BÖLÜM 12

Prostat Kanserinde Kullanılan Yeni Nesil Anti-Androjen Tedaviler

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GİRİŞ

Prostat kanseri, başlangıcı ve ilerlemesi androjen reseptörü (AR) sinyal yolunun aktivitesi ile yakından ilişkili olan, hormona bağımlı bir malignitedir. AR 'nin aktivasyonuna, sentezi hipotalamik-hipofiz-testis aksı tarafından düzenlenen androjenler aracılık eder. Bu nedenle anti-androjen ajanlar prostat kanseri tedavisinin temelini oluşturmuş ve hastalığın farklı evreleri için bir dizi anti-AR ilaç geliştirilmiş ve onaylanmıştır.

Birinci nesil AR antagonistler flutamid, nilutamid ve bikalutamidi içermektedir. Hastalar, hastalığın erken evrelerinde birinci kuşak AR antagonistlerine yanıt verirken, zamanla direnç kazanır ve kastrasyona dirençli prostat kanserine (CRPC) ilerlerler. CRPC'de dahi AR aşırı ekspresyonun hastalığın ilerlemesinde etkili olduğu görülmüş bu nedenle bu sinyal yolunun hedeflenmesi önem kazanmıştır. Bu sebeple AR sinyallemesini hedeflemek için daha yüksek AR bağlanma afinitesi ve özgüllüğüne sahip ikinci nesil AR antagonistleri geliştirilmiştir.

Bu ajanların kullanımı, 2011 yılında abirateron asetat, 2012'de Amerika Birleşik Devletleri Gıda ve İlaç İdaresi (FDA) tarafından enzalutamidin onaylanmasıyla başlayarak giderek yaygınlaşmıştır. Sonrasında 2018 ve 2019'da onay alan apalutamid ve darolutamid ile birlikte bu ajanlar, hem androjene bağımlı hem de kastrasyona dirençli hastalık uygulamalarıyla prostat kanserli hastaların sağkalımını iyileştirmiştir. (1)

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