Key Takeaways from the HBV Foundation Workshop on Challenges and Barriers to Early Detection of HCC

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Conflicts of Interest

- None

Outline of This Discussion

- Review recommendation from a previous workshop was held at the Hepatitis B Foundation to make recommendations on the treatment of chronic HBV and surveillance for HCC
- Discuss the pros and cons of universal treatment for all persons with HBV with detectable HBV DNA regardless of the level
- Review controversies on new AASLD HBV treatment guidelines
- Review Surveillance recommendations for early detection of HCC

The Controversy of Universal Treatment for HBV

- Pros: Prescribing antiviral therapy (Tenofovir-based or Entecavir) for all patients with chronic Hepatitis B infection (CHB) would very likely reduce the incidence of HCC and death from cirrhosis
- Cons:
  - AASLD Guidelines state that not all persons with CHB will benefit from treatment
  - While side effects of oral antiviral agents are minimal, cost could be high
  - Patients not infrequently come on and off antiviral therapies which can lead to flares that occasionally result in liver failure, even death
  - Tracking patients or just allowing them to continue treatment without regular monitoring is problematic.
  - Long-term randomized treatment/placebo trials are not available and unethical currently to answer benefits and harms of lifelong treatment

AASLD Hepatitis B Guidelines

- AASLD Guidelines recommend treatment be considered for those with HBV DNA > 2,000 IU/ml and ALT above normal levels
- Guidelines recommend shared decision making between provider and patient
  - This requires a provider very knowledgeable about HBV and would be difficult for many providers whether primary care or even Gastroenterologists who see limited numbers of patients with liver disease

Natural History of CHB

- HBV has a mind of its own
- You can't predict what will happen to an individual with CHB
- Patients can progress through the phases of CHB or revert back to an earlier phase
- Patients put on Tenofovir or Entecavir long-term have a lower probability of clearing HBsAg than those not on antiviral therapy
- We have seen clearance of HBsAg following flares of HBV
  - If patients do not have more than mild fibrosis, we sometimes monitor them closely if they have a flare (ALT 50 to 200) not accompanied by elevation of bilirubin and INR to see if they will clear HBsAg.

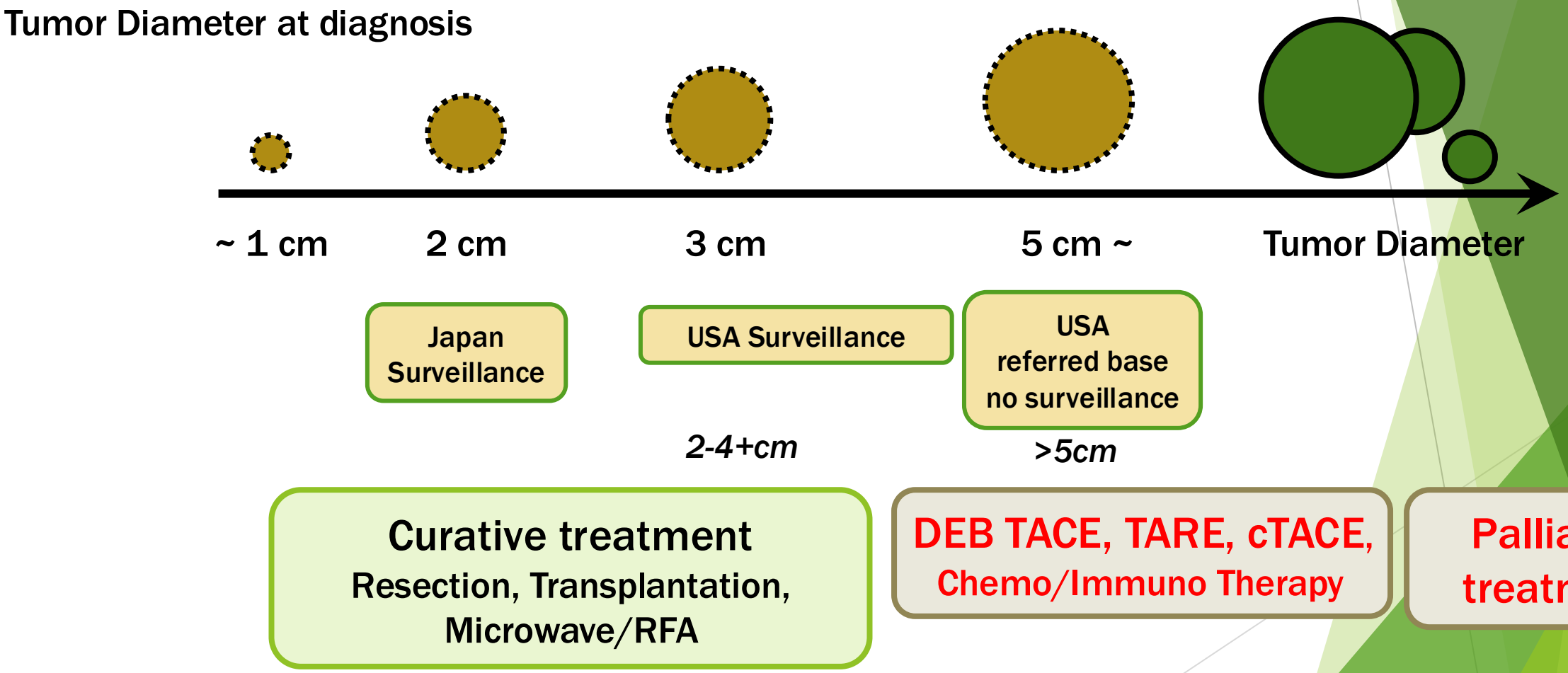
Our Definition of the Phases of Chronic HBV

Phase	HBeAg	HBV DNA	ALT	Liver Biopsy	Treatment
Immune Tolerant	Positive	Very high >200,000 IU/ml	Normal	No/mild inflammation/Fibrosis	Not Indicated
Immune Active	Positive or Negative	>2,000 IU/ml Usually >20,000	Elevated	Inflammation and Fibrosis; Degree Varies	Treatment Candidates
Inactive	Negative	<2,000 IU/ml	Normal	Normal or mild	Not Indicated
Grey Zone Phase or Indeterminate Phase	Negative	Fluctuating <2,000 to >2,000	Fluctuating Normal to Abnormal	Fibrosis/Inflammation Fluctuates	?
Partial Cure	Negative but HBsAg positive	<10	Normal	HBsAg gene integrated hepatocyte	Not Indicated
HBsAg Clearance Functional Cure	Negative	Not detected	Normal	No inflammation variable fibrosis	Not Indicated, Functional Cure

Regular Surveillance for Early Detection of Hepatocellular Carcinoma (HCC)

- This is not controversial as finding small tumors has been shown to dramatically improve over all and 5-year cancer free survival
- HCC doubling rate ranges from 1 month to twelve months but averages approximately 6 months, allowing ample time to find small HCC cancers
- Nationally only 15% to 20% of HCC tumors are found early enough to cure
- In some HBV endemic areas such as sub-Saharan Africa, <5% are found early
- In the Alaska Native population where we send letters reminding persons with CHB to have blood drawn for AFP and other labs and a list of persons under their care to providers and obtain a liver US, we find 40% of HCC early enough to cure
- The VA system finds approximately half of HCC tumors early but the etiology for most is not CHB

Why is HCC Surveillance Beneficial?
HCC Treatment Options: Earlier is Better



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Discussion Topics

- What are the benefits, risks, cost and potential savings of placing all persons with CHB on antiviral therapy
- If universal therapy is not preferred, can we expand the treatment guidelines to include persons at a higher risk of HCC using criteria such as
  - HBV Genotype
  - Moderate fibrosis on non-invasive testing
  - Presence of MASLD with evidence of MASH
    - In these persons would adding a GLP1 or similar medication be beneficial
  - Accompanying alcohol associated liver disease
  - Persons at high risk of acquiring hepatitis C infection
  - Other factors for discussion