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Take home message, Monday 11

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The Burden of Hepatitis C
Summary

- The burden of hepatitis C is immense and often underestimated
- Curing hepatitis C will have a positive impact by:

  -Decreasing the incidence of cirrhosis

  -Decreasing hepatocellular carcinoma

  -Improving overall quality of life for

  - Multiple common barriers exist for implementation of focused programs to control HCV across low, middle, and high income countries
  - We must continue to be the champions to effect change and to shape policies in our respective countries that will lead to greater access to care

Why Should I Treat My Patients With Mild Hepatitis C?

Available therapies are highly effective and safe

Disease staging is not faultless

HCV causes signif cant extra-hepatic morbidity

Best cost-effectiveness is obtained treating at an early stage of disease

Why Don’t I Treat My Patients with Mild Hepatitis?

- The first step is to prioritise access to antiviral treatment according to severity of fibrosis, the risk of progression to more advanced disease and the presence of severe extra-hepatic manifestations related to HCV
- Antiviral treatment can be deferred in patients with mild disease, except in genotype 3 patients
  - Very good short-term prognosis
  - Optimisation of the antiviral regimen (short duration, simplification, etc…)
  - Sequential decrease of the cost of the therapy
- However, universal access to treatment is a short-term objective with the aim of eradicating the hepatitis C epidemic in the next future

Is the Benefit to Treat Patients With Cirrhosis Proven?

Benef ts of an SVR:

Compensated: prevention of end stage complications and liver related mortality. Similar life expectancy as general population. Doubtful reduction of all cause mortality.

Decompensated: reversal of decompensation possible, durability and no-return point, unclear. Regression of cirrhosis and prevention of HCC doubtful. Reduction of liver related mortality likely, reduction of all-cause mortality unknown. Delisting possible, driven by local policies.

It Is Useful To Detect Ravs?

- Usefulness of RAV testing will be patiet population and treatment regimen dependent

- RAV testing most likely not required in patient populations with SVR rates >99%

- RAV testing most likely be clinical useful and cost effective in population with sub-optimal SVR rates (def nition <95%/90% & if population large enough
  - -regimens w/o very high barrier to resistance drug
  - -treatment experienced patients (in particular when exposed to DAAs)
  - -patients with cirrhosis
  - -When the shortest possible treatment duration is econmically important

Individual Optimisation of Therapy Theory

- Short course therapy with extended therapy for failures may be cost-effective
- Careful selection of patients will be critical
- Robust re-treatment regimens will be necessary
- Studies in the UK are on-going

HCV In Dialysis Patients And Kidney Recipients

- GFR> 30 ml/mn: all the therapeutic options
- GFR < 30 ml/mn:

GT1 or 4: GZP/EBV 12 weeks
GT1b: 3D 12 weeks
GT2/3/5/6: SOF (200 mg/d or 400 mg/d or each 2 days ???) + NS5A –DCV-/d
SOF/LDV?

- Kidney recipients:
  - GFR > 30 ml/mn GT1, 2, 4-5: SOF+LDV 12 weeks
    GT1 or 4: GZP/EBV 12 weeks?
    3D with adjustments of calcineurin inhibitors
    GT3: SOF + DCV
  - GFR < 30 ml/mn GT1 or 4: GZP/EBV 12 weeks?
    GT1b 3D with adjustments of calcineurin inhibitors

    GT2/3/5/6: SOF (200 mg/d or 400 mg/d or each 2 days?)
    + NS5A/j

Daas And Transplanted Patients

- Treat hepatitis C using DAA before or after LT? Both strategies are feasible with excellent efficacy results and good safety profiles
- Regarding efficacy, better results are achieved after LT than before in decompensated cirrhotic patients
- Regarding safety, drug-drug interactions and degree of hepatic impairment are still issues, and favor the use of NS5A inhibitors
- Withdraw patients of waiting list is feasible and should concern about 30% of patients.

HIV-HCV Co-infected Patients

- Data from phase 3 clinical trials indicate similar SVR rate in persons with and without HIV coinfection *with some caveats*
  - High rate of HCV relapse after 8 weeks of daclatasvir + sofosbuvir
  - High rate of HCV relapse among Black patients treated for 12 weeks with ledipasvir/sofosbuvir
- HCV disease progression is more rapid despite effective HIV treatment
- Incidence of reinfection may be higher after SVR
- Drug interactions must be carefully considered by clinicians with expertise in HIV and/or HCV

Sulkowski M, PHC 2016

How to Improve the Therapeutic Strategies ?

1 **E**ducation (medical education, sciences)
2 **R**esistance (salvage therapy, RAVs)
3 **A**ccess to Treatment
7 **D**uration (shorten, 6 or 8 weeks)
8 **I**ncreasing Screening (worldwide)
9 **C**ompliance
10 **A** la carte or Universal Treatment
11 **T**reatment Interraction (DDI)
12 **I**mproving Survival (HCC, ELD)
13 **O**ther populations (PWID, Decompensated cirrhosis,…

HCV ERADICATION WORLWIDE

How to Provide the Best Treatment With What Is Available?

- Six all-oral regimens are approved for chronic HCV treatment; two more coming in 2016
- Limited access and availability of some oral agents create the need to build the best treatment regimen from available drugs
- Treatment choice is often based on access, eff cacy, safety and cost balance
- Easy to treat populations allow more options for tailored therapy, while hard to treat populations (eg; gen 3, decompensated, renal failure) require more select treatment regimens

Universal Screening

- Birth cohort screening does not recognize a significant fraction of persons with chronic HCV and falls short of Universal screening.
- Improved strategies which link patients identified with HCV to providers who can properly evaluate and treat this disease is required.
- Restricted access to HCV medication by insurance carriers and governmental bodies is the single greatest impediment to treating HCV infection today.
- Universal screening for HCV can identify patients with chronic HCV and co-morbidities which enhance fibrosis progression.

EASL Guidelines. Post-treatment Follow-up of Patients Who Achieve an SVR

- Non-cirrhotic patients with SVR should be retested for ALT and HCV RNA at 48 weeks post-treatment, then discharged if ALT is normal and HCV RNA is negative (B1)….
- Patients with pre-existing cofactors for liver disease (notably, history of alcohol drinking and/or type 2 diabetes) should be carefully and periodically subjected to a thorough clinical assessment,……
- The exact duration of HCC surveillance in patients with advanced fibrosis or cirrhosis who achieve an SVR is unknown in the current state of knowledge, but is probably indefinite (B1).