Summary of PHC Day 2

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Disclosures
Michael W. Fried, M.D.

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Impact of HBV on Public Health

Prof. G. Dusheiko

- A better understanding of the prevalence of the disease and disease burden is still needed
- Awareness of HBV remains lower than that for HIV
- Treatment forms part of the control of HBV
- Only 30 million individuals (10%) diagnosed and of these perhaps approximately 5 million are currently receiving antiviral treatment: Great geographic disparity
- Drug costs are not the limiting factor for HBV
- Vaccination is widely accepted:
  - Screening, diagnosis, and treatment to prevent progression are often overlooked
- Unsatisfactory progress in some parts of the world in implementing treatment

Long-term Safety and Efficacy of Nucs

Prof. Buti

- Benefits of achieving viral suppression are well documented
- Decompensated cirrhosis can be dramatically improved with HBV treatment
- Long-term NUC therapy generally considered safe:
  - Modest changes in GFR associated with long term TDF with smaller decrease seen in those treated with TAF
  - Similar relationship seen with Bone Mineral Density
- TAF and ETV recommended for patients with risk of renal and bone disease

he Importance of Nuc-PEG Combination
rof. Lampertico

- The combination of PEG+NUC with NUC has a strong biological rationale
- Three strategies have been assessed (de-novo combo, switch to, add-on)
- Most studies showed a faster HBsAg decline in the Peg-IFN+NUC vs NUC. But never translated into long-term benefit
- Safety and cost issues must be also considered
- Combination strategies are not recommended by EASL guidelines for all patients but may be considered for selected patients with favorable baseline and week 12 predictors

Controversy: Stop the NUC!
Prof. Mangia

CHB Tx guidelines	EASL 2017	AASLD 2018	APASL 2015
HBeAg+ve	HBeAg seroconversion with 12 mos of consolidation + undetectable HBV DNA	HBeAg seroconversion with 12 mos of consolidation + undetectable HBV DNA	HBeAg seroconversion and after at least 1 yr of additional therapy
HBeAg-ve	may be considered after 3 yrs viral suppression	indefinite (may be considered after HBsAg loss)	-HBsAg seroconversion or HBsAg loss >1 yr -Rx for at least 2 yrs with HBV DNA undetectable on 3 separate occasions 6 months apart

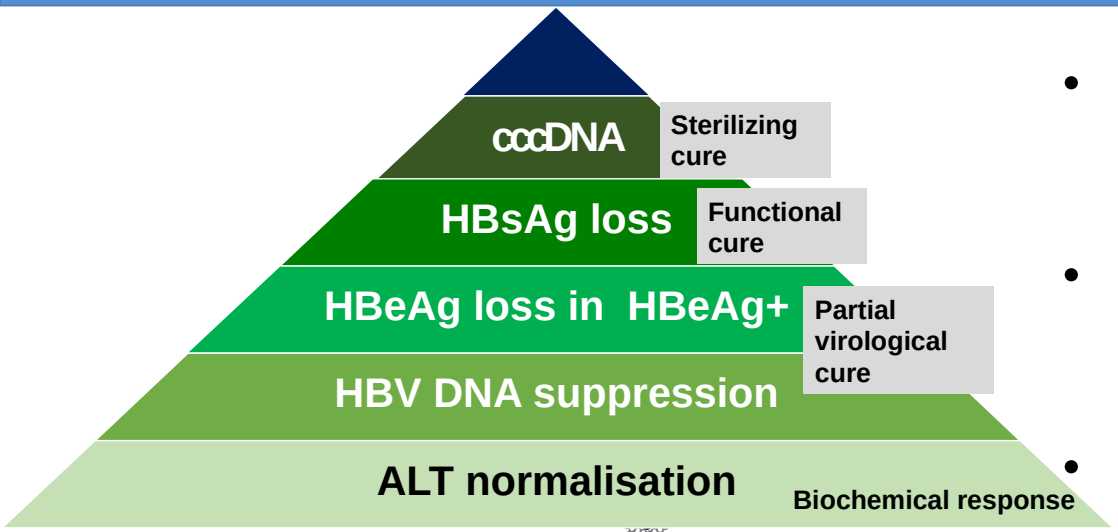
Withdrawal of NAs frequently results in ALT and HBV DNA flares which can be serious and even fatal: early, close and long term monitoring is mandatory for safe and effective NAs discontinuation

Controversy: Don't Stop the NUC!
Prof. Parana

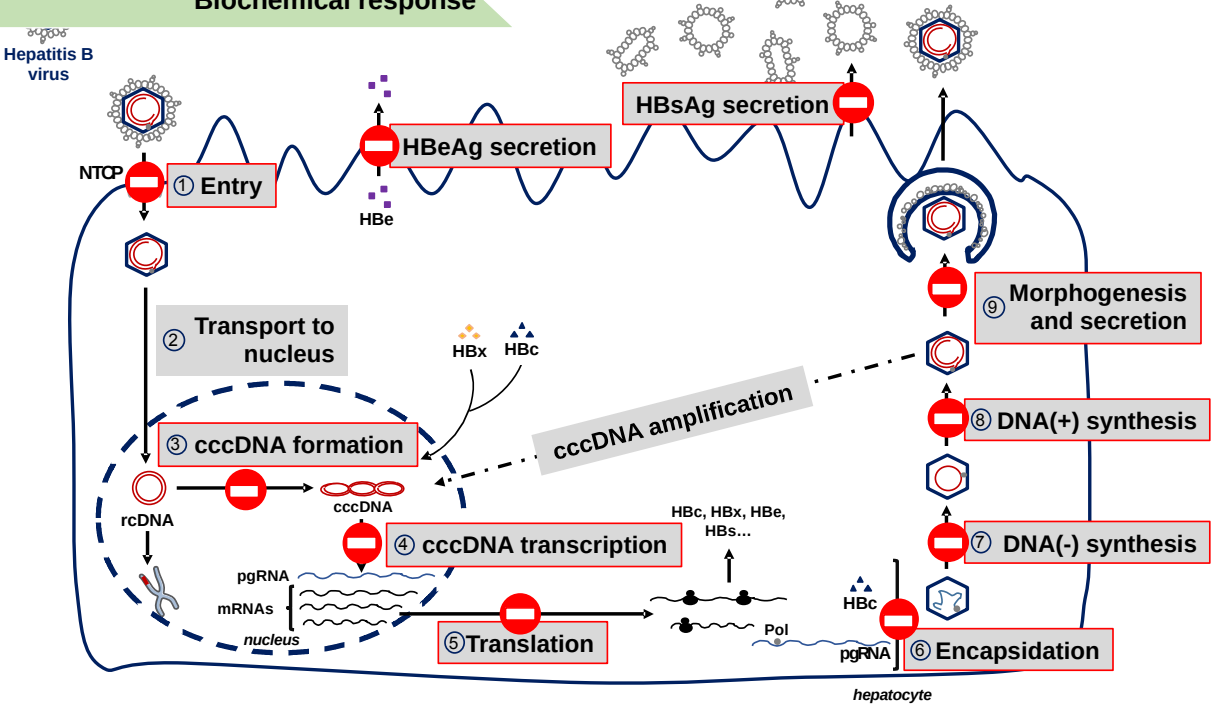
1. Stopping NUCs may be beneficial in some well selected non cirrhotic patients, mainly HBeAg +
2. There are no consensus on stopping NUCs among all Associations (EASL/ALEH/AASLD/APASL)
3. There are no adequate predictors of HBsAg clearance
4. Avoid stopping NUCs until better predictors of relapse are available
5. Need randomized trials with large Asian and non-Asian populations
6. Many other things to stop now (Climate change, Brexit, etc.), so focus on those instead of stopping NUCs

Targets and New Drugs for HBV

Prof. Asselah



- Excellent review of mechanisms and potential targets
- Highest Priority is therapy that achieve Functional Cure
- Numerous promising agents



Use of Quantitative HBsAg
Prof. Brunetto

- qtHBsAg provides additional and complementary information to that of viral replication markers.

- HBsAg levels may be influenced by features of the virus and/or viral infection, therefore the results need to be interpreted according to the clinical setting

- qtHBsAg is a major diagnostic tool for the management of chronic HBV carriers.

- Demonstrated role in quantifying likelihood of response and futility in PEG-IFN treated patients

- Low HBsAg levels (<100 IU/ml) may predict off-treatment response after cessation of NA

Magritte R, La voix des airs 1931

Treatment of Delta Hepatitis

Prof. Brunetto

- **PEG-IFN may control ~25% of patients with Delta hepatitis but high rate of off-treatment failure**
- **Multiple promising agents under develop evaluating different targets**
  - **Nucleic acid polymers (Rep 2139 + PEG)**
  - **Lonafarnib-farnesyltransferase inhibitor**
  - **Myrcludex: Entry inhibitor**
- **Major and immediate unmet need in viral hepatitis therapeutics**

Treatment of HBV During Pregnancy
Prof. Lim

HBV may complicate pregnancy with preterm labor and gestational diabetes

	AASLD	EASL	APASL
Antenatal testing of HBV	yes	yes	yes
HBV vaccination of newborn at birth	yes	yes	yes
Routine use of HBIg	yes	yes	yes
Antiviral Therapy in third trimester	yes	yes	yes
Criteria to start antivirals in third trimester	HBV DNA>200,000 IU/ml	HBV DNA>200,000 IU/ml or qHBsAg>4 log IU/ml	HBV DNA>6log IU/ml
Choice of antiviral	Tenofovir	Tenofovir	Tenofovir or telbivudine
Stopping antiviral therapy	Up to 4 weeks post partum	Up to 12 weeks post partum	At delivery

EASL, J Hepatol 2017;67:370-398.
Terrault NA et al, Hepatology 2016;63:261-283
Sarin SK et al, Hepatol Int 2016;10:1-98.

Management of Cholestatic Liver Disease
Prof. Beuers

- Discussion pathophysiology of PBC, including that related to disordered bicarbonate activity in cholangiocytes
- UDCA remains the backbone of therapy
  - Responders have excellent prognosis
- OCA approved for non-responders to UDCA
- Bezafibrates also demonstrate efficacy in PBC

- Primary sclerosing cholangitis: remains an unmet medical need
- UDCA may provide benefit
- Experimental therapies being evaluated
- Consider IgG4 disease: Older males, jaundice, weight loss, abdominal pain, specific pathologic definition. PCR-based testing possible

HCC and Metabolic Syndrome
Prof. Paradis

- NASH becoming the new driving force in HCC
- Discussed interesting aspects of pathogenesis of steatohepatitis and HCC
- Diabetes an obesity are independent factors for HCC
- Cofactors, such as alcohol, play a major role

- Major concern is high incidence of HCC in non-cirrhotic NASH which raises many unanswered questions as to screening recommendations

HCC Treatment: Discrepancies Across Guidelines

Prof. Galle

- Three major guidelines developed by leading hepatology societies (AASLD, EASL, APASL)
- **All guidelines agree that screening with ultrasound +/- AFP for patients with cirrhosis at risk for HCC**
- Use biopsy of suspected HCC sparingly
- Treatment recommendations may vary by regional guideline for different stages of HCC
- Optimal therapy for HCC remains controversial and will likely evolve as new therapeutic regimens are incorporated into treatment algorithms
- Don’t forget to drink coffee!

New Therapies for HCC

Prof. Sangro

- Making remarkable progress in therapy for advanced liver cancers
- Kinase inhibitors have consistent track record in improving survival
- New second line therapies for sorafenib failures are available including other kinase inhibitors (regorafenib, cabozantinib) and ramucirumab (monoclonal antibody)
- Immunotherapies (Nivolumab, Pembrolizumab) represent exciting new therapeutic options with prolonged survival for many patients

Liver Transplantation
Prof. Terrault

- **HCV continues to decline as indication**
  - More for HCC than for decompensated cirrhosis
- **ALD on the rise in US likely related to LT for AH and changing attitudes regarding sobriety requirements**
  - Infections, malignancy and relapse of alcohol are main areas to focus on for improving outcomes
- **NASH shows largest increases – both for cirrhosis and HCC**
  - Management of obesity and metabolic complications are main challenges (as they are pre-LT)
  - Recurrent NASH – need better natural history data

Management of End Stage Liver Disease
Prof. Durand

- Decompensated cirrhosis is still associated with high mortality rates in the absence of transplantation
- Bacterial infections are a major source of mortality
  - Multidrug resistance is common in Europe and Asia
- Long term administration of norfloxacin may improve survival in patients with ascites protein concentration < 15 g/L
  - Without increasing the incidence of multidrug resistant bacteria
- Long term administration of albumin may improve survival in patients with decompensated cirrhosis
- Could norfloxacin + albumin do better?
- TIPS may improve survival in patients with “persistent” ascites
  - Needs to be confirmed in refractory ascites
  - Use of TIPS limited by encephalopathy and disease severity (high MELD)
- New pump device could be an alternative to paracentesis or TIPS in patients awaiting transplantation

Management of Portal HTN

Prof. Gadano

- Cirrhosis should be managed in two distinct clinical stages, compensated and decompensated, defined by the presence or absence of overt clinical complications (ascites, VH, and HE).

- In patients with cirrhosis and CSPH but without varices, the objective of treatment is to prevent clinical decompensation.
- New data suggests that statins lower the incidence of decompensation (ascites and VH) and lower mortality.

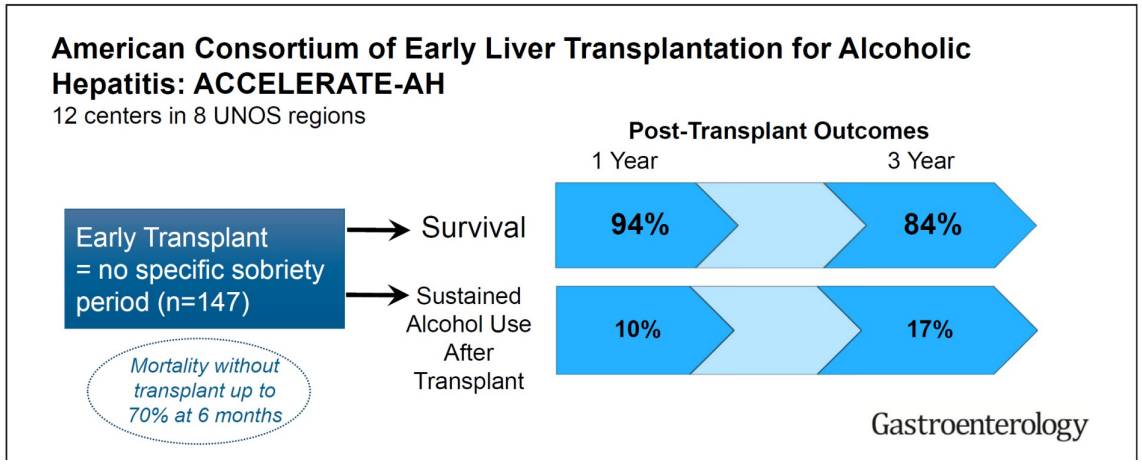
- Early TIPS within 72 hours of endoscopic control may benefit selected patients: Those at high risk of treatment failure or rebleeding (CTP class C cirrhosis or CTP class B with active bleeding on endoscopy)

- NSBB should not be used in patients with refractory ascites but they can benefit patients with ”non-

Liver Transplantation for Alcoholic Hepatitis

Prof. Mathurin

- **In an era of organ shortage, use of liver transplants in severe AH may negatively affect the public attitude on transplantation and organ donation**
  - **This may cause reluctance on the part of clinicians to modify guidelines for alcoholic patients**
  - **However, healthcare practitioners must inform the public that patients with self-inflicted disease warrant the same access to medical resources as other patients**



Until Next Year!

Jusqu'à l'année prochaine!