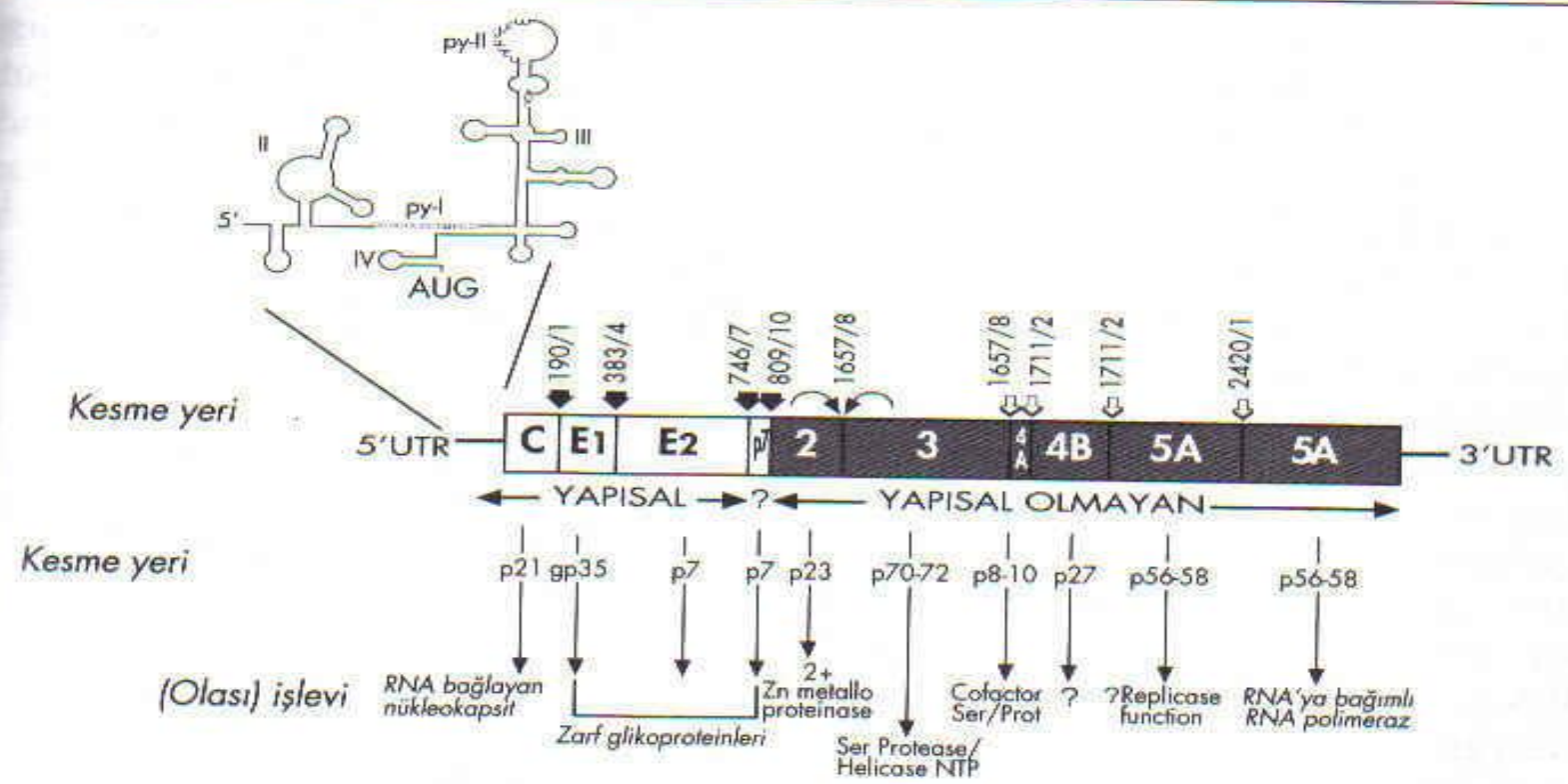
KRONİK HEPATİT C: OLGU

Dr. Reşit MISTIK

KLİMİK- VHÇG Abant Kampı
28.02-2.03.2014

- izole edilmeden antijenleri klonlanarak keşfedilen ilk virüs

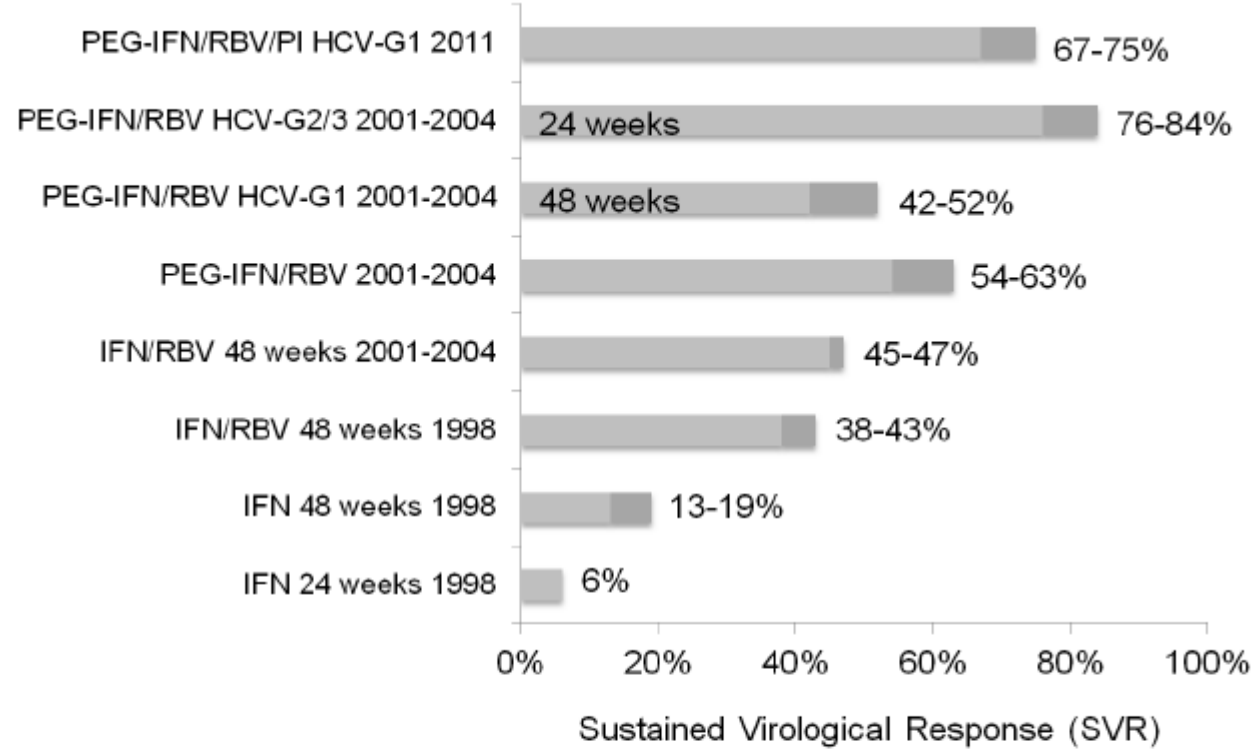
- zarflı, genomu 9600 bp



1. HCV Genom Organizasyonu

Table 2. Approved drugs for the treatment of chronic hepatitis C (2011)

Medication	Dosing
Type I interferons	Subcutaneous injection
Pegylated interferon α-2a (Pegasys®)	180 µg once weekly
Pegylated interferon α-2b (PEG-Intron®)	1.5 µg/kg once weekly
Interferon α-2a (Roferon®)	3 - 4.5 Mill IU three times weekly
Interferon α-2b (Intron A®)	3 Mill IU three times weekly
Consensus Interferon (Infergen®)	9 µg three times weekly
Ribavirin	Oral tablets or capsules
Ribavirin (Copegus®)	800 - 1200 mg daily (200 mg or 400 mg tablets)
Ribavirin (Rebetol®)	600 - 1400 mg daily (200 mg capsules or solution)
HCV protease inhibitors	Oral tablets or capsules
Boceprevir (Victrelis®)	800 mg (4 x 200 mg capsules) every 7-9 hours
Telaprevir (Incivek®, Incivo®)	750 mg (2 x 375 mg tablets) every 7-9 hours* *3 x 375 mg every 12 hours is as effective in treatment-naïve patients (Buti 2012)



IFN trials	PEG-IFN trials	PI trials
USA trial: McHutchison et al., NEJM 1998 Int. trial: Poynard et al., Lancet 1998	PEG-IFN2b: Manns et al., Lancet et al., 2001 PEG-IFN2a: Friedet al., NEJM 2002 PEG-IFN2a: Hadziyannis et al., Ann Int Med. 2004	Boceprevir: Poordad et al., NEJM 2011 (non-black cohort) Telaprevir: Jacobson et al., NEJM 2011

Figure 1. Development of chronic hepatitis C therapy. The sustained virologic response rates have improved from around 5% with interferon monotherapy in the early 90s to >70% today with triple therapy of PEG-IFN + ribavirin + PI (data for treatment-naïve patients)

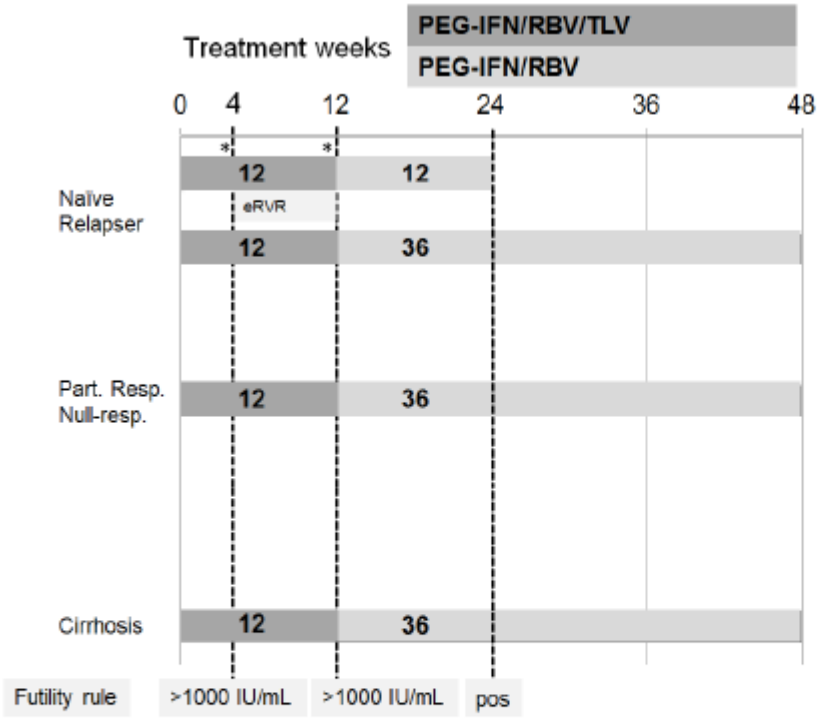


Figure 2B. Treatment with TLV/PEG-IFN/RBV: Approved treatment algorithm for HCV GT1 patients. *RGT if eRVR (HCV RNA LLD week 4-12)

***If patients have contraindications for BOC or TLV, dual therapy with PEG-IFN/RBV should be given for 24-72 weeks according to the HCV RNA decline at week 4 and week 12 (Sarrazin, Berg, Cornberg 2010 S3-Leitlinie). The treatment algorithm is similar to Figure 6

OLGU

- 49 y, kadın, evli, ev hanımı
- 5-10 adet/gün/ 20 yıl sigara
- Annesi serviks CA’dan eks

- 07.2010 da başvurdu,
- anti-HCV pozitif,

- Lökosit 6700, Hgb 13.7, Trombosit 201.000
- AKŞ 81, Üre 29, kreatinin 0.7,
- AST 41, ALT 39, ALP 116 İÜ/L, GGT 131 İÜ/L,

- Total protein 7.8 g/dL, albumin 3.9??? Trigliserit 114, kolesterol 142,
- protein elektroforezinde; albumin %47.8, gama globulin %24.2,
- AFP 15.1, INR 1.09

- HCV-RNA 406.000 İÜ/mL,
- G1,
- 65 kg, 152 cm,
- Batın USG KC ince granüler görünümlü,

Ne yapalım??

- Tedavi verelim mi? Evet.
- Ne zaman ve ne ile?

- Hemen tedavi başlayalım mı?
- Biyopsi yapıp sonra mı tedavi verelim?

Tedavide ne verelim?

- RBV/Peg-IFN
- RBV/Peg-IFN/PI

- ISHAK’a göre HAİ 17, Fibrozis 5

Kontrole üç yıl sonra 04.01.2013 te geldi;

- 2010’da kolesistektomi olmuş, halsizliği var

- KC USG aynı

- Lökosit 6700, Hgb 13.2, Trombosit 132.000

- AST 58, ALT 45, ALP 139, GGT 77,

- Total protein 8.0 g/dL, Albumin 2.9,
- AFP 15, TSH 2.3,
- PA %75, INR 1.17,
- HCV-RNA 14.500 İÜ/mL,

izlem

- 1.02.2013'te 3'lü tedavi (RIB, Peg-IFN, TLR) başlandı
- Tedavinin birinci ayında HCV-RNA negatif
- Anemi (8.2) ve trombositopeni (44.000) nedeniyle ribavirin ve peg-IFN bir hafta ara, 1 Ü kan transfüzyonu, ribavirin dozu önce 2x200 mg sonra 1x200 mg düşüldü, telaprevir kesilmedi,

- Anemi için tekrar 1 Ü kan
- Trombosit 66.000, Hgb 8.5-9.2 g/dL arasında tutuldu
- 3. ayın sonunda yüzde ve ekstremitelerde ödem, albumin 2.5 g/dL, Hgb 8.15, TSH 7.18, hipotiroidi için replasmöan tedavisi

tedaviyi ne yapalım???

- Keselim mi??
- Devam edelim mi?

- Hastanın genel durumu nedeniyle tedaviye 45 gün ara verildi
- TSH normal, Hgb 11.2, Trombosit 140.000,
- 45 gün ara verildikten sonra HCV-RNA yine negatif idi

- Tedaviye tekrar başlandı, peg-IFN alfa-2a 180 mic g flakon ve 2x400 mg ribavirin

- Hgb 8.5 g/dl, Trombosit 56.000,

- Ribavirin 600 mg a düşüldü,
- Hgb 10.1 g/dL, trombosit 55- 60.000 düzeyinde seyrediyor,
- toplam tedavinin 11. ayı, iki ay önce HCV-RNA negatif,

Sonuç

- İn-vitro olarak KC hücrelerinde kısa süreli proteaz inhibitör kombinasyon tedavilerinin virüsü kısa sürede eradike edebildiği gösterilmiş

  (Ohara E, et. al. J Hepatol 2011; 54: 872)

- Olgumuzda kısa süreli tedavi acaba KVY oluşturabilecek miydi?

- Çünkü FDA araştırmalarda tedavi sonrası 3 aylık izlemi yeterli görmekte (Hepatology 2013, Manns and et.al.)

Table 1. Relevant definitions for HCV treatment

Abbreviation	Term	Description
SVR	Sustained Virological Response	HCV RNA negative 6 months after the end of therapy
SVR-12	Sustained Virological Response	HCV RNA negative 12 weeks after the end of therapy; FDA-accepted endpoint for future trials
RVR	Rapid Virological Response	HCV RNA negative after 4 weeks of therapy
eRVR (BOC)	Extended Rapid Virological Response (for boceprevir)	HCV RNA negative (LLD, not LLQ) between week 8 and week 24 of BOC therapy: RGT criterion for BOC
eRVR (TLV)	Extended Rapid Virological Response (for telaprevir)	HCV RNA negative (LLD, not LLQ) between week 4 and week 12 of TLV therapy: RGT criterion for TLV
EVR	Early Virological Response	HCV RNA decline ≥2 $\log_{10}$ at week 12
cEVR	Complete Early Virological Response	HCV RNA negative at week 12
NR (BOC)	Non-response (boceprevir)	HCV RNA ≥100 IU/mL at week 12; or HCV RNA positive at week 24, futility rule for BOC
NR (TLV)	Non-response (telaprevir)	HCV RNA ≥1000 IU/mL at week 4 or week 12; or HCV RNA positive at week 12, futility rule for TLV
BT	Breakthrough	HCV RNA was LLD but increased to ≥100 IU/mL or increase of HCV RNA ≥ 1$\log_{10}$ during therapy
RL	Relapse	HCV RNA negative at EOT and recurrence of HCV RNA during the follow-up of 6 months
PR	Partial Response	HCV RNA decline ≥2 $\log_{10}$ at week 12 but positive at week 24 during PEG-IFN + RBV
NULR	Null response	HCV RNA decline <2 $\log_{10}$ at week 12 during PEG-IFN + RBV
LI	Lead-In	4 weeks PEG-IFN + RBV before adding a PI

LLD, lower limit of detection (<10-15 IU/mL; here indicated as negative); LLQ, lower limit of quantification; EOT, end of treatment; RGT, response-guided therapy

- teşekkürler