Bölüm
2

HEDEFE YÖNELİK TEDAVİLERİN ACİL YAN ETKİLERİ

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Tümör boyutunun 1-2 mm üzerine çıkması ile avasküler fazdan vasküler faza doğru ilerleme gerçekleşir. Bu fazda etkili olan hipoksi ile indüklenen faktör alfa (HIF-1a) ile vasküler endotelyal büyüme faktörü (VEGF), trombosit ilişkili büyüme faktörü (PDGF) gibi faktörlerin etkisi ile anjiogenezis süreci başlamış olur (1). Metastatik evre hastalık tedavisinde anjiogenezisi inhibe eden ajanların etkisiyle vasküler regresyon ve hastalık kontrolü sağlanabilmektedir. Tümör anjiogenezinin inhibisyonu için 2 ana mekanizma tanımlanmıştır: VEGF ligandı ile reseptörlerinin blokajı ve proanjiogenetik sinyalizasyonun, reseptor tirozin kinazlar ile inhibisyonu şeklindedir. Yüzlerce tirozin kinaz reseptörü bildirilmiştir. Küçük molekül yapıda hücre içi reseptör kinaz inhibisyonu sayesinde ile hem anti-anjiogenetik hemde anti-proliferatif yanıt elde edilebilmektedir. Tirozin kinaz inhibitörü (TKİ) sınıfında yer alan ilaçlara özgü sınıf etkisi olarak belirtilebilecek yan etkiler mevcuttur. Bu ilaçların yan etkileri şiddetine göre derecelendirilmeli ve gerekli tedavi bu derecelendirmeye göre düzenlenmelidir (Tablo-1).

Tablo 1: İlaca bağlı yan etkilerin derecelendirilmesi

Grade 1	Asemptomatik veya hafif semptomlar; sadece klinik veya tanısal gözlem yeterli, tıbbi müdale gerektirmeyen; hafif dereceli
Grade 2	Minimal tıbbi tedavi gereksinimi olan, lokal ya da non-invaziv olabilecek düzeyde; orta dereceli
Grade 3	Tıbbi açıdan müdahale gerektiren, hastane yatış endikasyonu oluşturan ya da yatan hastada yatışın uzamasına neden olabilen; şiddetli dereceli
Grade 4	Acil müdahale gerektiren; hayatı tehdit etmekte olan
Grade 5	Ölümle sonuçlanan yan etki

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siklibden farklı olarak abemasiklib kullanan hastalarda grade3 nötropeninin de dahil olduğu ilk episodun yaklaşık 29-33. gününde rastlanılmaktadır. İlaca ara verilmesi sonrası normal nötrofil değerlerine yaklaşık 7-12 günde ulaşılır. Bu nedenle ilacı kullanan kişilerde nötropenik ateşle acil servise başvuru gözlemlenebilir.

Pulmoner toksisite, öksürük, nefes darlığı, hipoksi bulguları olan hastalarda enfeksiyon veya neoplazinin dışlanması sonrasında ilaca bağlı pnömonitis akılda tutulmalıdır. Yaşamı tehdit edebilecek kadar ciddi intertisyel akciğer hastalığı gelişebilmektedir.

Kardiyak ileti bozukluğu, cQT uzaması günlük 600 mg doz alan hastalarda >500 msn veya bazale göre >60 msn uzama görülebilir. EKG de QT değişklikleri özellikle ilacın başlanmasından sonraki ilk 4 hafta içerisinde görülür. Beraberinde hipokalemi, hipokalsemi gibi elektrolit bozukluğu, geçirilmiş myokard enfarktüs öyküsü, ileri kalp yetersizliği ve bradiartimisi olan hastalarda Torsades de pointes ve ani kardiyak ölüm açısından dikkatli olunmalıdır.

Hepatobiliyer toksisite, serum ALT ve AST değerlerinde grade 3 ve 4 artış görülebilmektedir.

Gastrointestinal toksisite, özellikle daha çok abemasiklibe bağlı gelişmektedir. İshal şiddeti grade 3 düzeylerinde seyredebilmektedir. İshale bağlı dehidrtasyon görülebilmektedir. İlacın ilk haftasında gelişebilir ve yaklaşık 7-11 gün sürebilmektedir. Antidiyarel ilaçlar (loperamid vs) ve sıvı desteği verilmelidir.

Tromboembolism, CDK 4/6 inhibitörleri (daha çok abemasiklib) ile aromataz inhibitörleri ya da fulvestrant kombinasyonu ile ilişkili olarak venöz tromboz, pulmoner emboli, serebral sinüs trombozu ve aksiller ven trombozu bildirilmiştir.

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