

Bölüm 10

YENİ NESİL ANTI-CD 20 ANTİKORLAR

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GİRİŞ

CD20 molekülü, hem normal B hücreleri hemde B hücreli non-Hodgkin lenfoma hastalarının yaklaşık % 90 kadarı tarafından hücre yüzeyinde eksprese edilen bir hücre yüzeyi aktive-glikosile fosfoproteindir. CD20 işlevi iyi karakterize edilmemiştir, ancak B hücresinin büyümesinde ve farklılaşmasında, ayrıca kalsiyumun transmembran iletilmesinde rol oynadığı bilinmektedir. CD20'nin aktivasyonu, Lyn, Fyn, Lck ve Src ailesi kinazları gibi çeşitli hücre içi tirozin kinazların aktivasyonuna yol açar.^{1,2}

Anti-CD20 monoklonal antikorlarının bulunması kronik lenfositik lösemisinin (KLL) tedavisinde devrim etkisi yapmış ve köklü değişiklikler yaratmıştır. KLL hastalarında kullanılan ilk monoklonal antikor rituksimab olup, yapılan ilk çalışmada tedavi almamış KLL hastalarında fludarabin-siklofosamid (FC) kemo-terapisine rituksimabın eklenmesiyle sağ kalımda belirgin yararı gösterilmiştir.³ Rituximab, kimerik yapıdaki ilk anti-CD20 monoklonal antikordur ve KLL'de önceden herhangi bir tedavi almış veya tedavi-naive hastalarda başarılı bir şekilde kullanılmıştır. Rituksimabın KLL'deki immünoterapötik etkinliğini daha da ileri götürmek amacıyla yeni nesil alternatif anti-CD20 antikorları geliştirilmiştir.

Monoklonal antikorların (mAb) CD20-pozitif hücreleri hedef alması ve elimine edebilmesi için dört olası mekanizma vardır. Bu malign B-hücrelerinin yok edilmesi için monoklonal antikorlar; antikor bağımlı hücrel sitotoksinite (ADCC), antikor bağımlı hücrel fagositoz (ADCP), kompleman bağımlı sitotoksinite (CDC), programlı hücre ölümü (PCD) ve potansiyel olarak pasif immünizasyon gibi çeşitli farklı mekanizmalardan yararlanırlar. Bir antikorun bu me-

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sı etkinlik, yan etki profili ve çoklu ilaç tedavileri için uygun kombinasyonların belirlenmesine yardımcı olmaktadır. Süren bir dizi çalışmayla birlikte gelişmiş antikor hedefleme özelliklerine sahip yeni anti-CD20 ajanlarının geliştirilmesine devam edilmektedir.

Güncel klinik pratikte yeni ajanlar olan ofatumumab ve obinutuzumab hem tek ajan olarak hem de çeşitli klinik durumlarda kombinasyon halinde etkinlik göstermelerinden sonra KLL için kullanım onayı almışlardır. Daha yeni anti-CD20 antikorlar olan ocaratuzumab, veltuzumab ve ublituximabın immünoterapötik özellikleri ve bunların artırımı ile ilgili çalışmalar devam etmektedir.

Anahtar Kelimeler: Kronik lenfositik lösemi, yeni nesil anti-CD 20 antikorlar

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