I: Prostate Cancer: Initial Diagnosis and Treatment

Prostate Cancer Background

- Besides skin cancer, Prostate Cancer (PCa) is the most common cancer in American men.
- In the United States for 2016:
  - 180,890 new cases of PCa are expected
  - 26,120 deaths from PCa are expected
- Estimated cost of PCa care in 2010 was approximately $12B
- PCa is the second leading cause of cancer death in American men
  - One man in 39 will die from PCa

Disclosures

Jane Adams is an employee of Blue Earth Diagnostics, Inc., manufacturer of Axumin (fluorine F18) Injection

The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Agenda

1. Prostate Cancer: Initial Diagnosis and Treatment
2. Biochemically Recurrent Prostate Cancer
3. Detection and Localization of Biochemical Recurrent Prostate Cancer
4. Approved PET Imaging Agents for BCR Prostate Cancer

Prostate Cancer Imaging and Treatment:
List the approved positron emission tomography imaging agents for prostate diagnosis and their clinical application

Jane Adams
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BS Nuclear Pharmacy
Initial Diagnosis of Prostate Cancer

• Process consists of medical history and symptoms review, physical examination, and may include one or more of the tests below.

  • Prostate-specific antigen (PSA) measurement: PSA is a protein produced by the prostate that often is elevated if there is prostate cancer.
  • Digital Rectal Exam (DRE): During a DRE, the doctor gently inserts a lubricated, gloved finger into the rectum to feel for lumps, soft or hard spots, and other abnormalities in the prostate gland.
  • Transrectal Ultrasound (TRUS): Reflected sound waves from ultrasound probe inserted into rectum provide images of the prostate. Used to guide biopsies.
  • Biopsy: Ultrasound-guided removal of tissue samples from the prostate gland. The samples are subsequently analyzed under a microscope for the presence of cancer.

Initial Diagnosis of Prostate Cancer: Prostate-Specific Antigen (PSA)

• Prostate-specific antigen (PSA) measurement:
  • PSA is a protein produced by cells of the prostate and is often elevated in prostate cancer.
  • PSA is detected using a blood test, and is usually reported as nanograms of PSA per milliliter (ng/mL) of blood.\(^1\)
  • The standard PSA reference range is 0.0-4.0 ng/mL.
    1. Normal PSA levels for specific age ranges:\(^2,3\)
      a. 0.2-2.5 ng/mL for age 40-49 years
      b. 0.3-3.5 ng/mL for age 50-59 years
      c. 0.4-4.5 ng/mL for age 60-69 years
      d. 0.6-5.0 ng/mL for age 70-79 years.
  • A number of benign (not cancerous) conditions can cause an elevated PSA level:
    1. Prostatitis (inflammation of the prostate)
    2. Urinary tract infections
    3. Benign prostatic hyperplasia (BPH) (enlargement of the prostate)

Prostate Cancer: Treatment Options

• Treatment(s) selected depend on tumor location, grade and stage

  • Localized:
    1. Active surveillance
    2. Radical prostatectomy (RP)
    3. External beam radiation therapy (EBRT)
    4. Brachytherapy
  • Locally advanced:
    1. Surgery
    2. Radiation therapy (RT)
    3. Hormone therapy
  • Metastatic:
    1. Hormone therapy
    2. Chemotherapy
    3. Novel agents

Recurrent Prostate Cancer

• Up to one-third of men treated for primary prostate cancer will experience biochemical recurrent (BCR) prostate cancer within 10 - 15 years following treatment.\(^2,4\)
• Up to one-third of men demonstrating BCR will develop metastatic disease within 8 years.\(^5\)
• Evidence of recurrent disease is generally based on serial measurement of prostate-specific antigen (PSA) alone.\(^6\)
• Determining the location of the recurrence is critical, as this guides the optimal choice of therapy.
Following Treatment, Monitoring for Disease Recurrence with PSA is Standard of Care

- PSA tests administered:
  - Six weeks post-therapy
  - Every 3 months for 2 years
  - After 2 years, every 6 months
- Multiple thresholds for BCR dependent on type of primary treatment
- PSA levels above 0.2 ng/mL are considered biochemical PCa recurrence (BCR) for patients initially treated with RP
- PSA rise of 2.0 ng/mL above nadir
- PSA tests administered:
  - Every 3 months for 2 years
  - Multiple thresholds for BCR

Recurrent Prostate Cancer: Standard Imaging

- The diagnostic accuracy of standard imaging tests for the identification of sites of recurrence is low:
  - Almost 90% of the standard battery of imaging tests, including CT/MRI and bone scans, may be negative:
  - Some imaging procedures may be unable to detect:
    - Recurrent prostate tumor <1 cm in size
    - When PSA levels are <20 ng/mL
- More accurate, non-invasive imaging techniques for the detection of recurrent cancer are needed.

Local Salvage in BCR

- For presumed local BCR, potentially curative salvage options include:
  - Radiotherapy (RT), post surgery
  - Surgery+/-lymph node dissection (LND), post radiotherapy
  - Cryo, brachy, or high intensity focused ultrasound (HIFU) post therapy
- Long term biochemical control ranges between 30-70%
- RT expansion from prostate bed to pelvis may benefit some patients
- In general, failure and morbidity remain significant
- Better risk prediction and more efficient markers of progression are desperately needed

Systemic Treatment in BCR

- Although local treatment is increasing, most patients with PSA failure/progression eventually receive ADT, especially after RT:
- Although NCCN guidelines are clear on the use of ADT in metastatic disease, the recommendations for BCR without radiological evidence of metastases are more complex and confusing:
  - ADT can delay disease progression but is not curative and increasingly associated with negative sequelae such as:
    - Sexual dysfunction, hot flashes, osteoporosis and fracture, diabetes, kidney injury and cardiovascular disease
  - There is also increasing interest in use of taxol chemotherapy in BCR patients

Follow BCR, Clinically Recurrent Disease May Be Detected by Imaging Technologies*

- Currently employed techniques include:
  - Transrectal ultrasound (TRUS)
  - Computed tomography (CT)
  - Anatomical magnetic resonance imaging (MRI)
  - Advanced multi-parametric MRI (mpMRI)
  - Skeletal scintigraphy (bone scan)
  - Prostascint®
- No consistent and comprehensive imaging guidelines or appropriate use criteria exist:
- EAU recommends bone scan should be performed in symptomatic patients, independent of PSA level, Gleason score or clinical staging
- NCCN recommends bone scan for rapidly increasing PSA

*FET imaging reviewed in Section 4

III: Prostate Cancer: Detection and Localization of Biochemical Recurrent Prostate Cancer
**Summary of Imaging Techniques for Recurrent Prostate Cancer**

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*Indicate relative frequency of use

**Note:** Pelvic CT or MRI and bone scan are the most commonly used tests, indicating relative frequency of use.

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**99mTc Bone Scintigraphy is the Mainstay of Diagnosis of Bone Metastases**

- 99mTc method diphosphonate (MDP) is a marker of osteoblastic activity secondary to presence of cancer.
- Locators along mineralization fronts.
- Optically metastases at an advanced stage of tumor infiltration.
- Has lower spatial resolution than PET images with 18F NaF and has limited specificity.
- Bone trauma/injuries can appear positive.
- Bone healing responses after lesion treatment may look like progression (also known as LIES).
- Use of SPECT rather than planar imaging and addition of CT may improve performance.

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**Indium In 111 ProstaScint (Capromab Pendetide)**

- FDA Approved Indications for Use
  - Indium In 111 ProstaScint (Capromab Pendetide) is indicated as a diagnostic imaging agent in newly diagnosed patients with biopsy-proven prostate cancer, thought to be clinically localized after standard diagnostic evaluation (eg chest x-ray, bone scan, CT scan, or MRI), who are at high risk for pelvic lymph node metastases. It is not indicated for patients who are not at high risk.
  - Indium In 111 ProstaScint is also indicated as a diagnostic imaging agent in post-prostatectomy patients with a rising PSA and a negative or equivocal standard metastatic evaluation in which there is a high clinical suspicion of occult metastatic disease. The imaging performance of Indium In 111 ProstaScint following radiation therapy has not been studied.
  - The information provided by Indium In 111 ProstaScint imaging should be considered in conjunction with other diagnostic information. Scans that are positive for metastatic disease should be confirmed histologically in patients who are otherwise candidates for surgery or radiation therapy unless medically contraindicated. Scans that are negative for metastatic disease should not be used in lieu of histological confirmation.
  - ProstaScint is not indicated as a screening tool for carcinoma of the prostate nor for neoadministration for the purpose of assessment in response to therapy.

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**IV: Prostate Cancer: PET/CT Approved Imaging Agents**

- PET/CT can play an important role in the evaluation of prostate cancer:
  - Detecting metastatic disease
  - Restaging
  - Biochemical recurrence
  - Monitoring of treatment
  - Use in primary staging generally limited only to high risk disease
- PET Imaging Agents used in Prostate Cancer
  - F-18 FDG
  - F-18 NaF
  - C-11 Choline
  - Fluorovine F18 injection
18F FDG Injection for Intravenous Use

Indications and usage

- Fludeoxyglucose F 18 injection (18F FDG) is indicated for positron emission tomography (PET) imaging in the following settings:
  - **Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
  - **Cardiology:** For the identification of left ventricular myocardium with normal glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
  - **Neurology:** For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Limitations

FDG

While

Indications

Sodium


FDG

has

Positron

Significant

PCa,

FDG Injection; (PET) imaging of bone to define areas of altered osteogenic activity.1

Important Safety Information

- **Radiation Risk:** Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.
- **Blood Glucose Abnormalities:** In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to ensure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.
- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

18-F Fludeoxyglucose (FDG) Has Multiple Limitations in Detecting Prostate Cancer

Indications and usage

- While FDG is the most commonly employed PET tracer in oncology, it has multiple limitations in detecting prostate cancer (PCa):
  - PCa, unlike most malignancies, is characterized by low glycolysis and low FDG avidity on PET imaging.1
  - Low sensitivity for both regional spread and recurrent disease.
  - Significant overlap between FDG uptake in PCa and benign prostate hyperplasia1,2
  - Intense activity in urine, causes urinary bladder to obscure pelvis, interfering with identification of pelvic lymph nodes.
  - FDG may have some utility in late stage castrate-resistant metastatic prostate cancer.2
  - Castrate-resistant PCa (CRPC) is defined by disease progression despite androgen-deprivation therapy (ADT) and may present as one or any combination of a continuous rise in serum levels of PSA, progression of pre-existing disease, or appearance of new metastases.

18-F NaF PET-CT is Employed to Detect/Localize PCa Bone Metastases

**Indications and Usage**

- Sodium Fluoride F 18 injection is indicated for diagnostic positron emission tomography (PET) imaging of bone to define areas of altered osteogenic activity.1

**Important Safety Information**

- **Allergic Reactions:** As with other radiopharmaceuticals, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available.
- **Cancer Risk:** Sodium Fluoride F 18 injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.
- **Adverse Reactions:** No adverse reactions have been reported for Sodium Fluoride F 18 injection based on the available literature, publicly available reference sources, and adverse drug reaction reporting systems.

18F NaF Dosage and Administration

- Minimal patient preparation, no dietary restrictions, no activity restrictions
- Inject 8 to 12 mCi 18F NaF (adult) or 0.5 to 4 mCi (pediatric weight based dose)
- Encourage patient to drink fluids
- Encourage the patient to void immediately prior to imaging to evaluate suspected disease in the pelvic region
- Imaging can begin 1-2 hours after administration (optimally at 1 hour post administration)
- Image whole body or selected body areas, dependent on clinical indication

Sodium Fluoride F 18 Injection

Clinical studies- metastatic bone disease

- The doses used in reported studies ranged from 2.7 mCi to 20 mCi (100 MBq to 740 MBq), with an average median dose of 10 mCi (370 MBq) and an average mean dose of 9.2 mCi (340 MBq).
- In PET imaging of bone metastases with Sodium Fluoride F 18 Injection, locally increased tracer uptake is seen in both osteolytic and osteoblastic bone lesions.
- Negative PET imaging results with Sodium Fluoride F 18 Injection do not preclude the diagnosis of bone metastases.
- As benign bone lesions are also detected by Sodium Fluoride F 18 Injection, positive PET imaging results cannot replace biopsy to confirm a diagnosis of cancer.
Choline C11 PET Has a Role in the Detection/Localization of PCa

**INDICATIONS AND USAGE**
- Choline C11 Injection is a radioactive diagnostic agent for positron emission tomography (PET) imaging of patients with suspected prostate cancer recurrence and non-informative bone scintigraphy, computed tomography (CT) or magnetic resonance imaging. In these patients, 11C-choline PET imaging may help identify potential sites of prostate cancer recurrence for subsequent histologic confirmation. Suspected prostate recurrence is based upon elevated blood prostate specific antigen (PSA) levels following initial therapy. In clinical studies, images were produced with PET/CT coregistration.
- Limitation of Use: 11C-choline PET imaging is not a replacement for histologic verification of recurrent prostate cancer.

**Pharmacology**
- **Pharmacodynamics**
  - In a study of men with prostatic hyperplasia or primary prostate cancer, PET imaging showed 11C-choline radioactivity accumulated rapidly within the prostate.
  - Uptake appeared to peak by five minutes following injection of the drug and activity was retained over the subsequent 30 minute scanning period.
  - Little uptake was observed in the bladder and rectum.
- **Pharmacokinetics**
  - 11C-choline distributes mainly to the pancreas, kidneys, liver, spleen and colon.
  - Based upon the relatively low urinary excretion of radioactivity, renal distribution is predominantly to the organ itself, rather than via formation of urine.

**Pharmacodynamics**
- **Choline C11: Important Safety Information**
  - **Contraindications**
    - None
  - **Warnings and Precautions**
    - Imaging errors have been reported; blood PSA levels < 2 ng/mL have been associated with poor imaging performance.
    - Allergic reactions have been reported. Ensure safe handling to protect the patient and healthcare worker.
    - **Adverse Reactions**
      - Diaphoresis of an uncommon, mild injection site reaction, no other adverse reactions have been reported.
      - Drug Interactions
        - Choline and androgen deprivation therapeutic drugs may interfere with 11C-choline PET/CT imaging performance.
      - To report SUSPECTED ADVERSE REACTIONS, contact Zevaco Corporation at 844-364-4478 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**Pharmacodynamics**
- **Choline C11: Description**
  - Choline C11 injection is a positron emitting radiopharmaceutical that is used for diagnostic purposes in conjunction with PET imaging. The active ingredient, 11C-choline, has the molecular formula of C4H14NClO with a molecular weight of 136.63 g and has the following chemical structure:
  
  \[
  \text{CH}_3 \hspace{1cm} \left[ \text{H}_3\text{C}^1\text{C}-\text{N}^\cdot-\text{CH}_2\text{CH}_2\text{OH} \right]^\text{Cl}^- \\
  \text{CH}_3
  \]

  - Carbon 11 is a cyclotron-produced radionuclide that decays to Boron 11 by positron emission and has a physical half life of 20.4 minutes.

**Pharmacodynamics**
- **Choline C11: Mechanism of Action**
  - Choline 11 injection is a radiolabeled analog of choline, a precursor molecule essential for the biosynthesis of cell membrane phospholipids.
  - Choline is involved in synthesis of the structural components of cell membranes, as well as modulation of trans-membrane signaling.
  - Increased phospholipid synthesis (i.e., increased uptake of choline) has been associated with cell proliferation and the transformation process that occurs in tumor cells.

**Pharmacodynamics**
- **Choline C11: Clinical Pharmacology**
  - **Pharmacodynamic**
    - Administer 370 to 740 MBq (10 to 20 mCi) as a bolus intravenous injection.
    - The radioactivity dose (370 to 740 MBq, 10 to 20 mCi) is chosen based on patient body dimensions and the characteristics of the image acquisition system.
    - Initiate imaging immediately after administration of Choline C11 Injection and acquire static emission images 0 to 15 minutes from the time of injection.
    - The effective radiation absorbed dose from 740 MBq (20 mCi) dose of Choline C11 Injection is approximately 3.22 mSv (0.32 rem) in an adult.
Choline C11: Clinical Studies

- A systematic review of published reports identified four studies that contained data sufficient to compare 11C-choline PET imaging to histopathology (truth standard) among patients with suspected prostate cancer recurrence and non-informative conventional imaging (for most patients, CT or MRI).

  - In general, the suspected recurrence criteria consisted of at least two sequential PSA levels of >0.2 ng/mL for men who had undergone prostatectomy and PSA levels of >2 ng/mL above the posttherapy nadir for men who had undergone radiation therapy.
  - The studies were predominantly single-center experiences and image acquisition generally surveyed radioactive distribution from the base of the pelvis to the base of the skull.

Clinical Studies: Study 1

- In Study One:
  - 25 patients who underwent 11C-choline PET/CT and conventional imaging (CT or MRI) were scheduled to undergo pelvic or pelvic plus retropelvic lymphadenectomy following the imaging identification of suspected lymph node metastases.
  - The median PSA was 2.0 ng/mL (range 0.2 to 23.1 ng/mL).
  - The study excluded subjects with metastatic disease detected by bone scintigraphy or isolated prostatic fossa recurrence.
  - Among the 25 patients:
    - 22 had positive 11C-choline PET/CT scans; histopathology verified cancer in 19 of these patients.
    - Lymph node histopathology detected no cancer among the four patients who had surgery based only on positive conventional imaging.
    - 11C-choline PET/CT was negative in all four patients.
  - The study report included information for patients who had noninformative conventional imaging (CT or MRI, bone scintigraphy and transrectal ultrasound).

Clinical Studies: Study 2

- In Study Two:
  - 15 patients were scheduled to undergo pelvic or pelvic plus retropelvic lymphadenectomy solely based upon positive 11C-choline PET/CT imaging in the setting of negative conventional imaging (ultrasound and/or CT and/or MRI and/or bone scintigraphy).
  - The median PSA was 2.0 ng/mL (range 1.0 to 8.0 ng/mL); all patients had previously undergone radical prostatectomy.
  - Eight of the 15 patients had cancer verified by lymph node histology; histology detected no cancer in seven patients.

Clinical Studies: Study 3

- Retrospective Studies: Two studies were retrospective reviews of patients who underwent 11C-choline PET/CT and had histopathology obtained from biopsy of the prostatic fossa or other suspected recurrence sites.

  - In Study Three:
    - 11C-choline PET/CT imaging was performed among 36 patients with suspected prostate cancer recurrence and 13 subjects without suspected recurrence (controls). Prostatic fossa biopsies were performed among the patients with suspected recurrence.
    - All the patients and control subjects had previously undergone radical prostatectomy. None of the patients and only one control subject had no evidence of cancer during conventional clinical evaluations, including transrectal ultrasound and bone scintigraphy.
    - PET/CT scans were interpreted by readers masked to clinical information. Median PSA was 2.0 ng/mL (range 0.1 to 12.1 ng/mL) for patients with suspected recurrence and 0.1 ng/mL (range 0.0 to 0.2 ng/mL) for control subjects.
    - Prostatic fossa biopsy showed cancer in 33 of the 36 patients with suspected recurrence. PET/CT scans were positive in 25 of the 36 patients; two patients underwent surgery, and cancer was confirmed in both patients. Among the 11 control subjects, 0 had positive 11C-choline PET/CT scans.

Clinical Study: Study 4

- In Study Four:
  - 34 patients with negative conventional imaging underwent 11C-choline PET/CT and subsequently had biopsies of suspected recurrence sites.
  - The median PSA level of the 34 patients was 3.9 ng/mL (range 0.2 to 65.0 ng/mL).
  - 12 of the patients had previously undergone radical prostatectomy.
  - 12 had received other therapy (radiotherapy, anti-androgen therapy or cryotherapy).
  - 11C-choline PET/CT images were positive in 30 patients and negative in four patients.
  - Cancer was verified by histopathology in 29 patients.
  - 25 had positive PET/CT images and four had negative PET/CT images.
  - Five patients with positive PET/CT images did not have cancer confirmed with histopathology.
Clinical Study:

**Axumin™**

**Important Axumin™**

- FDA approved at Mayo Clinic 2012
- 11-C choline has demonstrated usefulness in detecting
- Choline uptake and incorporation into cell membranes is

**Imaging and Histopathology Truth Standard**

C11 – Choline PET/CT among Patients with Non-informative Conventional

Clinical Study Data

- In Studies Three and Four, PSA levels were generally lower for
  patients with negative 11C-choline PET/CT results than for
  patients with positive results.
  - In Study Three
    - The median PSA was 2.6 ng/mL (range 0.6 - 12.1 ng/mL) among the 25
    - Nine out of 11 patients with false negative or false positive images had PSA
    - .1 ng/mL
  - In Study Four
    - The median PSA was 6.2 ng/mL (range 0.2 - 65.0 ng/mL) among the 25
    - PSA levels < 2 ng/mL were observed in four of the nine patients with false
    - negative or false positive images.
  - These data, combined with other published reports, suggest
  that 11C-choline PET imaging performance may be more
  reliable among patients with blood PSA levels > 2 ng/mL,
  compared to patients with lower levels

Summary: Choline C11 PET Has an Emerging Role in the Detection/Localization of PCa

- Choline uptake and incorporation into cell membranes is increased in malignant tissues1
- 11-C choline has demonstrated usefulness in detecting distant metastases2
- FDA approved at Mayo Clinic 2012
- FDA approval required for each 11-C choline manufacturing site added to new drug application (NDA)
- Twenty-minute half-life necessitates production near site of patient administration (necessity for in-house or nearby cyclotron)

Axumin™ (fluciclovine F 18) Injection Indication

- Axumin™ (fluciclovine F 18) injection is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment.1

Axumin™ (fluciclovine F 18) Injection Important Safety Information

- Image interpretation errors can occur with fluciclovine PET imaging. A negative image does not rule out recurrent prostate cancer and a positive image does not confirm its presence.
- The performance of fluciclovine seems to be affected by PSA levels. Fluciclovine uptake may occur with other cancers and benign prostate hyperplasia or primary prostate cancer.
- Clinical correlation, which may include histopathological evaluation, is recommended.
- Hypersensitivity reactions, including anaphylaxis, may occur in patients who have received fluciclovine. Emergency resuscitation equipment and personnel should be immediately available.
- Fluciclovine use contributes to a patient’s overall long-term cumulative radiation exposure, which is associated with an increased risk of cancer. Safe handling practices should be used to minimize radiation exposure to the patient and health care providers.
- Adverse reactions were reported in 0.1% of subjects during clinical studies with fluciclovine. The most common adverse reactions were injection site pain, injection site erythema and edema.
- To report suspected adverse reactions to Axumin, call 1-855-450-AXUMIN (1-855-450-2966) or contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
- Please see full prescribing information at www.axumin.com. A hard copy of the Axumin Prescribing Information will also be distributed to you at the presentation.

Axumin: First F 18 Agent for PET Imaging in Biochemically Recurrent Prostate Cancer

- Fluciclovine F 18 is an synthetic amino acid PET imaging agent labelled with
  F18 (molecular weight 132).
- Recognized and taken up by amino acid transporters that are upregulated in many cancer cells, including prostate cancer.
- Fluciclovine F 18 is not metabolized or incorporated into newly synthesized proteins.
Axumin Chemical Structure

Axumin™ (fluciclovine F 18): Dosing, Administration & Image Acquisition

- Recommended dose is 370 MBq (10 mCi) administered as an intravenous (IV) bolus injection, followed by IV saline flush
- Avoid any significant exercise for at least one day prior to PET imaging
- Fast for at least 4 hours prior to administration
- Inject on PET scanner table
- Position the patient supine with arms above the head.
- CT for attenuation correction & anatomic correlation
- Begin PET scanning 3 to 5 minutes after completion of injection.
- Start acquisition at mid-thigh and proceed to the base of the skull.
- Typical total scan time is between 20 to 30 minutes

Axumin: Pharmacodynamics

- Imaging: begin within 3-5 minutes; complete within 20 – 30 minutes.

Axumin: Clinical Studies

- The safety and efficacy evaluated in two studies (Study 1 and Study 2) in men with suspected recurrence of prostate cancer, based on rising PSA levels following radical prostatectomy and/or radiotherapy.
- Study 1 evaluated 105 fluciclovine F 18 PET scans in comparison to histopathology obtained by biopsy of the prostate bed and biopsies of lesions suspicious by imaging. PET/CT imaging generally included the abdomen and pelvic regions. Images were originally read by on-site readers.
- In Study 2, 96 fluciclovine and 111 choline images were compared. The choline scans were read by on-site readers and the fluciclovine F 18 scans were read by the Study 1 blinded readers.

Axumin: Bio-distribution

- Amino acid (AA) transporters ubiquitous throughout body, upregulated in prostate cancer
- Distribution after IV dosing:
  - Liver: 15%
  - Kidney: 12%
  - Intestines: 1%
  - Brain: 3%
- Percent excreted in urine:
  - 1% by 4 hrs, post-injection

Axumin: Clinical Study 1

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Axumin: Clinical Studies Summary

- Images from 105 scans were evaluated by three independent readers who were unaware of the clinical details of each patient or whether the biopsy of the prostate gland was positive or negative for cancer.
- On average, a correct image finding was identified in 77% of patients (range: 75%-79%).
- For cancer outside the region of the prostate, a correct image finding for cancer was identified in an average of 60% of patients (range: 28%-92%).
- The results seem to be affected by PSA levels, with, in general, lower PSA levels in patients with negative scans than in those with positive scans. In patients with PSA levels ≤1.78 ng/mL, 10 of 25 had a positive scan, with 11 confirmed as positive by biopsy. In patients with PSA levels >1.78 ng/mL, only 1 of 10 had a positive scan, of which 5 were confirmed as positive.
- Agreement between fluciclovine and choline ranged from 61% to 77%.

Axumin™ (fluciclovine F 18) Case Study

- Post-radical prostatectomy, negative lymphadenectomy
- Rising PSA to 0.73 ng/mL
- Negative MRI for malignancy
- Negative digital rectal examination
- Imaging result:
  - left presacral node

Axumin™ (fluciclovine F 18) Summary

- There is a clinical need for new tools for the detection of biochemically recurrent prostate cancer.
- The diagnostic accuracy of standard imaging tests for the identification of sites of recurrence is low.
- Axumin contains fluciclovine, a fluorine (F 18) labeled synthetic amino acid analog with a 110 minute half life.
- Shown in clinical studies to be effective at detecting recurrent prostate cancer.
- Adverse reactions were reported in ≤3% of subjects during clinical studies. The most common adverse reactions were injection site pain, injection site erythema, and dysgeusia (abnormal sense of taste).
- Typical PET/CT scan time is 20 to 30 minutes.
- 110 minutes half life expands provider access through Siemens’ PETNET Solutions.