Bölüm
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İMMÜNOTERAPİ AJANLARININ ETKİNLİĞİNİ GÖSTEREN KLİNİK ÇALIŞMALAR VE ENDİKASYONLARI

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GİRİŞ

Sitotoksik T lenfosit antijen-4 (CTLA-4) ve programlanmış ölüm proteini 1 (PD-1) ve bunun ligandı olan PDL-1 i hedefleyen monoklonal antikor immun check point inhibitörleri bir çok kanser türünde kullanılmış ve gerek tek başına gerekse kemoterapi veya hedefe yönelik ajanlarla yada radyoterapi ile kombine olarak tedavi endikasyonu almışlardır (1-6). Bu bölümde Ocak 2020 tarihine kadar FDA tarafından onaylanmış CTLA-4 inhibitörleri ve PD-1 ve PDL-1 inhibitörleri ile endikasyon çalışmaları ve endikasyonlarına yer verilecektir.

CTLA-4 İNHİBİTÖRLERİ

İpilimumab:

Tam insan IgG1 yapısında monoklonal antikordur (7). T hücre yüzeyinde bulunan CTLA-4 ve CD80/CD86 arasındaki bağlanmayı bloke eder. Bu blokaj sayesinde T hücre aktivasyonu artar, T hücrelerinde artış hızlanır ve T hücrelerinin antitümör etkinlikleri artar(8). İpilimumab ilk defa 2010 yılında ileri evre malign melanomda yapılan faz 3 çalışmada etkinliğini gösterdi ve 2011 yılında immunoterapötik ajan olarak FDA onayı alan ilk ajan olmuştur(9). Rutin kullanım dozu 3 mg/kg 3 haftada birdir. İzotonik veya %5 dextroz ile kullanılır. Nihayi solusyon konsantrasyonu 1-2 mg/ml olmalıdr. En fazla 4 doz önerilmektedir. Diğer endikasyonları tablo-1'de verilmiştir. Ticari ismi YERVOY'dur.

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ATEZOLİZUMAB:

PDL-1 e karşı insan IgG4 monoklonal antikorudur. 840 mg veya 1200 mg sabit dozda 3 haftada bir uygulanır. Sadece 250 ml izotonik ile karıştırılarak ilk dozda 60 dakikada, reaksiyon gelişmezse sonraki dozlarda 30-60 dakikada infüze edilir. Piyasa ismi TECENTRİQ'tir (60). Atezolizumab'ın Ocak 2020 tarihi itibari ile FDA tarafından onaylanan endikasyonları Tablo-6 dadır.

Tablo-6. Atezolizumab FDA endikasyonları

Onay tarihi	Çalışma	faz	Endikasyon	Doz
11.03.2019	Impassion130 (61)	3	Triple negatif metastatik meme kanserinde 1. Basamakta nab-paclitaxel ile	840 mg
06.12.2018	Impower150 (62)	3	Nonskuamöz küçük hücre dışı akciğer kanseri 1. Basamakta kemoterapi +/-bevacizumab ile	1200 mg
18.10.2016	OAK (63)	3	Daha önce tedavi almış non small cell akciğer kanserinde tek başına	840 mg-1200 mg
18.03.2019	Impower133 (64)	3	Küçük hücreli akciğer kanseri 1. Basamakta kemoterapi ile	1200 mg
18.05.2016	(65)	2	Sisplatin bazlı tedavi için uygun olmayan üretelyal karsinom 1.basamak tedavisinde	1200 mg

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