Treatment options for recurrent prostate cancer

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Reston Hospital

Treatment options for recurrent prostate cancer

- Background
- Radiation
- Hormone treatment
- Chemotherapy
- New agents

Treatment options for recurrent prostate cancer

- **Background**
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Background

- Prostate cancer is the most commonly diagnosed solid organ cancer in the United States
  - 240,000 in 2012
- Prostate cancer is the second leading cause of cancer deaths among American men
  - 28,000 in 2012

Yesterday and today

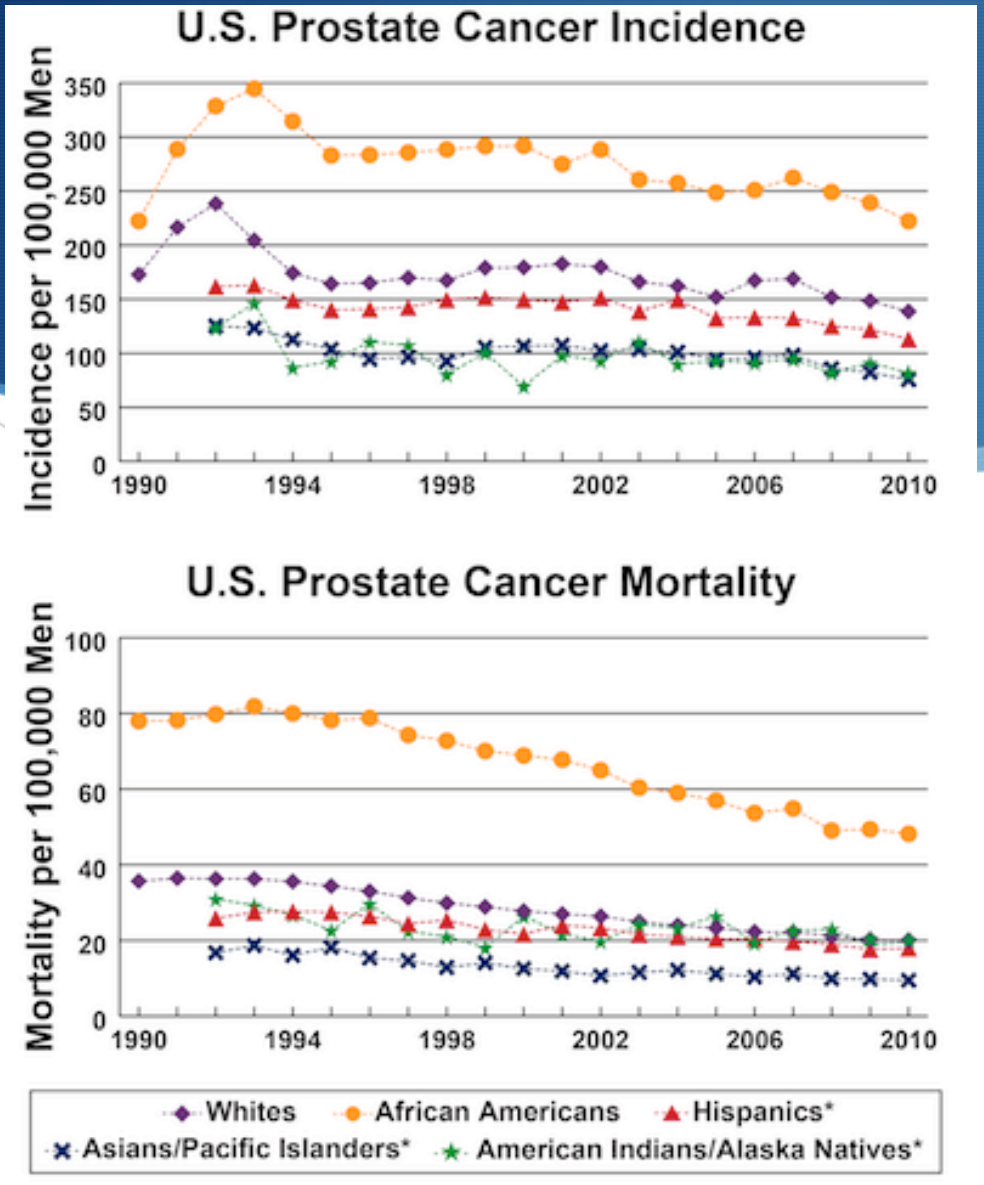
1975

- 94 new cases per 100,000 men
- 31 deaths per 100,000 men
- 1986 FDA approves PSA
  - Increase in diagnosis
  - 1992: peaked at 237 cases per 100,000 men

2007

- 116 cases per 100,000 men
- 24 deaths per 100,000 men
- 90% of cancers diagnosed at early stage

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate



Source: Surveillance, Epidemiology, and End Results (SEER) Program and the National Center for Health Statistics. Additional statistics and charts are available at the SEER Web site.

PSA came into use 1980s – increased incidence of prostate cancer

www.cancer.gov/researchandfunding/snapshots/prostate

Treatment localized cancer

1975

- Surgery
  - Open prostatectomy
- Radiation
  - External beams

2007

- Surgery
  - Nerve-sparing prostatectomy
  - Laparoscopic and robotic prostatectomy
- Radiation
  - External beams
  - Seeds (brachytherapy)
- Active surveillance for early, low grade cancer

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate

Hormone therapy

1975

- Removal of the testicles
- Estrogen
  - Diethylstilbestrol (DES)
    - Cardiovascular side effects

2007

- 1985: Gonadotropin-releasing hormone agonists
  - leuprolide (Lupron), goserelin (Zoladex), triptorelin (Trelstar), histrelin (Vantas)
- 1997: Anti-androgens
  - bicalutamide (Casodex), flutamide (Eulexin), nilutamide (Nilandron)
- 2008: Gonadotropin-releasing hormone agonists
  - degarelix (Firmagon)
- Ketoconazole (Nizoral)

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate

Chemotherapy

1975

- none

2007

- 2004: docetaxel (Taxotere)
- 2010: cabazitaxel (Jevtana)
  - Men who no longer respond to docetaxel

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate

Immunotherapy

1975

- none

2007

- 2010: sipuleucel T (Provenge) vaccine

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate

Bone agents

1975

- none

2007

- Bisphosphonates
  - zolendronic acid (Reclast, Zometa), alendronate (Fosamax), ibandronate (Boniva) risedronate (Actonel)
- Selective estrogen receptor modulators
  - raloxifene (Evist) and toremifene (Fareston)
- Teriparatide (Forteo)
- RANK ligand inhibitor
  - denosumab (Xgeva, Prolia)
- Calcitonin

American Urological Association 2013 San Diego, CA Annual Meeting Highlights. P 7-9

Radiation to bone

1975

- none

2013

- Injectable radiation
  - Radium-223 dichloride (Xofigo)

American Urological Association 2013 San Diego, CA Annual Meeting Highlights. P 7-9

Prevention

1975

- none

2007

- 2003: finasteride (Proscar) decreases risk of prostate cancer 25%
- 2010: dutasteride (Avodart) decreases risk of prostate cancer in high risk men

www.cancer.gov/cancertopics/factsheet/cancer-advances-in-focus/prostate

Background

- The most common treatment for prostate cancer is surgery
  - Radical prostatectomy
- In 2/3 of men, prostatectomy cures prostate cancer
- In 1/3 of men, prostate cancer will come back within 10 years

Why does it come back?

- A microscopic amount of cancer cells left behind at surgery
- Spread of cancer outside the pelvis (low belly)

Risks for recurrent cancer

- Worrisome pathology after surgery
  - Positive margins – cancer seen at edge of removed prostate
  - Cancer in the glands behind the prostate (seminal vesicles)
  - Cancer bulging outside the capsule of the prostate
  - Higher Gleason score

Treatment options for recurrent prostate cancer

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- **Radiation**
- Hormone treatment
- Chemotherapy
- New agents

New guidelines for radiation after surgery

- Radiation after Prostatectomy Panel
  - American Urological Association Education and Research, Inc. (AUA)
  - American Society for Radiation Oncology (ASTRO)
- Panel created in 2011
- Guidelines approved in 2013

American Urological Association (AUA) Guideline

ADJUVANT AND SALVAGE RADIOTHERAPY AFTER PROSTATECTOMY: ASTRO/AUA GUIDELINE

Ian Murchie Thompson,* Richard Valicenti,* Peter C. Albertsen, Brian Davis, S. Larry Goldenberg, Carol A. Hahn, Eric A. Klein, Jeff Michalski, Mack Roach III, Oliver Sartor, J. Stuart Wolf Jr. and Martha M. Faraday

Approved by the AUA Board of Directors
April 2013

How can you tell when cancer has come back?

- Check PSA blood test regularly after surgery
- Rising PSA after surgery means a higher risk of:
  - Spread of prostate cancer throughout the body (metastasis)
  - Death from prostate cancer
- *Clinical Principle*

Guideline Statement 4. Radiation after Prostatectomy: ASTRO/AUA Guideline

What PSA level indicates cancer has come back?

- Detectable or rising PSA value after surgery $\geq$ 0.2 ng/ml
- Second test that confirms PSA $\geq$ 0.2 ng/ml

- *Recommendation;* Evidence Strength: Grade C

Guideline Statement 5. Radiation after Prostatectomy: ASTRO/AUA Guideline

Do I need any more tests?

- Restaging evaluation may be considered
  - Bone scan
  - CT scan of the pelvis (low belly)

- *Option;* Evidence Strength: Grade C

Guideline Statement 6. Radiation after Prostatectomy: ASTRO/AUA Guideline

Should I get radiation?

- Radiation should be offered to men with PSA recurrence after surgery if there is no evidence of distant spread of cancer (scans show prostate cancer, bone pain)

- *Recommendation;* Evidence Strength: Grade C

Guideline Statement 7. Radiation after Prostatectomy: ASTRO/AUA Guideline

When should I get radiation?

- Radiation for PSA recurrence is most effective when given at lower levels of PSA

- *Clinical Principle*

Guideline Statement 8. Radiation after Prostatectomy: ASTRO/AUA Guideline

What are the benefits of radiation?

- Potential benefits of controlling recurrent prostate cancer

Guideline Statement 9. Radiation after Prostatectomy: ASTRO/AUA Guideline

What are the risks of radiation?

- Short-term and long-term side effects
  - Urinary: urinary frequency and urgency, blood in the urine, scar tissue in the bladder tube
  - Bowel: bowel frequency and urgency, diarrhea, blood in the stool
  - Sexual: erectile dysfunction
- *Clinical Principle*

Guideline Statement 9. Radiation after Prostatectomy: ASTRO/AUA Guideline

Treatment options for recurrent prostate cancer

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- Radiation
- **Hormone treatment**
- Chemotherapy
- New agents

AUA Update Series 2011

Lesson 11 Volume 30

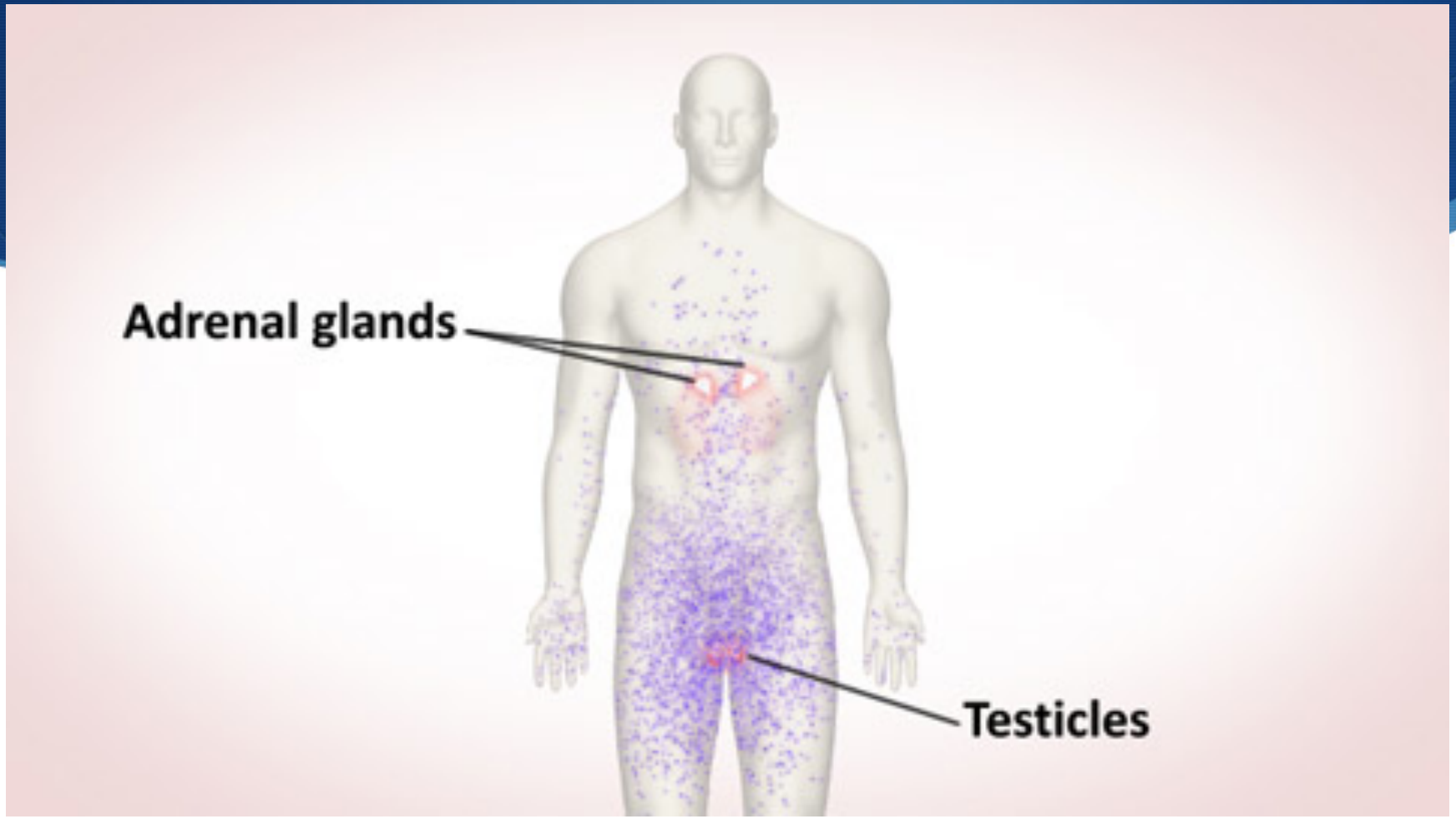
Appropriate Use of Androgen Deprivation for the Management of Prostate Cancer

Wilson SS and Glode LM. Appropriate use of androgen deprivation for the management of prostate cancer. AUA Update Series, Volume 30, Lesson 11. American Urological Association Education and Research, Inc, 2011.

Hormone (androgen deprivation) therapy

- Hormone therapy is also called *androgen deprivation therapy* (ADT) or *androgen suppression therapy*
- The goal is to reduce levels of male hormones, called *androgens*, in the body, or to prevent them from reaching prostate cancer cells

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy



- The main androgens in men's blood is testosterone and dihydrotestosterone (DHT)
- 85-90% is made in the testicles. 10-15% is made by the adrenal glands and other parts of the body

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page2

Hormone (androgen deprivation) therapy

- Androgens stimulate prostate cancer cells to grow
- Lowering androgen levels or stopping them from getting into prostate cancer cells makes prostate cancers shrink or grow more slowly
- Hormone therapy alone does not cure prostate cancer
- Eventually hormone therapy stops working

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy

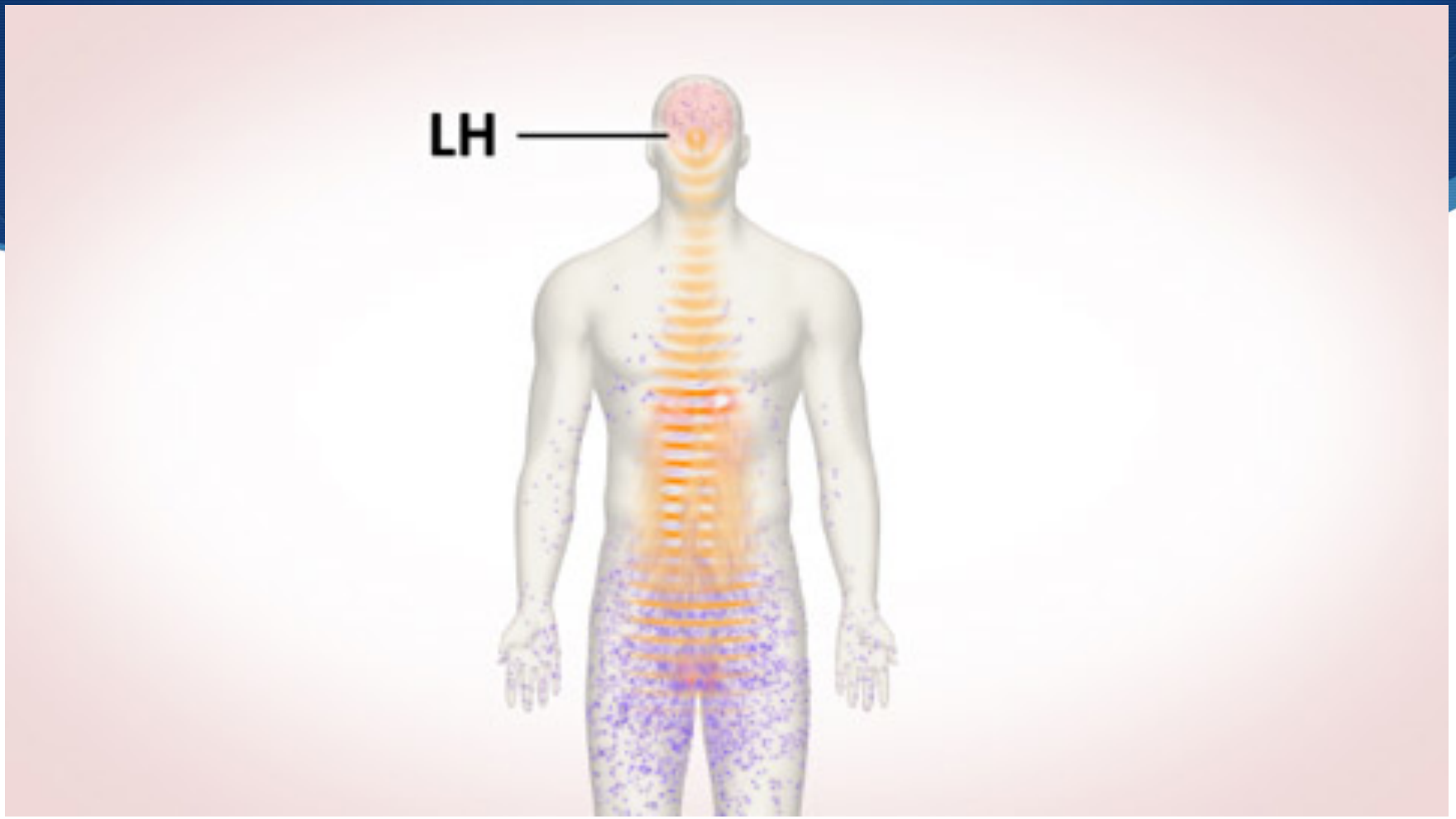
Treatments to lower androgen levels

- Orchiectomy (surgical castration)
- Luteinizing hormone-releasing hormone (LHRH) analogs
  - Similar to LHRH
- Luteinizing hormone-releasing hormone (LHRH) antagonists
  - Block LHRH

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy

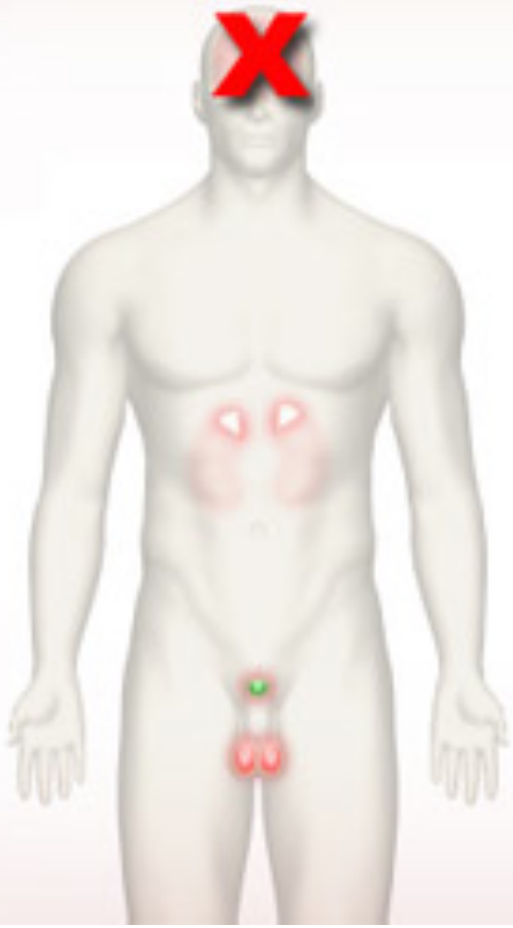
Orchiectomy (surgical castration)

- Surgical removal of the testicles
- Outpatient surgery
- Simple, least expensive
- Permanent
- Testicle prostheses available



- The brain sends chemical signals (LHRH/GnRH) to the pituitary gland
- The pituitary gland sends chemical signals (LH) to the testicles to make testosterone
- When testosterone is detected, these signals shut off

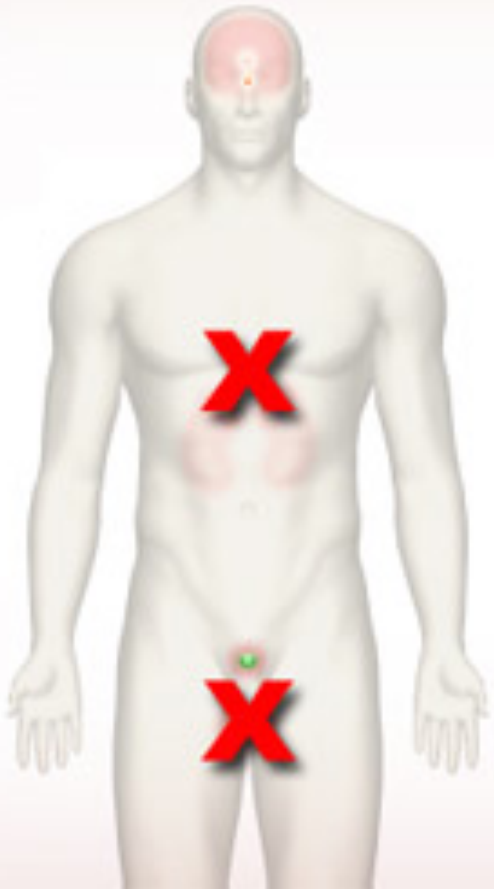
www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page2



- LHRH agonists
  - leuprolide (Lupron, Viadur, Eligard)
  - histrelin (Vantas)
  - goserelin (Zoladex)
  - triptorelin (Trelstar)

- LHRH agonists suppress the pituitary gland's call for testosterone
- Injection in the muscle every 3 to 6 months
- Testosterone flare - bone pain, block ureter, spinal cord compression

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page2



- **LHRH antagonists**
  - degarelix (Firmagon)
  - abarelix (Plenaxis)
    - Withdrawn from US 2005, used in Germany

- LHRH antagonists stop the production of testosterone in the testes and adrenal glands
- Injection into skin (belly) every 28 days
- No testosterone flare

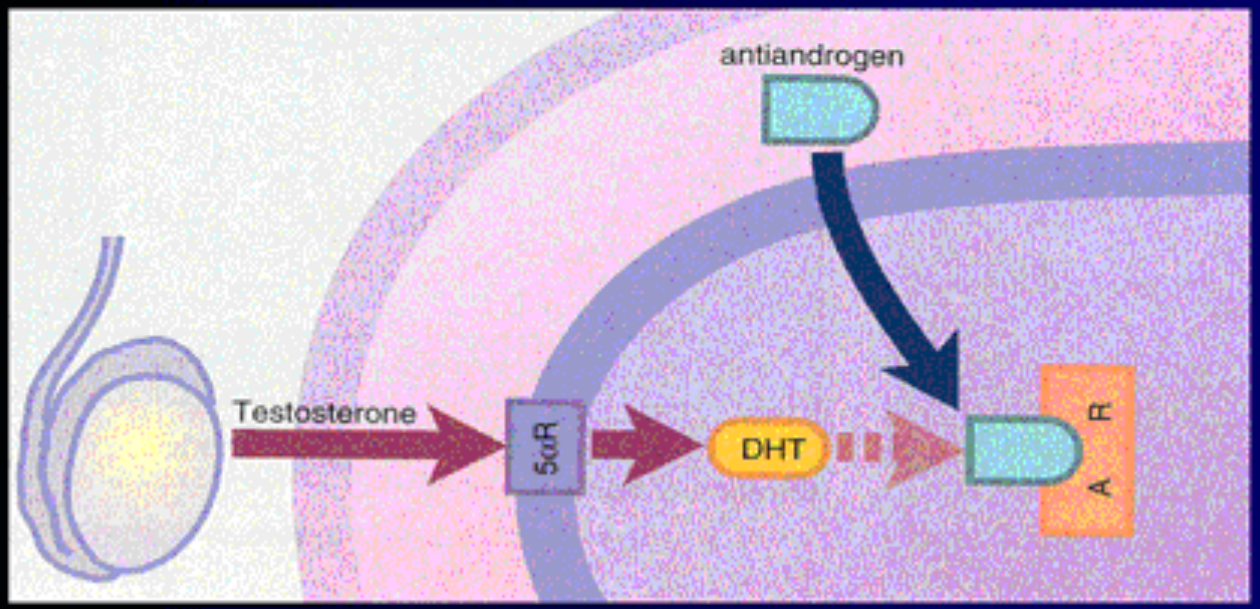
www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page2

Drugs that stop androgens from working

- Anti-androgens
  - casodex (bicalutamide), nilandron (nilutamide), eulexin (flutamide)
- Androgen synthesis inhibitors ("super-antiandrogens")
  - Abiraterone (Zytiga)
- Next generation androgen receptor blockers
  - Enzalutamide (Xtandi)

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy

Antiandrogens – Androgen Receptor Antagonists



- casodex (bicalutamide)
- nilandron (nilutamide)
- eulexin (flutamide)

- Blocks androgens from androgen receptor
- Oral pills taken daily
- Usually given before treatment with, or in combination with, an LHRH agonist

www.medscape.org/viewarticle/416543_6

Other androgen-suppressing drugs

- estrogens (female hormones)
  - Diethylstilbestrol (DES): cardiovascular side effects
- ketoconazole (Nizoral)
  - Dramatically decreases testosterone level in 4 hours
- aminoglutethimide (Cytadren)
  - Blocks steroid synthesis, including testosterone

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy
http://www.healthline.com/health/prostate-cancer-drugs?toptoctest=expand

Side effects of blocking testosterone

- Osteoporosis (bone thinning), broken bones
- Reduced or absent libido (sexual desire)
- Impotence (erectile dysfunction)
- Shrinking of testicles and penis
- Hot flashes, may get better or even go away with time
- Breast tenderness, growth of breast tissue
- Anemia (low red blood cell counts)
- Decreased mental sharpness
- Loss of muscle mass
- Weight gain
- Fatigue
- Increased cholesterol, possible cardiovascular problems (heart attack, death)
- Depression

www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-treating-hormone-therapy

Prevention

- Calcium and vitamin D
- Regular, weight-bearing exercise
- Bone density scans

When cancer no longer responds to hormone therapy

- Prostate cancer spreads throughout the body
- Historically, average survival was less than 2 years
- New treatments, longer survival
- Remains an incurable disease

Treatment options for recurrent prostate cancer

- Background
- Radiation
- Hormone treatment
- **Chemotherapy**
- New agents

Chemotherapy for prostate cancer

- For metastatic cancer (spread beyond the prostate), no longer responsive to hormone therapy
- Kill cancer cells or prevent them from multiplying
- Given through the vein (intravenous) or by mouth

www.prostate.net/prostate-cancer/chemotherapy-for-prostate-cancer/

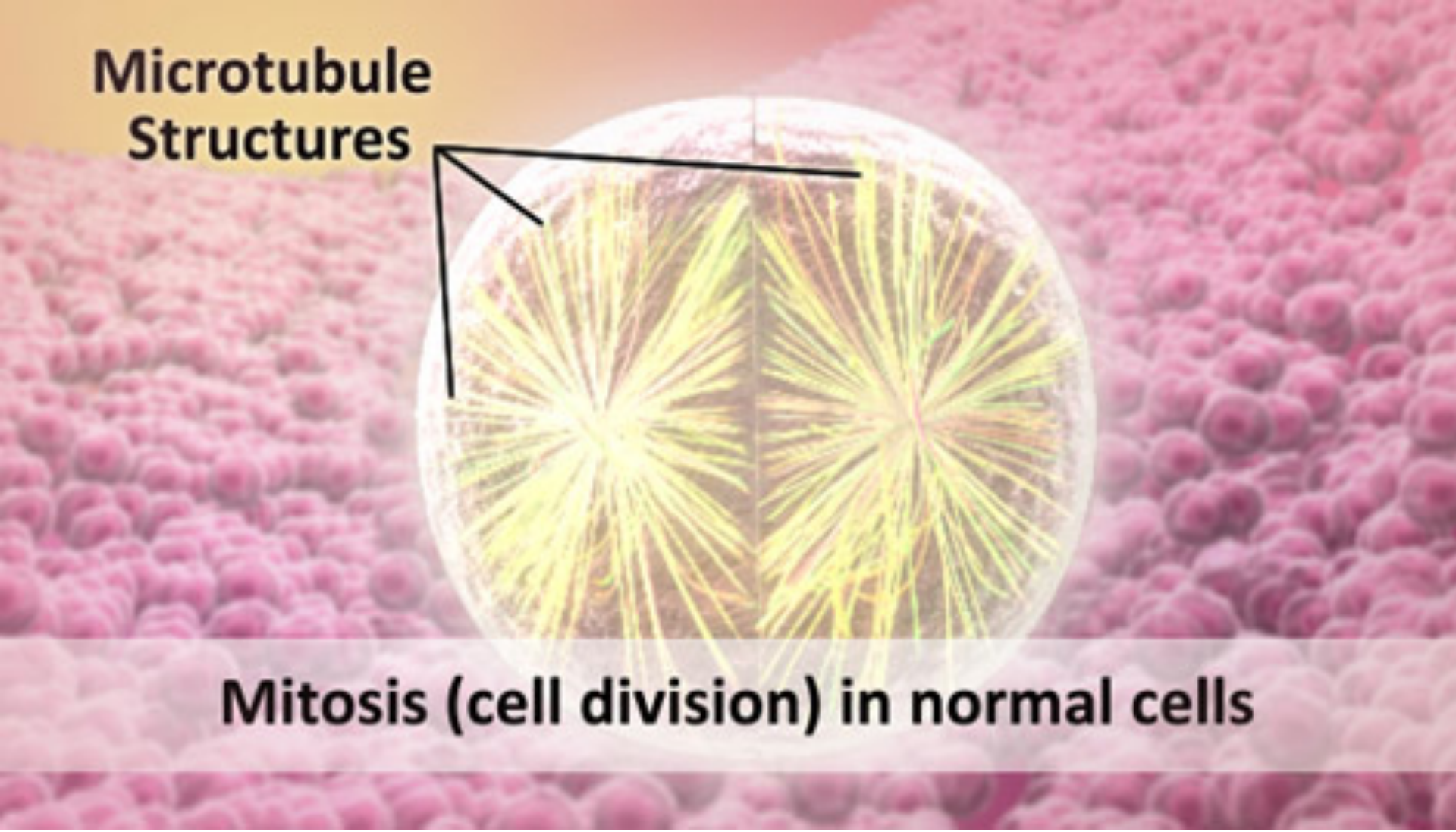
Chemotherapy

- doxetaxel (Taxotere): intravenous, with other drugs
- cabazitaxel (Jevtana): injectable, with prednisone, if no response to docetaxel. Approved 2010
- mitoxantrone (Novantrone): with steroids, treats pain in advanced cancer
- estramustine (Emcyt): orally, sometimes with other drugs
- paclitaxel (Taxol): intravenous
- etoposide (Vepsid, V-16): intravenous and by mouth, combined with other drugs
- doxorubicin (Adriamycin): intravenous, an antibiotic. Risk of heart damage.
- vinblastine (Velban): intravenous, often with other drugs

www.prostate.net/prostate-cancer/chemotherapy-for-prostate-cancer/

docetaxel (Taxotere)

- One of the main types of chemotherapy to treat hormone-refractory prostate cancer
- Prevents cell growth
  - Inhibits microtubule assembly and disassembly


Microtubule
Structures
Mitosis (cell division) in normal cells

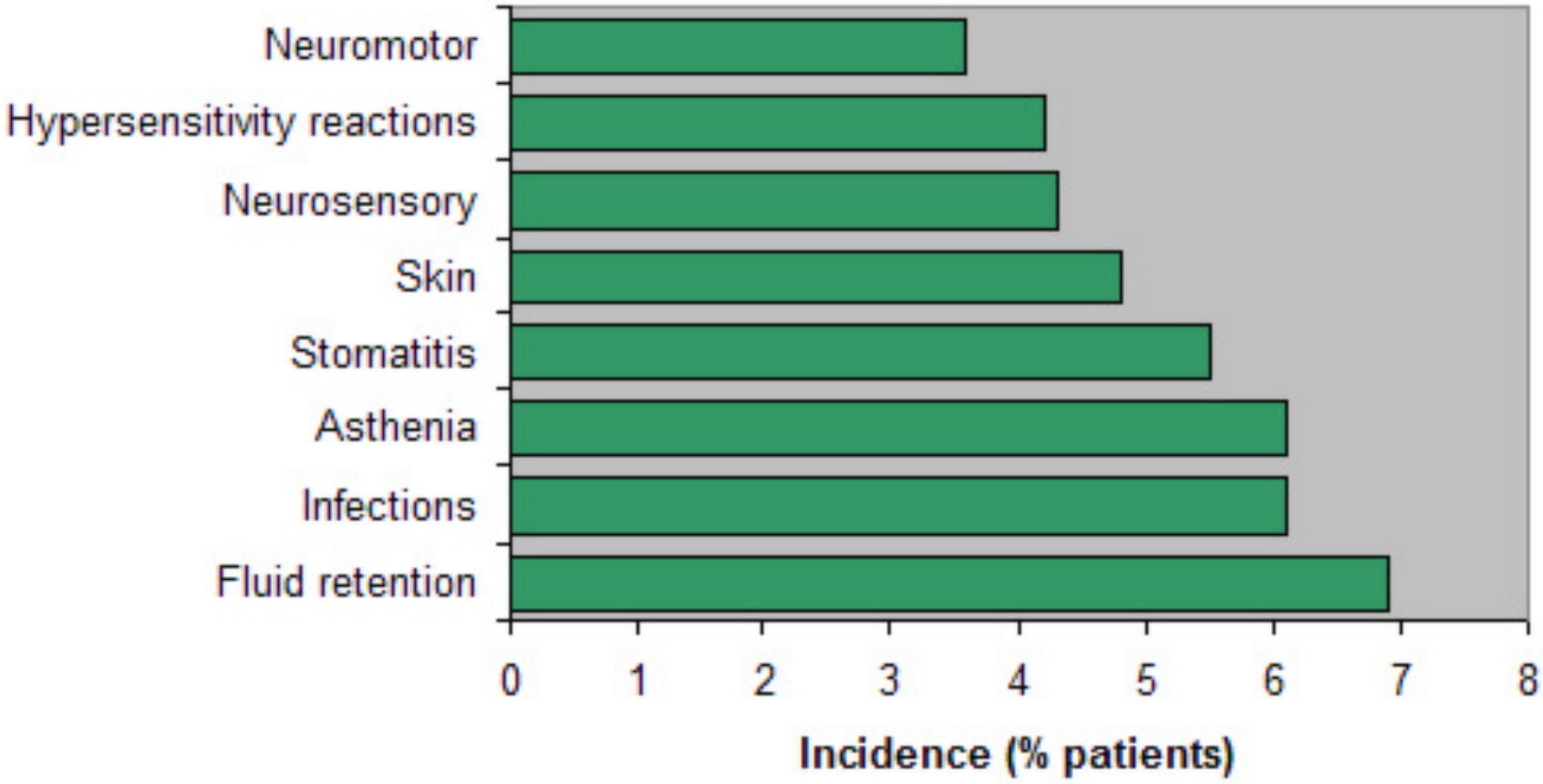
Cancer.gov

docetaxel (Taxotere)

- Effectiveness:
  - 17.5 month survival compared to 15.6 months with mitoxantrone chemotherapy
  - 18.9 month survival compared to 16.5 month survival with mitoxantrone
- Side effects: 26% had serious side effects
  - 11% stopped treatment

SWOG 9916; TAX-327

Severe adverse effects in patients undergoing treatment with docetaxel n=2045



Treatment options for recurrent prostate cancer

- Background
- Radiation
- Hormone treatment
- Chemotherapy
- **New agents**

New agents

- Immunotherapy
  - Sipuleucel-T (Provenge)
- Androgen blockers
  - abiaterone (Zytiga)
  - enzalutamide (Xtandi)
- Injectable radiation
  - Radium-223 dichloride (Xofigo)

sipuleucel-T (Provenge)

sipuleucel-T (Provenge)

- Immunotherapy
- Approved by FDA 2010
- First and only cancer vaccine ever approved by the FDA

IMPACT trial 2008

sipuleucel-T (Provenge)

- Autologous cellular immunotherapy,
  - Uses a man's own immune cells (autologous) to battle prostate cancer
- Series of carefully orchestrated steps to make a drug that is personalized for each patient

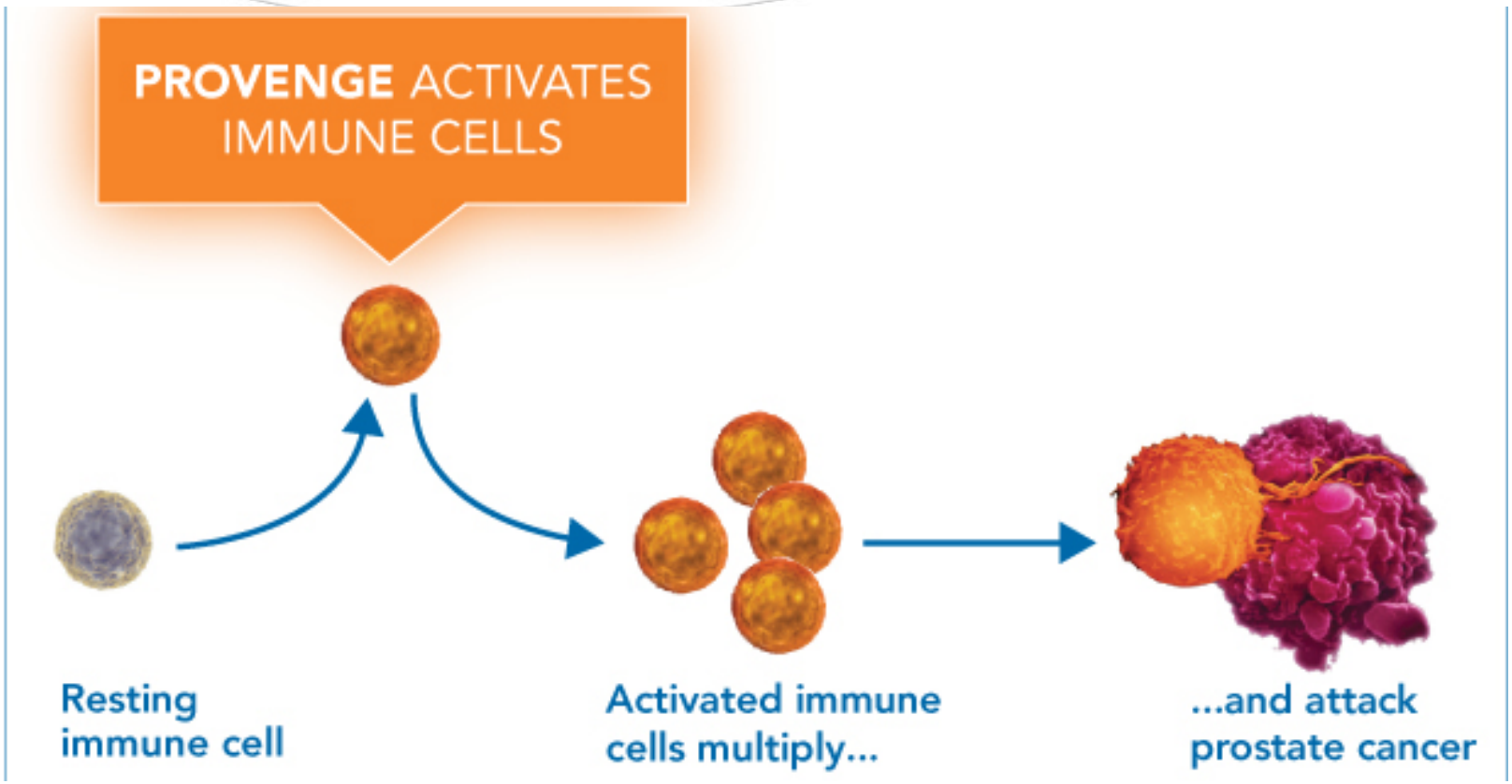
www.prostate.net/2012/prostate-cancer/provenge/

sipuleucel-T (Provenge)

- Other therapies work against the body
  - Hormone therapy stops production of hormones
  - Chemotherapy therapy are toxic and focus on killing cancer cells
- Provenge is an approach that makes use of the body's *own* immune cells (dendritic or T cells) which have been activated in a lab so they can recognize and battle prostate cancer cells

www.prostate.net/2012/prostate-cancer/provenge/

sipuleucel-T (Provenge)



Who can take sipuleucel-T (Provenge)?

- No or few symptoms: no cancer pain or, pain does not require narcotic pain medicine
- Cancer has spread to other areas in the body, such as bone (metastatic)
- Cancer has worsened despite hormone treatment (androgen resistant)
- Lower amount of cancer, healthy immune system

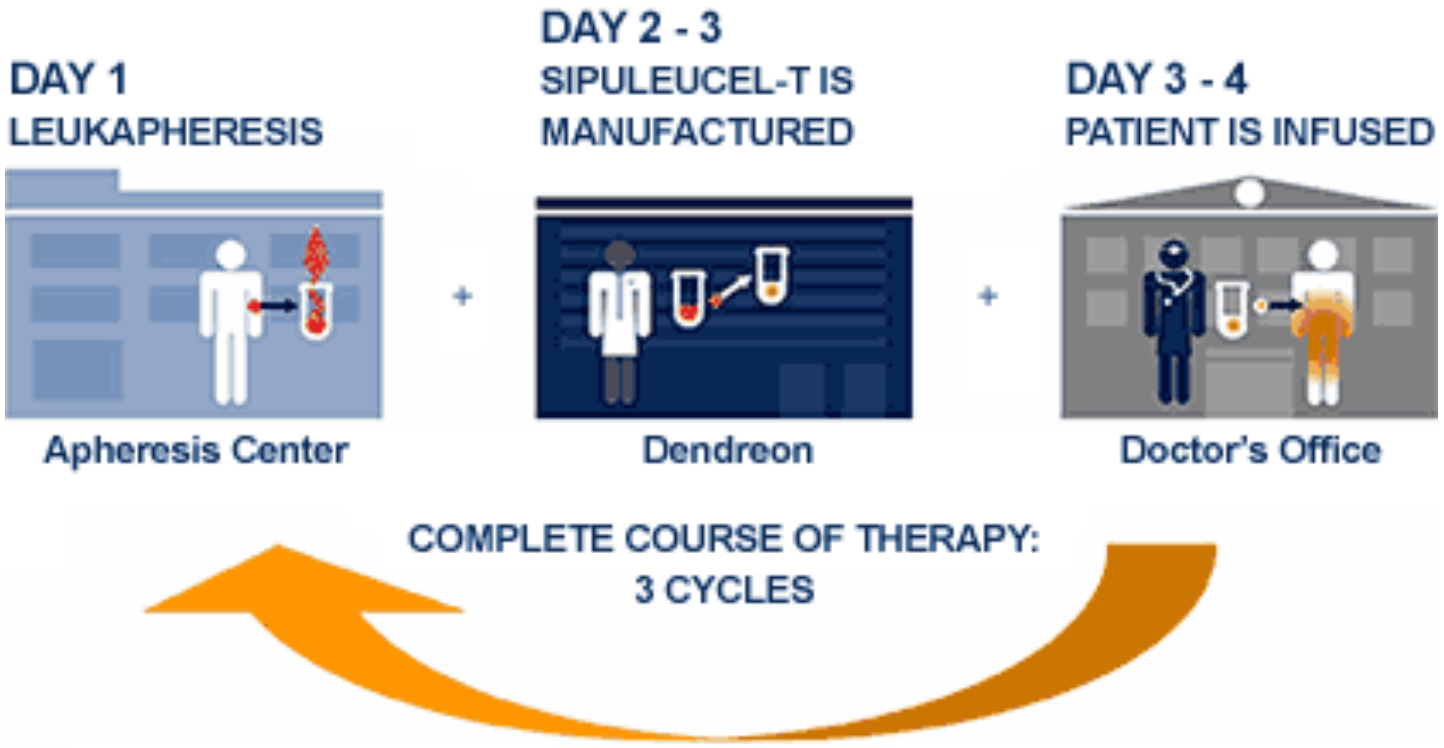
www.prostate.net/2012/prostate-cancer/provenge/
The National Comprehensive Care Network

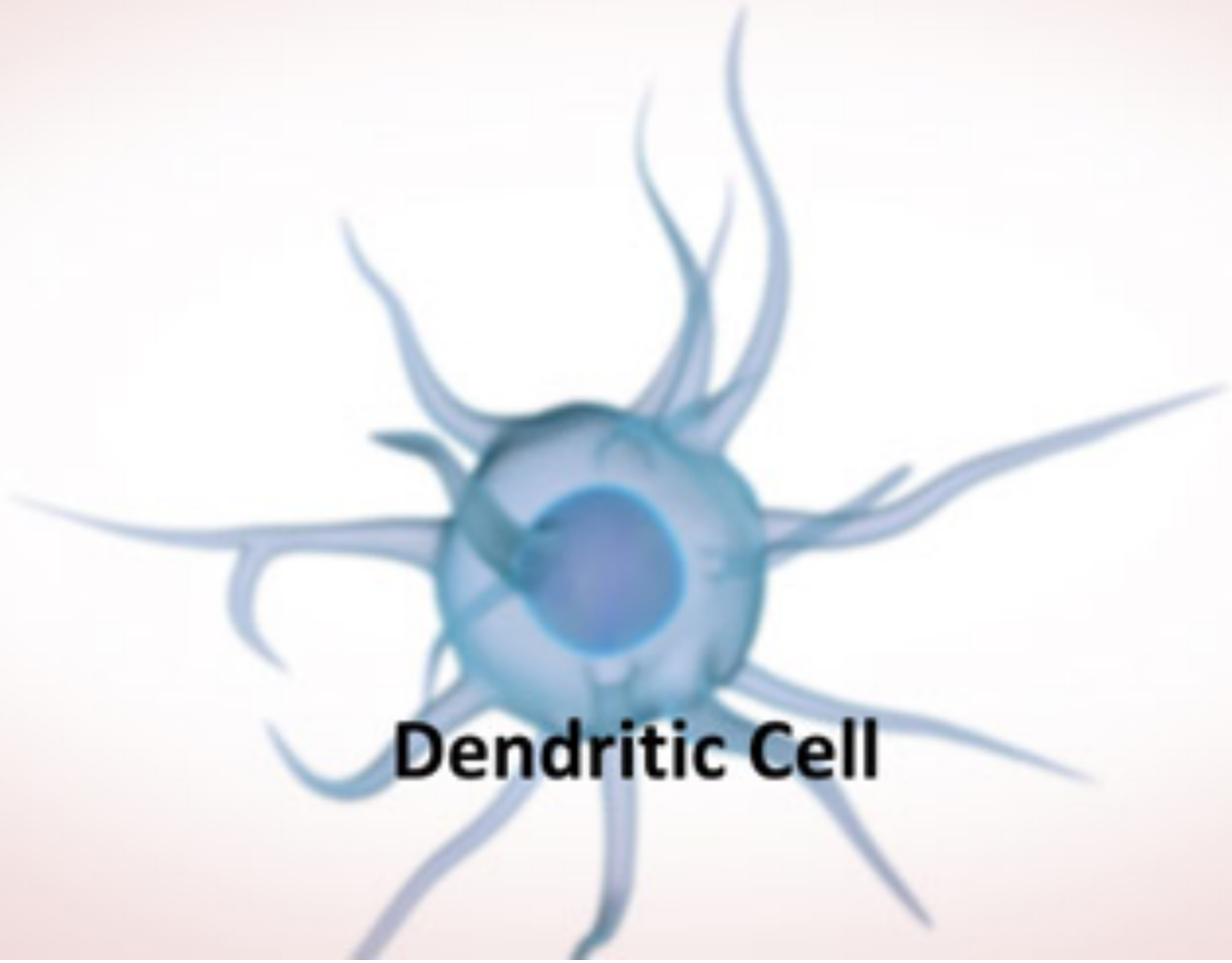
How sipuleucel-T (Provenge) is prepared

- Leukopharesis: blood drawn through a large vein, goes into a machine where immune cells (dendritic or T cells), clotting proteins (platelets) and red blood cells are extracted. 3-4 hours
- Cells sent to a lab where the are activated to prompt the immune cells to look for and attack prostate cancer cells. 2- 3 days
- Activated immune cells (personalized drug) is infused 3 days later. 2 hours
- 3 doses total. Treatment period: 5 weeks

www.prostate.net/2012/prostate-cancer/provenge/

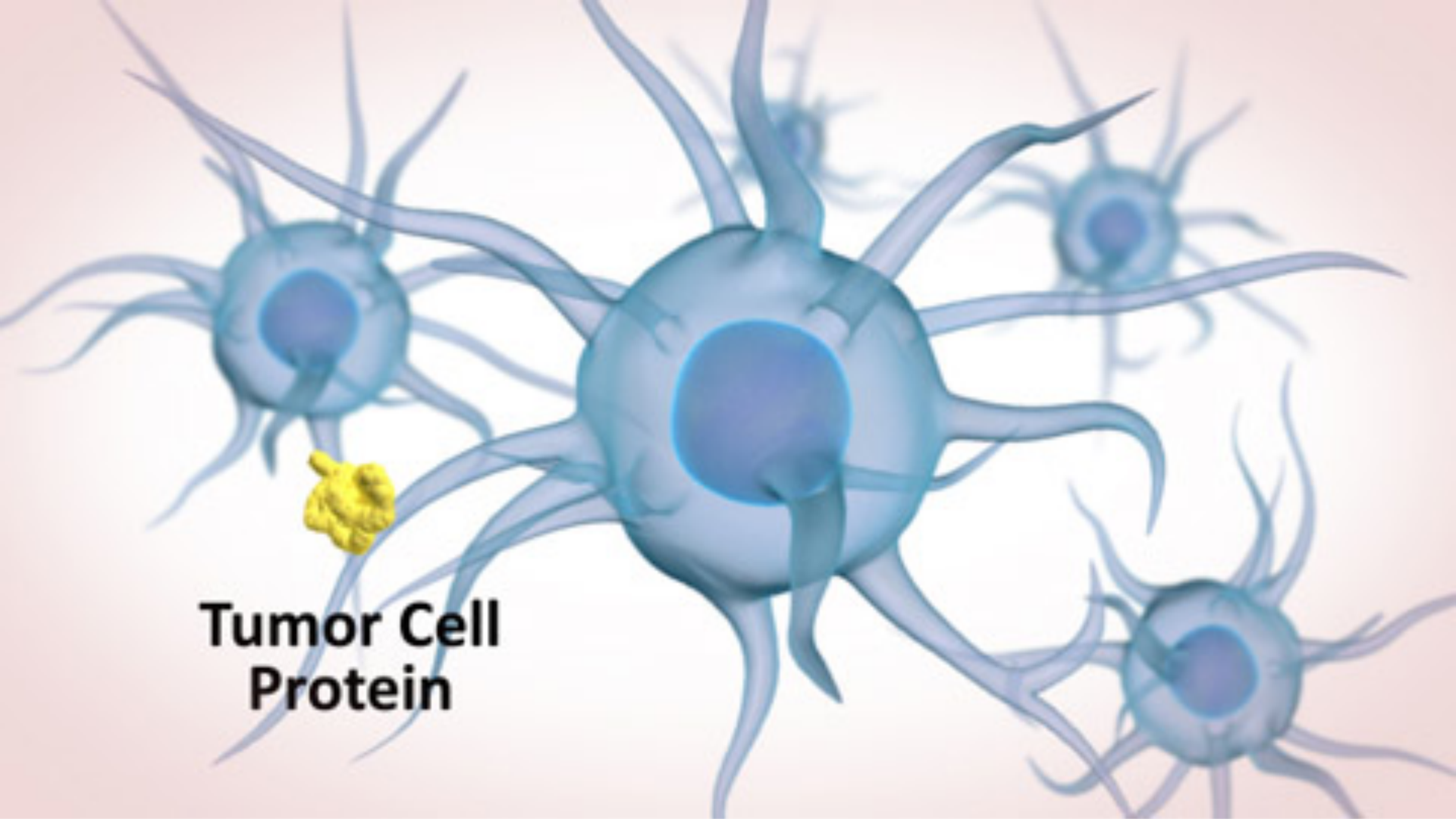
sipuleucel-T (Provenge)





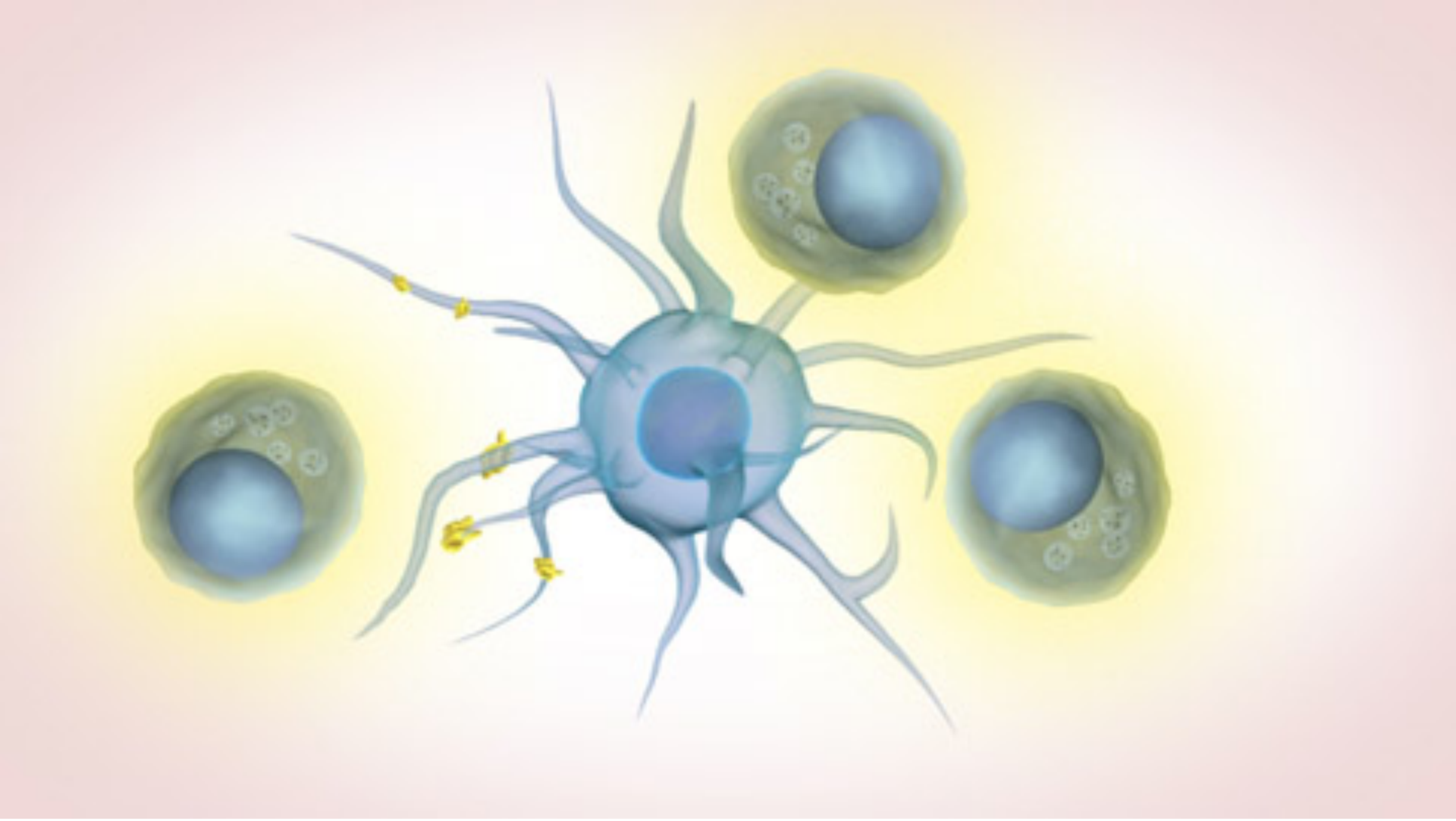
- The blood of the cancer patient is collected and enriched to increase the population of immune cells (dendritic or T cells)

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page3



- These cells are then grown in the laboratory in the presence of a protein or part of a protein that is present in or on the patient's tumor cells

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page3



- When the dendritic cells are put back into the patient, they signal the body's own immune system to destroy all cells with the telltale protein, including cancer cells

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page3

sipuleucel-T (Provenge)

- <10% of patients show a response in symptoms, PSA or on xray
  - Don't expect to see a response
- Side effects:
  - Common: back pain, chills, fatigue, fever, headache, joint ache, and nausea (15%)
  - Less common: stroke or severe infusion reactions: breathing problems, chills, dizziness, fatigue, fever, headache, high blood pressure, muscle ache, nausea, vomiting, and weakness (3.5%)
  - Less than 1.5% stopped treatment because of side effects

www.prostate.net/2012/prostate-cancer/provenge/

sipuleucel-T (Provenge)

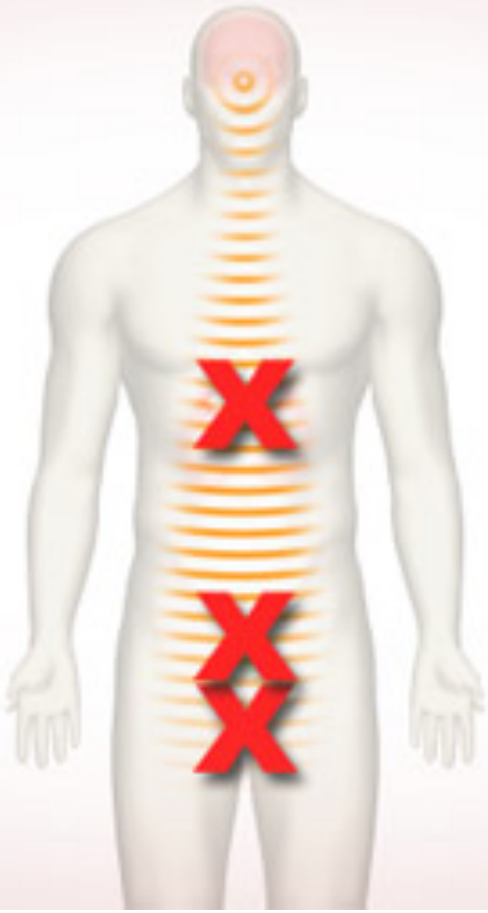
- Cost: $93,000
  - $31,000 per infusion; $23,000 per month of life
  - Insurance may cover, ¼ patients have co-payment up to 22%
- Effectiveness
  - 512 patients
  - Median overall survival: 25.8 months compared to 21.7 months
  - 22% decrease risk of death
  - Median extended survival: 4.1 months

www.prostate.net/2012/prostate-cancer/provenge/
www.xconomy.com/seattle/2010/04/29/dendreon-sets-provenge-price-at-93000-says-only-2000-people-will-get-it-in-first-year/
http://www.provenge.com/reimbursement.aspx

abiaterone (Zytiga)

abiaterone (Zytiga)

- For metastatic, androgen-resistant prostate cancer before or after chemotherapy
- Androgen synthesis inhibitor ("super anti-androgen")
- Blocks production of testosterone early on
  - Testes, adrenal glands and prostate cancer cells
- Drops testosterone lower than any other known treatment
  - Can work even once other forms of androgen blockage have stopped working



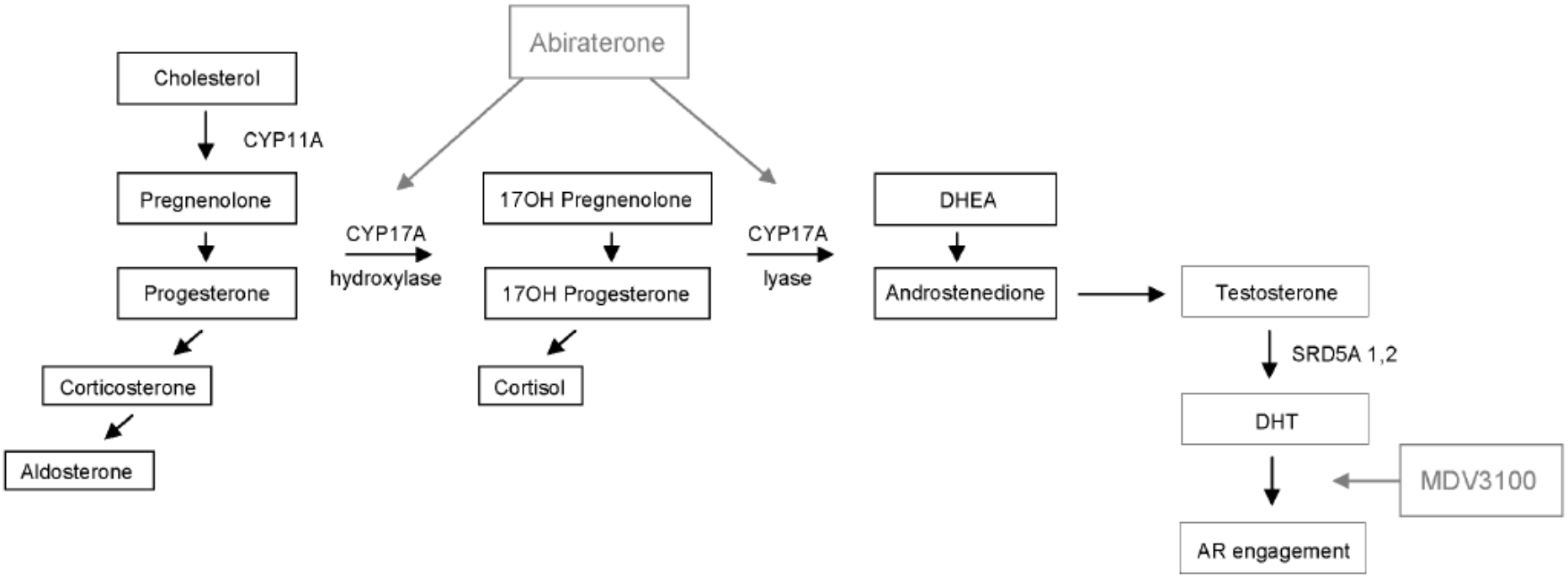
Androgen synthesis inhibitors (“super-antiandrogens”)

abiraterone (Zytiga)

- Blocks testosterone production from from testes, adrenal glands and prostate cancer cells

www.cancer.gov/cancertopics/understandingcancer/targetedtherapies/prostatecancer_htmlcourse/page2

Androgen production



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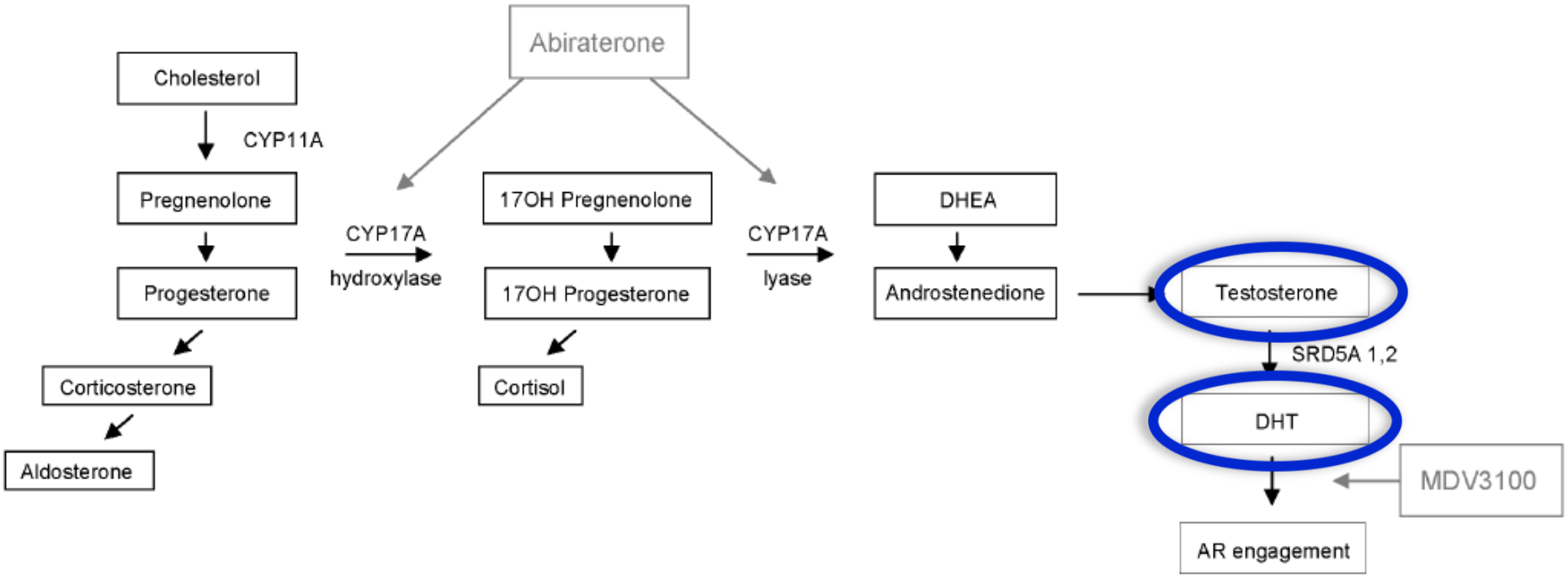
Androgen production



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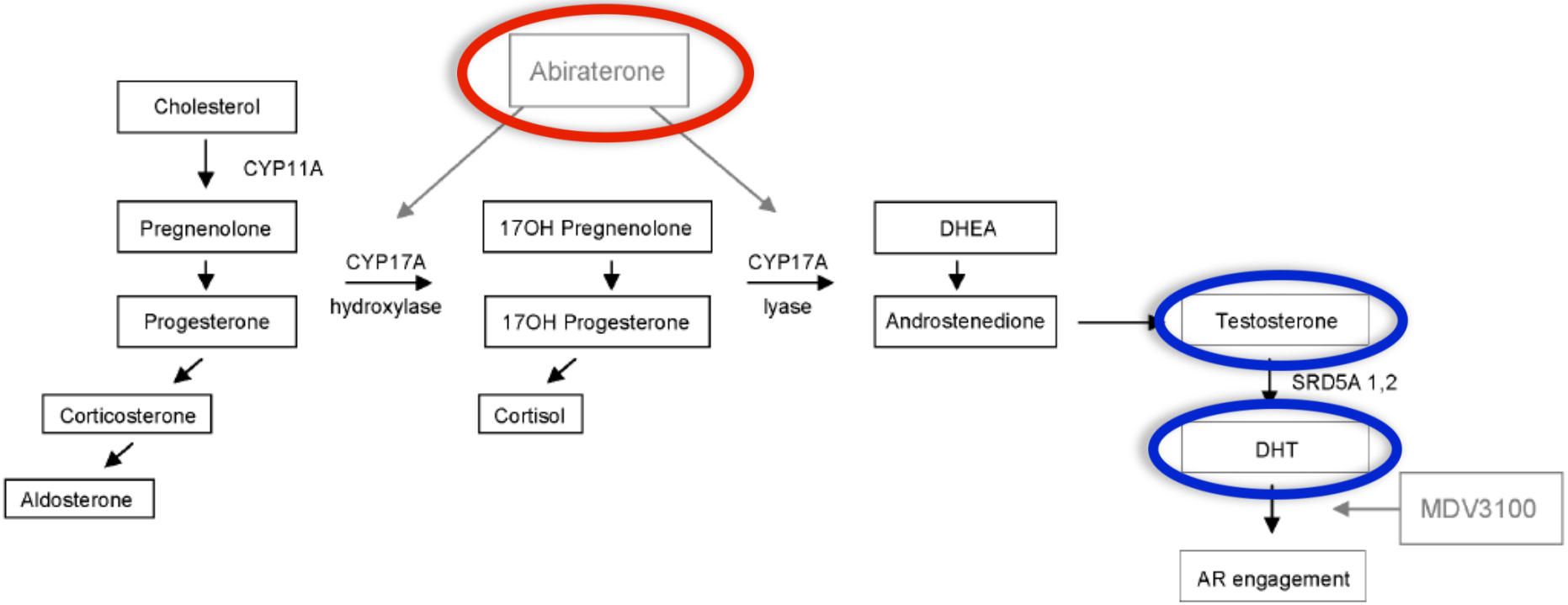

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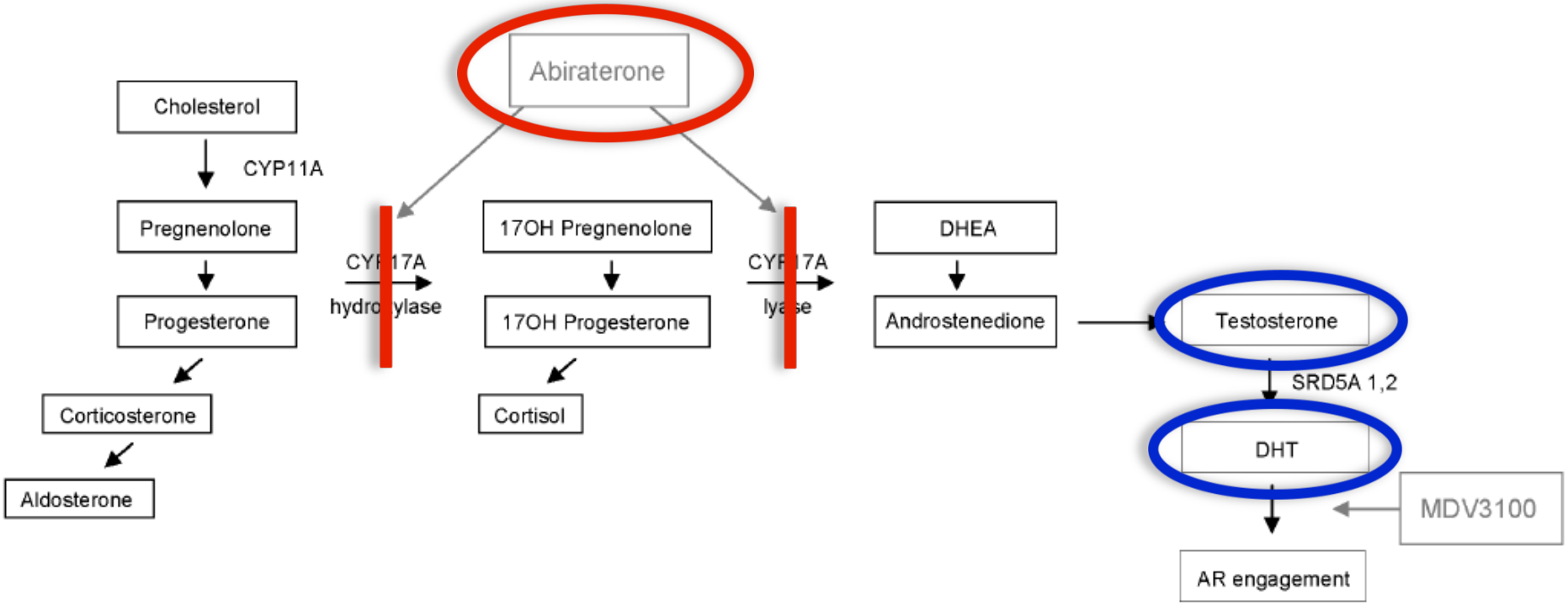
Stops enzymes (CYP17A) from working



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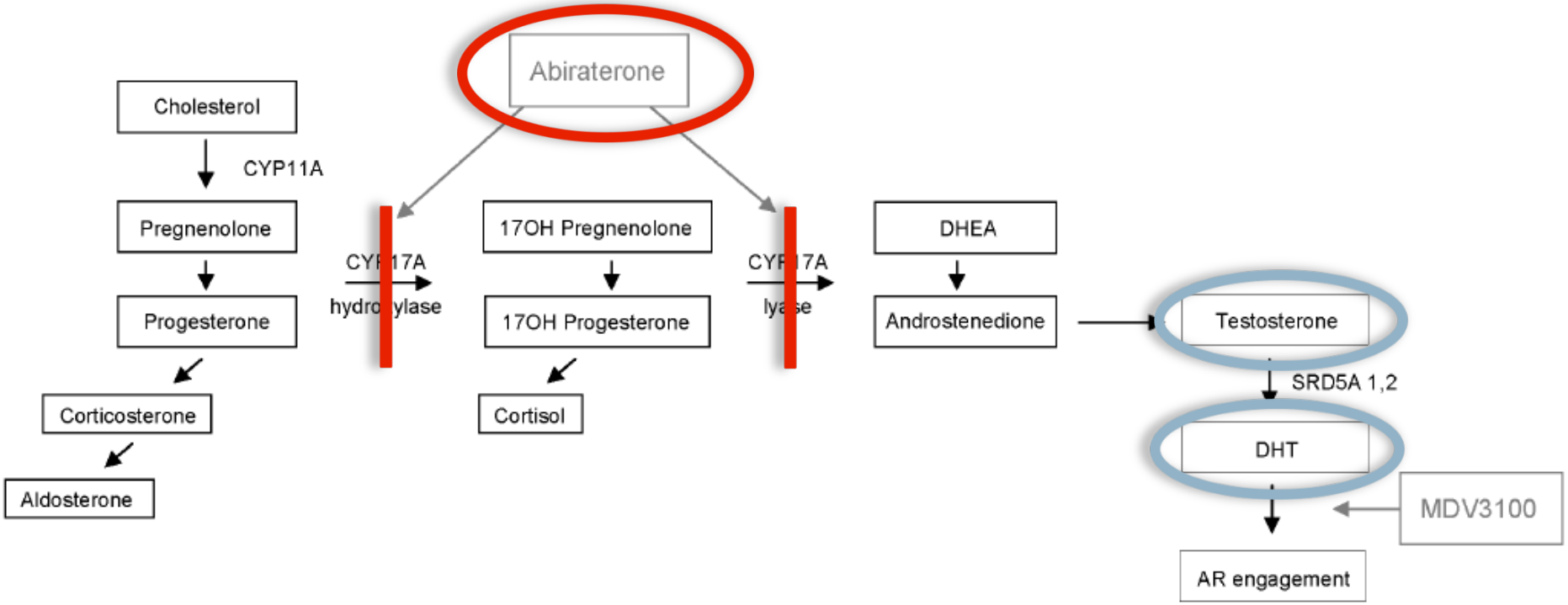
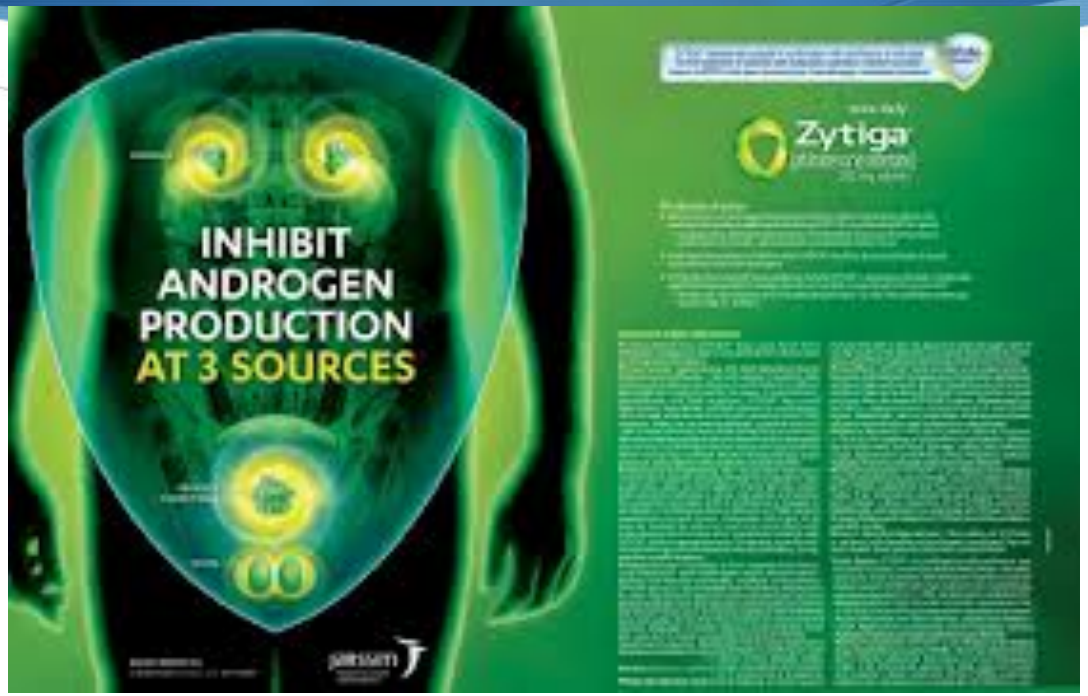
Stops enzymes (CYP17A) from working



Mostaghel EA and Lin DW. Treatment of metastatic prostate cancer: How urologists should sequence available agents. AUA Update Series, Volume 31, Lesson 4. American Urological Association Education and Research, Inc, 2012.

abiaterone (Zytiga)



abiaterone (Zytiga)

- Oral pill that is taken daily with steroid (prednisone) twice daily
- Average treatment period: 8 months.
- Side effects: cough, diarrhea, fluid retention, heartbeat disorders, high blood pressure, hot flashes, joint swelling, low potassium levels, muscle aches, upper respiratory tract infection, upset stomach, urinary frequency, and urinary tract infection.
- Steroid: weakening of the immune system
  - More susceptible to infection

www.prostate.net/2012/prostate-cancer/xtandi-vs-zytiga-comparison/

abiaterone (Zytiga)

- Cost: $5,000 per month
  - Covered by Medicare and most insurance companies
- Effectiveness
  - 1,195 patients
  - Median overall survival 14.8 months compared with 10.9 months
  - Median extended survival: 3.9 months

www.prostate.net/2012/prostate-cancer/xtandi-vs-zytiga-comparison/

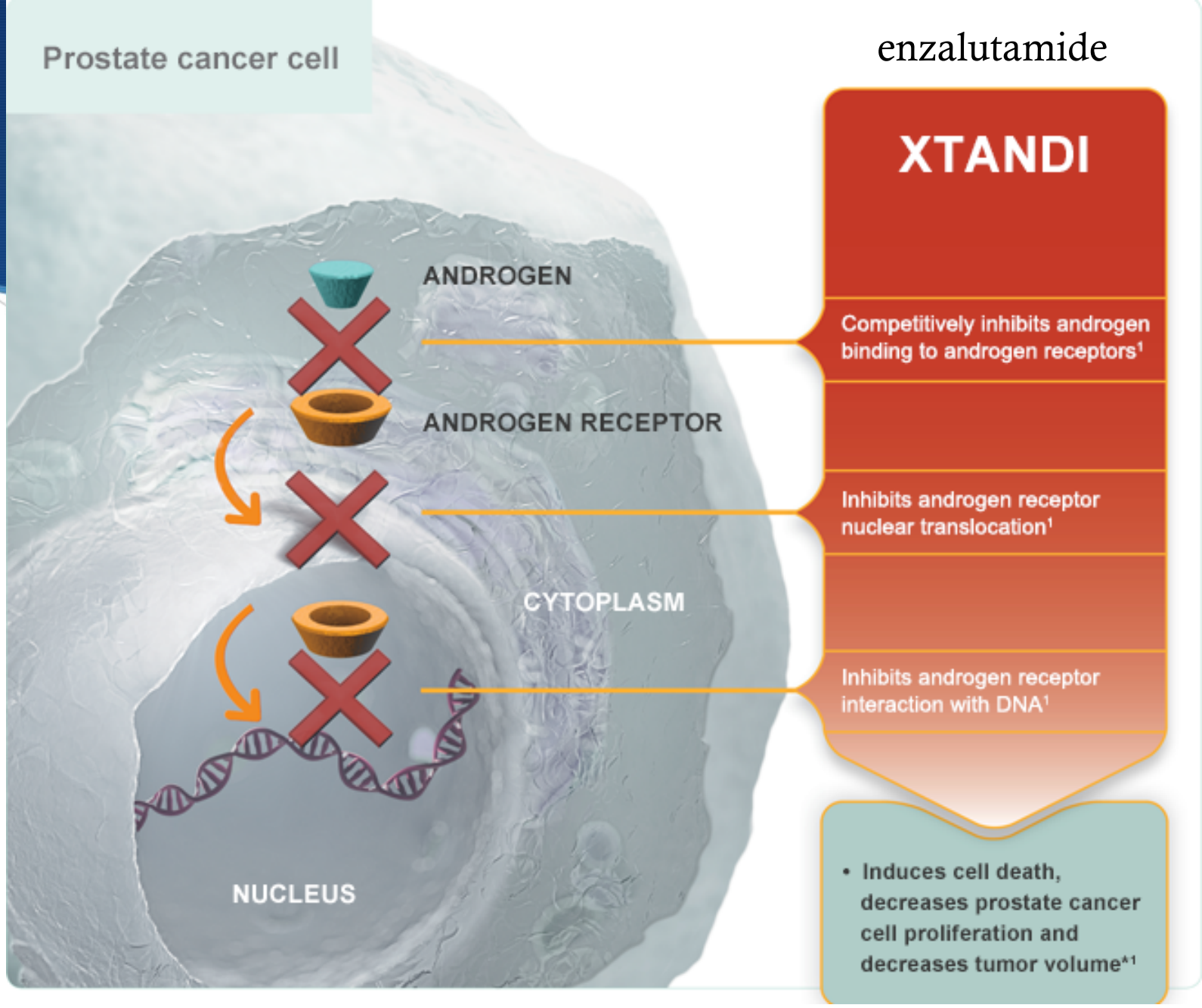
enzalutamide (Xtandi)

enzalutamide (Xtandi)

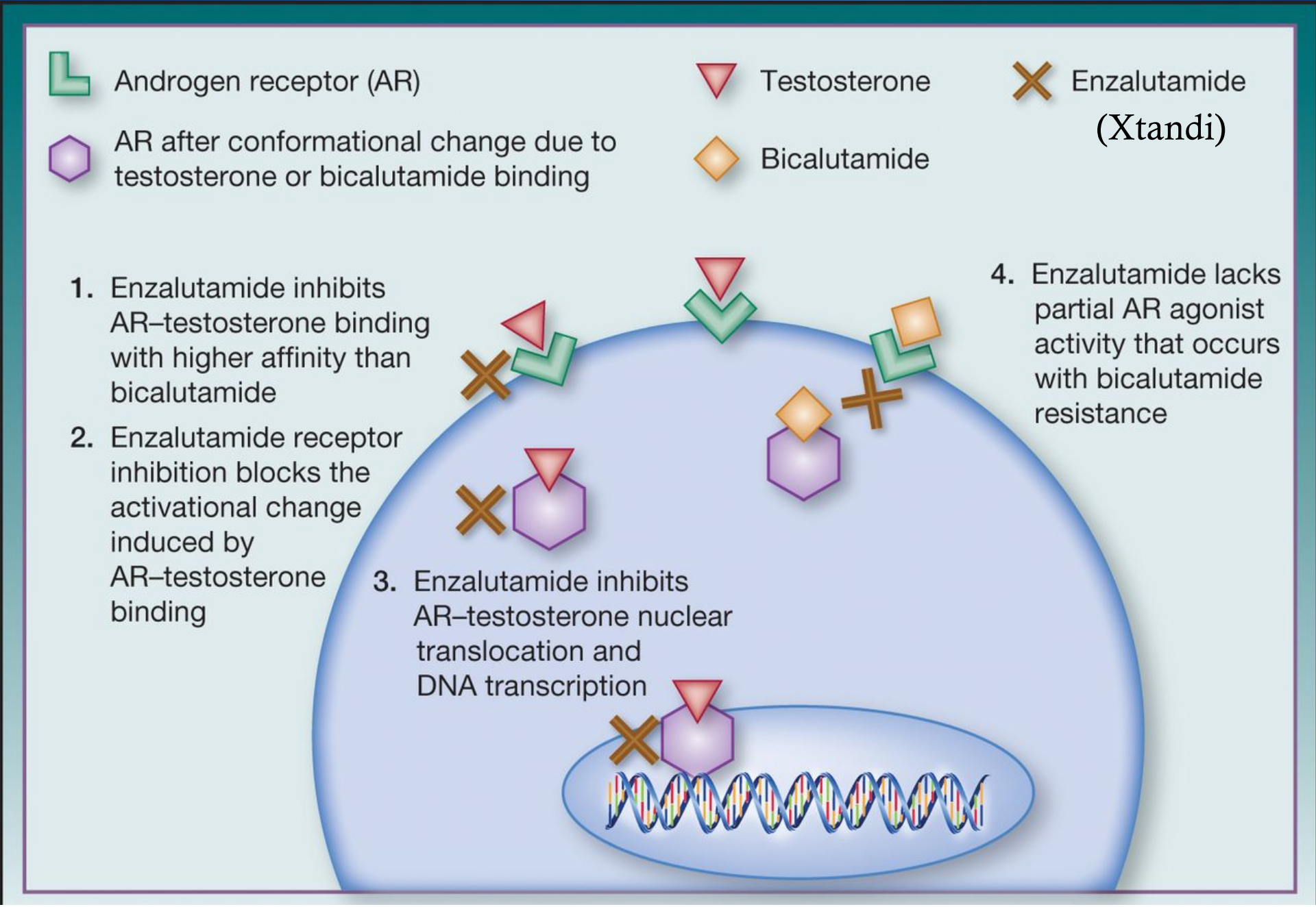
- For metastatic, androgen-resistant prostate cancer after docetaxel chemotherapy
- Androgen receptor blocker, works at several different steps
- Binds androgen receptor 5-8 times stronger than first generation androgen blockers

Mostaghel EA and Lin DW. Treatment of metastatic prostate cancer: How urologists should sequence available agents. AUA Update Series, Volume 31, Lesson 4. American Urological Association Education and Research, Inc, 2012.
NCCN Guidelines for Prostate Cancer

enzalutamide



www.xtandihcp.com/mechanism-of-action



clincancerres.aacrjournals.org/content/19/6/1335/F1.expansion.html

enzalutamide (Xtandi)

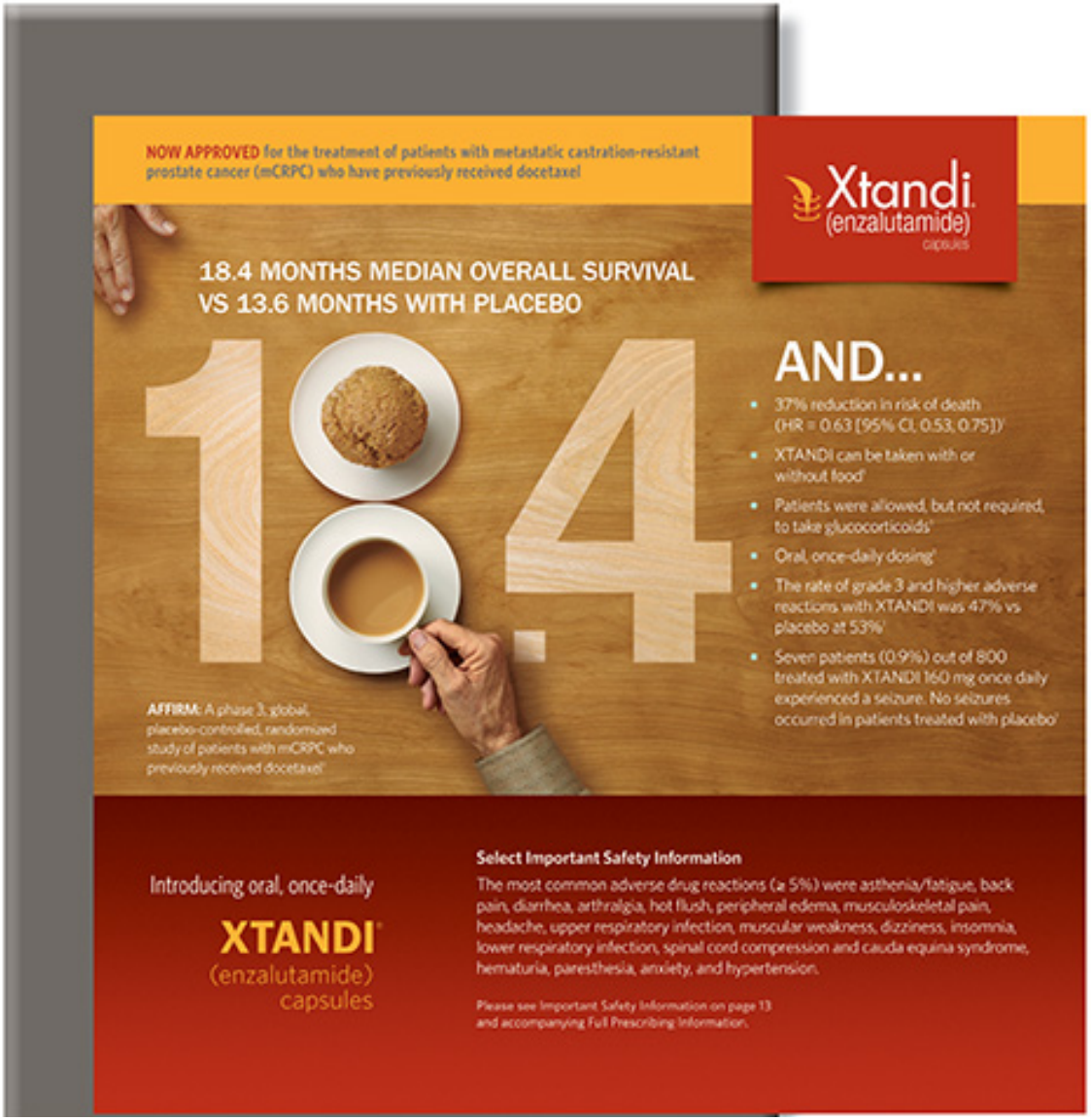
- Oral pill taken daily
- Average treatment period: 8 months
- Side effects: anxiety, back pain, bloody urine, diarrhea, dizziness, fatigue, headache, hot flashes, joint pain, muscle weakness, musculoskeletal pain, respiratory infections, sleep problems, spinal cord compression, tingling sensation, and tissue swelling, seizures (1%)

www.prostate.net/2012/prostate-cancer/xtandi-vs-zytiga-comparison/

enzalutamide (Xtandi)

- Cost: $7,450 per month
  - Medicare and most insurance companies will likely cover but need to check with insurance
- Effectiveness:
  - 1,199 men
  - Median overall survival 18.4 months compared with 13.6 months
  - Median extended survival: 4.8 months

www.prostate.net/2012/prostate-cancer/xtandi-vs-zytiga-comparison/



www.pm360online.com/wp-content/uploads/2013/06/f5_Giant.jpg

Osteoporosis in men

- 7% white men, 5% African-American men, and 3% Hispanic men (Qaseem 2008)
- Risks: hormone therapy (androgen blockage), 65 and older, medications (steroids), not enough calcium, not enough exercise, smoking, excess alcohol, family history, thin
- 20% of men who are on hormone therapy for prostate cancer will experience a fracture within 5 years. (Adler 2011)

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Bone therapy: bisphosphonates

- Slow the rate of bone loss and can also lead to an increase in bone density
- alendronate (Fosamax), ibandronate (Boniva), risedronate (Actonel), and zoledronic acid (Reclast), FDA approved
  - Most orally daily, weekly or monthly
  - ibandronate (Boniva) is typically given IV every 3 months.
  - zoledronic acid (Reclast) is given intravenously yearly
- Effectiveness: 112 men, alendronate for 1 year: bone mineral density had increased in the hip by 2.3%, spine by 5.1%

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Selective estrogen receptor modulator (SERM) medications

- Oppose the actions of estrogen in the body, slow bone thinning, and can cause some increase in bone thickness.
- Two SERMs prescribed for off-label use in men are raloxifene (Evist) and toremifene (Fareston)

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Synthetic parathyroid hormone

- Teriparatide (Forteo) is a synthetic form of the natural parathyroid hormone FDA approved for use in men who have severe osteoporosis
- Forms new bone, increases both bone mineral density and bone strength, reduces the risk of fracture
- Once daily as a subcutaneous injection

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Humanized monoclonal antibody and antiresorptive agent

- Denosumab (Prolia)
- Reducing the activity of a specific receptor activator: RANK (Receptor Activator of Nuclear factor kB) ligand inhibitor
- FDA approval for postmenopausal women with osteoporosis, used off-label for men on hormone therapy
- Increase bone density and decrease vertebral fractures in men on hormone therapy (Adler/Gill 2011)
- Injection given every six months

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Calcitonin

- Naturally occurring hormone that helps regulate calcium levels and slows the rate of bone thinning
- Injection or nasal spray
- Rarely used
  - Possible increased risk of prostate, skin, bone cancer

www.prostate.net/2011/prostate-cancer/prostate-cancer-and-osteoporosis-what-men-should-know/

Radium-223 dichloride (Xofigo)

Radium-223 dichloride (Xofigo)

- Approved by FDA May 15, 2013
- For symptomatic, metastatic, androgen-resistant prostate cancer that has spread to bones but not to other organs
- Delivers radiation to tumor in bone without much damage to surrounding tissues
- Injection monthly for 6 weeks
- Side effects: nausea, diarrhea, vomiting, swelling of arms or legs, low blood cell counts

www.prostate.net/2013/prostate-cancer/xofigo-compared-to-xtandi/

Radium-223 dichloride (Xofigo)

- Cost: $69,000 for complete course
  - New, check with insurance for coverage
- Effectiveness
  - 809 men
  - Median overall survival: 14 months versus 11 months
  - Median extension in survival: 3 months

www.prostate.net/2013/prostate-cancer/xofigo-compared-to-xtandi/
http://www.cancer.org/cancer/news/fda-approves-xofigo-for-advanced-prostate-cancer

Guideline on hormone resistant prostate cancer

- The American Urological Association commissioned an independent group to conduct a review and analysis of the literature on therapies for hormone resistant prostate cancer
- Literature reviewed from 1996 to 2013
- 303 eligible studies included

American Urological Association (AUA) Guideline

Approved by the AUA Board of Directors April 2013

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

CASTRATION-RESISTANT PROSTATE CANCER: AUA GUIDELINE

Michael S. Cookson, Bruce J. Roth, Philipp Dahm, Christine Engstrom, Stephen J. Freedland, Maha Hussain, Daniel W. Lin, William T. Lowrance, Mohammad Hassan Murad, William K. Oh, David F. Penson and Adam S. Kibel

When cancer no longer responds to hormone therapy

- Prostate cancer deaths are typically due to prostate cancer that no longer responds to hormone treatment and has spread throughout the body.
- Historically the average survival for men with this type of cancer was less than two years.
- We now have a variety of new treatments and longer survival.
- Remains an incurable disease.

Which treatment is right for me?

- Symptoms
- Spread of cancer throughout the body (metastasis)
- Performance status
- Previous chemotherapy

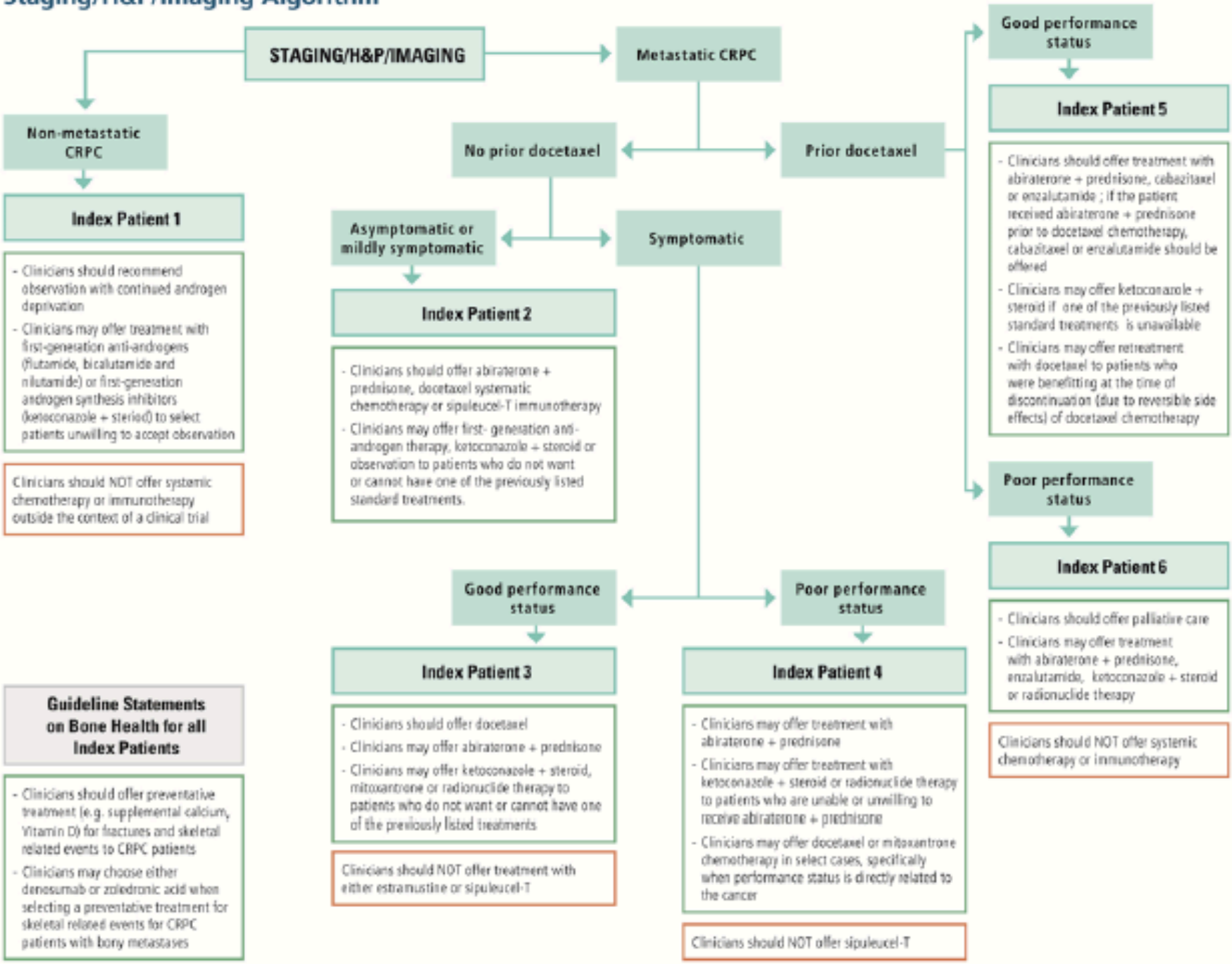
Appendix A: ECOG Performance Status

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

5 Index patients

1. Asymptomatic non-metastatic CRPC
2. Asymptomatic or minimally-symptomatic, mCRPC without prior docetaxel chemotherapy
3. Symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy
4. Symptomatic, mCRPC with poor performance status and no prior docetaxel chemotherapy
5. Symptomatic, mCRPC with good performance status and prior docetaxel chemotherapy
6. Symptomatic, mCRPC with poor performance status and prior docetaxel chemotherapy

Staging/H&P/Imaging Algorithm



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