cERianna™
(FLUOROESTRADIOL F 18) INJECTION

CERIANNA USER'S GUIDE

The only Estrogen-Receptor
Targeted Radiotracer that enables

SEEING CLEAR ER+

Cerianna PET reveals whole-body ER+ lesion status in patients with recurrent or metastatic breast cancer that may help guide clinical decisions.

INDICATIONS AND USAGE

CERIANNA is indicated for use with positron emission tomography (PET) imaging for the detection of estrogen receptor (ER)-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer.

Limitations of Use

Tissue biopsy should be used to confirm recurrence of breast cancer and to verify ER status by pathology. CERIANNA is not useful for imaging other receptors, such as human epidermal growth factor receptor 2 (HER2) and the progesterone receptor (PR).

CONTRAINDICATIONS

None.

ADVERSE REACTIONS

In Clinical Trials (n=1207) the most common adverse reactions seen occurred at a rate <1%: were injection-site pain and dysgeusia.

Please see additional Important Safety Information on inside front cover. Full Prescribing Information is available on Cerianna.com/PI, in the pocket of this piece, or from your GE Healthcare representative.

cERianna™
(FLUOROESTRADIOL F 18) INJECTION

Important Safety Information **Continued**

WARNINGS AND PRECAUTIONS

Risk of Misdiagnosis

Inadequate Tumor Characterization and Other ER-Positive Pathology: Breast cancer may be heterogeneous within patients and across time. CERIANNA images ER and is not useful for imaging other receptors such as HER2 and PR. The uptake of fluoroestradiol F18 is not specific for breast cancer and may occur in a variety of ER-positive tumors that arise outside of the breast, including from the uterus and ovaries. Do not use CERIANNA in lieu of biopsy when biopsy is indicated in patients with recurrent or metastatic breast cancer.

False Negative CERIANNA Scan: A negative CERIANNA scan does not rule out ER-positive breast cancer. Pathology or clinical characteristics that suggest a patient may benefit from systemic hormone therapy should take precedence over a discordant negative CERIANNA scan.

Radiation Risks

Diagnostic radiopharmaceuticals, including CERIANNA, expose patients to radiation. Radiation exposure is associated with a dose-dependent increased risk of cancer. Ensure safe drug handling and patient preparation procedures (including adequate hydration and voiding) to protect patients and health care providers from unintentional radiation exposure.

Pregnancy Status

Assessment of pregnancy status is recommended in females of reproductive potential before administering CERIANNA.

ADVERSE REACTIONS

In Clinical Trials (n=1207) the most common adverse reactions seen occurred at a rate <1%: were injection-site pain and dysgeusia.

USE IN SPECIFIC POPULATIONS

Pregnancy Risk Summary

All radiopharmaceuticals, including CERIANNA, have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of radiation dose. Advise a pregnant woman of the potential risks of fetal exposure to radiation from administration of CERIANNA.

There are no available data on CERIANNA use in pregnant women. No animal reproduction studies using fluoroestradiol F18 have been conducted to evaluate its effect on female reproduction and embryo-fetal development.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation Risk Summary

There are no data on the presence of fluoroestradiol F18 in human milk, or its effects on the breastfed infant or milk production. Lactation studies have not been conducted in animals. Advise a lactating woman to avoid breastfeeding for 4 hours after CERIANNA administration in order to minimize radiation exposure to a breastfed infant.

Pediatric Use

The safety and effectiveness of CERIANNA in pediatric patients have not been established.

Geriatric Use

Clinical studies of fluoroestradiol F18 injection did not reveal any difference in pharmacokinetics or biodistribution in patients aged 65 and over.

DRUG INTERACTIONS

Systemic Endocrine Therapies that Target Estrogen Receptors

Certain classes of systemic endocrine therapies, including ER modulators and ER down-regulators, block ER, reduce the uptake of fluoroestradiol F18, and may reduce detection of ER-positive lesions after administration of CERIANNA. Drugs from these classes such as tamoxifen and fulvestrant may block ER for up to 8 and 28 weeks, respectively. Do not delay indicated therapy in order to administer CERIANNA. Administer CERIANNA prior to starting systemic endocrine therapies that block ER.

To report SUSPECTED ADVERSE REACTIONS, contact Zionexa US Corp, a GE Healthcare Company at +1.800.654.0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

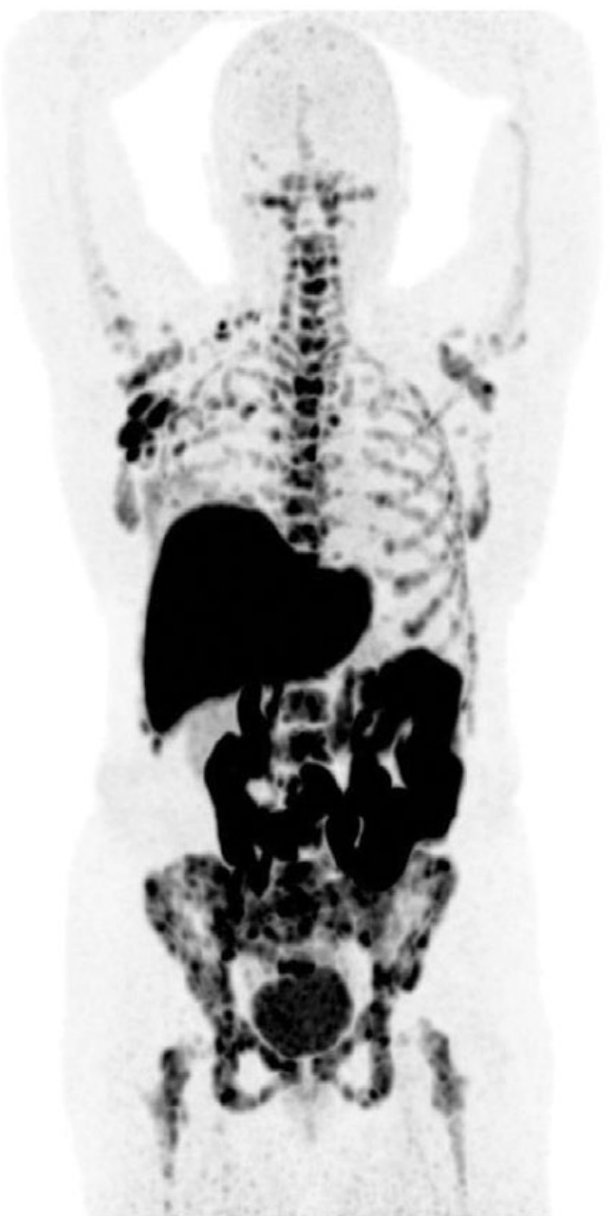
Table of contents

Product overview

Description

- Cerianna is a diagnostic radioactive tracer for PET imaging,[1] alone or in conjunction with computed tomography (CT)
- The product contains fluoroestradiol fluorine 18 (F 18), a synthetic estrogen analog radiolabeled with F 18, a cyclotron produced radionuclide that decays by positron emission[1]
- Cerianna strongly binds to ER and enables visualization of receptor expression via molecular imaging[1]

Cerianna PET/CT Imaging Detects ER-Positive (ER+) Lesions in Breast Cancer (BC)*



Critical organs include the liver, gallbladder, urinary bladder, and uterus[1,2]

- Metabolized in the liver[1]
- Eliminated by biliary and urinary excretion[1]
- Distributed systemically with high physiological uptake in the uterus and ovaries[1]

*Image provided courtesy of the Assistance Publique – Hôpitaux de Paris (APHP).

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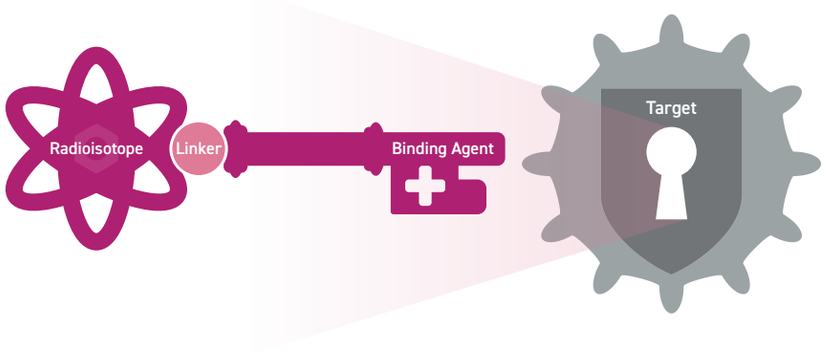
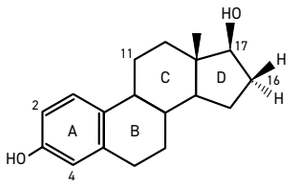
Mechanism of action

Estrogen-receptor targeted radiotracer (e-RTR)

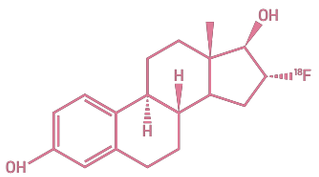
Molecular PET/CT Tracer Binds to Target Receptors Using "Lock-and-Key" Mechanism



Endogenous Estradiol[3]*



Cerianna (Fluoroestradiol F 18)[1]†



*Endogenous estradiol, or more properly 17β-estradiol, consists of four cycloalkane rings and two hydroxyl groups.[3] The numbers in the chemical structure for estradiol indicate commonly used positions for substituents,[3] such as fluorine 18 in the case of Cerianna.

†Chemically, fluoroestradiol F 18 is [18F]16α-fluoro-3,17β-diol-estratriene-1,3,5(10).[1]

Accumulates in Tissues Expressing ER

- Following intravenous (IV) administration, Cerianna accumulates in tissues expressing ER for approximately 80 minutes (20-80 minutes) prior to initiating the PET/CT[1]

Binds ER with High Affinity

- Cerianna mimics endogenous estradiol (i.e., "key") and binds to the ER (i.e., "lock") in BC cells with high affinity (60-100%)[1,3]

Detects Functional ER Expression

- The accumulated tracer eventually decays by positron emission, resulting in a reaction that produces two γ-ray photons that are sensed by the PET/CT camera and eventually converted to images for detection of lesions that express functional ER[1,3]

Cerianna PET/CT enables a non-invasive, comprehensive assessment of whole-body ER+ lesion status[3-5]

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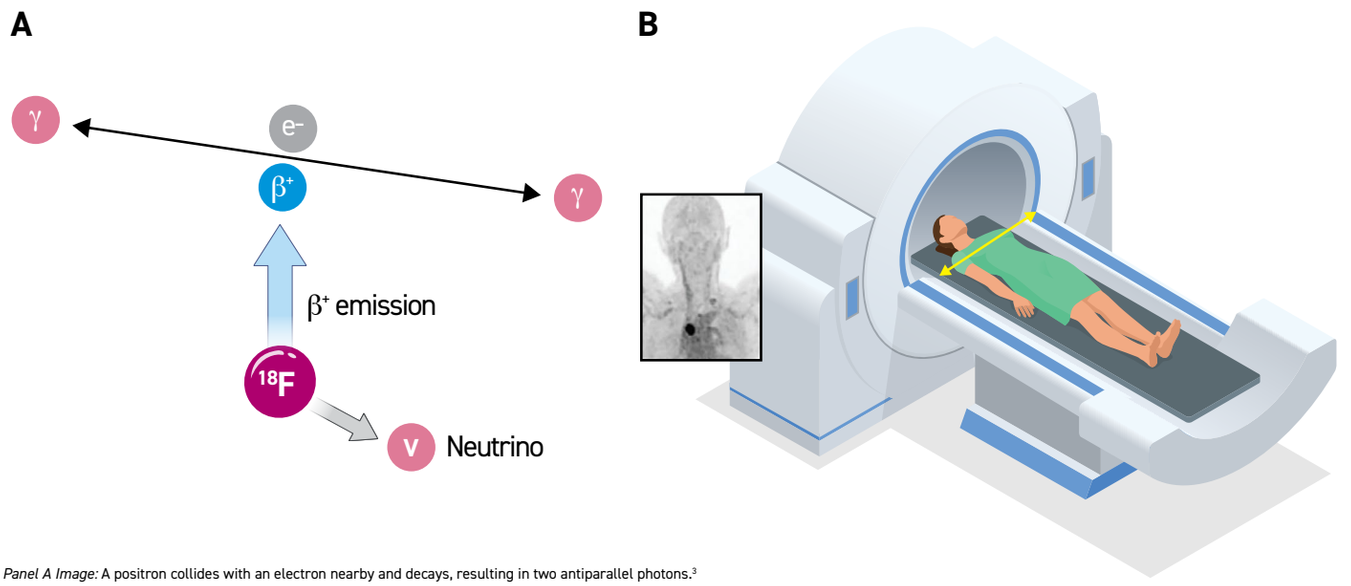
Mechanism of action Continued

Estrogen-receptor targeted radiotracer (e-RTR)

Mechanism of PET/CT Imaging with Cerianna[3]



Panel A Image: A positron collides with an electron nearby and decays, resulting in two antiparallel photons.[3]

Panel B Image: The accumulated fluoroestradiol F 18 is detected by the γ camera.[3]

Cerianna is different from metabolic activity radiotracers

- Molecular imaging with Cerianna and ^{18}F-fluorodeoxyglucose (FDG) answer fundamentally different questions
  - Imaging with Cerianna answers the question of whether BC tumors have functional ER[1,4,6]
  - Imaging with FDG answers the question of whether diseases exhibit glucose metabolic activity[6-8]
- Cerianna is a radiolabeled estrogen analog that detects ER+ lesion status by binding to functional estrogen receptors[1]
  - Cerianna images ER and is not useful for imaging other receptors such as HER2 and PR[1]
  - The uptake of fluoroestradiol F 18 is not specific for BC and may occur in a variety of ER+ tumors that arise outside of the breast, including from the uterus and ovaries[1]
- FDG is a radiolabeled glucose analog that is not a cancer-specific radiotracer and does not assess ER status[6-9]
  - False-positive results with FDG PET/CT may occur in infectious and/or inflammatory processes, post-radiation changes, and post-surgical changes, since intensified glycolytic or hypermetabolic activities result in increased FDG uptake[7,9,10]
  - False-negative results with FDG PET/CT may occur in cancers with low metabolic rates, such as invasive lobular carcinomas (ILC)7,10-12 and when there is suboptimal preparation of patients with glucose intolerance or diabetes, since elevated serum glucose levels result in decreased FDG uptake[10]

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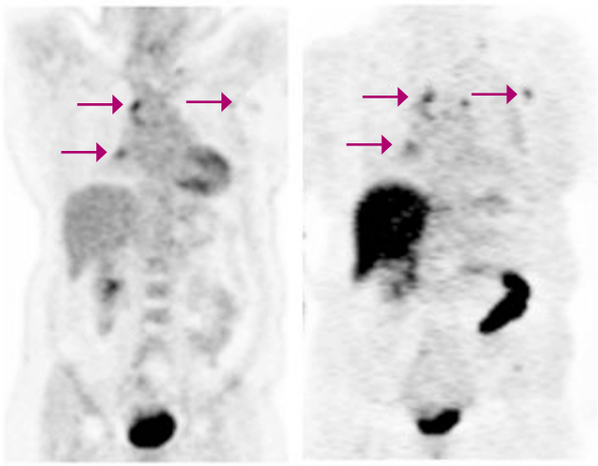
Examples of Receptor Function Imaging Contrasted with Metabolic Activity Imaging[13*†]

Patient 1
Biopsy = ER+

High FES Uptake

FDG **FES**

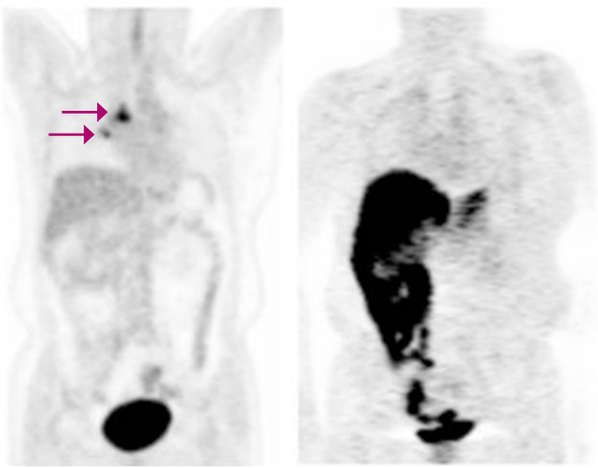


Glucose Metabolism Estradiol Binding

Patient 2
Biopsy = ER-

Low or Absent FES Uptake

FDG **FES**



Glucose Metabolism Estradiol Binding

*FDG = ^{18}F-fluorodeoxyglucose, FES = F18 fluoroestradiol.

†The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Imaging examples from two patients with newly diagnosed metastatic BC who underwent both FDG and FES scans before starting endocrine therapy. Both patients had lymph node metastases from ER+ BC. *Left Panel:* Patient 1 had mediastinal lesions appreciated by both FDG and FES. *Right Panel:* Patient 2 also had mediastinal disease clearly seen by FDG PET but not visible on FES PET. The core biopsy of a metastatic axillary lesion from Patient 1 showed ER+ BC, while the needle biopsy of a vertebral lesion from Patient 2 showed ER- BC.[13]

cERianna™
(FLUOROESTRADIOL F 18) INJECTION

Cerianna workflow implementation

Patient preparation

- Instruct the patient to drink water to ensure adequate hydration prior to Cerianna administration[1]
- Otherwise, Cerianna PET/CT imaging has no required pre-imaging laboratory work or immediate pre-imaging patient preparation,[14] which differs from FDG PET/CT imaging requirements
  - Fasting ahead of the FDG PET/CT study is a prerequisite to minimize interference with tracer uptake[15,16]
  - Checking blood glucose levels and ensuring euglycemia (to the extent possible) is necessary prior to FDG PET/CT imaging[15]
  - Refraining from talking, moving, or engaging in physical activity before and during the FDG PET/CT scan is required to minimize tracer uptake in muscles[15]
  - Keeping the patient warm before the injection of FDG and continuing throughout the subsequent uptake period and examination is needed to minimize tracer accumulation in brown fat[15]
- Before administering Cerianna, assess pregnancy status in a female of reproductive potential[1]
  - Refer to Use in Specific Populations section (page 14) for additional information
- Review past oncology therapies and current medications to assess for drug interactions in advance of Cerianna administration

Drug interactions

- Certain classes of systemic endocrine therapy (ET) that block ER, including selective ER modulators (SERMs) and selective ER down-regulators (SERDs), reduce the uptake of fluoroestradiol F 18 and may reduce detection of ER+ lesions after administration of Cerianna[1]
- Drugs from these classes such as tamoxifen (SERMs) and fulvestrant (SERDs) may block ER for up to 8 and 28 weeks, respectively[1]
  - Therefore, a special consideration for Cerianna PET/CT imaging is washout of prior ER antagonists[4]
- Administer Cerianna prior to starting systemic ET that block ER[1]
  - Do not delay indicated therapy in order to administer Cerianna[1]
- Unlike SERMs and SERDs, the aromatase inhibitor (AI) class of drugs (e.g., anastrozole) deplete levels of the ER ligand (i.e., estrogen) but do not interfere with the ER or Cerianna binding[17]
  - Thus, a Cerianna PET/CT scan may be performed to assess ER status during AI therapy[2,4]

Washout Period for Cerianna Drug Interactions[1]

	Duration
ER modulator (e.g., tamoxifen)	8 weeks
ER down-regulator (e.g., fulvestrant)	28 weeks

The table indicates the approximate duration in weeks that ET may reduce Cerianna uptake.

The AIs have neglible impact on estrogen binding and Cerianna uptake, in comparison to SERMs and SERDs[17]

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Cerianna workflow implementation Continued

Dosing principles

Recommended Dosage

The recommended amount of radioactivity to be administered for Cerianna imaging is 222 MBq (6 mCi), with a range of 111 MBq to 222 MBq (3 mCi to 6 mCi).[1]*

Radiation Dosimetry

- Radiation dosimetry studies show that organ doses from Cerianna imaging are comparable with those from other commonly performed nuclear medicine studies, and potential radiation risks are well within acceptable limits[2]
- The radiation effective dose resulting from administration of 222 MBq (6 mCi) of Cerianna to an adult weighing 70 kg is estimated to be 4.9 mSv[1]*
- A Cerianna PET scan may impart a radiation dose to the patient comparable to about one year of natural background radiation, according to estimates reported by the SNMMI,[18]* and roughly equivalent to the radiation burden of FDG[2,15]
  - The average exposure to natural radiation for a person living in the United States is estimated to be 3 mSv per annum[19]
  - Comparably, the estimated radiation effective dose resulting from FDG PET scanning is about 4 mSv[15]
- When PET/CT imaging is performed, exposure to radiation will increase by an amount dependent on the settings used for the CT acquistion[1]

*kg = kilogram, MBq = megabecquerel, mCi = millicurie, mSV = millisievert, SNMMI = Society of Nuclear Medicine and Molecular Imaging.

Administration instructions

Administration instructions

Product Preparation and Administration

- Use aseptic technique and radiation shielding when withdrawing and administering Cerianna[1]
- Visually inspect the radiopharmaceutical solution prior to administration[1]
  - Do not use if the solution contains particulate matter or if it is cloudy or discolored[1]
- After visual inspection of the solution, administer Cerianna as a single IV injection of 10 mL or less over 1 to 2 minutes[1†]
  - Cerianna may be diluted with 0.9% Sodium Chloride Injection, USP, when the dose is prepared[1†]
  - Assay the dose in a suitable dose calibrator prior to administration[1]
- Preferably inject Cerianna at a site contralateral to the primary tumor site, analogous to guideline recommendations for FDG administration[16]
  - Ensure good venous access, but the needle gauge does not impact image quality
  - Note that central port utilization for Cerianna administration is not contraindicated but may decrease image quality due to tracer accumulation (i.e., radioisotope hang-up) at the port site

Post-Administration

- Follow the Cerianna injection with an adequate amount of 0.9% Sodium Chloride Injection, USP, to ensure full delivery of the dose[1†]
- Dispose of any unused Cerianna in compliance with applicable regulations[1]
- Recall that restricted talking, moving, or engaging in physical activity before and following Cerianna administration is not required[2,4]
- Advise the patient to void immediately prior to the Cerianna PET/CT scan to reduce urinary bladder activity[15]
- Instruct the patient to continue drinking water and voiding frequently during the first hours following Cerianna administration to further reduce radiation exposure[1]

†mL = milliliter, USP = United States Pharmacopeia.

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(FLUOROESTRADIOL F 18) INJECTION

Image acquisition and interpretation

Acquisition guidelines

Recommended Imaging Technique

- In general, for scan acquisition and processing of Cerianna imaging, the same protocol can be followed as for FDG imaging[2]
- The recommended start time for image acquisition is 80 minutes, with an adaptable range of 20 to 80 minutes, after the IV administration of Cerianna[1]
  - Many institutions use a start time of 45 to 60 minutes after radiotracer administration for logistical reasons[2]
- The patient should void immediately before Cerianna scanning[15]
- During the scan, position the patient supine with arms supported above the head, if possible, to avoid artifacts[1,2,15]
  - Refer to Physiological Uptake Image on accompanying page
  - If this is not possible, one arm can be kept above the head with the other positioned alongside the body, or both arms can be positioned alongside and close to the body[2,15]
- Cerianna scanning should include the entire area from skull vertex to mid-thigh or knee[2,4]
- Total scan time is approximately 20 to 30 minutes,[1,4] but scan duration for optimal image quality varies based on equipment used and patient and tumor characteristics[1]
  - Follow your institutional protocol for scan duration with Cerianna

Interpretation principles

Clinical Pharmacology

- After IV administration, fluoroestradiol F 18 distributes primarily to the hepatobiliary system, and also to the small and large intestines, kidneys, bladder, and uterus, as well as the blood and heart wall[1]
  - At 20 minutes after injection, ~20% of circulating radioactivity in the plasma is in the form of non-metabolized fluoroestradiol F 18[1]
- Fluoroestradiol F 18 is metabolized in the liver[1]
  - At 2 hours after injection, circulating fluoroestradiol F 18 levels are < 5% of peak concentration[1]
- These two principles reemphasize that the preferred imaging start time is between 20 and 80 minutes (e.g., 45 minutes) after Cerianna administration to allow ample physiological distribution and forego complete hepatic metabolism, respectively[1]
- Elimination of fluoroestradiol F 18 is by biliary and urinary excretion[1]

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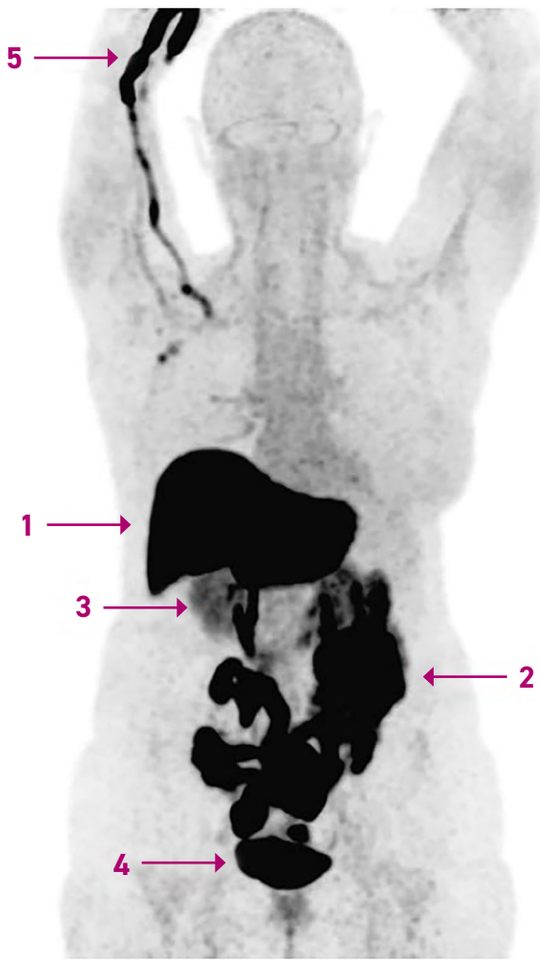
Physiological Uptake

- Uptake of fluoroestradiol F 18 depends on ER density and function in tumors and physiologic tissue, including in liver, ovary, and uterus[1]
  - Fluoroestradiol F 18 uptake assessed by PET/CT in human tumors is directly proportional to tumor ER expression measured by *in vitro* assays[1]
- Detection of ER+ tumors should be based on comparison with tissue background outside of organs with high physiologic uptake and regions with high activity due to hepatobiliary and urinary excretion[1]
  - As a general rule, all lesions with fluoroestradiol F 18 uptake greater than background (e.g., physiological liver uptake) are considered ER+ (i.e., evidence of the presence of ligand binding function of ER)[2]
- Cerianna is not useful for assessing ER expression in regions with high activity, particularly metastatic liver lesions[2,4,20]

Physiological Uptake of Fluoroestradiol F 18 on PET Imaging[2]*



The image shows the physiological distribution of fluoroestradiol F 18 during PET scan, with accumulation in the liver (1) and excretion by the gastrointestinal tract (2), kidneys (3), and urinary bladder (4). In most patients, high uptake also is seen in the injected vessel (5).[2] The cause of this accumulation at the injection site and in blood vessels is unknown but is probably due to sticking of the tracer to the vessel wall and/or endothelial cells. As the amount of tracer in these blood vessels is negligible (< 1% of the administered dose), no influence is to be expected for uptake in the tumors.[2]

*The F18 fluoroestradiol used in this scan was not equivalent to the FDA-approved formulation of Cerianna.

Special considerations

Risk of misdiagnosis

Inadequate Tumor Characterization and Other ER-Positive Pathology

- Breast cancer may be heterogeneous within patients and across time[1]
- Cerianna images ER and is not useful for imaging other receptors such as HER2 and PR[1]
- The uptake of fluoroestradiol F 18 is not specific for BC and may occur in a variety of ER+ tumors that arise outside of the breast, including from the uterus and ovaries[1]
- Do not use Cerianna in lieu of biopsy when biopsy is indicated in patients with recurrent or metastatic BC[1]

False Negative Cerianna Scan

- A negative Cerianna scan does not rule out ER+ BC[1]
- Pathology or clinical characteristics that suggest a patient may benefit from systemic hormone therapy should take precedence over a discordant negative Cerianna scan[1]

Use in specific populations

Pregnancy

- There are no available data on Cerianna use in pregnant women[1]
  - No animal reproduction studies using fluoroestradiol F 18 have been conducted to evaluate its effect on female reproduction and embryo-fetal development[1]
- All radiopharmaceuticals, including Cerianna, have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of radiation dose[1]
- Advise a pregnant woman of the potential risks of fetal exposure to radiation from administration of Cerianna[1]

Lactation

- There are no data on the presence of fluoroestradiol F 18 in human milk, or its effects on the breastfed infant or milk production[1]
  - Lactation studies have not been conducted in animals[1]
- Advise a lactating woman to avoid breastfeeding for 4 hours after Cerianna administration to minimize radiation exposure to a breastfed infant[1]

Pediatric Use

The safety and effectiveness of Cerianna in pediatric patients have not been established.[1]

Geriatric Use

Clinical studies of Cerianna did not reveal any difference in pharmacokinetics or biodistribution in patients aged ≥ 65 years.[1]

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Safety information

Adverse reactions

Clinical Trials Experience

The safety of Cerianna was evaluated from published clinical trials of 1,207 patients with BC receiving at least one fluoroestradiol F 18 administration.[1]

The following adverse reactions occurred at a rate < 1%:[1]*

- *General disorders:* injection-site pain
- *Neurological and gastrointestinal disorders:* dysgeusia

In a clinical trial of F18 fluoroestradiol that was pivotal for obtaining Food and Drug Administration (FDA) approval of Cerianna, no serious adverse events occurred during the trial and there were no treatment-related deaths.[5]

To report SUSPECTED ADVERSE REACTIONS, contact Zionexa US Corp, a GE Healthcare Company, at +1.800.654.0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

*Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.[1]

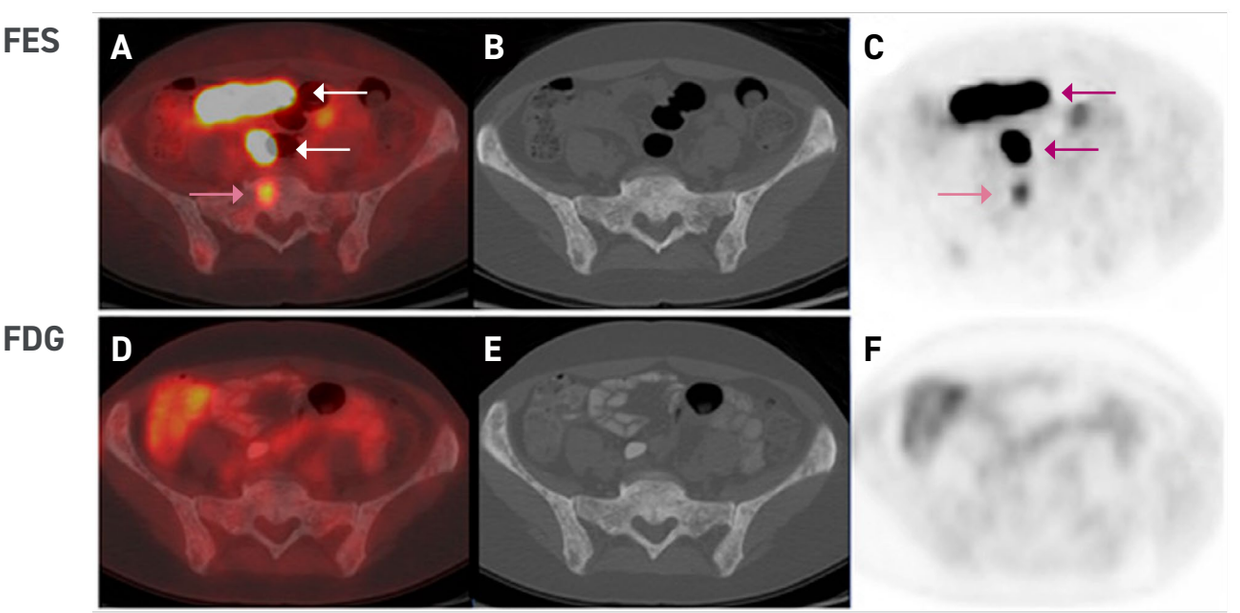
Imaging cases

Confirming ER+ metastatic disease

Patient 1

Images of metastatic disease apparent on F18 fluoroestradiol imaging but not on FDG imaging in a patient with biopsy-proven metastatic ILC. This patient had extensive sclerotic osseous lesions on CT and known active osseous metastases from a biopsy used to enroll the patient in a prospective clinical trial.[12]

Confirmation of ER+ Osseous Lesions in Metastatic ILC with F18 Fluoroestradiol[12*†]



Upper Panel Images (FES): Axial F18 fluoroestradiol PET/CT (A), CT (B), and F18 fluoroestradiol PET (C) demonstrated F18 fluoroestradiol-avid osseous foci (pink arrows), consistent with avid malignancy. Physiologic activity was also seen in the bowel (white/magenta arrows).[12]

Lower Panel Images (FDG): Axial FDG PET/CT (D), CT (E), and FDG PET (F) did not demonstrate any FDG-avid foci suspected of being malignancy.[12]

*FES = F18 fluoroestradiol.

†The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Images from a retrospective evaluation of 6 prospective clinical trials using F18 fluoroestradiol PET/CT in 92 patients with metastatic breast cancer (MBC), of whom 14 (15%) had ILC histology. Seven of the 14 patients had synchronous F18 fluoroestradiol and FDG PET/CT imaging, which allowed comparison of these two PET tracers. For these 7 patients, the F18 fluoroestradiol and FDG PET/CT scans were analyzed to determine the total number of tracer-avid lesions, organ systems of involvement, and measurable uptake of each organ system for both tracers.[12]

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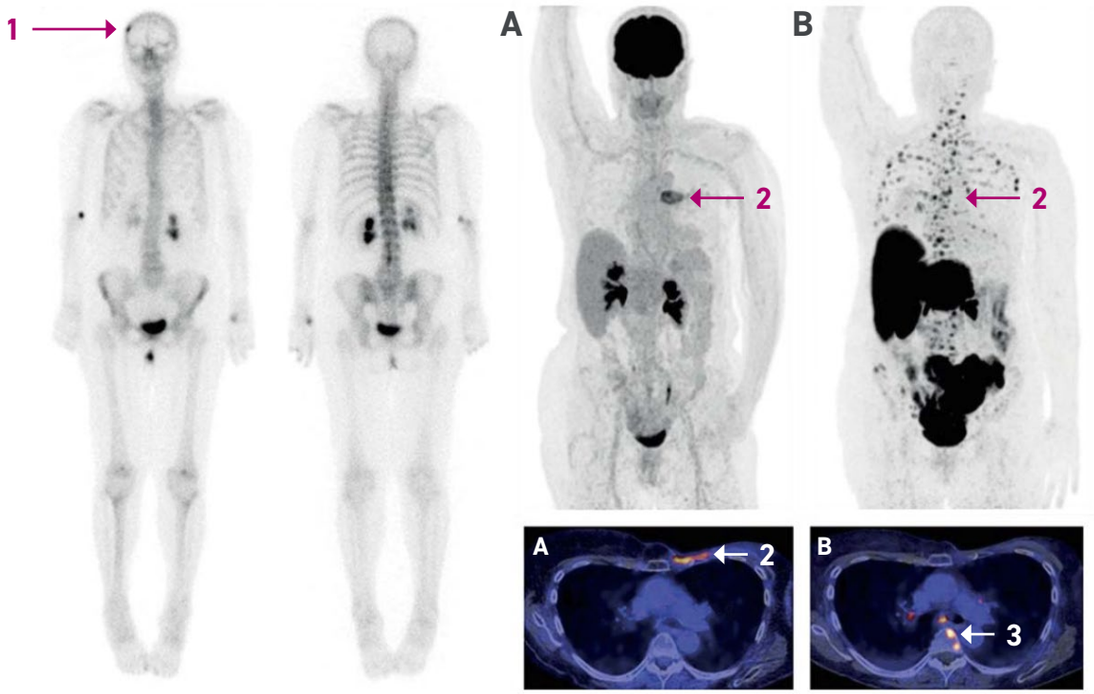
Patient 2

Images of a patient with local recurrence of ILC in whom biopsy was not feasible. Contrast-enhanced CT suggested metastatic bone lesions, but these were not confirmed by bone scintigraphy or FDG PET.[21]

Confirmation of ER+ Lesions in Suspected Metastatic ILC with F18 Fluoroestradiol[21]*



The bone scintigraphy showed one skull lesion (arrow 1), which was not confirmed by FDG PET (A). Conversely, FDG PET showed only increased uptake at the excision site (arrow 2) due to recent surgery. PET findings with F18 fluoroestradiol (B), on the other hand, were compatible with ILC metastases in lymph nodes and bone (arrow 3). Treatment with AI therapy was started as first-line palliative hormone therapy.[21]

*The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Images from three lobular BC cases in whom staging with conventional imaging yielded equivocal results and a biopsy was not feasible. In contrast, F18 fluoroestradiol PET confirmed ER+ metastatic disease and contributed to clinical decision making in these patients.[21]

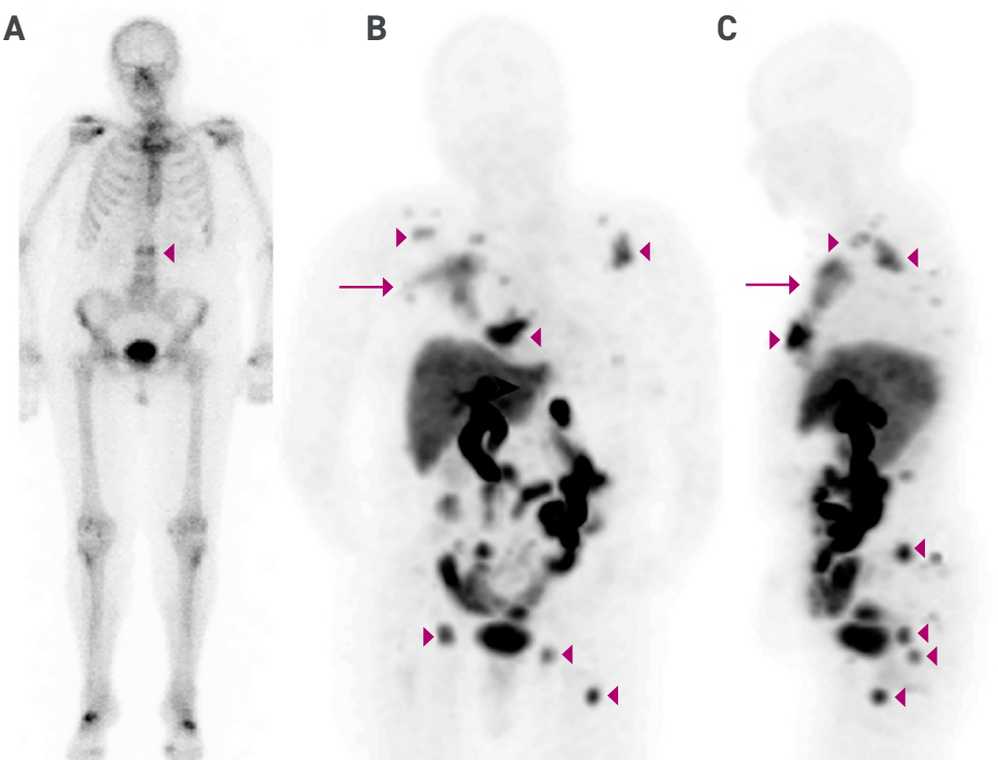
Imaging cases Continued

Resolving clinical dilemmas

Patient 1

Images of a patient with suspected distant BC recurrence on conventional imaging. Molecular imaging with F18 fluoroestradiol was performed because biopsy did not show malignancy, but bone scan suggested possible malignant lesion.[20]

Confirmed Recurrence and Diagnosed Metastases with F18 Fluoroestradiol[20]*



Bone scan (A) of patient showed suggestive lesion at L2 (arrowhead). Biopsy of this lesion did not confirm malignancy. Coronal (B) and sagittal (C) images of F18 fluoroestradiol PET showed tracer uptake in vertebra L2 and multiple other bone metastases (arrowheads), as well as large locoregional recurrence in soft tissue (arrow). Only the most intense lesions are indicated.[20]

*The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Images from a retrospective study of 33 patients with histologically-proven ER+ BC and suspected distant recurrence or metastases that evaluated the value of PET imaging with F18 fluoroestradiol as a diagnostic tool when, despite complete standard workup, patients presented a clinical dilemma for their treating physician. F18 fluoroestradiol PET or PET/CT imaging was requested to evaluate ambiguous findings or equivocal lesions on standard workup (n=21), ER status in patients with metastases who progressed on hormone therapy (n=10), and the origin of metastases (n=2). Validated questionnaires were used to collect the insight of the referring physician to ascertain the value of molecular imaging with F18 fluoroestradiol in resolving clinical dilemmas.[20]

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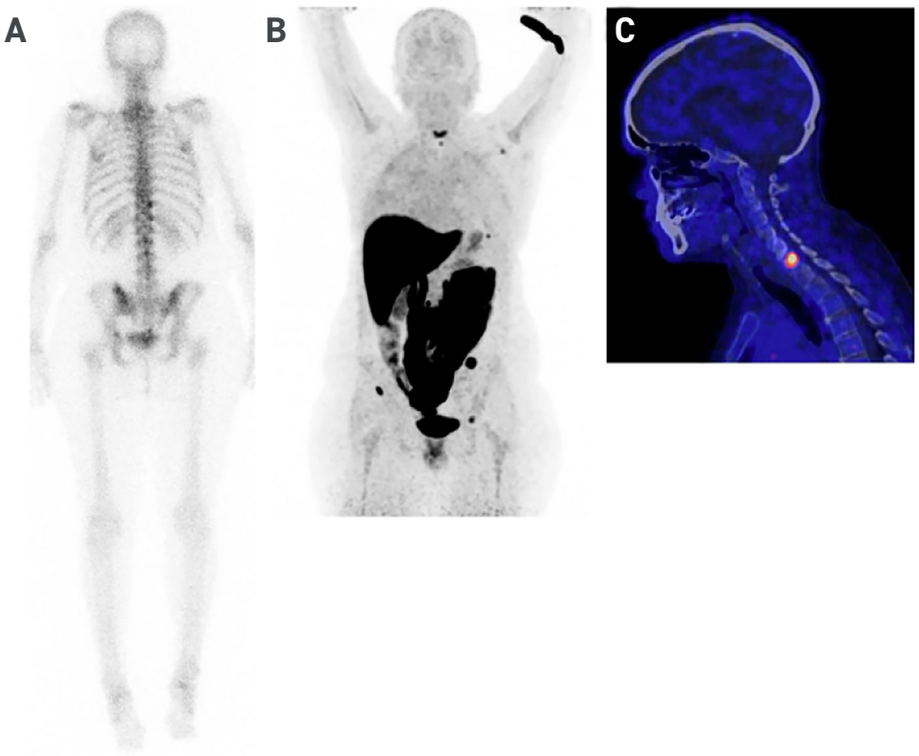
Patient 2

Images of a patient known to have Bechterew disease and diagnosed with primary ER+ BC two years previously. Molecular imaging with F18 fluoroestradiol was performed because of equivocal lesions on standard workup.[22]

Differentiated Bone Metastases with F18 Fluoroestradiol[22]*



Conventional bone scanning was performed because of pain in neck region and showed heterogenous uptake in pelvis and spine, shown in the static image posterior view (A). To differentiate between presence of bone metastases and lesions associated with Bechterew, F18 fluoroestradiol PET scan was performed. Increased F18 fluoroestradiol uptake was seen in multiple skeletal lesions, including the rib, left scapula, pelvis, and spine, as seen in the maximum-intensity-projection (MIP) view (B) and PET/CT sagittal view of cervical spine (C). Based on these findings, diagnosis was settled on MBC and the clinical dilemma was resolved. The patient was started on first-line ET and received radiation to the cervical spine.[22]

*The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Images from a retrospective study of 100 consecutive F18 fluoroestradiol PET scans performed in 83 patients with confirmed or suspected ER+ MBC that assessed whether molecular imaging with F18 fluoroestradiol aided in resolving clinical dilemmas that persisted after standard workup. Clinical dilemmas were categorized as inability to determine the extent of metastatic disease (n=52), unclear ER status of the tumor (n=31), and inability to determine which primary tumor caused the metastases (n=17). A clinical dilemma was considered resolved if the F18 fluoroestradiol PET results provided a solution or if a treatment decision (i.e., change or continue) was based directly on the F18 fluoroestradiol PET results.[22]

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Imaging cases Continued

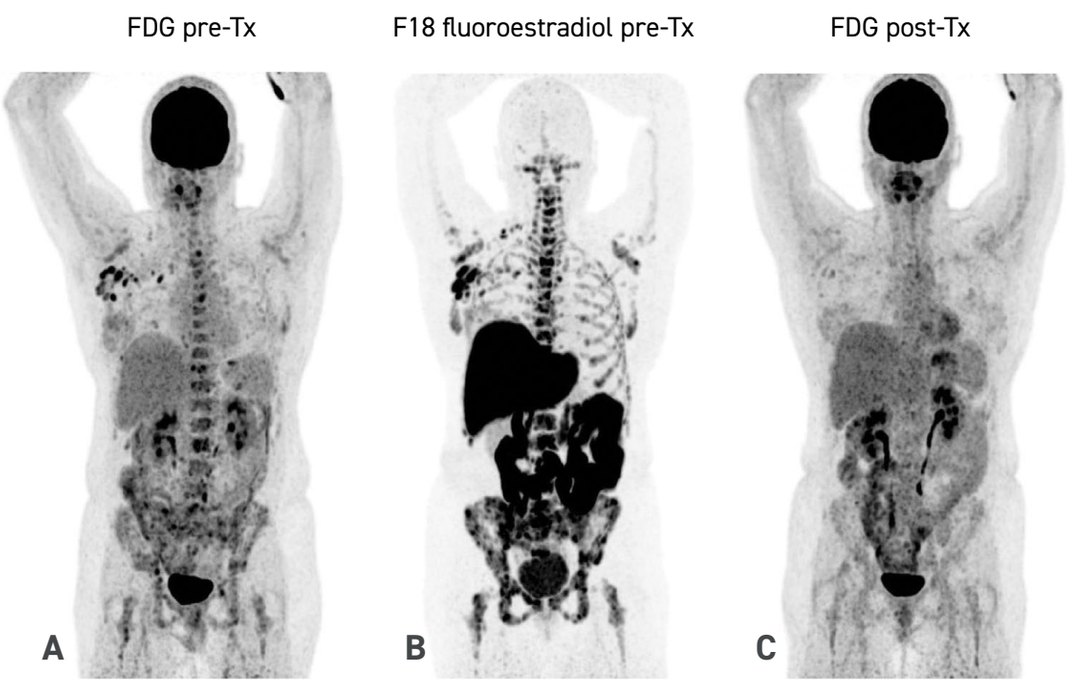
Helping inform clinical decisions

Patient 1
Anterior/Superior

Molecular images of a patient whose disease responded to treatment with an AI and a CDK 4/6 inhibitor.[23]

- FDG PET images depicted in A and C
- F18 fluoroestradiol PET image depicted in B

F18 Fluoroestradiol and FDG PET Images in a Treatment Responder and Non-Responder[23*†]



Upper Panel Images (MBC Treatment Responder): Baseline FDG PET (A) showed pathological uptake in axillary lymph nodes (right side) and in nearly all vertebrae and pelvic bones. Image B showed the baseline F18 fluoroestradiol PET with pathological ER expression in the axial skeleton (including vertebrae, pelvic bones, proximal humeri and femora) and in axillary lymph nodes (right side). After 8 weeks, the FDG PET (C) showed almost complete metabolic response (just some slightly elevated uptake in the axillary lymph nodes). The patient had been on treatment for > 70 weeks.[23]

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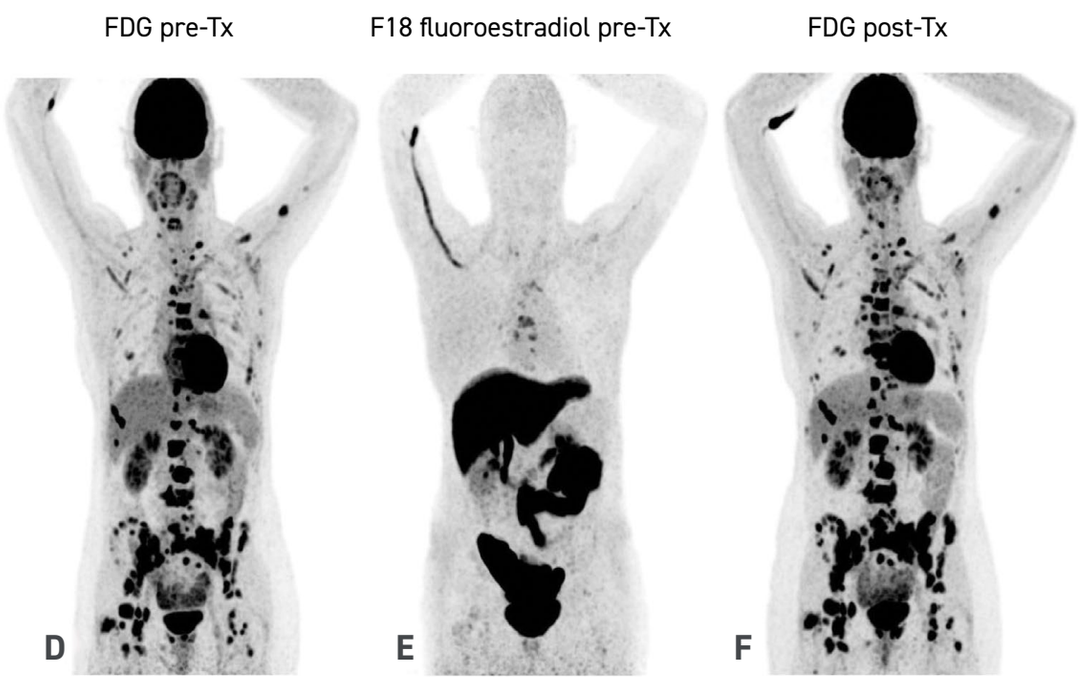
Patient 2

Anterior/Superior

Molecular images of another patient whose disease did not respond to treatment with an AI and a CDK 4/6 inhibitor.[23]

- FDG PET images depicted in D and F
- F18 fluoroestradiol PET image depicted in E



Lower Panel Images (MBC Treatment Non-Responder): Baseline FDG PET (D) showed pathological uptake in multiple skeletal lesions. Image E showed the baseline F18 fluoroestradiol PET with only some increased ER expression in thoracic vertebrae. After 8 weeks, the FDG PET (F) showed no metabolic response, even some increase in the pathologic uptake in the multiple skeletal lesions.[23]

*CDK = cyclin-dependent kinase, Tx = treatment.

†The F18 fluoroestradiol administered in this study was not equivalent to the FDA-approved formulation of Cerianna.

Images from a prospective, single-center, feasibility study that aimed to explore whether baseline F18 fluoroestradiol PET discordance and F18 fluoroestradiol uptake were correlated with outcome and response to concomitant treatment with an AI and a CDK 4/6 inhibitor. Thirty patients with ER+ MBC were included in the study, including 87% who received at least one previous line of ET in the metastatic setting.[23]

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Appendix

Cerianna imaging checklist

For any questions related to imaging with Cerianna, reach out to your GE Healthcare Oncology Clinical Applications Specialist

PATIENT PREPARATION—TO DO

- Drinking water beforehand is necessary
- Talking, moving, and engaging in physical activity before administration is permitted
- Assessing pregnancy status is recommended
- Assessing for drug interactions is required
  - The SERM and SERD drug classes may block ER and interfere with fluoroestradiol F 18 uptake for up to 8 and 28 weeks, respectively*
  - Administering Cerianna prior to starting systemic ET that block ER is advised*

—NOT TO DO

- Fasting is not required
- Checking blood glucose levels is not necessary
- Keeping warm is not required

DOSING AND ADMINISTRATION—TO DO

- Dosing with 222 MBq (6 mCi) of Cerianna is recommended*†
- Using aseptic technique and radiation shielding is mandatory
- Inspecting the radiopharmaceutical solution visually is requisite
  - Cerianna is a clear, colorless solution
- Injecting in an arm contralateral to the primary tumor site is preferred
- Administering as a single IV injection of ≤ 10 mL over 1 to 2 minutes is recommended*
  - Cerianna may be diluted with NSS*
- Assaying the dose in a calibrator is advised
- Ensuring good venous access is necessary (but the needle gauge is not impactful)
- Following the injection with an adequate amount of NSS is advised*
- Disposing unused product in compliance with applicable regulations is expected
- Talking, moving, and engaging in physical activity after administration is permitted
- Having the patient void just before imaging is advised
- Continuing to drink water and void afterwards is necessary

—NOT TO DO

- Using an unclear or colored radiopharmaceutical solution is discouraged
- Administering Cerianna through a central port is not contraindicated but is dissuaded

ACQUISITION AND INTERPRETATION—TO DO

- Following your institutional protocol for FDG imaging and timing parameters is suggested
- Voiding prior to scanning is urged
- Positioning the patient supine with arms above the head is preferred
- Scanning from skull vertex to mid-thigh or knee is advised
- Imaging for about 20 to 30 minutes is suggested
- Detecting ER+ lesion status based on fluoroestradiol F 18 uptake greater than background is endorsed*

—NOT TO DO

- Assessing ER expression in regions with normally high physiological activity (e.g., liver) is not advised*

*AI = aromatase inhibitor, ER = estrogen receptor, ET = endocrine therapy, IV = intravenous, MBq = megabecquerel, mCi = millicurie, mL = milliliter, NSS = normal saline solution (0.9% Sodium Chloride), SERD = selective estrogen receptor down-regulator or degrader, SERM = selective estrogen receptor modulator.

†The recommended amount of radioactivity to be administered for Cerianna PET imaging ranges from 111 MBq to 222 MBq (3 mCi to 6 mCi).[1]

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Cerianna resource contact list

CERIANNA ACCESS SUPPORT℠

For specific product or indication questions on Cerianna, please contact your local Account Manager

For coverage, reimbursement, or other payment support questions, please contact the Cerianna Access Support Line:

1-833-946-6392

For scientific or medical inquiries, please contact Medical Affairs

Medical Information:

1-800-654-0118 (Option 2, then 3) medical.affairs@ge.com

For delivery or logistical questions, please contact PETNET

PETNET Customer Care Center:

1-877-473-8638

For questions about how to use Cerianna in your imaging center, please contact your local senior Clinical Application Specialist (CAS)

To report SUSPECTED ADVERSE REACTIONS, contact Zionexa US Corp, a GE Healthcare Company, at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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To report SUSPECTED ADVERSE REACTIONS, contact Zionexa US Corp, a GE Healthcare Company, at +1.800.654.0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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August 2022 JB06804US