I guai non vengono mai da soli

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MARCO

- 2013:
- HA 35 anni TD, AFFETTO DA EPATITE CRONICA HCV GENOTIPO 3 ,
- STADIAZIONE DELLA SUA EPATOPATIA
  FIBROSCAN …KpA 7.
- HBs Ag:neg, HIV Ab: neg
- HCVRNA 1.200.000 UI/L, GOT x5 vn GPTx7 vn.
- Ecografia epatica: nella norma
- Terapia Peg ifn plus Ribavirina 800mg/die
- HCVRNA non rilevabile e transaminasi nella norma dopo 28 gg
- Prosegue terapia per 24 weeks

- Durante il trattamento, compare alla XXIII settimana febbre persistente, spenomegalia, leucopenia con più marcata linfopenia, prurito.
- Transaminasi aumentate di circa 3 volte la norma linfoadenopatia laterocervicale bilaterale ,
- Nuova rivalutazione: HCV RNA, CMV , EBV, NEGATIVI, HBsAg resta assente.

Quale sospetto diagnostico

Effetto collaterale della terapia anti HCV?

Esordio di Linfoma ? altro?

Deduzioni

- Non ha linfoma!
- Dopo couselling, il paziente riferisce elementi nascosti in precedenza: numerosi rapporti sessuali “promiscui” e “non protetti”

  ed abuso alcolico
- Esegue HIV AB:

PRESENTI (sieroconversione)

Stadiazione della infezione da HIV

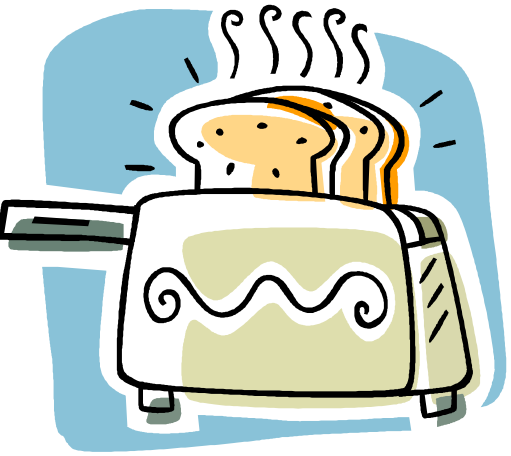
- Nel frattempo ha concluso con successo terapia anti HCV
- CD4 580 cell /mmc , HIV RNA 11.500 copie/ ml, plt 190.000
- INFEZIONE ACUTA? Riteniamo di si. Decidiamo di non trattarlo
- Ai controlli successivi: progressivo miglioramento immunologico,
- Eco Epatica : conferma di epatospenomegalia , con linfonodi reattivi all'ilo
- transaminasi ancora alterate: fino a GOT x 2v.n. GPT x 2 v.n
- HCV RNA risulta di nuovo presente: riattivazione di HCV

Ma

Ipertransaminasemia non solo persiste ma progredisce fino a x 10, con netta impronta colestatica .

HEV AB negativa, IgM HAV assenti, a sorpresa: HBsAg IgM e anti HBc presenti

Si era beccato anche una epatite acuta da HBV Genotipo A



IL NOSTRO PAZIENTE AVEVA CONTRATTO DUE NUOVE INFEZIONI :HIV ED HBV

A PARTE HCV

considerazioni

- NON TUTTO E’ SCONTATO
- il paziente dopo l’infezione da hcv ha contratto l’infezione da hiv
- Quindi una infezione da HBV

CONCLUSIONI

oggi

HBsAg presente, HBeAb presenti, HBV DNA non rilevabile

HCV è replicante

HIV è replicante

Quale conduttore ha questa troica?

- Haart per hiv e hbv
- Ritrattare hcv ? E con cosa?
- Terapia contemporanea per i tre virus? Magari!

AASLD/IDSA Recommendations for Genotype 3 HCV Treatment-Naive Pts

Population	Recommended Regimen	Duration
Regardless of IFN eligibility	Sofosbuvir 400 mg + RBV 1000-1200 mg/day	24 wks

Population	Alternative Regimen	Duration
Only consider if eligible for IFN	Sofosbuvir 400 mg + pegIFN + RBV 1000-1200 mg/day	12 wks

Not recommended:

- PegIFN/RBV for 24-48 wks
- Monotherapy with pegIFN, RBV, or a DAA
- Telaprevir, boceprevir, simeprevir

AASLD/IDSA treatment recommendations.

AASLD/IDSA Recommendations for Genotype 3 HCV Treatment-Experienced

Population	Recommended Regimen	Duration
Regardless of IFN eligibility	Sofosbuvir 400 mg + RBV 1000-1200 mg/day	24 wks

Population	Alternative Regimen	Duration
Consider only if eligible for IFN	Sofosbuvir 400 mg + pegIFN + RBV 1000-1200 mg/day	12 wks

Not recommended:

- PegIFN/RBV ± telaprevir, boceprevir, simeprevir
- Monotherapy with pegIFN, RBV, or a DAA

AASLD/IDSA treatment recommendations.

AASLD/IDSA Guidance: When to Start Treatment in HCV/HIV-Coinfected Patients

- Treatment is recommended for patients with chronic HCV infection
- Treatment should be prioritized in patients at high risk for liver-related complications
  - Includes patients with HCV/HIV coinfection, regardless of fibrosis stage
- Treating patients at high risk for transmitting HCV to others may decrease transmission and HCV disease prevalence
  - Includes MSM with high-risk sexual practices and active injection drug users

9. AASLD and IDSA. HCV Management Guidance. September 2014.

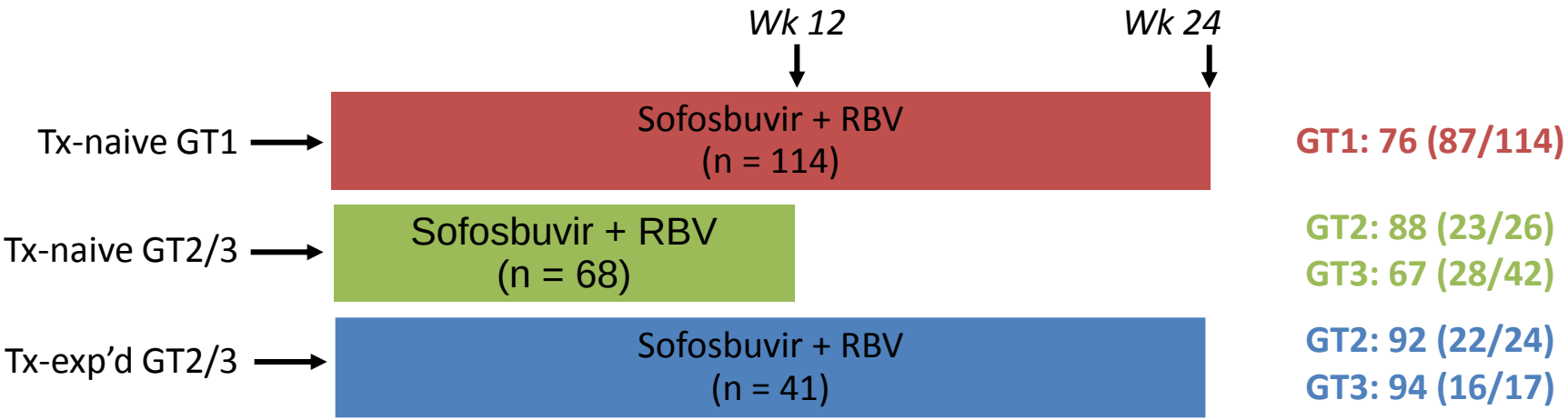
AASLD/IDSA Guidance: HCV Regimens NOT Recommended in HIV-Coinfected Pts

- The following are NOT recommended for treatment-naive or treatment-experienced HCV/HIV-coinfected patients:
  - Telaprevir- or boceprevir-containing therapy
  - Monotherapy with pegIFN, RBV, or a DAA

19. AASLD and IDSA. HCV Management Guidance. September 2014.

PHOTON-1: Sofosbuvir + RBV in GT1-3 HCV Patients Coinfected With HIV

- Nonrandomized, open-label phase III study; primary endpoint: SVR12
- Stable ART (HIV-1 RNA < 50 copies/mL for > 8 wks before enrollment)
  - 95% on ART: TDF/FTC, 100%; EFV, 35%; ATV/RTV, 17%; DRV/RTV, 15%; RAL, 16%; RPV, 6%
- Cirrhosis at baseline: GT1, 4%; GT2/3 tx naive, 10%; GT2/3 tx-exp'd: 24%

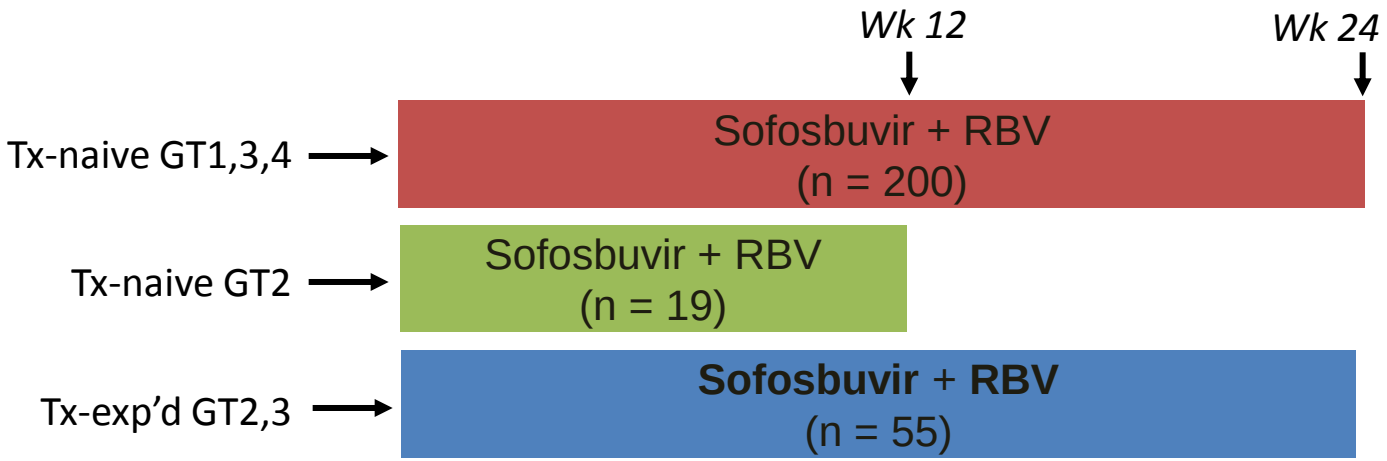


Sofosbuvir 400 mg QD; weight-based RBV 1000 or 1200 mg/day

22. Sulkowski MS, et al. JAMA. 2014;312:353-361.

PHOTON-2: Sofosbuvir + RBV in GT1-4 HCV Patients Coinfected With HIV

- Nonrandomized, open-label phase III study; primary endpoint: SVR12
- Stable ART (HIV-1 RNA < 50 copies/mL for ≥ 8 wks before enrollment)
  - 97% on ART: TDF/FTC, 100%; EFV, 25%; ATV/RTV, 17%; DRV/RTV, 21%; RAL; 23%; RPV, 5%
- Cirrhosis at baseline: All pts, 20%; tx-naive patients, 13%; tx-exp'd patients, 45%



Sofosbuvir 400 mg QD; weight-based RBV 1000 or 1200 mg/day

29. Molina JM, et al. AIDS 2014. Abstract MOAB0105LB.

AASLD/IDSA Guidance: Allowable ARVs in HCV/HIV-Coinfected Pts Receiving DAAs

- Sofosbuvir: ALL *except* didanosine, zidovudine, and tipranavir[1]
- Simeprevir: raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, and abacavir[15]
  - Clinically significant drug interactions were observed when simeprevir coadministered with ritonavir or with efavirenz in healthy volunteers[17]

15. AASLD and IDSA. HCV Management Guidance. September 2014. 17. Simeprevir [package insert].

AASLD/IDSA Guidance: Recommended Regimens for HCV/HIV-Coinfected Pts

Genotype	Recommended Regimens
Genotype 1	
HCV treatment naive and prior PR relapsers ▪ IFN eligible	Sofosbuvir + pegIFN/RBV for 12 wks
▪ IFN ineligible	Sofosbuvir + RBV for 24 wks Sofosbuvir + simeprevir ± RBV for 12 wks
HCV treatment experienced*	Sofosbuvir + simeprevir ± RBV for 12 wks
Genotype 2	
Regardless of HCV treatment history	Sofosbuvir + RBV for 12 wks
Genotype 3	
Regardless of HCV treatment history	Sofosbuvir + RBV for 24 wks
Genotype 4	
Regardless of HCV treatment history ▪ IFN eligible	Sofosbuvir + pegIFN/RBV for 12 wks
▪ IFN ineligible	Sofosbuvir + RBV for 24 wks
Genotype 5 or 6	
Regardless of HCV treatment history	Sofosbuvir + pegIFN/RBV for 12 wks

*Previous PR nonresponders regardless of IFN eligibility.

12. AASLD and IDSA. HCV Management Guidance. September 2014.

Considerations Regarding Treatment Initiation in HCV/HIV-Coinfected Pts

- Is the pt ready and able to start therapy?
- Pts not receiving ART
  - Treat HCV now and defer ART?
- Pts receiving ART
  - Is there an HCV regimen available that can be coadministered with current ART or is ART switch needed?
  - Should ART interruption ever be considered?
    - Associated with increased risk of OI/death in HIV infected pts[1]
    - Associated with increased risk of fibrosis progression in HCV/HIV-coinfected pts[2]

69. El-Sadr WM, et al. N Engl J Med. 2006;355:2283-2296. 70. Thorpe J, et al. AIDS. 2011;25:967-975.

Drug–Drug Interactions With ARVs

ARV	Simeprevir	Sofosbuvir
DTG	No interaction expected	No interaction expected
RAL	Use standard doses	Use standard doses
EFV	Do not coadminister	Use standard doses
DLV, ETR, NVP	Do not coadminister	Use standard doses
RPV	Use standard doses	Use standard doses
Any PI	Do not coadminister	
DRV/RTV	Do not coadminister	Use standard doses
RTV	Do not coadminister	Use standard doses
TPV/RTV	Do not coadminister	Do not coadminister
TDF	Use standard doses	Use standard doses
COBI	Do not coadminister	Use standard doses

63. Sofosbuvir [package insert]. 64. Simeprevir [package insert]. 65. Kirby B, et al. AASLD 2012. Abstract 1877. 66. Ouwerkerk-Mahadevan S, et al. IDSA 2012. Abstract 49.

Summary

- Sofosbuvir and simeprevir are currently recommended as part of preferred or alternative regimens for HCV/HIV-coinfected patients
  - Boceprevir and telaprevir are not recommended
- SVR rates in HCV/HIV-coinfected patients treated with sofosbuvir or simeprevir are comparable to those in HCV- monoinfected patients
- Management of drug–drug interactions between HCV DAAs and ART remains important
- Additional all-oral regimens expected to be approved in late 2014