

# Some Current Trials – In the Field of Biomarkers

Clinical trials are constantly changing. But to offer our readers some current options that might be worth researching, here is what I found for clinical trials using BRCA testing, or AR-V7 testing – both of which are mentioned in [Dr Eshaghian's article here](#).

## **CURRENT TRIALS IN PROSTATE CANCER, USING BRCA 1 OR BRCA 2 TESTING**

\*Note – ask trial site how they are doing BRCA testing. Are they offering in trial? Or does it need to be done beforehand? Are they using the blood test or the pathology test?

### **1) [A Phase II Study of the Chk1/2 Inhibitor \(LY2606368\) in BRCA1/2 Mutation Cancers, Including Metastatic Castrate-Resistant Prostate Cancer](#) Phase 2, NO Placebo**

#### **Basic Eligibility Criteria:**

- Must be on hormone therapy, with cancer progressing
  - Must have soft tissue mets that can be biopsied (lymph node, lung, bladder, etc)
  - Must have had prior Xtandi OR Zytiga (for 1 month or more)
  - No limit to the number of prior therapies
- (For full eligibility criteria, check with contacts below)

#### **Location: Bethesda, MD (NIH)**

Contacts – Anna Couvillon, CRNP, (301) 443-6211, [couvilla@mail.nih.gov](mailto:couvilla@mail.nih.gov)  
or Cynthia Boyle, R.N, (301) 496-0932, [helsabec@mail.nih.gov](mailto:helsabec@mail.nih.gov)

### **2) [Pilot Trial of BMN 673, an Oral PARP Inhibitor, in Patients](#)**

## With Advanced Solid Tumors and BRCA Mutations

### Phase 1/2, NO Placebo

#### **Basic Eligibility Criteria:**

- Must be metastatic with at least 1 standard treatment for metastatic cancer
- Must be willing to undergo tumor biopsies
- At least 4 weeks since surgery, radiation, or chemo  
(For full eligibility criteria, check with contact below)

#### **Location: Bethesda, MD (NIH)**

Contact: Melanie M. Herrin, (301)  
402-5640, [melanie.herrin@nih.gov](mailto:melanie.herrin@nih.gov)

## 3) TOPARP: A Phase II Trial of Olaparib [Lynparza] in Patients With Advanced Castration Resistant Prostate Cancer (TOPARP)

### Phase 2, NO Placebo

#### **Basic Eligibility Criteria:**

- On hormone therapy, or previous orchiectomy
- CTC blood test of 5 or more
- Previous Taxane chemotherapy – 1 or 2 cycles
- At least 4 weeks since chemotherapy  
(For full eligibility criteria, check with contact below)

**Location: United Kingdom** – London and Sutton, Surrey Contact:  
TOPARP Trial Manager, 020 8722 4156,  
[toparp-icrctsu@icr.ac.uk](mailto:toparp-icrctsu@icr.ac.uk)

## **CURRENT TRIALS IN PROSTATE CANCER, USING AR-V7 BLOOD TESTING**

\*Note – AR-V7 blood testing is only available through Johns Hopkins, and for mCRPC patients. For more information about how to obtain AR-V7 testing through a local laboratory (your blood must be shipped to Johns Hopkins), please contact Katie Beierl, [molecularpathresults@jhmi.edu](mailto:molecularpathresults@jhmi.edu). Or ask the trial site

how they are doing their AR-V7 blood testing.

**1) Biomarker-Driven Therapy with Nivolumab [Opdivo] and Ipilimumab [Yervoy] Treating Patients with Metastatic Hormone-Resistant Prostate Cancer Expressing AR-V7 (STARVE-PC) Phase 2 – NO placebo**

**Basic Eligibility Criteria:**

- On hormone therapy, with progressing disease
  - Two or more bone metastases
  - At least 4 weeks since radiation or major surgery
  - At least 4 weeks since use of antiandrogens
- (For full eligibility criteria, check with contact below)

**Location: Baltimore, MD**

Contact: Rana Harb, MS, (443) 287-6662, [Rharb1@jhmi.edu](mailto:Rharb1@jhmi.edu)

**2) Niclosamide and Enzalutamide [Xtandi] in Treating Patients With AR Splice Variant [7]-Positive, Castration-Resistant, Metastatic Prostate Cancer Phase 1 – NO placebo**

**Basic Eligibility Criteria:**

- On hormone therapy, with progressing disease
  - Must be metastatic
  - Must have taken, and failed abiraterone (Zytiga)
- (For full eligibility criteria, check with contact below)

**Location: Seattle, WA**

Contact: Michael Schweizer, (206) 288-6252, [schweize@uw.edu](mailto:schweize@uw.edu)

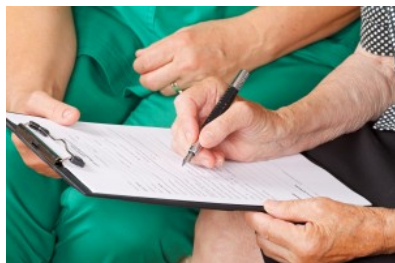
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**TIPS FOR PATIENTS & CAREGIVERS – CLINICAL TRIALS:**

Think of a clinical trial as another treatment choice. Therefore, weigh the Risks and Benefits with your doctors and nurses, just like any other treatment.

Here are some things to consider & ask:

- How long is the enrollment paperwork & process for this trial? (it's usually 3-4 weeks) How does that affect your current cancer situation? What is your PSA Doubling Time (PSADT), for example?



- Can you do anything (as a patient or caregiver) to speed up the paperwork and enrollment process? Ask to speak directly to the clinical trial nurse, who is usually a different nurse than your regular nurses. Develop a relationship with them, and hand them any medical records they may not have.

- How much testing is involved? Is the patient willing to do the testing?

- Is there any travel or cost involved? Is the patient willing to travel? (There is usually no cost for a trial, but ask – there are always a few exceptions.)

*Remember, clinical trials are voluntary and you can pull out of a clinical trial any time you want.*

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## **On the Horizon-Individualized**

# Biomarker Driven Therapy for CRPC

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The past decade has brought many advances for the treatment of CRPC, or MCRPC (metastatic CRPC). This includes the remarkable approval of at least 5 novel treatment options for these patients, who are on hormone therapy, with progressing disease. In previous years, we have called them hormone refractory (or androgen independent) prostate cancer patients:

- Novel anti-androgens: Abiraterone acetate (Zytiga) & Enzalutamide (Xtandi)
- Second line chemotherapy: Cabazitaxel (Jevtana)
- Immunotherapy: Sipuleucel-T (Provenge)
- Radiopharmaceutical therapy: Radium-223 (Xofigo)

Although these agents have improved the progression free survival & overall survival in CRPC patients, the disease unfortunately still remains incurable. So, what does the future hold for patients that have progressed past these novel lines of therapies?

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‘Novel’ – a term in medicine used to describe something “new,

different, or unusual.”

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Attending conferences & meetings and exploring various clinical journals & NCCN guidelines, the one common answer usually is – enrollment in a clinical trial. Although, we fully support enrollment in clinical trials, as a medical oncologist for almost a decade, I have seen that such a route is not always an option or desire for patients. Understandable information on trials is also difficult for patients to find. (However, please see PAACT’s corresponding article on current clinical trials using biomarkers here ) Still, if a trial isn’t a reasonable option, what else is left for an oncologist and patient to do? One answer that I have found in our clinic is individualized biomarker driven oncology treatment based on novel molecular tests that may help guide a personalized decision. Below, I will briefly discuss and review a few such options that can be offered to patients.

One option would include, assessing for alterations in the expression of the androgen receptor (AR). It has been demonstrated that splice variant AR-V7 predicts a likely low response rate to androgen pathway therapies ([REF](#)). Additionally, such a finding might even imply the transition to a distinct new more aggressive histology, which is now termed: intermediate atypical carcinoma (IAC). Prior to this new classification, tumors were traditionally classified as adenocarcinoma or small cell cancer. Although no standard therapy has yet to be established for the treatment of IAC tumors, it would not be unreasonable to consider treatment with chemotherapy (possibly a platinum based chemotherapy regimen) – instead of pursuing additional anti-androgen treatment options.



FROM PAACT: NOTE - **The AR-V7 blood test** recently became available for **mCRPC (metastatic castrate-resistant PC)** patients - only through Johns Hopkins. **MCRPC** patients should ask and make sure they are eligible for the AR-V7 blood test. They should also ask about cost, insurance, turnaround time, and how to get their blood drawn locally to be sent to Johns Hopkins. Contact *Katie Beierl* at Johns Hopkins - [molecularpathresults@jhmi.edu](mailto:molecularpathresults@jhmi.edu). For more detailed information, call PAACT at (844) PAACT 4U.

Additionally, an image guided biopsy (usually bone or lymph node) can be pursued with the help of a skilled radiologist. The tissue sample can then be tested for a possible novel targeted pathway. For many patients, this would also be their first biopsy since being diagnosed with prostate cancer – sometimes many decades ago and the pathology of a patient’s tumor now can certainly be different than it was at the time of their original diagnosis.

An example of testing for a novel pathway would be assessing for BRCA1 and/or BRCA2 mutations that tend to predict a more aggressive phenotype of disease; but, one that might demonstrate response to novel poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors. Although these mutations are rare (estimate <5% of MCRPC patients will harbor a BRCA1 or 2 mutation), such a finding can lead to a novel approach of therapy with a possible prolong response to treatment.

There are various labs that can offer such personalized genomic analysis. A reputable lab we have come to rely on in our clinic (COMG) to analyze a comprehensive genomic profile for our patients is: FoundationOne ([www.foundationone.com](http://www.foundationone.com)). Please visit their website for more information and details about their various testing options. This test is normally covered by most insurance carriers and has a turnaround time of 2 weeks.

Finally, more and more serum liquid biopsies are becoming commercially available in the clinic and might one day replace the need for invasive biopsies. These liquid biopsies can possibly also identify a potentially novel targeted signal pathway, which can lead to the utilization of an

individualized treatment plan. Again there are various labs that offer such services and one that we have become most familiar with has been the Guardant360 ([www.guardanthealth.com](http://www.guardanthealth.com)). Again, please visit their website for additional information and testing options. This test is also usually covered by most insurance plans and has a turnaround time of approximately 1 week.

As most readers like to end with a real life case example, I will briefly review a recent case example at Compassionate Oncology Medical Group (COMG) utilizing such methods:

**Case Report – JM: 66-year-old male with no significant medical problems.**

- **2001:** Diagnosed at age 50 with Gleason 3+4 prostate adenocarcinoma, PSA 2.9. He underwent radical prostatectomy. PSA was zero post-operatively and surgical margins were free of cancer.
- **2004:** Biochemical (PSA) recurrence and underwent salvage radiation therapy followed by androgen deprivation therapy (hormone therapy).
- **2006:** Castrate resistant & established care at COMG with Dr. Bob Leibowitz. By 2009 had progressive bone metastasis & was treated with Dr. Bob's three-prong therapy including: Taxotere/Emcyt /Carboplatin (TEC) x5-cycles + Triple Hormone Blockade x9-months.
- **2011-15:** Zytiga (2011-12), Xtandi (2012-13), Jevtana x21-cycles (2013-15). Briefly treated with Cometriq and then did not qualify for any clinical trials. He deferred Xofigo given rapidly rising PSA (194) & CTC (158) with progressing & symptomatic (painful) bone metastasis.
- **2015:** Bone biopsy done & sent to FoundationOne that demonstrated BRCA -2 positivity. Some extensive paperwork granted compassionate approval through FDA (read more below) of Lynparza (olaparib) and he has been on oral Lynparza daily since October 2015. Since then, bone pain has resolved and PSA (94) & CTC (1) are decreasing, and follow up is continuing. He continues to work daily and lives an active lifestyle.



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Lynparza (olaparib) is not currently available commercially for prostate cancer in the U.S. There is presently one clinical trial in Europe – See article, [Some Current Trials – In the Field of Biomarkers](#) .

\*Trial info is constantly changing. Check [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) for latest info.

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In conclusion, the future continues to hopefully look more promising for patients with MCRPC and more personalized therapies are likely in the landscape for a select group of patients.

This article is not meant to be an endorsement for any one test or lab and is meant to serve as a review for the reader, which will hopefully start a conversation with their own personal oncologist &/or physician about what individualized biomarker driven therapies might be available for them, like the AR-V7 blood test, and BRCA 1 or 2 – if ever needed. If I can be of any assistance, please feel free to contact me via phone (310)229-3555 or email ([eshaghian@compassionateoncology.org](mailto:eshaghian@compassionateoncology.org)).