ANTİ/HER2 TEDAVİLER İLE İLİŞKİLİ KARDİYOMYOPATİLER

5. BÖLÜM

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TRANSTUZUMAB

İnsan epidermal büyüme faktörü reseptörü 2'yi (HER2, ErbB2 olarak da adlandırılır) hedefleyen monoklonal bir antikordur. Tümörleri HER2'Yİ aşırı eksprese eden meme kanseri hastalarının yüzde 15 ila 20'si için transtuzumab tedavisi hem erken hem de ileri hastalığın tedavisinde önemlidir. Bununla birlikte, kullanımı, tipik olarak sol ventrikül ejeksiyon fraksiyonunda asemptomatik bir azalma ve daha az sıklıkla klinik kalp yetmezliği ile kendini gösteren kardiyotoksisite için hafif-orta risk taşımaktadır.

Transtuzumab'ın klinik kullanımından sonra HER2'yi aşırı ekspere eden meme kanserli hastaların tedavisi için transtuzumabın dışında 3 yeni Anti-HER2 ajan geliştirilmiştir.

Bunlardan bir tanesi olan **lapatinib**, bir trozinkinaz inhibitörüdür ve EGFR 1 ve 2 (erb1 ve erb2) reseptörlerinin hücre içi dimerlerinin fosforilasyonunu engeller. Bir diğeri antikor-ilaç konjugatı olan ve **transtuzumab** ile antimitotik bir ajan olan **maytansine'nin** komposizyonundan oluşan **ado-transtuzumabemtasine(T-DM1)** ve son olarak **Pertuzumab**, HER2'nin ekstrasellüler parçasının altpraçası2(subdomain2)'e bağlanarak HER2'nun HER reseptör ailesinin diğer üyeleriyle homo-hetero dimerizasyonunu engeller

Pertuzumab ve T-DM1'ın kardiyotoksisitesi hakkındaki bilgilerimiz sınırlı olasa da mevcut bilgiler pertuzumab ve T-DM1'in transtuzumab'a göre daha az kardiyotoksik olduğu yönündedir.

Trastuzumab ve ilgili HER2 hedefli ajanlarla ilgili kardiyotoksisite burada sunulacaktır. Antrasiklinler ve taksanlar da dahil olmak üzere diğer antineoplastik ilaçlara bağlı kardiyotoksisite, kalp yetmezliğinin yönetimi ve trastuzumab ve diğer HER2 hedefli tedavilerin klinik kullanımı ayrı ayrı tartışılmalıdır.

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- Adjuvan ilaç alan hastalarda, trastuzumab başlamadan önce bir başlangıç değerlendirmesi ve seri LVEF izlenmesi (trastuzumab'ı başlattıktan 3, 6 ve 12 ay sonra ve bir antrasiklin veya diğer kemoterapiyi başlattıktan 18 ay sonra) kardiyak disfonksiyonu taramak için uygundur.
- Metastatik hastalarda, başlangıç değerlendirmesinden sonra, LVEF semptomların yokluğunda nadiren izlenir
- Trastuzumab ile ilişkili kardiyotoksisite geliştiren hastalar için trastuzumab dozajı için kılavuzlar, LVEF deki azalma hasta semptomlarına dayanmaktadır
- Trastuzumab ile ilişkili kardiyotoksisite birçok hastada geri dönüşümlüdür ve kalp yetmezliği için standart tedaviye yanıt verir. Birçok hasta devam veya trastuzumab ile tekrar tedaviyi tolere eder
- Trastuzumab, taksanlar, radyasyon tedavisi ve endokrin tedavisi ile güvenli bir şekilde uygulanabilir

Diğer HER2 hedefli ajanlar

- Trastuzumabın aksine, kardiyotoksisite riski, lapatinib, ado-trastuzumab emtansine (T-DM1) ve pertuzumab gibi diğer insan epidermal büyüme faktörü reseptörü 2 (HER2) hedefli ajanlarla daha az görünmektedir. Bununla birlikte, bu ajanların üçü ile ilgili deneyim sınırlıdır ve tüm ajanlarla potansiyel bir kardiyotoksisite riski vardır.
- Transtuzumab da oladuğu gibi LVEF'nin tedavi öncesi bazal değerlendirmesi uygundur. Yine Trastuzumab'da olduğu gibi, metastatik hastalarda, tedavi sırasında semptomların yoksa semptomların yokluğunda LVEF nadiren izlenir.
- Bu ajanlarla tedavi sırasında kardiyotoksisite geliştiren hastalarda doz ayarlaması ile ilgili kılavuzlar mevcuttur

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