APTITUDE HEALTH®

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Conference Coverage: ESMO 2024 – Focus on Genitourinary (GU) Malignancies

September 24, 2024

Report Contents

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Meeting Snapshot

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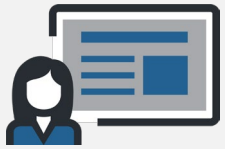
VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
September 24, 2024



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in GU malignancies

- 6 from the US
- 2 from Europe

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

Panel Consisting of 6 US and 2 European GU Cancer Experts

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Terence Friedlander, MD
University of California,
San Francisco

Scott Tagawa, MD, FACP, FASCO
Weill Cornell Medicine

Leonard Gomella, MD, FACS
Thomas Jefferson University

Joaquim Bellmunt, MD, PhD
Dana-Farber Cancer Institute

CHAIR:
Daniel Petrylak, MD
Yale Cancer Center

Susan Slovin, MD, PhD
Memorial Sloan Kettering Cancer Center

Karim Fizazi, MD, PhD
Institut Gustave Roussy

Manuela Schmidinger, MD
Medical University of Vienna

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Meeting Agenda

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Time (EST)	Topic	Presenter
9.00 AM – 9.05 AM / 15.00 – 15.05	**Welcome and Introductions**	Daniel Petrylak, MD
9.05 AM – 9.15 AM / 15.05 – 15.15	**Bladder Cancer Part 1 – NMIBC and MIBC**	Leonard Gomella, MD, FACS; Terence Friedlander, MD
9.15 AM – 9.35 AM / 15.15 – 15.35	**Discussion and Key Takeaways**	Moderator: Daniel Petrylak, MD
9.35 AM – 9.45 AM / 15.35 – 15.45	**Bladder Cancer Part 2 – Metastatic Urothelial Cancer**	Joaquim Bellmunt, MD, PhD
9.45 AM – 10.05 AM / 15.45 – 16.05	**Discussion and Key Takeaways**	Moderator: Daniel Petrylak, MD
10.05 AM – 10.15 AM / 16.05 – 16.15	**Renal Cell Carcinoma**	Manuela Schmidinger, MD
10.15 AM – 10.35 AM / 16.15 – 16.35	**Summary and Key Takeaways**	Moderator: Daniel Petrylak, MD
10.35 AM – 10.40 AM / 16.35 – 16.40	**BREAK**	
10.40 AM – 10.50 AM / 16.40 – 16.50	**Hormonal, Cytotoxic, and Targeted Therapies for Metastatic Castration-Resistant Prostate Cancer**	Scott Tagawa, MD, FACP, FASCO
10.50 AM – 11.05 AM / 16.50 – 17.05	**Discussion and Key Takeaways**	Moderator: Daniel Petrylak, MD
11.05 AM – 11.15 AM / 17.05 – 17.15	**Radioligand Therapies for Prostate Cancer**	Karim Fizazi, MD, PhD
11.15 AM – 11.35 AM / 17.15 – 17.35	**Discussion and Key Takeaways**	Moderator: Daniel Petrylak, MD
11.35 AM – 11.45 AM / 17.35 –17.45	**Localized and Hormone-Sensitive Prostate Cancer**	Susan Slovin, MD, PhD
11.45 AM – 12.00 PM / 17.45 – 18.00	**Discussion and Key Takeaways**	Moderator: Daniel Petrylak, MD
12.00 PM / 18.00	**Summary and Closing Remarks**	Daniel Petrylak, MD

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Conference Highlights

Bladder Cancer Part 1 – NMIBC and MIBC

TAR-200 + cetrelimab (CET) or CET alone as neoadjuvant therapy in patients with MIBC who are ineligible for or refuse Cis-based NAC: SunRISe-4

Necchi et al. ESMO 2024; LBA84

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STUDY POPULATION AND METHODS

> Pts with cT2-T4a N0M0 MIBC were randomized to 12 wk of

EFFICACY BY TAR-200 DOSE EXPOSURE

TAR-200 ± cetrelimab (CET) and CET alone in patients with BCG-unresponsive high-risk NMIBC: Updated results from SunRISe-1

Van der Heijden et al. ESMO 2024; LBA85

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STUDY POPULATION AND METHODS

> Pts with BCG-unresponsive high-risk NMIBC were randomized to

DURABILITY OF RESPONSES

Nivolumab + chemoradiotherapy in patients with nmMIBC not undergoing cystectomy: Phase II, randomized study by the Hellenic GU Cancer Group

Kougioumtzopoulou et al. ESMO 2024; 1961O

EPICS

STUDY POPULATION AND METHODS

> 77 pts with nonmetastatic MIBC who were not candidates for

OVERALL SURVIVAL

JCOG1019: Phase III study comparing watchful waiting and intravesical BCG in high-grade pT1 bladder cancer with pT0 on the second TUR

Kitamura et al. ESMO 2024; 1963MO

EPICS

STUDY POPULATION AND METHODS

> 263 pts with high-grade pT1 bladder cancer resected to PT0 on

RELAPSE-FREE SURVIVAL

Phase III trial of neoadjuvant durvalumab + chemotherapy followed by radical cystectomy and adjuvant durvalumab in MIBC (NIAGARA)

Powles et al. ESMO 2024; LBA5

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STUDY POPULATION AND METHODS

> 1,063 pts with cisplatin-eligible MIBC were randomized to

OVERALL SURVIVAL

Alliance A031501: AMBASSADOR study of adjuvant pembrolizumab in MIUC vs observation – extended follow-up

Apolo et al. ESMO 2024; 1964MO

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STUDY POPULATION AND METHODS

- 702 pts with MIBC (≥T2) were randomized to receive 1 yr of

DISEASE-FREE SURVIVAL

Identification of patients with bladder cancer who could benefit from early post-cystectomy immunotherapy based on serial ctDNA testing: TOMBOLA

Jensen et al. ESMO 2024; 1960O

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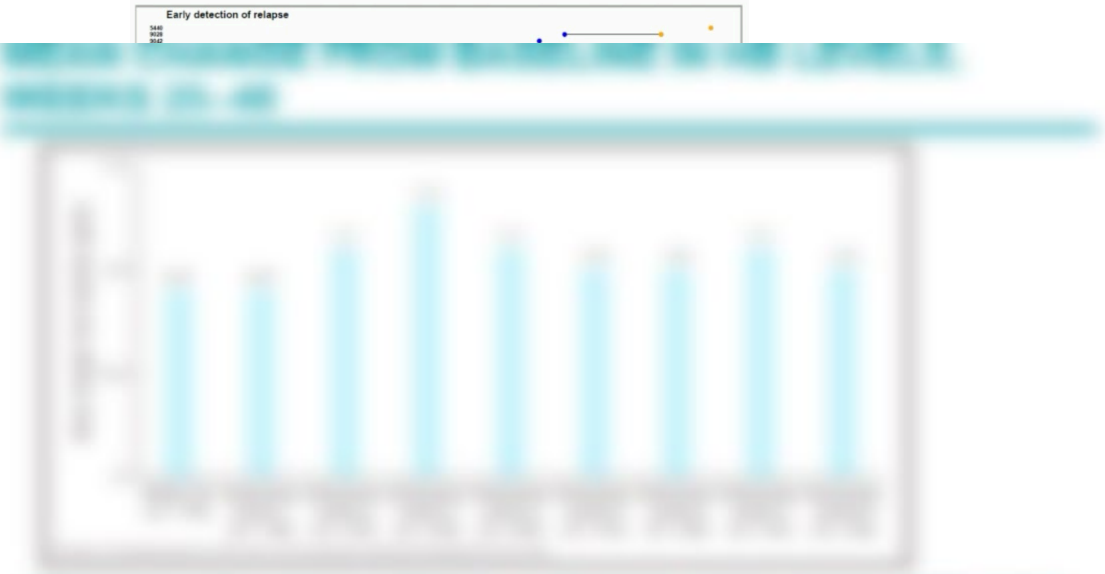
STUDY POPULATION AND METHODS

> 190 pts with cT2-4a N0-1 M0 MIBC received NAC and underwent

RELAPSE FOLLOWING CYSTECTOMY



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Key Insights

Bladder Cancer Part 1 – NMIBC and MIBC

Experts Considered the Implications of the NIAGARA Trial for the Management of MIBC

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NIAGARA: PERIOPERATIVE DURVALUMAB

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a [redacted] 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 [redacted] 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.

[redacted]

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 Adjuvant Immunotherapy for MIBC, and the Potential for ctDNA-Guided Adjuvant Decision-Making

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AMBASSADOR

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Experts Discussed Intravesical Therapies for Patients With NMIBC and MIBC

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SunRISE-1

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Congress Highlights

Bladder Cancer Part 2 – Metastatic Urothelial Cancer

BL-B01D1, an EGFR x HER3 bispecific antibody-drug conjugate, in patients with locally advanced or metastatic urothelial carcinoma

Ye et al. ESMO 2024; 1959O

EPICS

STUDY POPULATION AND METHODS

- 27 pts with previously treated mUC received treatment with BL-

DEPTH AND DURATION OF RESPONSE

HRQOL from the CheckMate 901 trial of nivolumab as first-line therapy for unresectable or metastatic urothelial carcinoma

Bedke et al. ESMO 2024; 1962O

EPICS

STUDY POPULATION AND METHODS

- 608 pts with previously untreated mUC were randomized to

LEAST SQUARES MEAN CHANGES: BASELINE–WK 16

Phase II study of futibatinib + pembrolizumab in patients with mUC: Final analysis

Koshkin et al. ESMO 2024; 1965MO

EPICS

STUDY POPULATION AND METHODS

- Pts with previously untreated mUC received the FGFR inhibitor

ANTITUMOR ACTIVITY (COHORT A)

EV-302: Exploratory analysis of nectin-4 expression and response to 1L enfortumab vedotin (EV) + pembrolizumab in previously untreated la/mUC

Powles et al. ESMO 2024; 1966MO

EPICS

STUDY POPULATION AND METHODS

- 886 pts with previously untreated la/mUC eligible for platinum-

OVERALL SURVIVAL

Efficacy and safety of disitamab vedotin (DV) with pembrolizumab in treatment-naive HER2-expressing la/mUC: RC48G001 Cohort C

Galsky et al. ESMO 2024; 1967MO

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STUDY POPULATION AND METHODS

> Pts with HER2-expressing, previously untreated mUC received

ANTITUMOR ACTIVITY

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Key Insights

Bladder Cancer Part 2 – Metastatic Urothelial Cancer

Experts Discussed Selecting Patients With mUC for Treatment With EV-Pembrolizumab

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ENFORTUMAB VEDOTIN + PEMBROLIZUMAB

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a [redacted] regimen (a taxane plus trastuzumab and pertuzumab) first-line, followed by T-DM1 second-line, for most patients.
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- 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.

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Experts Debated the Use of Sacituzumab Govitecan for mUC in the Wake of TROPiCS-04

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SACITUZUMAB GOVITECAN

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Experts Considered Novel Investigational Therapies for mUC

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CheckMate 901

The addition of nivolumab to first-line gem-cis did not have a detrimental effect on

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Congress Highlights

Renal Cell Carcinoma

NKT2152, a novel oral HIF-2α inhibitor, in patients with previously treated accRCC: Preliminary results of a phase I/II study

Jonasch et al. ESMO 2024; 1690O

EPICS

STUDY POPULATION AND METHODS

> 113 pts with heavily pretreated advanced ccRCC were treated

ADVERSE EVENTS

Tivozanib ± nivolumab in patients with RCC following 1 or 2 prior therapies including an ICI: Results of the phase III TiNivo-2 study

Choueiri et al. ESMO 2024; LBA73

EPICS

STUDY POPULATION AND METHODS

- 343 pts with advanced/metastatic ccRCC after progression on 1–2

TUMOR RESPONSE

Final analysis of the phase III LITESPARK-005 study of belzutifan vs everolimus in patients with previously treated advanced ccRCC

Rini et al. ESMO 2024; LBA74

EPICS

STUDY POPULATION AND METHODS

- 746 pts with metastatic ccRCC previously treated with 1–3 lines of

PROGRESSION-FREE SURVIVAL

Randomized phase II trial of ipilimumab-nivolumab vs SOC in non-clear cell RCC: Results of the SUNNIFORECAST trial

Bergmann et al. ESMO 2024; LBA75

EPICS

STUDY POPULATION AND METHODS

- 306 pts with advanced/metastatic non-clear cell RCC were

OVERALL SURVIVAL: CPS ≥1

Anlotinib + anti–PD-L1 antibody benmelstobart (TQB2450) vs sunitinib in first-line treatment of advanced RCC: Phase III study (ETER100)

Sheng et al. ESMO 2024; LBA76

EPICS

STUDY POPULATION AND METHODS

- 531 pts with previously untreated advanced/metastatic ccRCC

PROGRESSION-FREE SURVIVAL

Fecal microbiota transplantation (FMT) vs placebo in patients receiving pembrolizumab + axitinib for mRCC: Phase II TACITO trial

Ciccarese et al. ESMO 2024; LBA77

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STUDY POPULATION AND METHODS

- 50 pts with RCC of any histology, initiating treatment with axitinib

12-MO PROGRESSION-FREE SURVIVAL

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Key Insights

Renal Cell Carcinoma

Experts Discussed Results From Investigational Agents and Strategies for Advanced/Metastatic ccRCC

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ETER100

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a [redacted] regimen (a taxane plus tivozanib and pembrolizumab) first-line, followed by T-DXd second-line, for most patients.
- Most experts are using tivozanib deruxtecan third-line, but will prioritize the lucitinib triplet for patients with evidence of brain metastases.
- The lucitinib triplet may also be used in the second-line setting, before T-DXd, for patients with documented brain metastases.
  - If lucitinib is used second-line, experts are divided on whether they would currently use T-DXd or tivozanib deruxtecan third-line.
    - Results of the ongoing [redacted] trial comparing tivozanib deruxtecan vs T-DXd will help to clarify the optimal sequence of these ADCs.
- Tivozanib deruxtecan and the lucitinib triplet may also be used earlier than third-line in patients who recur following treatment with tivozanib, pembrolizumab, and T-DXd 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 tivozanib deruxtecan and the lucitinib regimen have pushed other options, such as tivozanib-chemotherapy combinations, nivolumab, and inarigivimab, to later lines of therapy.

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We used to run out of good options and we would just default to the mean of chemotherapy plus tivozanib 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.

Experts Considered Treatment Options for Patients With Advanced/Metastatic Non-Clear Cell RCC

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SUNNIFORECAST

ongoing trials will help clarify the optimal sequencing of agents

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Experts Discussed Sequencing Therapies for Metastatic ccRCC

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TiNivo-2

Results of the phase III TiNivo-2 study comparing tivozanib ± nivolumab in

Experts Discussed Later-Line Trials for Metastatic ccRCC

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LITESPARK-005

Longer follow-up of the LITESPARK-005 trial comparing belzutifan vs everolimus

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Congress Highlights

Hormonal, Cytotoxic, and Targeted Therapies for Metastatic Castration-Resistant Prostate Cancer

Clinical activity of BMS-986365 (CC-94676), a dual AR ligand-directed degrader and antagonist, in heavily pretreated mCRPC

Rathkopf et al. ESMO 2024; 1597MO

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STUDY POPULATION AND METHODS

- 68 pts with mCRPC previously treated with at least 1 ARPI and a

PSA RESPONSE

Nivolumab 3 mg/kg and ipilimumab 1 mg/kg in molecularly selected patients with mCRPC

Mehra et al. ESMO 2024; LBA72

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STUDY POPULATION AND METHODS

- 69 pts with previously treated, molecularly selected mCRPC

PROGRESSION-FREE SURVIVAL

Cabozantinib + atezolizumab vs second novel hormonal therapy (NHT) in mCRPC: Final OS results of the phase III CONTACT-02 study

Agarwal et al. ESMO 2024; LBA67

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STUDY POPULATION AND METHODS

- 580 pts with mCRPC that had progressed on 1 prior ARPI

OVERALL SURVIVAL BY SUBGROUP

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Key Insights

Hormonal, Cytotoxic, and Targeted Therapies for Metastatic Castration-Resistant Prostate Cancer

Experts Considered Emerging AR-Targeted Agents for mCRPC

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BMS-986365

BMS-986365 (CC-94676), a first-in-class dual AR ligand-directed degrader and

Experts Debated the Role of TKIs and Immunotherapies in mCRPC

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CONTACT-02

ongoing trials will help clarify the optimal sequencing of agents

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Congress Highlights

Radioligand Therapies for Prostate Cancer

Ra-223–docetaxel vs docetaxel–Ra-223 sequence in mCRPC with prospective biomarker evaluation (RAPSON study)

Conteduca et al. ESMO 2024; LBA71

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STUDY POPULATION AND METHODS

- 70 pts with mCRPC and symptomatic bone-dominant metastases,

CHANGE IN HRQOL SCORES: BASELINE TO WK 12

First results of phase III EORTC-GUCG 1333/PEACE-3: Enzalutamide ± Ra-223 in asymptomatic/mildly symptomatic bone-metastatic mCRPC

Gillessen et al. ESMO 2024; LBA1

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STUDY POPULATION AND METHODS

- 446 pts with asymptomatic or mildly symptomatic mCRPC with

OVERALL SURVIVAL

UpFrontPSMA: A phase II study of sequential 177Lu-PSMA-617 and docetaxel vs docetaxel in mHSPC

Azad et al. ESMO 2024; LBA66

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STUDY POPULATION AND METHODS

- 122 pts with mHSPC

PSA RESPONSE

Symptomatic skeletal events, HRQOL, and pain in PSMAfore: [177Lu]Lu-PSMA-617 in taxane-naive patients with PSMA-positive mCRPC

Fizazi et al. ESMO 2024; 1599P

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STUDY POPULATION AND METHODS

- 468 pts with mCRPC (≥1 PSMA-positive metastatic lesion)

TIME TO WORSENING OF FACT-P TOTAL SCORE

Hematologic impact of [177Lu]Lu-PSMA-617 vs ARPI change in patients with mCRPC in PSMAfore

Chi et al. ESMO 2024; 1611P

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STUDY POPULATION AND METHODS

- Adults with PSMA-positive mCRPC and 1 progression on prior

HEMATOLOGIC TEAEs BY NO. OF BONE METASTASES

Efficacy of 177Lu-PNT2002 in PSMA-positive mCRPC following progression on an ARPI (SPLASH)

Sartor et al. ESMO 2024; LBA65

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STUDY POPULATION AND METHODS

- 412 pts with mCRPC (PSMA-avid PET) that progressed after 1

PROGRESSION-FREE SURVIVAL

Lutetium-177–Prostate-Specific Membrane Antigen (177Lu-PSMA) therapy in patients treated with prior Ra-223

Rahbar et al. ESMO 2024; 1629P

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STUDY POPULATION AND METHODS

- 198 pts with heavily pretreated mCRPC, including prior Ra-223

SAFETY

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Key Insights

Radioligand Therapies for Prostate Cancer

Experts Considered New Data From Trials Evaluating Ra-223

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PEACE-3

Experts believe PEACE-3 data are practice changing and support the combination of

Experts Discussed Implications of Recent Trials Investigating 177Lu-PSMA in mPC

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PSMAfore

Experts Assessed Novel PSMA-Targeted Radioligands

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SPLASH

The SPLASH trial investigating 177Lu-PNT2002 vs second ARPI in PSMA-positive

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Congress Highlights

Localized and Hormone-Sensitive Prostate Cancer

Decipher mRNA score for prediction of survival benefit from docetaxel at start of ADT for advanced PC: An ancillary study of the STAMPEDE trials

Grist et al. ESMO 2024; 1596O

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STUDY POPULATION AND METHODS

- Retrospective analysis of tissue samples from 895 pts enrolled in

IMPACT OF DECIPHER SCORE

Phenotypic and genomic characterization of de novo metastatic prostate cancer: An ancillary study of the PEACE-1 phase III trial

Pobel et al. ESMO 2024; 1595MO

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STUDY POPULATION AND METHODS

> Samples from 350 pts enrolled in the PEACE-1 trial (abiraterone-

OVERALL SURVIVAL

Phase III evaluation of transdermal estradiol (tE2) vs LHRHa for androgen suppression in M0 prostate cancer

Langley et al. ESMO 2024; LBA69

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STUDY POPULATION AND METHODS

> 1.360 pts with M0 PC were randomized to transdermal estradiol

METASTASIS-FREE SURVIVAL

Efficacy and safety of darolutamide + ADT in patients with mHSPC from the phase III ARANOTE trial

Saad et al. ESMO 2024; LBA68

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STUDY POPULATION AND METHODS

- 669 pts with mHSPC were randomized 2:1 to ADT + darolutamide

SAFETY PROFILE

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Key Insights

Localized and Hormone-Sensitive Prostate Cancer

Experts Discussed Hormonal Therapy Options for Patients With Advanced Prostate Cancer

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ARANOTE

ongoing trials will help clarify the optimal sequencing of agents

- Experts are still using a [redacted] 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 Considered Potential Biomarkers for Guiding Treatment Decision-Making in Prostate Cancer

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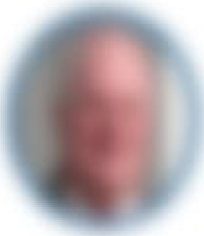
STAMPEDE



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