLUSIONS

IO-based regimens showed superior efficacy compared to VEGF TKI in S/R nccRCC



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

McGregor, et al. 2023, ASCO 4520

STUDY POPULATION AND METHODS

- > 40 pts with RCC with variant histologies

TOXICITY

STUDY POPULATION

40 pts with RCC with variant histologies... (text is blurred)

RESULTS

... (text is blurred)

CONCLUSIONS

... (text is blurred)



EPICS

Key Insights

Non-clear Cell Renal Cell Carcinoma

Experts Discussed Treatment Paradigms for Non-clear Cell RCC

IMMUNOTHERAPY VS VEGFR TKIs


Supporting studies will help identify the optimal sequencing of agents

- 1. Treatment will start with a combination of immunotherapy and antiangiogenic therapy, followed by TKI monotherapy, for most patients
- 2. Most experts are using immunotherapy + antiangiogenic therapy, but will prioritize the second-line agent for patients with evidence of prior progression
- 3. The second-line agent may also be used in the maintenance setting, before TKI, for patients with documented prior progression
 - 1. Preferred to used sequentially, experts are divided on whether they would currently use TKI + immunotherapy + antiangiogenic therapy
 - 1. Results of the ongoing IM+TKI+antiangiogenic vs immunotherapy + antiangiogenic + TKI will help to clarify the optimal sequencing of these agents
- 4. Immunotherapy + antiangiogenic and the second-line agent may also be used earlier than starting a patient who was following treatment with immunotherapy + antiangiogenic + TKI in the maintenance setting, but this represents a small fraction of patients
- 5. Future preferences will also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, versus what has been in practice)
- 6. The comparative efficacy of immunotherapy + antiangiogenic and the second-line agent have opened other options, such as immunotherapy + antiangiogenic + TKI, and immunotherapy + antiangiogenic + TKI + antiangiogenic, in the first-line setting



Dr. [Name]
The combination of immunotherapy and antiangiogenic therapy is the standard of care for non-clear cell RCC. The addition of TKI to this combination is a topic of ongoing discussion. The sequencing of these agents is a key consideration. The combination of immunotherapy and antiangiogenic therapy is preferred to used sequentially. The results of the ongoing IM+TKI+antiangiogenic vs immunotherapy + antiangiogenic + TKI will help to clarify the optimal sequencing of these agents. Immunotherapy + antiangiogenic and the second-line agent may also be used earlier than starting a patient who was following treatment with immunotherapy + antiangiogenic + TKI in the maintenance setting, but this represents a small fraction of patients. Future preferences will also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, versus what has been in practice). The comparative efficacy of immunotherapy + antiangiogenic and the second-line agent have opened other options, such as immunotherapy + antiangiogenic + TKI, and immunotherapy + antiangiogenic + TKI + antiangiogenic, in the first-line setting.





US 5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

[aptitudehealth.com](https://www.aptitudehealth.com)

