Us TOO University Presents:
Understanding Diagnostic Testing for Prostate Cancer Patients

Today’s speaker is Manish Bhandari, MD
Program moderator is Pam Barrett,
Us TOO International

Made possible by a contribution from Veridex LLC, a Johnson & Johnson company
Agenda

• 7:00 pm  Welcome & Introductions

• 7:04 pm  Presentation by Dr. Bhandari begins
  – Overview of Different Diagnostic Testing
  – Prostate Cancer Staging
  – Monitoring Tools

• 7:45 pm  Live Q&A Begins

• 7:58 pm  Wrap-up

• 8:00 pm  Call/Webinar Ends
Manish Bhandari, MD

Dr. Bhandari is a practicing oncologist in Cincinnati, OH and focuses on genito-urinary cancers including systemic therapy for prostate cancer. He did his medical school training in Boston at Harvard Medical school and Oncology training at University of Michigan at Ann Arbor.
“I already diagnosed myself on the Internet. I’m only here for a second opinion.”
Diagnostic tests are useful tools to help your physician manage your care throughout your journey with prostate cancer.
# The Initial Diagnosis

## Key tools to confirm diagnosis:

| Fluids          | Measure levels of hormones and proteins in your blood or urine | • Testosterone & DHT  
|                 |                                                                 | • PSA  
|                 |                                                                 | • free PSA  
| Touch           | Feeling the prostate for changes or abnormalities             | • Digital Rectal Exam (DRE)  
| Tissue          | Samples taken from the prostate to analyze for cancer          | • Biopsy  
|                 |                                                                 | • Lymph Node Dissection  
|                 |                                                                 | • Cellular & Molecular Analysis  
| Image           | Taken of internal organs and bones to help determine disease stage | • MRI  
|                 |                                                                 | • CT Scan  
|                 |                                                                 | • Ultrasound  
|                 |                                                                 | • P.E.T. Scan  
|                 |                                                                 | • Bone Scan  

## Staging

- MRI
- CT Scan
- Ultrasound
- P.E.T. Scan
- Bone Scan

## Gleason Score
BUT only 1/2 of nodules are CA and most men with CA have no nodules.
Prostate Cancer Diagnosis
Prostate Specific Antigen (PSA)

- Glycoprotein (mw=34kD) secreted exclusively by prostate epithelium; a protease

- Enters serum in prostate disease/trauma states

- If serum level 4-10 ng/ml ~1/4 chance of CaP; >10 ng/ml ~ 2/3 chance of CaP

- Highest positive predictive value of any single test, but not specific for CaP:
  - Many men with BPH have PSA > 4.0 ng/ml
  - 25% of men with CaP have PSA < 4.0 ng/ml
Prostate Cancer Diagnosis
Free PSA (fPSA or PSA-f)

• Most PSA are bound to proteins in the blood; however some are free-floating
• The free PSA test measures the proportion of free PSA to bound PSA in your blood sample
• Most men with prostate cancer have a low f-PSA (<15%)
• Percentages >25% are much less likely associated with prostate cancer
• The free PSA test may spare you an unnecessary biopsy
Gleason Score – How is it calculated?

• Calculated from tissue obtained during biopsy
  – Biopsy needle used to remove several cores of tissue from various areas on prostate gland

• Describes different types of cells to help estimate
  – How fast the cancer is likely to grow
  – A patient’s life expectancy

• Two numbers determined by the pathologist
  – First number indicates type of cancer cells that are most numerous in the tissue
  – Second number indicates the type of cancer cell that is second most numerous in the tissue
  – **Gleason Score = first number + second number**
### Gleason Score – What does it mean?

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 4</td>
<td>Cancer is very low on aggression scale</td>
</tr>
<tr>
<td>5 to 6</td>
<td>Cancer is mildly aggressive</td>
</tr>
<tr>
<td>7</td>
<td>Cancer is moderately aggressive</td>
</tr>
<tr>
<td>8 - 10</td>
<td>Cancer is highly aggressive</td>
</tr>
</tbody>
</table>

Note: 3+4 ≠ 4+3
# Cancer Staging

| Stage I   |  • Cancer is found only in the prostate  
|           |  • Small enough that no tumor is felt by the physician during the DRE |
| Stage II  |  • Cancer is found only in the prostate  
|           |  • May be big enough to be felt by the physician during the DRE |
| Stage III |  • No longer confined to just the prostate  
|           |  • Has not yet spread (metastasized) to tissues outside the pelvic area.  
|           |  • Tumors may have spread to nearby seminal vesicles |
| Stage IV  |  • Cancer is detected in tissue far from prostate  
|           |  • N+ indicates cancer has spread to lymph nodes  
|           |  • M+ indicates the cancer has metastasized or spread to distant tissue or bone |
Tumor Burden refers to the number of cancer cells, the size of a tumor, or the amount of cancer in the body. Also called tumor load.
Disease Course of Prostate Cancer:

Primary = FIRST, LOCAL prostate treatment
Disease Course of Prostate Cancer:

Biochemical progression = “PSA relapse”
Disease Course of Prostate Cancer:

Hormone responsive = “Androgen sensitive”  Prostate Cancer
Disease Course of Prostate Cancer:

Hormone refractory (HRPC) = “Androgen resistant” PSA-only Prostate Cancer
Disease Course of Prostate Cancer:
Metastatic HRPC = Stage D2, D3 = Bone scan positive Prostate Cancer
Disease Course of Prostate Cancer

Earlier Intervention to Bypass Resistance

Adjuvant/Neo

Local RX

Biochem Prog

Rising PSA

Androgen Ablation

Hormone Refract Biochem Prog

Stage D3

HRPC

TIME

TUMOR BURDEN
## Monitoring Your Condition

Many of the same tools can be used for monitoring after initial diagnosis:

| Fluids          | Measure levels of hormones and proteins in your blood or urine | • Testosterone & DHT  
|                 |                                                              | • PSA, free PSA  
|                 |                                                              | • free PSA  
|                 |                                                              | • Circulating Tumor Cells (CTCS) |
| Touch           | Feeling the prostate for changes or abnormalities             | • Digital Rectal Exam (DRE) |
| Tissue          | Samples taken from the prostate to analyze for cancer          | • Biopsy  
|                 |                                                              | • Cellular & Molecular Analysis |
| Image           | Taken of internal organs and bones to help determine disease stage | • MRI  
|                 |                                                              | • CT Scan  
|                 |                                                              | • Ultrasound  
|                 |                                                              | • P.E.T. Scan  
|                 |                                                              | • Bone Scan |
## Monitoring Tools

### A closer look at some key tools:

<table>
<thead>
<tr>
<th>Tool</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imaging</strong></td>
<td>Used to monitor whether cancer has spread to near or distant tissue or to the bones</td>
</tr>
<tr>
<td><strong>PSA</strong></td>
<td>One indicator of abnormal activity in the prostate gland</td>
</tr>
<tr>
<td><strong>Testosterone &amp; DHT</strong></td>
<td>Measures the effectiveness of hormonal blockade treatment. It also is useful in assessing causes of sexual dysfunction.</td>
</tr>
<tr>
<td><strong>Cellular / Molecular Analysis</strong></td>
<td>Used to develop a better understanding of the underlying biology of the tumor cell</td>
</tr>
<tr>
<td><strong>Circulating Tumor Cells (CTCs)</strong></td>
<td>The number of circulating tumor cells in your blood is predictor of progression free and overall survival and is monitored for change in prognosis over time</td>
</tr>
</tbody>
</table>
# Imaging

| **MRI**  | Takes cross-sectional slices (views) from several angles  
| Magnetic resonance imaging | Looks for signs that cancer may have metastasized (spread) |
| **CT Scan**  | Scans show a slice, or cross-section, of the body  
| (Computed tomography scan) | Image is created using controlled amounts of x-rays -- beams of high-energy radiation that are passed through the body |
| **Ultrasound**  | Creates images called sonograms by giving off high-frequency sound waves that go through your body  
|  | Ultrasound cannot tell a benign (not cancer) tumor from one that is cancer |
| **P.E.T Scan**  | Used to find tumors, especially in the bones and thyroid gland. They are also used to study a cancer's stage (extent of its spread) and to evaluate whether treatment is working  
| (nuclear imaging) |  |
| **Radionuclide Bone Scan**  | Small amount of radioactive material is injected into a vein and travels through the bloodstream. The radioactive material collects in the bones and is detected by a scanner  
|  | Used to check for cancer cells in the bone |
Testosterone & DHT*

• Prostate cancer cells utilize male hormones known as androgens (testosterone is the most well known)
• Blocking these hormones generally reduces prostate cancer growth, at least temporarily and sometimes for a very long time
• Levels of these hormones are assessed using a blood test which measures the effectiveness of hormonal blockade treatment

* Dihydrotestosterone
PSA for Monitoring

- Your doctor may monitor for a rise in your PSA level over time to watch for signs of recurrence or metastatic disease.
- If your PSA continues to rise, your doctor is likely to order additional tests (e.g. imaging) to decide whether additional treatment may be necessary.
- A rise in PSA does not always mean your cancer has recurred or spread.
  - Prostate inflammation or enlargement may cause PSA to rise.

Prostate cancer is a complex disease. PSA along with other variables should be considered by you and your doctor to make the best decision for you.
PSA Doubling Time (PSADT)

PSA Doubling Time = time it takes for PSA to double

- Used to help predict risk of recurrence, metastases, and cancer related death
  - < 3 months associated with higher risk of a poor outcome
  - >15 months associated with a more favorable outcome
  - 3-15 months – other clinical factors are better for determining risk

- See Memorial Sloan Kettering online tool for calculating PSA doubling time
  http://www.mskcc.org/applications/nomograms/prostate/PsaDoublingTime.aspx

Reference: http://prostatecancerinfolink.net/2008/05/29/guidelines-on-psa-doubling-time
What is a Circulating Tumor Cell?

A Circulating Tumor Cell (CTC) is a cancer cell that has detached from a solid tumor lesion and entered the peripheral blood circulation.
Why are CTCs Important?

CTCs are rarely found in healthy patients or patients with non-malignant or other benign diseases.

Certain number of CTCs in the blood stream are correlated with poor prognosis in metastatic breast, prostate, & colorectal cancer patients.

* In Controls (Subjects without Cancer) and Patients with MBC1, MCR2, or MPC3 before Initiation of a new line of Therapy (Baseline) and ~2-5 weeks After the Initiation of Therapy.
How are CTCs Measured?

- A tube of blood is drawn & sent to a lab for testing
- The blood sample is processed on an automated system
- Antibodies are added to the blood to capture CTCs & to differentiate them from other cells (e.g. white cells)
- Images of cells are reviewed by the lab to determine if the cells are CTCs
- The system reports out the total number of CTCs found in the tube of blood
CTC Count – What does it mean?

- Patients with <5 CTCs (GREEN) have greater median overall survival (almost double) versus patients with ≥5 CTCs (RED)

Data from CELLSEARCH® CTC Test Clinical Trials

Results are similar for predicting progression free survival
The Value of Monitoring CTCs

Prognosis can change

- **GREEN LINE**: Patients with <5 CTCs at all measurement points
- **RED LINE**: Patients with ≥5 CTCs at all measurement points
- **BLUE LINE**: Patients who started off with ≥5 CTCs but changed to <5 CTCs
- **ORANGE LINE**: Patients who started off with <5 CTCs but changed to ≥5 CTCs

Results are similar for predicting progression free survival

Data from CELLSEARCH® CTC Test Clinical Trials

VX10530
CTC Summary

- A monitoring tool for patients with Metastatic Prostate Cancer
- A simple blood test that provides your physician with additional information to help manage your overall care
- Obtain initial CTC count prior to initiation of a new line of therapy
- Monitor CTC count over time to detect changes in prognosis

Limitations:

- CTCs are not used for initial diagnoses of prostate cancer
- If you are a patient with metastatic prostate cancer, your doctor must use your CTC count along with other medical information, including tests like imaging and PSA, to monitor how you are doing
- CTC tests cannot be used to determine how you will respond to treatment
Actions You Can Take

- Keep an eye on other indicators and make sure to talk to your doctor if you have any questions or concerns!
- Some considerations include
  - Diet / Nutrition
  - Exercise / Flexibility
  - Weight
  - Incontinence
  - Sexual Function
Diagnostic Resources

• There are a variety of diagnostic tests designed to identify how you are doing and to assist in determining the most appropriate actions to take for YOU.

• Continue to educate yourself about these options so that you can provide input into your care.

Recommended resource available at www.ustoo.org
Questions / Discussion

- Web participants can ask a question by typing it in the CHAT box.
- Callers can ask a question by pressing *1 on their telephone keypad, and will initially talk with Jackie from Us TOO.
For More Information

- An audio and video archive and transcription of this presentation will be available at www.ustoo.org

- Read these Us TOO educational brochures:
  - Prostate Cancer Patient’s Guide to Hormone Therapy
  - What You Need to Know for Better Bone Health
  - What now? Hope and options when experiencing a rising PSA
  - The Prostate Cancer Playbook: For Prostate Cancer Recurrence, Rising PSA, and Advanced Disease

- Participate in an online discussion group

- Thank you!

www.ustoo.org
1-800-80-Us TOO (1-800-808-7866)