Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

Prostate Cancer

Tuesday, December 1, 2020
5:00 PM – 6:00 PM ET

Faculty
Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM

Moderator
Neil Love, MD
Commercial Support

This activity is supported by educational grants from Astellas and Pfizer Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Clovis Oncology, Merck, and Sanofi Genzyme.
Dr Love — Disclosures

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.
# Dr Antonarakis — Disclosures

<table>
<thead>
<tr>
<th><strong>Consulting Agreements</strong></th>
<th>Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Clovis Oncology, Dendreon Pharmaceuticals Inc, ESSA Pharma Inc, GlaxoSmithKline, Janssen Biotech Inc, Lilly, Medivation Inc, a Pfizer Company, Merck, Sanofi Genzyme</th>
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<tr>
<td><strong>Contracted Research</strong></td>
<td>AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Dendreon Pharmaceuticals Inc, Genentech, a member of the Roche Group, Janssen Biotech Inc, Johnson &amp; Johnson Pharmaceuticals, Merck, Novartis, Sanofi Genzyme, Tokai Pharmaceuticals Inc</td>
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<td><strong>Ownership Interest</strong></td>
<td>QIAGEN</td>
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## Dr Armstrong — Disclosures

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<tr>
<th><strong>Advisory Committee</strong></th>
<th>Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Merck</th>
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<tr>
<td><strong>Speakers Bureau</strong></td>
<td>Bayer HealthCare Pharmaceuticals, Dendreon Pharmaceuticals Inc</td>
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</table>
We Encourage Clinicians in Practice to Submit Questions

Feel free to submit questions now before the program begins and throughout the program.
Familiarizing Yourself with the Zoom Interface

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When a poll question pops up, click your answer choice from the available options.
Results will be shown after everyone has answered.
Upcoming Webinars

Wednesday, December 2, 2020
12:00 PM – 1:00 PM ET

Meet The Professor: Management of Lung Cancer

Faculty
Ramaswamy Govindan, MD

Moderator
Neil Love, MD

Friday, December 4, 2020

Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Hematologic Cancers

A 4-Part Friday Satellite Symposia Live Webinar Series Preceding the 62nd ASH Annual Meeting

Moderator
Neil Love, MD
Upcoming Webinars

**Tuesday, December 8, 2020**
5:00 PM – 6:00 PM ET

**Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology**

**Colorectal and Gastroesophageal Cancers**

**Faculty**
Peter C Enzinger, MD
Zev Wainberg, MD, MSc

**Moderator**
Neil Love, MD

**Thursday, December 10, 2020**
8:30 PM – 10:00 PM ET

**Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer**

**Faculty**
Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

**Moderator**
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Friday, December 11, 2020
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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

Faculty
P Kelly Marcom, MD
Joyce O’Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

Moderator
Neil Love, MD
Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.
ONCOLOGY TODAY
WITH DR NEIL LOVE
CURRENT AND FUTURE ROLE OF IMMUNE CHECKPOINT INHIBITORS AND OTHER NOVEL THERAPIES IN UROTHELIAL BLADDER CANCER

DR ASHISH KAMAT
UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

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Neil Love, MD
YiR Prostate Cancer Faculty

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Professor of Oncology and Urology  
Johns Hopkins University  
The Sidney Kimmel Comprehensive Cancer Center  
Baltimore, Maryland

Andrew J Armstrong, MD, ScM  
Professor of Medicine, Surgery, Pharmacology and Cancer Biology  
Director of Research  
Duke Cancer Institute Center for Prostate and Urologic Cancers  
Divisions of Medical Oncology and Urology  
Duke University  
Durham, North Carolina
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**Friday, December 4, 2020**

**Multiple Myeloma**
8:30 AM – 10:00 AM Pacific Time (11:30 AM – 1:00 PM ET)

**Chronic Lymphocytic Leukemia**
12:00 PM – 1:30 PM Pacific Time (3:00 PM – 4:30 PM ET)

**Acute Myeloid Leukemia**
3:00 PM – 4:30 PM Pacific Time (6:00 PM – 7:30 PM ET)

**Hodgkin and Non-Hodgkin Lymphoma**
7:00 PM – 8:30 PM Pacific Time (10:00 PM – 11:30 PM ET)
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Key Prostate Cancer Clinical Algorithms: What We’ve Learned This Year – Part 1

In the treatment algorithm, when should the following generally be recommended?

- Post-prostatectomy radiation therapy – *Dr Armstrong*
- Oral GnRH receptor antagonist relugolix – *Dr Antonarakis*
- Androgen deprivation therapy (ADT) for PSA-only relapse after local therapy (M0) – *Dr Armstrong*
- Adding an antiandrogen agent to ADT in castration-resistant M0 disease – *Drs Antonarakis and Armstrong*
- Utilizing prostate-directed local therapy for metastatic hormone-sensitive prostate cancer (mHSPC) – *Dr Antonarakis*
- Adding an antiandrogen, abiraterone or docetaxel to ADT for mHSPC – *Drs Armstrong and Antonarakis*
In the treatment algorithm, when should the following generally be recommended?

• Endocrine treatment versus chemotherapy after first-line endocrine therapy for metastatic castration-resistant prostate cancer (mCRPC) – Drs Antonarakis and Armstrong

• Radium-223 in mCRPC – Dr Armstrong

• PARP inhibitors in mCRPC; recommended genomic evaluation – Drs Antonarakis and Armstrong

• PSMA-targeted treatment and imaging – Drs Armstrong and Antonarakis

• TMPRSS2 and COVID-19 – Dr Antonarakis
Four Key Advances in 2019-20 in Advanced Prostate Cancer

1. Improved survival in nmCRPC with new AR therapies
2. Improved survival in mHSPC with new AR therapies
3. Cabazitaxel solidified as 3rd line therapy in mCRPC: the CARD trial
4. Precision medicine comes in mCRPC: homologous repair and PARP inhibition

Courtesy of Andrew J Armstrong, MD, ScM
Treatment Evolution in Metastatic Prostate Cancer


2021: PSMA therapeutics?

Courtesy of Andrew J Armstrong, MD, ScM
Module 1

In the treatment algorithm, when should post-prostatectomy radiation therapy generally be recommended?

Discussant: Dr Armstrong
3 Trials, Same Result: Evidence-Based Medicine!

**TROG 08:** Kneebone et al. Lancet Oncol 2020

**GETUG-AFU 17:** Sargos P et al. Lancet Oncol 2020

**RADICALS:** Parker CS et al. Lancet Oncol 2020

**Implications for men:** avoidance of the side effects of radiation in many situations without compromising cure, such as erectile dysfunction and bowel/bladder risks

Courtesy of Andrew J Armstrong, MD, ScM
In the treatment algorithm, when should the oral GnRH receptor antagonist relugolix be recommended if it were available?

Discussant: Dr Antonarakis
HERO Phase III Trial: Results Comparing Relugolix, an Oral GnRH Receptor Antagonist, versus Leuprolide Acetate for Advanced Prostate Cancer

Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer

1 Shore N et al. 
ASCO 2020; Abstract 5602.

2 Shore ND et al. 
HERO: Ongoing Phase III Trial of Relugolix versus Leuprolide Acetate for Advanced HSPC

Men with Advanced Prostate Cancer
N = 934

2:1

Men with Advanced Prostate Cancer
N = 934

Relugolix
360 mg Loading Dose on Day 1
120 mg Orally Once Daily
N = 624

Leuprolide Acetate
22.5* mg SC Injection Every 3 Months
N = 310

*11.25 mg in Japan and Taiwan
SC, subcutaneous; D, day

Primary Endpoint
Week 48

Secondary Endpoints
Castration D4, D15
Profound Castration D15
PSA Response D15
FSH End Week 24

Testosterone Recovery
N = 184

HERO: Primary Endpoint – Sustained Castration
Key Secondary Endpoint – Noninferiority to Leuprolide

HERO: Mean Testosterone Level among All Patients

HERO: Mean Testosterone Level in Subgroup Followed for Testosterone Recovery

# HERO: Cardiovascular Adverse Events

<table>
<thead>
<tr>
<th>Adverse Cardiovascular Events</th>
<th>Relugolix (N = 622)</th>
<th>Leuprolide (N = 308)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Major Adverse Cardiovascular Events (MACE)</td>
<td>2.9%</td>
<td>6.2%</td>
</tr>
<tr>
<td>Ischemic Heart Disease</td>
<td>2.4%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>History of MACE</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>Relugolix 84 (13.5%)</td>
<td>Leuprolide 45 (14.6%)</td>
</tr>
<tr>
<td>MACE</td>
<td>3.6%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>Leuprolide vs Relugolix 5.8 (1.5, 23.3)</td>
<td>1.5 (0.7, 3.4)</td>
</tr>
</tbody>
</table>
| MACE = non-fatal myocardial infarction + non-fatal stroke + all-cause mortality

Shore N et al. ASCO 2020;Abstract 5602.
HERO: Cumulative Incidence of Major Adverse Cardiovascular Events (MACE)

In the treatment algorithm, when should ADT for PSA-only relapse (M0) after local therapy be recommended?

Discussant: Dr Armstrong
What PSA doubling time will generally lead you to initiate ADT for hormone-naïve M0 prostate cancer?

a. Less than 4 months
b. Less than 6 months
c. Less than 10 months
d. Less than 12 months
e. Less than 18 months
f. Less than 24 months
g. I don’t generally use PSA doubling time as the critical decision factor
Module 4

In the treatment algorithm, when should an antiandrogen agent be added to ADT for castration-resistant M0 prostate cancer? (Selection of agent)

Discussants: Drs Antonarakis and Armstrong
In general, which is your preferred antiandrogen agent to add to ADT for patients with castration-resistant M0 prostate cancer?

a. I don’t have a preferred antiandrogen agent in this setting
b. Enzalutamide
c. Darolutamide
d. Apalutamide
# Recent FDA Approvals of Next-Generation Antiandrogens in Nonmetastatic Castration-Resistant Prostate Cancer

<table>
<thead>
<tr>
<th>Agent</th>
<th>Approval date</th>
<th>Pivotal study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darolutamide</td>
<td>July 30, 2020</td>
<td>ARAMIS</td>
</tr>
<tr>
<td>Enzalutamide</td>
<td>July 12, 2018</td>
<td>PROSPER</td>
</tr>
<tr>
<td>Apalutamide</td>
<td>February 14, 2018</td>
<td>SPARTAN</td>
</tr>
</tbody>
</table>

[https://www.fda.gov/drugs/resources-information-approved-drugs/](https://www.fda.gov/drugs/resources-information-approved-drugs/)
Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide

### Overall Survival: Darolutamide, Enzalutamide, Apalutamide

<table>
<thead>
<tr>
<th></th>
<th>ARAMIS(^1)</th>
<th>PROSPER(^2)</th>
<th>SPARTAN(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiandrogen</td>
<td>Darolutamide</td>
<td>Enzalutamide</td>
<td>Apalutamide</td>
</tr>
<tr>
<td>Median follow-up</td>
<td>49 mo</td>
<td>47 mo</td>
<td>52 mo</td>
</tr>
<tr>
<td>Median OS</td>
<td>Not estimated</td>
<td>57 vs 56 mo</td>
<td>74 vs 60 mo</td>
</tr>
<tr>
<td>OS hazard ratio</td>
<td>0.69 ((p = 0.003))</td>
<td>0.73 ((p = 0.001))</td>
<td>0.78 ((p = 0.0161))</td>
</tr>
</tbody>
</table>

\(^3\) Smith MR et al; SPARTAN Investigators. *Eur Urol* 2020;[Online ahead of print].
## Comparison of Toxicities: Darolutamide, Enzalutamide, Apalutamide

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>ARAMIS</th>
<th>PROSPER</th>
<th>SPARTAN</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Darolutamide</td>
<td>Placebo</td>
<td>Enzalutamide</td>
</tr>
<tr>
<td>Fatigue/asthenia</td>
<td>16%</td>
<td>11%</td>
<td>33%</td>
</tr>
<tr>
<td>Falling</td>
<td>4%</td>
<td>5%</td>
<td>11%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5%</td>
<td>4%</td>
<td>10%</td>
</tr>
<tr>
<td>Mental impairment</td>
<td>1%</td>
<td>2%</td>
<td>5%</td>
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Small EJ et al; SPARTAN Investigators. ASCO 2020;Abstract 5516.
Module 5

In the treatment algorithm, when do you use prostate-directed local therapy for mHSPC?

Discussant: Dr Antonarakis
Module 6

In the treatment algorithm, when do you add an antiandrogen agent, abiraterone or docetaxel to ADT for mHSPC? (Selection of agent)

Discussants: Drs Antonarakis and Armstrong
What is your most likely treatment approach for a 75-year-old man presenting de novo with prostate cancer with multiple symptomatic bone metastases and 2 lung metastases?

a. ADT alone
b. ADT and enzalutamide
c. ADT and apalutamide
d. ADT and abiraterone
e. ADT and docetaxel
f. ADT with docetaxel and endocrine treatment
Recent FDA Approvals of Next-Generation Antiandrogens in Metastatic Hormone-Sensitive Prostate Cancer

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<tr>
<th>Agent</th>
<th>Approval date</th>
<th>Pivotal study</th>
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<tbody>
<tr>
<td>Enzalutamide</td>
<td>December 16, 2019</td>
<td>ARCHES</td>
</tr>
<tr>
<td>Apalutamide</td>
<td>September 17, 2019</td>
<td>TITAN</td>
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</table>

https://www.fda.gov/drugs/resources-information-approved-drugs/
ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer

Andrew J. Armstrong, MD, ScM1; Russell Z. Szumilewitz, MD2; Daniel P. Petrylak, MD2; Jeffrey Holzbeierlein, MD2; Arnauld Villers, MD2; Arun Azad, MBBS, PhD3; Antonio Alcaraz, MD, PhD2; Boris Alekseev, MD4; Taro Iguchi, MD, PhD5; Neal D. Shore, MD6; Brad Rosbrook, MS12; Jennifer Sugg, MS12; Benoit Baron, MS13; Lucy Chen, MD12; and Arnulf Stenzl, MD14


Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D., Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D., Axel S. Merseburger, M.D., Mustafa Özgür oglu, M.D., Hirotsugu Uemura, M.D., Dongwei Ye, M.D., Kris Deprince, M.D., Vahid Naini, Pharm.D., Jinhui Li, Ph.D., Shinta Cheng, M.D., Margaret K. Yu, M.D., Ke Zhang, Ph.D., Julie S. Larsen, Pharm.D., Sharon McCarthy, B.Pharm., and Margaret Chowdhury, M.D., for the TITAN Investigators*

Survival Analyses for ARCHES and TITAN: ADT + Enzalutamide or Apalutamide in Metastatic HSPC

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ARCHES (N = 1,150)</th>
<th>TITAN (N = 1,052)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• 2/3rd high volume</td>
<td>• 2/3rd high volume</td>
</tr>
<tr>
<td></td>
<td>• 17% prior docetaxel</td>
<td>• 10% prior docetaxel</td>
</tr>
<tr>
<td></td>
<td>• 25% prior RP/XRT</td>
<td>• 17% prior RP/XRT</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiographic PFS</th>
<th>ADT + enzalutamide (n = 574)</th>
<th>ADT (n = 576)</th>
<th>ADT + apalutamide (n = 955)</th>
<th>ADT (n = 554)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (overall): 0.39</td>
<td>NR</td>
<td>19.0 mo</td>
<td>NR</td>
<td>22.1 mo</td>
</tr>
<tr>
<td>HR (prior docetaxel): 0.52</td>
<td></td>
<td></td>
<td>HR (prior docetaxel): 0.47</td>
<td></td>
</tr>
<tr>
<td>HR (high volume): 0.43</td>
<td></td>
<td></td>
<td>HR (high volume): 0.53</td>
<td></td>
</tr>
<tr>
<td>HR (low volume): 0.25</td>
<td></td>
<td></td>
<td>HR (low volume): 0.36</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall survival</th>
<th>NR</th>
<th>NR</th>
<th>NR</th>
<th>NR</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR: 0.81 (immature)</td>
<td></td>
<td></td>
<td>HR (overall): 0.67</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR (prior docetaxel): 1.27</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR (high volume): 0.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR (low volume): 0.67</td>
<td></td>
</tr>
</tbody>
</table>

NR = not reached

Abiraterone Acetate plus Prednisolone for Hormone-Naïve Prostate Cancer (PCa): Long-Term Results from Metastatic (M1) Patients in the STAMPEDE Randomised Trial (NCT00268476)

James N et al.
ESMO 2020;Abstract 611O.
STAMPEDE — SOC + AAP vs SOC: Overall Survival

HR  0.60  
95%CI  0.50 to 0.71  
P-value  0.0000000003

Median survival (years)
SOC=3.8  SOC+AAP=6.6

Events
SOC=329  SOC+AAP=244

2017 (M1 only)
HR  0.61  
95%CI  0.49 to 0.75

James N et al. ESMO 2020;Abstract 611O.
STAMPEDE: Overall Survival by Risk Group (LATITUDE)

Low risk

HR 0.55 (0.41-0.76)
p=0.00001

High risk

HR 0.54 (0.43-0.69)
P<0.00001

HR 0.66 (0.44-0.98)
p=0.041

HR 0.54 (0.41-0.70)
P<0.001

James N et al. ESMO 2020;Abstract 611O.
In the treatment algorithm, how do you generally approach the selection of endocrine treatment versus chemotherapy after first-line endocrine therapy for mCRPC?

Discussants: Drs Antonarakis and Armstrong
A 75-year-old man presents with prostate cancer (BRCA wild type) metastatic to the bone and receives ADT + docetaxel with disease progression 1 year later. He responds to enzalutamide for 9 months, then has symptomatic progression in the bone along with new lung lesions. What is your most likely treatment?

a. Abiraterone  
b. Apalutamide  
c. Docetaxel  
d. Cabazitaxel  
e. Other
CARD: Overall Survival Analysis of Patients with Metastatic Castration-Resistant Prostate Cancer Receiving Cabazitaxel vs Abiraterone or Enzalutamide

Tombal B et al.
ASCO 2020;Abstract 5569.
CARD Study of Cabazitaxel: Survival Analyses

rPFS (primary endpoint)

OS (key secondary endpoint)

Tombal B et al. ASCO 2020;Abstract 5569.
Module 8

In the treatment algorithm, how do you generally approach the use of radium-223 for mCRPC?

Discussant: Dr Armstrong
Safety and Overall Survival in Patients with mCRPC Treated with Radium-223 plus Subsequent Taxane Therapy: Second Interim Analysis of REASSURE

Higano CS et al.
ASCO 2020;Abstract 5542.
REASSURE: Overall Survival

Higano CS et al. ASCO 2020;Abstract 5542.
REASSURE: Incidence of Treatment-Emergent Adverse Events with Radium-223 and Grade 3/4 Hematologic AEs During Subsequent Chemotherapy

Higano CS et al. ASCO 2020;Abstract 5542.
Conclusions: REASSURE

• Clinical Implications:
  - Radium-223 can be administered safely either before or after docetaxel
  - If docetaxel is given after radium-223, myelosuppression remains minimal
  - Remember to co-administer with denosumab (fragility fracture risk)

• Future Directions:
  - What combinations will be synergistic (and safe) with radium-223?
    - radium-223 + enzalutamide (PEACE III)
    - radium-223 + sipuleucel-T
    - radium-223 + PARP/ATR inhibitors
  - We still need biomarkers (clinical, genomic) of radium-223 sensitivity
Module 9

In the treatment algorithm, how do you generally approach the use of PARP inhibitors for mCRPC?

Discussants: Drs Antonarakis and Armstrong
At what point, if any, do you generally recommend a PARP inhibitor to a patient with metastatic prostate cancer and a germline BRCA mutation?

a. As part of first-line treatment, alone or as maintenance therapy
b. After 1 line of hormonal therapy
c. After 1 line of chemotherapy
d. After at least 1 line of both hormonal therapy and chemotherapy
e. Other
f. I generally would not administer a PARP inhibitor
# Recent FDA Approvals of PARP Inhibitors for mCRPC

<table>
<thead>
<tr>
<th>PARP inhibitor</th>
<th>Approval date</th>
<th>Pivotal study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib</td>
<td>May 19, 2020</td>
<td>PROfound</td>
</tr>
<tr>
<td>Rucaparib</td>
<td>May 15, 2020</td>
<td>TRITON2</td>
</tr>
</tbody>
</table>

[https://www.fda.gov/drugs/resources-information-approved-drugs/](https://www.fda.gov/drugs/resources-information-approved-drugs/)
Olaparib for Metastatic Castration-Resistant Prostate Cancer


PROfound Primary Endpoint: Imaging-Based PFS with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

![Graph with survival curves and table showing median iPFS, HR, and p-value.]

<table>
<thead>
<tr>
<th></th>
<th>Olaparib (n = 162)</th>
<th>Control (n = 83)</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median iPFS</td>
<td>7.4 mo</td>
<td>3.6 mo</td>
<td>0.34</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

PROfound: Overall Survival with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

Overall survival

- Olaparib: 91/162 (56.4%)
- Control: 57/83 (68.3%)

Median Overall Survival (95% CI)
- Olaparib: 19.1 (17.4–23.4) mo
- Control: 14.7 (11.9–18.8) mo

Cross-over adjusted overall survival

- Patients who crossed over: 67% (56/83)
- Hazard ratio for death: 0.42 (95% CI, 0.19–0.91)

Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial

Joaquin Mateo*, Nuria Porta*, Diletta Bianchini, Ursula McGovern, Tony Elliott, Robert Jones, Isabel Syndikus, Christy Ralph, Suneil Jain, Mohini Varughese, Omi Parikh, Simon Crabb, Angus Robinson, Duncan McLaren, Alison Birtle, Jacob Tanguay, Susana Miranda, Ines Figueiredo, George Seed, Claudia Bertan, Penny Flohr, Berni Ebbs, Pasquale Rescigno, Gemma Fowler, Ana Ferreira, Ruth Riisnaes, Rita Pereira, Andra Curcean, Robert Chandler, Matthew Clarke, Bora Gurel, Mateus Crespo, Daniel Nava Rodrigues, Shahneen Sandhu, Aude Espinasse, Peter Chatfield, Nina Tunario, Wei Yuan, Emma Hall†, Suzanne Carreira†, Johann S de Bono†
TOPARP-B: Antitumour Activity by Gene Aberration Subgroup (ITT Population, Pooled 300 mg and 400 mg Cohorts)

TOPARP-B: Duration of Response by Gene Aberration Subgroup (ITT Population, Pooled 300 mg and 400 mg Cohorts)

Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a BRCA1 or BRCA2 Gene Alteration

Wassim Abida, MD, PhD; Akash Patnaik, MD, PhD, MMSc; David Campbell, MBBS; Jeremy Shapiro, MBBS; Alan H. Bryce, MD; Ray McDermott, MD, PhD, MBA; Brieuc Sautois, MD, PhD; Nicholas J. Vogelzang, MD; Richard M. Bambury, MD; Eric Voog, MD; Jingsong Zhang, MD, PhD; Josep M. Puiats, MD; Charles J. Ryan, MD; Axel S. Merseburger, PhD; Gedske Daugaard, DMSc; Axel Heidenreich, MD; Karim Fizazi, MD, PhD; Celestia S. Higano, MD; Laurence E. Krieger, MBChB; Cora N. Sternberg, MD; Simon P. Watkins, PhD; Darrin Despain, MStat; Andrew D. Simmons, PhD; Andrea Loehr, PhD; Melanie Dowson, BA; Tony Golsorkhi, MD; and Simon Chowdhury, MD, PhD; on behalf of the TRITON2 investigators

J Clin Oncol 2020;[Online ahead of print].
TRITON2: Response to Rucaparib in Patients with mCRPC Harboring a BRCA1 or BRCA2 Gene Alteration

ORR per independent radiology review: 43.5%

Confirmed PSA response rate: 54.8%

Conclusions: TRITON2

• Clinical Implications:
  - Rucaparib has robust activity in mCRPC pts with BRCA1/2 mutations
  - TRITON2 led to accelerated FDA approval of rucaparib in prostate cancer
  - Side effects: myelosuppression, fatigue, anorexia, rash, teratogenic

• Future Directions:
  - Initial FDA approval is contingent upon positive Phase III TRITON3 trial
  - Unlikely to get approved for non-BRCA and non-ATM mutations
  - CASPAR trial: rucaparib + enzalutamide for first-line mCRPC
  - CheckMate 9KD: rucaparib + nivolumab in second-line mCRPC

Courtesy of Emmanuel S Antonarakis, MD
Module 10

What is known about PSMA-targeted treatment and imaging in prostate cancer?

Discussants: Drs Armstrong and Antonarakis
The U.S. Food and Drug Administration approved Gallium 68 PSMA-11 (Ga 68 PSMA-11) – the first drug for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) positive lesions in men with prostate cancer.

Ga 68 PSMA-11 is indicated for patients with suspected prostate cancer metastasis (when cancer cells spread from the place where they first formed to another part of the body) who are potentially curable by surgery or radiation therapy. Ga 68 PSMA-11 is also indicated for patients with suspected prostate cancer recurrence based on elevated serum prostate-specific antigen (PSA) levels. Ga 68 PSMA-11 is a radioactive diagnostic agent that is administered in the form of an intravenous injection.

Once administered via injection, Ga 68 PSMA-11 binds to PSMA, which is an important pharmacologic target for prostate cancer imaging because prostate cancer cells usually contain elevated levels of the antigen. As a radioactive drug that emits positrons, Ga 68 PSMA-11 can be imaged by PET to indicate the presence of PSMA-positive prostate cancer lesions in the tissues of the body.
TheraP: A Randomised Phase II Trial of $^{177}$Lu-PSMA-617 (LuPSMA) Theranostic versus Cabazitaxel in Metastatic Castration Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel: Initial Results (ANZUP Protocol 1603)

Hoffman S et al.
ASCO 2020;Abstract 5500.
$^{177}$Lu-PSMA-617 is a small molecule RLT targeting PSMA

Hoffman S et al. ASCO 2020;Abstract 5500.
TheraP: $^{177}$Lu-PSMA-617 Theranostic versus Cabazitaxel

**KEY ELIGIBILITY**
- mCRPC post docetaxel suitable for cabazitaxel
- Progressive disease with rising PSA and PSA ≥ 20 ng/mL
- Adequate renal, hematologic, and liver function
- ECOG performance status 0-2

$^{68}$Ga-PSMA + $^{18}$F-FDG PET/CT
- PSMA SUVmax > 20 at any site
- Measurable sites SUVmax > 10
- No FDG positive/PSMA negative sites of disease
- Centrally reviewed

**$^{177}$Lu-PSMA-617**
- 8.5 GBq IV q6 weekly
- ↓ 0.5 GBq each cycle
- Up to 6 cycles

**SPECT/CT @ 24 hours**
- suspend Rx if exceptional response; recommence upon progression

**200 men 1:1 randomisation**
**11 sites in Australia**
- Stratified by:
  - Disease burden (>20 sites vs ≤ 20 sites)
  - Prior enzalutamide or abiraterone
  - Study site

**CABAZITAXEL**
- 20 mg/m² IV q3 weekly,
- Up to 10 cycles

80% power to detect a true absolute difference of 20% in the PSA response rate (from 40% to 60%), with a 2-sided type 1 error of 5% and allowance of 3% for missing data.

Hoffman S et al. ASCO 2020;Abstract 5500.
Primary endpoint: PSA ≥50% response (PSA50-RR)

Lu-PSMA: 29% absolute (95% CI 16%-42%, p<0.0001) greater PSA50-RR compared to cabazitaxel
For sensitivity analysis per-protocol, the difference was 23% (95% CI 9%-37%; p=0.0016)

Hoffman S et al. ASCO 2020;Abstract 5500.
Module 11

What is known about TMPRSS2 and COVID-19?

Discussant: Dr Antonarakis
Compared to women, men...

a. Are more likely to contract COVID-19
b. Are more likely to contract COVID-19 and develop complications
c. Are not more likely to contract COVID-19 but are more likely to develop complications if they do contract COVID-19
d. There are currently not enough data
e. I don’t know
In Focus

**TMPRSS2 and COVID-19: Serendipity or Opportunity for Intervention?**

Konrad H. Stopsack¹, Lorelei A. Mucci², Emmanuel S. Antonarakis³, Peter S. Nelson⁴, and Philip W. Kantoff¹

**Summary:** *TMPRSS2* is both the most frequently altered gene in primary prostate cancer and a critical factor enabling cellular infection by coronaviruses, including SARS-CoV-2. The modulation of its expression by sex steroids could contribute to the male predominance of severe infections, and given that *TMPRSS2* has no known indispensable functions, and inhibitors are available, it is an appealing target for prevention or treatment of respiratory viral infections.

Meet The Professor
Management of Lung Cancer

Wednesday, December 2, 2020
12:00 PM – 1:00 PM ET

Faculty
Ramaswamy Govindan, MD

Moderator
Neil Love, MD
Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.