

BÖLÜM 26

AROMATAZ İNHİBİTÖRLERİ

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GİRİŞ

Östrojenlerin hem menopoza öncesi hem de menopoza sonrası kadınlarda meme kanserlerinin gelişmesinde önemli olduğu bilinmektedir. Meme kanseri hastalarının sayısı yaşla birlikte arttığından meme kanseri hastalarının çoğunluğunu post menopoza kadınlara oluşturmaktadır. Menopozdan sonra östrojenler artık overlerde yapılmazsa da, periferik dokular tümör büyümesini uyarmak için yeterli olan konsantrasyonlarda östrojen üretir. Aromataz enzimi (AI), östrojen biyosentezindeki son ve hız kısıtlayıcı adımı katalize ettiğinden, bu enzimin inhibitörleri meme kanseri için etkili, hedefe yönelik bir tedavi modelitesidir. Üç aromataz inhibitörü (Eksemestan, Anastrozol, Letrozol) mevcuttur ve anti-östrojen tamoksifeninden daha etkili oldukları ve iyi tolere edildikleri gösterilmiştir. AI'ler artık menopoza sonrası meme kanseri olan hastalar için standart bir tedavidir. AI'ler adjuvan, birinci ve ikinci basamak metastatik hastalıkta etkilidir.

Aromataz Enzimi

Östrojenler, normal kadın fizyolojisi ve üremesi için gerekli olan bir grup steroid hormondur. Östrojen sinyal yolu, özellikle hücre proliferasyonu ve hücrenin hayatta kalması gibi çeşitli hücresel süreçlerde yer alır. Östrojenlerin üreme sisteminin yanı sıra kas-iskelet sistemi, kardiyovasküler sistem ve beyinde de önemli işlevleri vardır (1). Kadınlardaki üç ana doğal östrojen, estrone (E1), estradiol (E2) ve estriol (E3) içerir. Estradiol veya 17 β -estradiol, üreme çağındaki kadınlarda östrojenlerin ana formudur. Buna karşılık, estrone ağırlıklı olarak post menopoza

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daha az görülmüşken (10-yıllık insidans %0.4 vs %1.2; RR:0.33), kemik kırıkları tamoksifen kolundan daha fazlaymış (5-yıllık risk %8.2 vs %5.5; RR:1.42). Meme kanseri dışı ölümler açısından (tromboembolik, serebrovasküler ve kardiyak ölümler) gruplar arasında fark görülmemiş (41).

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