Bölüm
**17**

# METASTATİK GASTROİNTESTİNAL STROMAL TÜMÖRDE SİSTEMİK TEDAVİ YAKLAŞIMLARI

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## GİRİŞ

Gastrointestinal stromal tümör (GİST), gastrointestinal sistemin en sık görülen mezenkimal kökenli tümörüdür. Yumuşak doku sarkomlarının % 20'sini oluşturmaktadır ve yıllık insidansı yaklaşık olarak milyonda 10 olarak bildirilmiştir (1). İlk kez 1980'li yılların başlarında Mazur ve Clark tarafınca tanımlanmıştır (2). Her yaşta tanı konulmasına rağmen 60'lı yaşlarda en sık görülmektedir (3). GIS'in herhangi bir yerinden kaynaklanabilir. Fakat, mide (% 60) ve ince barsak (% 30) en sık yerleşim yeridir. Daha az sıklıkla duodenum (% 4-5), rektum (% 4), özofagus (< %1) ve kolon (% 1-2) yerleşimlidir (4). %5'den daha az oranda omentum, mezenter ve retroperiton gibi gastrointestinal sistem ile bağlantısı olmadan abdominal boşluktan gelişmektedir, bu tümörler ekstra gastrointestinal GİST olarak tanımlanmaktadır (5). Sıklıkla karaciğer, omentum ve peritoneal yüzeylere metastaz yapmaktadır. Diğer sarkomlardan farklı olarak daha az sıklıkla akciğer ve nadiren lenf nodu ve kemik metastazı görülmektedir (3).

1998 yılında Hirota ve arkadaşları tarafınca GIST'de KIT mutasyonu saptanması üzerine hastalığın biyolojisi ve tedavi seçenekleri üzerine gelişmeler yaşanmıştır (6). KIT, transmembran yerleşimli protein kinaz olup, KIT proto-onkogeni tarafınca kodlanmaktadır (3). GİST vakalarının çoğunda (% 95) KIT(CD117) ekspresyonu saptanır. Bunun yanı sıra CD34 (% 70), aktin (% 25), desmin (< %5) ve DOG1 ekspresyonu gözlenir (7). Vakaların % 80'inde KIT reseptörü mutasyonu, % 5-10'da platelet kökenli büyüme faktörü-alfa (PDGFRA) reseptör mutasyonu saptanır. %1 0-15 vaka ise GİST wild tip olarak tanımlanır ve KIT veya PDGFRA mutasyonu gözlenmez (8). PDGFRA mutasyonu olanlarda KIT ekspresyonu düşük iken DOG1 ekspresyonu oranı yüksektir (9). GİST wild tip olanların büyük çoğunluğunda süksinat dehidrogenaz (SDH) geni mutasyonu veya SDH bağlayıcı

15.3 hafta; kombine kolda 12 hastanın birinde parsiyel yanıt, ikisinde stabil yanıt, PSK 18 hafta olarak saptanmıştır (45).

## SONUÇ

GİST, gastrointestinal sistemin en sık görülen mezenkimal tümörüdür. Cerrahi tedavi ve yüksek riskli hastalarda adjuvan imatinib tedavisi sonrası veya de novo olarak metastaz gelişmektedir. Karaciğer, mezenter ve omentum metastazı sıktır. Rutin pratikte bakılmamakla birlikte mutasyon analizi yapılması önerilmektedir. FDA tarafınca 1. basamak tedavide imatinib, 2. basamak tedavide sunitinib ve 3. basamak tedavide ise regorafenib onay almıştır. İmatinib standart dozu 400 mg/gün'dür. Fakat progresyon gelişen hastalarda doz artırılması ile yüksek doz (800 mg/gün) ve ya KIT ekzon 9 mutasyonu olanlarda 800 mg olarak tedaviye devam edilmesi önerilmektedir. Onaylı ilaçlar haricinde klinik çalışmalarda etkinlikleri gösterilen tirozin kinaz inhibörleri (sorafenib, pazopanib, nilotinib, dasatinib, masatinib, pocatinib ), PI3K/AKT/mTOR yolağı inhibörleri, HSP90 inhibitörleri, IGFR inhibitörleri ve immünoterapiler ileri evre GIST hastalarında alternatif tedavi seçenekleri oluşturmaktadır. Figür 1'de tedavi seçenekleri gösterilmektedir.

**Anahtar Kelimeler:** Gastrointestinal stromal tümör; imatinib; KIT

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