HHV-6 Project

The way forward?

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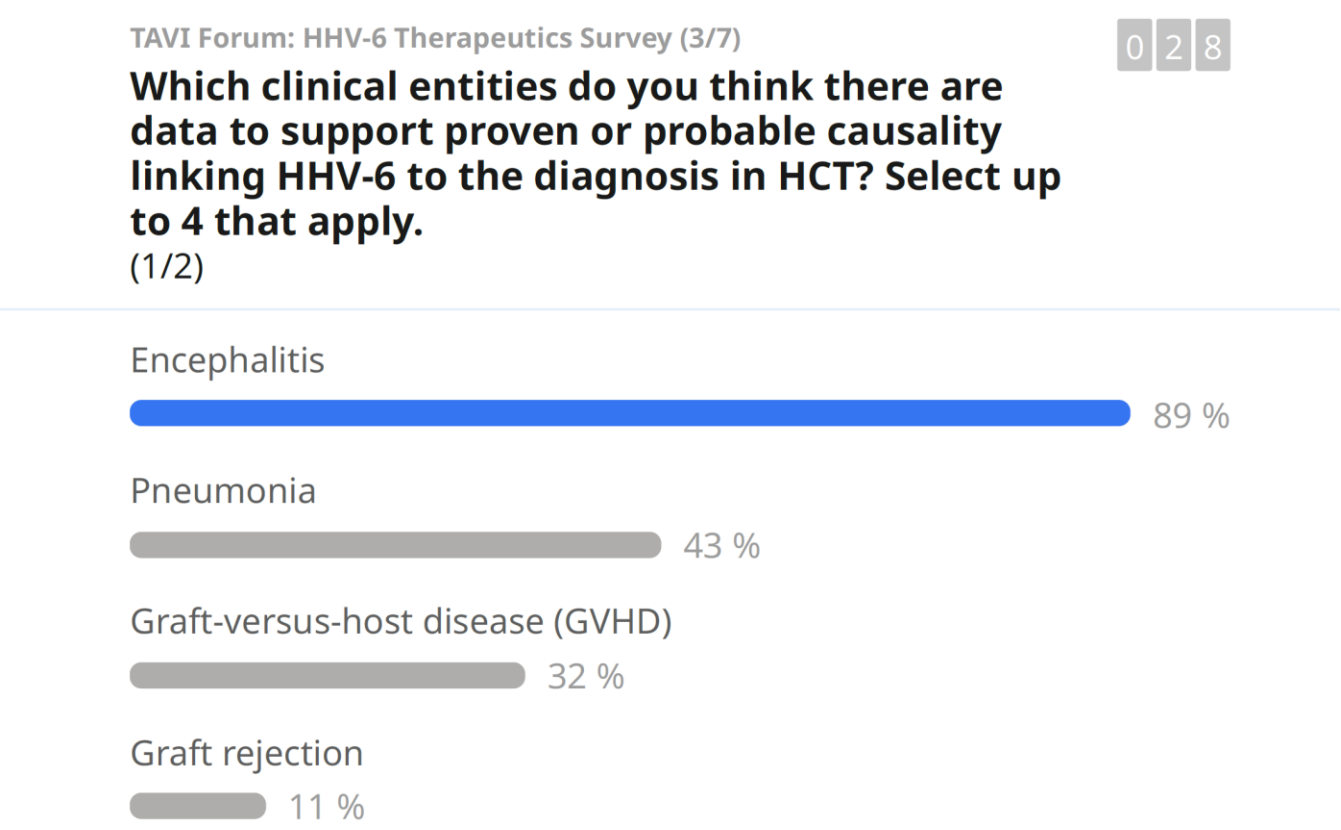
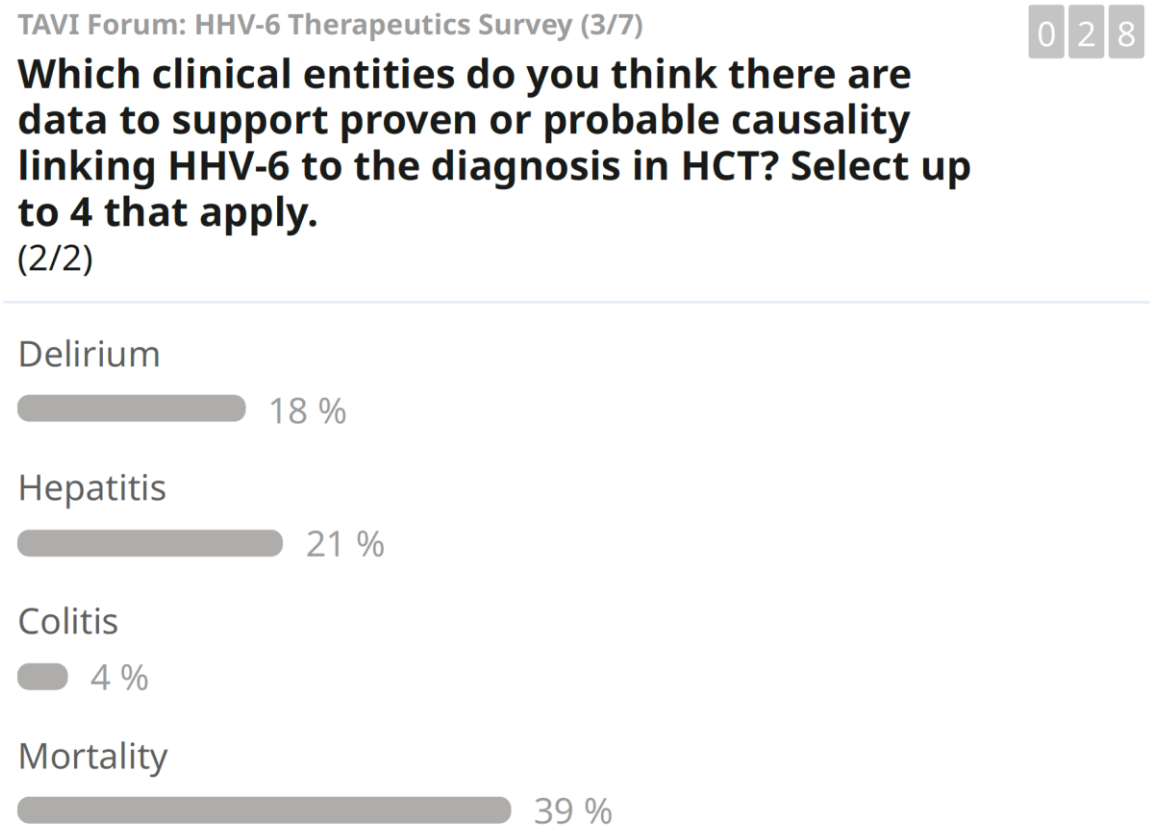
TAVI and HHV-6 until now

- Has been a possible topic for a manuscript or other actions now for a few years.
- Josh Hill has been the major driver of this topic
- A set of focussed interviews have been performed.
- A interactive survey among the participants were performed at the October 2024 TAVI-meeting in LA.
- 29 participants gave their input to the survey

Some key results from the survey - HCT



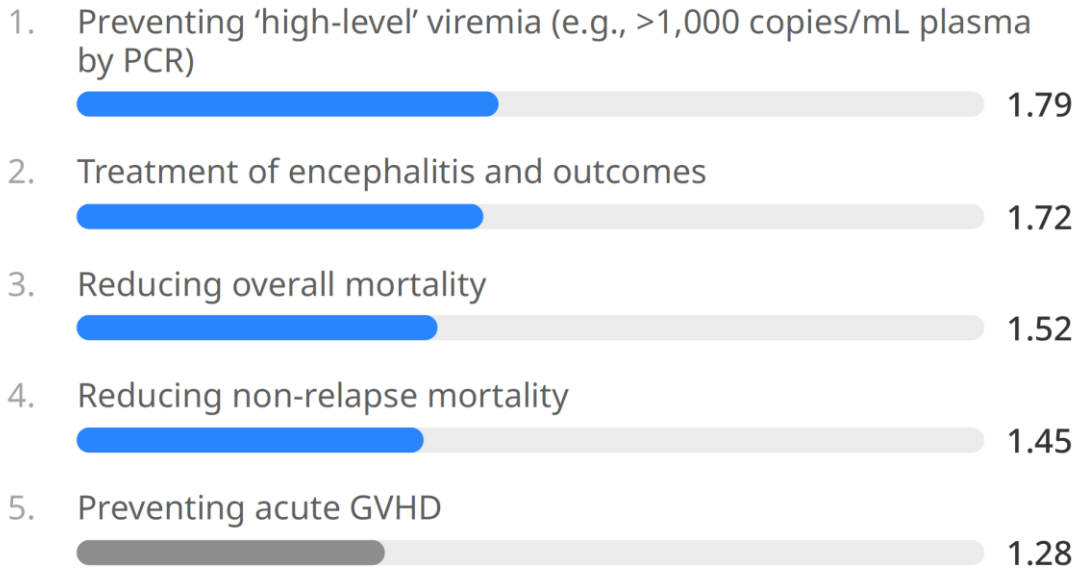


Some key results from the survey - HCT

TAVI Forum: HHV-6 Therapeutics Survey (5/7)

0 2 9

Please rank the following items in order of practicality and priority for potential clinical trial endpoints in HCT (top 4):
(1/2)



TAVI Forum: HHV-6 Therapeutics Survey (7/7)

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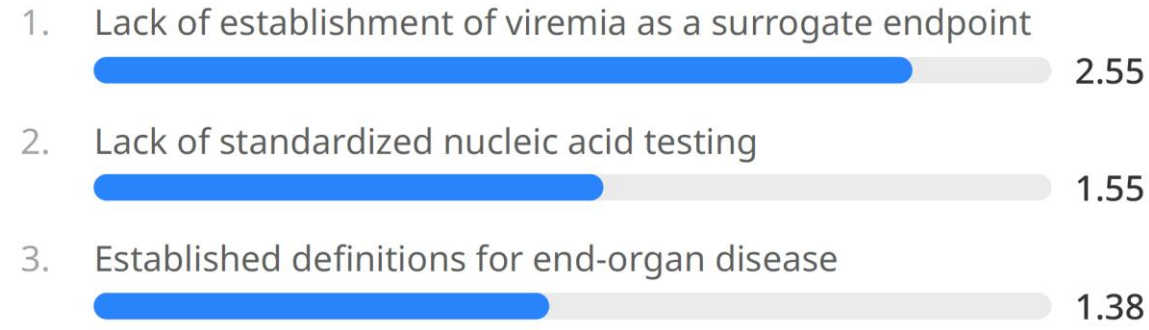
What are potential challenges for obtaining regulatory approval for trials and therapeutics for HHV-6 in HCT and SOT (assuming availability of new therapeutic options)? Rank in order of most significant challenge (1) to least (3).



Group discussion to look at a way forward

- It was agreed that the best group to focus on would be high-risk HCT. HHV-6 as an important pathogen is rarer and more difficult to assess after SOT.

- It was acknowledged that encephalitis, although the most meaningful clinical endpoint, is a difficult to study due to the rarity of the condition making it almost impossible to power a clinical trial on encephalitis alone. However, the severity of the condition would allow a smaller sample size.

- An alternative option would be to look at the prevention of CNS symptoms more general including encephalitis, cognitive dysfunction, and delirium based on previous studies by Zerr et al and Ogata et al.

- There are also now sensitive dysfunction assessment tools including advanced radiology (PET, MRI) and different functional tests that could be incorporated in such a study design.

- Virologic endpoints could be included in a design to allow collection of supportive evidence for such endpoints to be used in future trials.

Group discussion continued

- A manuscript describing the TAVIs opinion regarding what is known/what is feasible could be written as a position paper.

- The group suggested adding a simple conceptual model/figure for how evidence/endpoint development could be matured (drawing from CMV/adeno/HIV lessons).

- It was suggested the manuscript's value-add could be a framework for next steps—how the field should design studies and build evidence toward endpoints/registrational thinking, informed by other viral blueprints