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Anastrozole – Breast Cancer Prevention

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Patented in 1984 and approved for medical use in 1995, Anastrozole has become one of the most prescribed drugs for postmenopausal women to prevent the development of breast cancer. It works by lowering the oestrogen levels of postmenopausal women and slows or reverses the growth of hormone receptor-positive breast cancer. Anastrozole is often given to patients whose cancer has progressed even after taking the drug Tamoxifen, which also works by lowering oestrogen levels. There are many side effects that come with Anastrozole, and so precaution must be taken when prescribing the drug because the side effects will vary depending on how it interacts and metabolises within the patient's body. Research is being conducted to test if the effectiveness of Anastrozole can be increased if taken with other drugs, such as palbociclib; however, the economic costs on health institutions around the world must be considered. It may also be possible for Anastrozole to be genotyped for a specific individual to maximise its affect and reduce the risk of developing the side effects.

Anastrozole is one of the hormonal treatments for breast cancer. Sold under the brand name, Arimidex, Anastrozole is a nonsteroidal aromatase inhibitor (AI) and is most often prescribed to postmenopausal women suffering from breast cancer[3]. It works by blocking the enzyme aromatase, lowering the oestrogen levels lowered (Figure 1). Breast cancer is an oestrogen-dependent cancer. Postmenopausal women usually suffer from a type of breast cancer, wherein hormone-receptor-positive tumours are prevalent and spread if oestrogen concentrations are high. Anastrozole is usually taken as tablets once a day for five years. The patients who are prescribed Anastrozole experience a variety of side effects, such as hot flushes, vaginal dryness or bleeding, difficulty sleeping, tiredness, nausea, muscle or bone pain, skin rash, hair loss, low mood or depression, headaches, nausea, joint pain, tiredness, bone thinning, allergic reactions, liver injury that may result in autoimmune hepatitis, carpal tunnel syndrome, and severe skin reactions[9] . Furthermore, older women and women who drink alcohol or smoke have some predisposing risk factors. Your doctor must be consulted if you are affected by any of these risk factors. Older women are more likely to have osteoporosis, cardiovascular disease, or other health problems due to Anastrozole. Women who smoke have an increased risk of lung damage and reduced bone density and in turn an increased risk of bone fracture, whilst women who drink alcohol have an increased risk of liver damage and face interferences with the absorption of Anastrozole. Women who smoke and drink alcohol are both at risk of high blood pressure and the recurrence of breast cancer due to Anastrozole. It is advised that women on Anastrozole take Calcium and Vitamin D supplements to prevent bone loss and fractures. Those who smoke and drink alcohol are advised to quit so heart, lung, and liver problems can be avoided. In addition to this, exercising regularly will help maintain a healthy weight, improve your mood, energy, and overall health. It is advised to seek support from healthcare, family, and friends to help deal with the emotional and physical effects of Anastrozole.

As of November 7th, 2023, around 289,000 postmenopausal women in England are at moderate or high risk of developing breast cancer, based on their family history[2] . As a result, Anastrozole has been made accessible through the NHS. After a consultation with their GP, women can be referred for treatment.

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Anastrozole is a prophylactic treatment that can reduce the risk of breast cancer by up to 50% of women, depending on if they have a family history of the cancer.

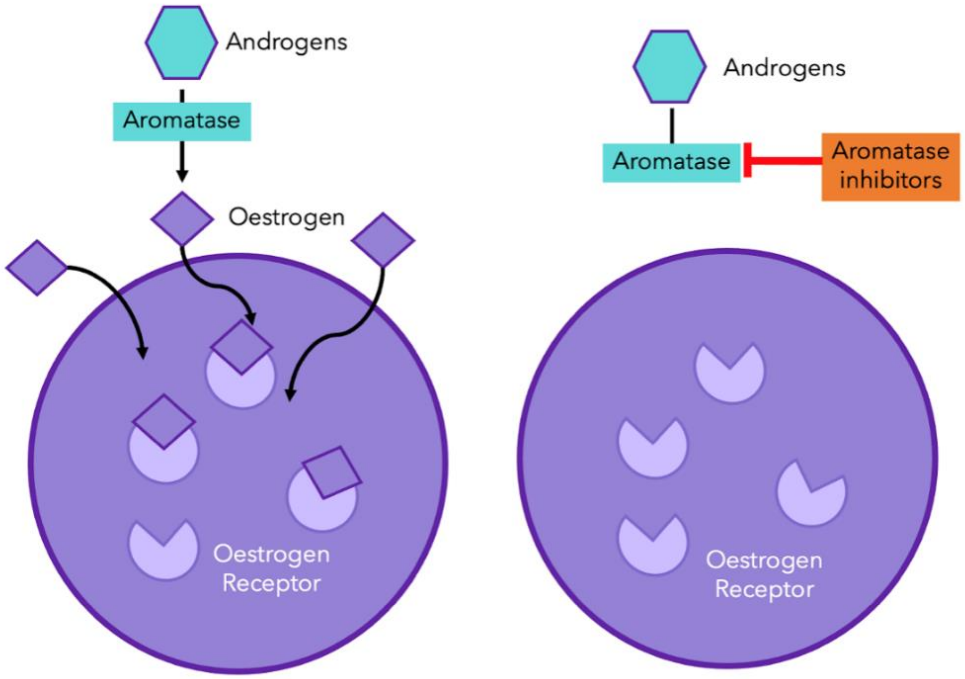

Figure 1: Inhibition of the aromatase enzyme. Aromatase inhibitors (AIs) bind to oestrogen receptors and prevent the Aromatase enzymes from working. This stops oestrogen levels rising, which stops the proliferation of cancer cells[6].

Currently, research is being conducted to determine the efficacy of Anastrozole along with other drugs for breast cancer prevention. Anastrozole was paired with baseline oestradiol serum and a case-control study was carried out based on the IBIS-II prevention trial, which investigated the effect of Anastrozole on preventing breast cancer in postmenopausal women. Overall, the study found that the drug was effective in preventing the risk of breast cancer by 49% compared to the placebo over a median follow-up of 131 months; however, the benefit was limited to women with a ratio of medium or high levels of oestradiol to sex hormone binding globulin (SHBG). Women with a low ratio of oestradiol to SHBG did not benefit from the anastrozole treatment[5]. The study concluded that measuring serum hormone concentrations could help identify which women would benefit from being treated with anastrozole, which could improve the risk management and personalised treatment of postmenopausal women at high risk of breast cancer. Despite the results, the study also acknowledges the limitations with case-control studies, such as a lack of hormone receptor data, which is a key prognostic and predictive factor for breast cancer, as well as to identify if the effects of Anastrozole will vary depending on the different subtypes of hormone receptors. Furthermore, an unproportionally representative sample due to the study population being comprised mainly of White European women at high risk of breast cancer because of their family history, which means ethnicity and those at lower risk have been disregarded so the findings may not be applied to women of these backgrounds. Further research must be carried out to verify these findings.

Another study was conducted using AIs in tandem with palbociclib for the treatment of advanced breast cancer[1]. Anastrozole is one of the AIs used to evaluate the effectiveness of palbociclib. The results were then compared to the results of the PALOMA-2 trial. The PALOMA-2 trial was a double-blind, phase 3 randomised controlled trial that evaluated the efficacy and safety of palbociclib in combination with Letrozole, which is an

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AI, for the treatment of ER-positive and HER2-negative advanced breast cancer. The study used a population-based registry (RON) to identify all patients who received AIs along with palbociclib in Portugal between 2017 and 2019. Overall, the combination of AIs with palbociclib had agreeable effectiveness in terms of progression-free survival (PFS), especially when used on patients with similar characteristics to the patients used in the PALOMA-2 trial, the median PFS was 19.5 months, which means half of the patients had disease progression or died before 19.5 months and the other half had it after, whilst the 1 year PFS was 67.9% and the 2 year PFS was 42.0%; however, similar to the oestradiol combination, the effectiveness varied. With palbociclib, the effectiveness of the treatment differed on the prognostic status of each patient, such as the presence of visceral metastases, which have a poorer PFS than those with bone-only or non-visceral metastases[4].Therefore, the future of anastrozole prescriptions will depend on the individual assessments of each patient's clinical situation and the expected outcomes. Furthermore, the study states that the cost of palbociclib will have a major impact on health systems and should be considered. During a cost-effectiveness analysis of palbociclib and other endocrine therapies, compared to placebo and endocrine therapy, in the UK, it was found that palbociclib-Anastrozole had an Incremental Cost-Effectiveness Ratio (ICER) of £79,947 per Quality-Adjusted Life Year (QALY)[7]. This far exceeds the willingness-to-pay threshold of £20,000-£30,000 per QALY. The study concludes that the combination of palbociclib-Anastrozole is not cost-effective in the UK.

The future of breast cancer prevention in postmenopausal women looks to be steady. With the current scheme of making the treatment much more accessible to postmenopausal women who may be at risk, a step in the right direction is being taken. One possible avenue of exploration is genotyping, which is a process that determines the genetic makeup of an individual by examining their DNA sequence. It is possible to use Anastrozole in conjunction with genotyping to identify genetic factors that may affect how receptive or resistant an individual is to the drug. Studies were conducted to review the mechanisms of resistance to Ais. It was found that single-nucleotide polymorphisms (SNPs), variations in a single base pair of DNA that occur in a certain percentage of the population, are one of the factors that may affect the effectiveness of AI therapy[8].

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