2018 11th Paris Hepatology Conference

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Summary of Day 2

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Who and When to Treat

- ✓ Prof. Papatheodoridis:
- ✓ Reviewed phases of HBV infection
- ✓ Discussed indications for HBV therapy
  - Standard (ie, HBeAg+)
  - Special populations (ie, pregnancy, HIV/HBV, etc)
- ✓ Compared the many differences across international HBV treatment guidelines
  - Untangled complicated algorithms

Is There Still A Role for Interferon?

- ✓ Prof Lampertico: PEG-IFN is a comfortable, old friend
  - Short answer is YES, for selected patients
    - ~20-30% of patients will respond
    - Improve selecion by looking at baseline characteristics
  - Utilize HBsAg for a stopping rule to define futility
  - New strategies to consider:
    - Switch to PEG-IFN after prolonged NUC
      - Associated with high rate of HBeAg-seroconversion
    - Add on PEG to NUC
  - New markers under investigation to predict response
    - HBcore antigen
    - Ultrasensitive HBV DNA
    - Others

Long-term Safety and Effectiveness of NUC Thearpy

- ✓ Prof Buti:
  - Prolonged viral suppression decreases decompensation, mortality and decreases incidence of HCC
  - NUCs highly effective; >97% remain HBV DNA suppressed after 5 yrs
  - BUT only 1%-2% of HBeAg- patients have HBsAg seroconversion
  - Persistent low level viremia while on NUC is associated with disease progression in patients with cirrhosis: Consider combination NUCs Prevalence of comorbidities in patients with CHB is increasing and may impact safety of long-term NUCS
    - However, overall safety profile remains exemplary
  - TAF, prodrug of tenofovir, has similar efficacy and better renal safety profile compared to TDF: especially important for patients with comorbid conditions like HTN, DM

Controversies: To Stop or Not to Stop a NUC

- ✓ Prof Berg:
  - Endpoints differ between HBeAg+ (HBeAg loss) vs HBeAg- (HBsAg loss)
  - Randomized trial of NUC discontinuation in non-cirrhotic HBeAg- patients
    - Transient flare of HBV DNA and ALT may be seen but subsequent loss of HBsAg may occur in high percentage of patients
    - Defer retreatment to determine if HBsAg loss may occur
    - Close post-NA monitoring is critical for safety
- ✓ Prof Gadano:
  - Provided data to suggest that most patients require continuous therapy to prevent relapse
  - Few downsides to continuing therapy indefinitely
- ✓ Hence why stopping NUCs is still controversial

New HBV Therapies

- ✓ Prof Schinazi:
  - HBV Eradication? Everything is theoretically impossible until it's done
  - Current goals: Functional cure (HBsAg-) vs Complete cure (-cccDNA)
  - Many approaches and targets:
    - CRISPR
    - Viral entry inhibitors, Targeting cccDNA, HBsAg targeted therapies (siRNA)
    - Enhance immune response: PD1 blockade enhances T-cell function
  - Capsid protein plays important role in HBV replication
    - Capsid inhibitors can decrease cccDNA (GLP26)
    - Prolonged suppression demonstrated in animal models
  - Long list of research priorities and caveats before achieving HBV cure
  - Collaboration across academia, industry, government agencies is critical to achieving HBV cure

Delta Hepatitis Revisited

- ✓ Prof Rizzetto
  - New therapies target:
    - Attachment of HDV
    - Assembly of HDV
  - Drugs impairing entry of HBV/HDV: Myrcludex
  - Prenylation inhibitors: Lonafarnib affects ability of HDV to combine with HBsAg and inhibit viral assembly
    - Phase 2a study shows transient decrease in HDV RNA
    - Another study suggested boosting with ritonovir potentiates the affect
    - Side effects may be problematic
  - Nucleic Acid Polymers (NAPS): blocks subviral HBsAg particles
    - REP2139 Phase 2a study: 58% HDV RNA-negative,
    - 50% lost HBsAg and developed anti-HBs
    - AEs? Needs confirmation in randomized controlled trial

Improving Access to HBV Therapies

- ✓ Prof Zoulim:
- ✓ HBV remains a major public health crisis
- ✓ Universal vaccination highly effective but global uptake has varied:
- ✓ Focus on eliminating vertical transmission
  - Better access to HBIG and antivirals should be considered if high maternal viral load
- ✓ Focus on screening and treating immigrant populations
- ✓ Point of care screening, Lower cost assays
- ✓ Better training of physicians
- ✓ National policies to implement the above

How to Control HBV in High Endemic Regions

- Prof Jia (Asia):
  - Huge disease burden driven by MTCT
  - Great strides have been made in universal vaccination +/- Maternal NA therapy with reduction in MTCT
  - Achieved WHO targets to reduce HBsAg+ in children
  - Liver cancer rates decreasing associated with HBV vaccine uptake
  - Improved access to NUCs is needed
- Prof Diouf: Sub-Saharan Africa
  - Horizontal transmission most common, MTCT also frequent
  - Very low uptake of HBV vaccinations at birth; HBIG not available
  - Must improve HBV screening programs
  - Better education and training of HCW and birth attendants

Revolution in Liver Imaging

- Prof Vilgrain:
- HCC screening every 6 months is optimal for optimizing patient survival
- Properly applied MR technologies are crucial to patient management with chronic liver disease and differentiating benign from malignant lesions
- Where is the revolution?
  - Quantitative imaging: Liver volume, Fat, Iron, Liver stiffness
  - 3D assessments

Infections Complicating Cirrhosis

- Prof Angeli:
  - GLOBAL Study: 1300 patients with cirrhosis and bacterial infection
    - Etiology: Alcohol>HCV>others
    - Gram-negative organisms most common
    - 34% Multidrug resistant, 8% Extended resistance
    - MDR varies by geography: 70% in India vs 30% in other regions
    - Predictors of MDR: NOT related to prophylaxis of SBP or HE treatment
    - Need extended antibiotics, MDR led to more frequent sepsis complications
    - SOFA score: low BP, high RR, altered mental status-performed better than SIRS
    - Failure of first line antibiotic is greatest predictor of mortality:
      - Hit them fast and hit them hard

Allocation of Liver Grafts Around the World

- Prof Clavien:
  - Case examples that challenged organ allocation policies
  - Reviewed various policies from around the world
  - Discussed methods to assess quality outcomes after liver transplantation
  - Discussed BAR score to predict outcome after transplant
    - BAR Score >18 suggestive of poor outcome
  - Example criteria to deny transplant including:
    - Ventilatory support
    - Pressors
    - Ongoing sepsis

Improving Long Term Outcomes After Liver Transplantation

- Prof Durand:
  - Liver mortality only accounts for ~25% of late mortality post transplant
    - Cancer and cardiovascular disease play a large role
  - Post-OLT outcome is multifactorial:
    - Etiology of liver disease
    - Higher cardiovascular risk (NASH)
    - More impaired renal function at transplant
  - Post-OLT management improves outcomes
    - Treat disease recurrence (HCV is now an easy target)
    - Manage metabolic syndrome and CNI complications
    - Prevent/cure de novo malignancy: No smoking, minimize immunosuppression
    - Protect the kidney

Vascular Liver Disease: New Concepts and Treatment

- Prof Valla:
  - Cumulative incidence of PVT ~10-20% at 5 years
  - PVT was not associated with progressive liver disease
  - Benefits of anticogulation from controlled trial
    - Recanalization
    - No clot progression
    - Diminished varices
    - Prevention of decompensation
  - Reviewed new paradigms for management of vascular disease in patients with cirrhosis

New Perspectives on HCC

- Prof Galle:
- Prof Samuel:
- Prof Sangro

- I hope everyone has enough short-term memory and will recall the important details from this last session

Closing Attestation

PHC is a truly unique meeting that brings together faculty and participants from all over the world with the common goal of improving the care for patients with liver disease

- On behalf of all the faculty, thank you to the audience for your interested participation

- Many thanks to Prof Marcellin and his colleagues for another outstanding PHC!