

İMMÜN KONTROL NOKTASI İNHİBİTÖRLERİ İLE İLİŞKİLİ PULMONER TOKSİTELER VE YÖNETİMİ

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18. BÖLÜM

GİRİŞ

Günümüzde kanser immünoterapisi denilince akla ilk olarak immün kontrol noktası inhibitörleri (KNİ) gelmektedir. İmmün sistem içindeki kontrol noktaları, immün hücrelerin belirli hücre veya dokulara saldırmasını önleyen inhibitör yollar içerir. Böylece immün yanıt sırasında sağlıklı dokuların zarar görmesi yani otoimmünite engellenmiş olur. Tümör hücreleri bu noktaları, konakçı immün sisteminden kaçmak için kullanabilmektedirler. KNİ'leri (Tablo 1), Programlanmış hücre ölüm-1 (PD-1), PD-1 ligandı (PD-L1) reseptörleri ve Sitotoksik T-lenfosit-ilişkili antijen 4 (CTLA-4) gibi immün kontrol noktası proteinlerinin negatif yöndeki düzenleyici etkisini bloke ederek tümöre spesifik immüniteyi güçlendirmektedirler. Bu yönleriyle KNİ'leri, özellikle ileri evre malignitesi olan hastalarda sağladıkları sağkalım oranlarıyla kanser tedavisinde çığır açmışlardır(1). Diğer yandan aktif T lenfositleri üzerindeki freni kaldırarak tetikledikleri otoantikorlar, inflamatuvar sitokinler ve komplemanlar birçok doku ve organda immün aracılı yan etkilere yol açarlar (2-3). KNİ ile ilişkili pnömonitis (KNİ-P), deri toksitesi, hepatit, tiroidit ve kolitten sonra en sık görülen immün aracılı yan etkidir. Bunlar arasında KNİ-P göreceli olarak nadir olmasına rağmen, daha ağır ve ölümcül seyredebilmektedir (4-6).

Tablo 1. Kontrol Noktası İnhibitörleri

Anti - CTLA-1 antikoru	İpilimumab, Tremelimumab
Anti - PD-1 Antikoru	Nivolumab, Pembrolizumab
Anti - PD-L1 antikoru	Atezolizumab, Avelumab, Durvalumab

CTLA: Sitotoksik T-lenfosit ilişkili protein, PD: Programlı hücre ölümü, PD-L: Programlı hücre ölümü ligandı

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