ARCH
Annual Review of Changes in Healthcare

Novel Drug Review of Approved 2020 Breast Cancer Agents

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Abstract

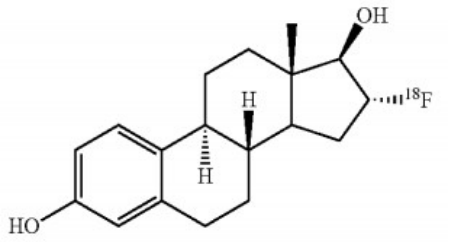
Annually, The Food and Drug Administration's Center for Drug Evaluation and Research publishes a report containing the latest drugs approved. In this review, the following breast cancer agents; Cerianna™ (fluoroestradiol F-18), Trodelvy (sacituzumab govitecan-hziy), and Tukysa (tucatinib), are evaluated for their drug properties including dosing and administration, absorption, distribution, metabolism, excretion, and adverse effects & warnings. In addition to their pharmacological parameters, review of the National Comprehensive Cancer Network (NCCN) Breast Cancer clinical guidelines assess how these agents may impact current clinical practice.

The Food and Drug Administration's Center for Drug Evaluation and Research annually publishes a report containing the latest drugs approved.[1] This report provides a list of novel agents with links to their drug trial snapshots and press releases.[1] In 2020 there were 40 newly approved drugs, three of which are the following breast cancer agents; Cerianna™ (fluoroestradiol F-18), Trodelvy (sacituzumab govitecan-hziy), and Tukysa (tucatinib).[1] These newly approved agents may add to the arsenal of treatment options to be used throughout the different stages and specific tumor characteristics of breast cancers.

Background

For women between the ages of 20-59 years old, breast cancer is the leading cause of cancer death.[2] Breast cancer is estimated to occur in about one-in-eight women as a result of endocrine, genetic, environmental, and lifestyle factors.[2] In 2019, there were 62,930 non-invasive breast cancer cases among women and 271,270 cases of invasive breast cancers that resulted in 42,260 deaths.[2] Prevention, early detection, breast cancer conserving surgery, and mastectomy are fundamental to the treatment of breast cancers, however, later stages require additional pharmacologic treatment regimens specific to tumor characteristics (e.g. hormone receptor positive [HR(+)], human epidermal growth factor receptor 2 positive [HER2(+)], and triple negative breast cancer [TNBC]).[2] The objective of this article is to describe characteristics of Cerianna™, Trodelvy™, and Tukysa™ while considering their potential use in clinical practice guidelines for the treatment of breast cancers.

Cerianna™ (fluoroestradiol F-18)



Cerianna™ is a parenteral radiopharmaceutical agent approved for the detection of estrogen-receptor-positive (ER+) lesions with the use of positron emission tomography (PET) scans in patients with recurrent or metastatic breast cancers.[3,4] Cerianna™ is only useful for the detection of estrogen receptors and is not effective for the detection of progesterone receptors (PR) or human epidermal growth factor receptor 2 (HER2).[3] As a radiopharmaceutical agent, safety precautions must be taken prior to administration. Only experienced and trained providers can administer Cerinna™. They must wear waterproof gloves and radiation shielding.[3] Patients must adequately hydrate before and after receiving Cerianna™.[3]

Dosing & Administration:

For PET imagining, a single bolus dose of 6mCi (222MBq) IV infused over 1-2 minutes, with a maximum amount allowed of 10mL or less.[3,4] Cerianna™ does not require renal or hepatic dose adjustments.[3] PET imagining should commence 80 minutes after Cerianna™ injection.[3]

ADME:

Cerianna™ is highly protein bound and distributes to the hepatobiliary system, is metabolized by the liver, and is eliminated via biliary and urinary excretion.[3]

Adverse Effects & Warnings:

Distortion of sense of taste and injection site pain are adverse effects reported with Cerianna™.[3] Pregnancy and lactation have not been extensively studied but there is still potential for harm of fetal development.[3]

Trodelvy (sacituzumab govitecan-hziy)

Trodelvy™ is a parenteral, topoisomerase inhibitor, Trop-2 antibody that is approved for treatment of adult patients who have received two prior therapies for metastatic disease with triple-negative breast cancer (TNBC).[5] Trodelvy™ should NOT be substituted for or used with other medications containing its active metabolite SN-38 or irinotecan.[5]

Dosing & Administration:

Prior to administration, Trodelvy™ must only be reconstituted with 20mL of 0.9% NaCl for each 180 mg Trodelvy™ vial.[5] The vial must be swirled and not shaken for 15 minutes.[5] Following reconstitution, Trodelvy™ should be diluted with 0.9% NaCl Inj (maximum 500mL) to obtain a concentration between 1.1 mg/mL-3.4 mg/mL.[5] The mixture may then be stored in the refrigerator for up to 4 hours and must not be frozen or shaken.[5] Protect Trodelvy™ from light.[5]

Trodelvy™ consists of a 21-day treatment cycle including weight-based dosing of 10mg/kg on administration days 1 and 8 for a first infusion of 3 hours and subsequent infusions over 1-2 hours.[5] For example, on day 1 the infusion must be given over 3 hours and on day 8 it can be given over 1-2 hours if prior infusions were tolerated.[5] Both must be monitored for at least 30 minutes after infusion.[5]Treatment with Trodelvy™ should be limited to a maximum of 10mg/kg and may be continued until disease progression or intolerable toxicity.[5] Upon completion of administration, the line used should be flushed with 20mL of 0.9% NaCl.[5]

ADME:

Trodelvy™ has an average volume of distribution of 0.045 L/kg.[5] Its half-life is 16 hours.[5] The half-life of its active metabolite free SN-38 is 18 hours.[5] Trodelvy™ has an average clearance rate of 0.002 L/h/kg.[5] The metabolism of Trodelvy™ cannot be concluded due to lack of studies conducted.[5]

Adverse Effects & Warnings:

Trodelvy™ has many adverse effects/warnings which include nausea & vomiting, diarrhea, hypersensitivity, and neutropenia.[5]

Nausea and vomiting occurred in 69% (74/108) and 49% (53/108) of patients respectively during clinical trials.[5] Trodelvy™ is emetogenic and it is recommended to premedicate patients with antipyretics, H1/H2 blockers, and corticosteroids prior to infusion to prevent chemotherapy induced nausea and vomiting (CINV).[5]

Diarrhea occurred in 63% (68/108) of patients during clinical trials.[5] Trodelvy™

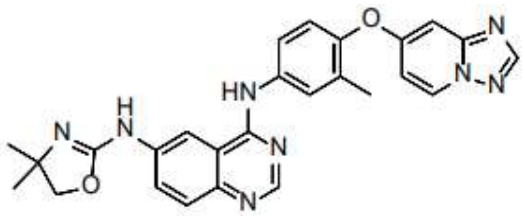
should be withheld for patients experiencing GRADE 3-4 diarrhea and may be resumed when GRADE ≤1.[5] Under negative infectious causes, loperamide can be used to treat diarrhea starting with an initial dose of 4 mg followed by 2 mg with every episode of diarrhea.[5] The maximum allowable dose of loperamide is 16 mg/day.[5]

Hypersensitivity reactions occurred in 37% (151/408) of patients receiving Trodelvy™. Patients must be observed for at least 30 mins after infusion of Trodelvy™.[5] The rate of infusion may be slowed down or interrupted if the patient is experiencing a reaction and promptly discontinued if the reaction becomes life-threatening.[5]

Neutropenia occurred in 54% (220/408) of all patients receiving Trodelvy™ and 6% (24/408) experienced febrile neutropenia.[5]

Dose modifications are needed for many of the side effects associated with Trodelvy™.[5] Health care professionals should consult the package insert to adjust these doses.

Tukysa (tucatinib)



Tukysa™ is an oral tyrosine kinase inhibitor of HER2 approved for the treatment of adult patients with advanced or unresectable metastatic HER2-positive breast cancer who have received one or more anti-HER2 based regimens in the metastatic setting.[7,8] Tukysa is used in combination with trastuzumab and capecitabine.[7,8] This combination includes treatment for patients with brain mestases.[7,8]

Dosing & Administration:

Tukysa™ has a recommended dose of 300 mg taken by mouth twice daily with trastuzumab and capecitabine.[7] Tukysa may be taken with or without food and it is advised that patients separate doses by 12 hours and they should take the medication at the same time each day.[7] It is supplied in 50 mg and 150 mg tablets and it must be stored in its original container.[7] Once opened, Tukysa™ must be used within 3 months.[7] Treatment with Tukysa™ continues until disease progression or intolerable toxicity. [7] Tukysa tablets must be swallowed whole and not chewed, crushed, or split when administered.[7] Capecitabine is contraindicated in severe hepatic impairment (CrCl <30 mL/min) and therefore the use of Tukysa™ cannot be continued.[8]

ADME:

Tukysa™ achieves peak plasma concentration at ~2 hours with a volume of distribution of 1670L with 97.1% protein binding. Tukysa™ is cleared at a rate of 148L/h, metabolized by CYP2C8, and excreted mainly through feces.

Adverse Effects & Warnings:

Tukysa™ carries adverse effects and warnings which include diarrhea, hepatotoxicity, and embryo-fetal toxicity.[7]

Diarrhea occurred in 81% of patients treated with Tukysa™.[7] Severe diarrhea may

cause acute kidney injury, dehydration, hypotension, and even death.[7]

Hepatotoxicity occurred in 8% of patients treated with Tukysa™.[7] Monitoring parameters for hepatotoxicity include: ALT, AST, and bilirubin.[7] For severe hepatotoxicity, it is recommended to reduce the dose or discontinue permanently.[7]

Embryo-fetal toxicity can result in fetal harm when Tukysa™ is used in the treatment of pregnant patients. It is advised that both male and females use appropriate contraceptives for at least 1 week after the last dose.[7] It is important to advise pregnant females and females with reproductive potential about the possible risks of fetal harm while being treated with Tukysa™.[7]

Discussion

As of 2020, The FDA approved the reviewed drugs Cerianna™, Trodelvy™, and Tukysa™ as novel agents for the diagnoses and treatment of certain breast cancers. Because clinical guidelines for breast cancer are ever-changing, it is necessary to consider how these novel agents may impact current clinical practice.

Cerianna™ may have an impact on staging and diagnosing of breast cancer. Alongside with the use of PET scans, Cerianna™ can help determine the hormone receptor status of breast cancer.[3] It must be noted that Cerianna™ can only determine estrogen receptor status and does not include diagnoses of progesterone receptor or human epidermal growth factor 2 receptor status.[3] According to NCCN guidelines, staging is needed to determine treatment regimens. [9] During staging, tumor size (T), number of lymph nodes involved (N), spread of cancer (M), and estrogen, progesterone, or HER2 status is gathered as information to characterize the cancer.[9] Primary treatment for breast cancer is lumpectomy or total mastectomy followed by hormone therapy or chemotherapy.[10] The use of hormone therapy vs chemotherapy is dependent on the breast cancer characteristic, (T/N/M/Receptor status).[9] Therefore, using Cerianna™ to determine the hormone status can help with determining approriate therapeutic regimens for patients.[10]

Trodelvy™ is a later stage agent for the treatment of triple-negative breast cancer for patients that have received two prior therapies for metastatic disease.[5] Trodelvy™ functions as a topoisomerase inhibitor, Trop-2 antibody.[5] Per NCCN 2020 treatment guidelines, Trodelvy™ has been included for the treatment of TNBC.[10] The use of Trodelvy™ is listed as an alternative agent only after the use of a platinum agent and a taxane agent for metastatic disease.[10]

Tukysa™ acts as a tyrosine kinase inhibitor of HER2-positive.[7] Current NCCN guidelines list pertuzumab + trastuzumab + docetaxel (category 1) as the recommended first line regimen for metastatic HER2-positive breast cancer.[10] Tukysa™ has been included in the NCCN guidelines as an "other" recommended regimen including tucatinib + trastuzumab + capecitabine (category 1).[10]

Conclusion

The Food and Drug Administration annually releases a report of novel agents that are introduced to the market. This report provides information on new medications For the purposes of breast cancer, Trodelvy™, Tukysa™, and Cerianna™ were recently approved by the FDA. Development of new agents is important to continue to to help treat and diagnose cancer.

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