Supplementary file 3. Delphi round-two questions for TITAN HSV/VZV study

- **Diagnosis and investigation to guide treatment**

1. From Delphi 1, consesus was reached that a unilateral, hypertensive AU without synechiae and anterior chamber flare is specific for HSV/VZV related viral AU. Corneal sensation, corneal oedema, stellate KPs and sectorial iris atrophy and iridoplegia were found to be useful to some experts but not others. No consensus was achieved on their specificity towards diagnosing HSV/VZV related viral AU. What ADDITIONAL clinical signs will you consider CRITICAL to assist you in making a better diagnosis of HSV/VZV related viral AU at the first presentation of the patient above - focus on how SPECIFIC these signs are with respect to the condition?

HSV		VZV	
Corneal sensation	Select Yes or No	Corneal sensation	Select Yes or No
Corneal oedema	Select Yes or No	Corneal oedema	Select Yes or No
Stellate KPs	Select Yes or No	Stellate KPs	Select Yes or No
Iridoplegia	Select Yes or No		
Sectorial iris atrophy	Select Yes or No		
Engorged iris vessels	Select Yes or No		
Anterior chamber cells	Select Yes or No	Anterior chamber cells	Select Yes or No

2. From Delphi 1, consesus was reached that an aqueous tap was important to perform if you suspect HSV/VZV related viral AU. The experts do it sometimes to further confirm the diagnosis i.e. if no characteristic skin lesions are absent. If an aqueous tap is performed, consesus was reached that QUALITATIVE multiplex PCR should be ordered. Almost 50% of experts will also send the aqeuous for QUANTITATIVE multiplex PCR. Will you consider QUANTITATIVE multiplex PCR as an important adjunct and under what circumstances?

Quantitative multiplex PCR		
HSV/VZV		
I routinely perform both qualitative and quantitative multiplex PCR for suspected HSV/VZV viral AU cases		Select one only
I do not perform quantitative multiplex PCR because it is not available. If it is available, I will order it as quantitative results are relevant to my management		Select one only
I do not perform quantitative multiplex PCR because it is not useful for my management		Select one only

- **Treatment**

1. From Delphi 1, consensus is resolution of clinical signs of inflammation i.e. cells / KPs / flare and normalization of IOP is the clinical treatment endpoint for HSV/VZV related viral AU. A significant propotion of experts (68 and 69%) also require resolution of corneal oedema as a clinical treatment endpoint for HSV and VZV viral AU respectively. Do you feel it is NECESSARY for corneal oedema to resolve as a clinical treatment endpoint?

HSV/VZV	
Yes, if significant corneal oedema persist despite no intraocular inflammation and normal IOP, I will continue to treat the patient	Please select any or all
No, corneal edema sometimes may lag behind the other clinical signs such as IOP, cells, KPs, flare which are more sensitive	Please select any or all
No, corneal edema sometimes may persist because of cornea decompensation (despite it being the first episode)	Please select any or all

2. From Delphi 1, consensus is if HSV/VZV viral AU presents more as a chronic AU as opposed to episodic hypertensive flares, long term maintenance oral antiviral +/- topical steroids should be considered. No consensus however can be found if the patient presents with recurrent episodic hypertensive HSV/VZV viral AAU although 50% of experts will alter their management in some way of which most will consider maintenance therapy if there are 3 episodes in a year. How will you alter your treatment plan for the treatment of a HSV/VZV related viral AU that recurrs as

separate episodic bouts of hypertensive uveitis - (Up to 4 separate episodes per year based on SUN criteria for recurrence)?

HSV/VZV
I agree with starting long term maintenance therapy (PO antivirals +/- topical steroids and IOP lowering drops) if there are 2 or more episodes of hypertensive uveitis per year
I agree with starting long term maintenance therapy (PO antivirals +/- topical steroids and IOP lowering drops) if there are 4 episodes of hypertensive uveitis per year

3. From Delphi 1, consensus from experts is that systemic +/- topical antivirals should be used for initial antiviral therapy for HSV/VZV related viral AU respectively. 96% of experts will use systemic antivirals (valacyclovir most commonly used), of which 40% of them will also use a topical antiviral (acyclovir most commonly used) concurrently. When do you decide topical antivirals is necessary? Please select any of the choices you deem appropriate

HSV/VZV	Check boxes so more than 1 can be selected
I consider adding on topical antivirals only if there is corneal involvement	
I consider adding on topical antivirals if it is a severe cause of HSV/VZV viral AU (highly inflammed, very high IOP)	
I consider adding on topical antivirals as a cover to prevent corneal involvement (as topical steroids are used)	
No, I do not use topical antivirals for HSV/VZV viral AU if systemic antivirals are already used	

4. From Delphi 1, consensus from experts is the first line systemic antiviral for VZV viral AU is PO Valacyclovir. Consensus was not reached (i.e. <70%) for HSV viral AU as only 66% used PO Valacyclovir for HSV viral AU as their first line systemic antiviral. How do you decide which systemic antiviral therapy to use? Please select any of the choices you deem appropriate

HSV	Check boxes so more than 1 can be selected
I prefer to use PO Valacyclovir because of its simpler dosing regimen	
I prefer to use PO Valacyclovir because it is more effiacious	
I prefer to use PO acyclovir because of its lower cost	
I prefer to use PO acyclovir because of its larger body of published evidence i.e. HEDS results	

5. From Delphi 1, the most common dosage and duration for INITIAL SYSTEMIC antiviral therapy for HSV/VZV related viral AU if used is: HSV: PO Valacyclovir 1g BD to TDS for 10-14 days; VZV : PO Valacyclovir 1g TDS for 10-14 days. OR HSV: PO Acyclovir 400-800mg 5x per day for 10-14 days; VZV : PO Acyclovir 800mg 5x per day for 10-14 days. Do you agree that this will be a good general guideline for initial antiviral therapy for HSV/VZV related viral AU?

HSV		VZV	
Yes, I agree with Valacyclovir dosage and duration	Please select one	Yes, I agree with Valacyclovir dosage and duration	Please select one
Yes, I agree with Acyclovir dosage and duration	Please select one	Yes, I agree with Acyclovir dosage and duration	Please select one
Yes, I agree with both Valacyclovir and Acyclovir dosage and duration	Please select one	Yes, I agree with both Valacyclovir and Acyclovir dosage and duration	Please select one
No, I disagree with both	Please select one	No, I disagree with both	Please select one

6. From Delphi 1, the most common dosage and duration for INITIAL TOPICAL antiviral therapy for HSV/VZV related viral AU if used is: HSV : Occ acyclovir (3%) 5 times a day for 1 month; VZV : Occ acyclovir (3%) 5 times a day for 1 month. Do you agree that this will be a good general guideline for initial topical antiviral therapy for HSV/VZV related viral AU?

HSV		VZV	
Yes, I agree with both topical dosage and duration	Please select one	Yes, I agree with both topical dosage and duration	Please select one
No, I agree with only the topical dosage but prefer a shorter duration	Please select one	No, I agree with only the topical dosage but prefer a shorter duration	Please select one
No, I agree with only the topical duration but prefer a tapering dosage (i.e. fewer nu	Please select one	No, I agree with only the topical duration but prefer a tapering dosage	Please select one
No, I disagree with both	Please select one	No, I disagree with both	Please select one

7. From Delphi 1, the most common dosage and duration for MAINTENANCE antiviral therapy for HSV/VZV related viral AU if used is: HSV: PO Valacyclovir 500mg BD to TDS for 3-12 months; VZV : PO Valacyclovir 500mg BD to TDS for 3-12 months. OR HSV: PO acyclovir 200-400mg BD for 3-12 months; VZV : PO acyclovir 400mg BD for 3-12 months. Do you agree that this will be a good general guideline for maintenance antiviral therapy for HSV/VZV related viral AU?

HSV		VZV	
Yes, I agree with both topical dosage and duration	Please select one	Yes, I agree with both topical dosage and duration	Please select one
No, I agree with only the topical dosage but prefer a shorter duration	Please select one	No, I agree with only the topical dosage but prefer a shorter duration	Please select one
No, I agree with only the topical duration but prefer a tapering dosage (i.e. fewer nu	Please select one	No, I agree with only the topical duration but prefer a tapering dosage	Please select one
No, I disagree with both	Please select one	No, I disagree with both	Please select one

8. From Delphi 1, consensus was achieved on NOT starting topical steroids without antiviral coverage in a case of HSV/VZV related viral AU. Consensus was almost achieved (69%) on NOT starting topical NSAIDs without antiviral coverage i.e. while aqueous tap results are pending. Will you be comfortable starting topical NSAIDs without antiviral coverage for a case you suspect is HSV/VZV related viral AU?

Yes, I am comfortable to start topical NSAIDs without antiviral coverage while results are pending	Please select one
No, I will not do so and will give empirical topical antiviral coverage if I were to start topical NSAIDs while results are pend	Please select one
No, I will not do so and will give empirical oral antiviral coverage if I were to start topical NSAIDs while results are pending	Please select one
No, I will not do so and will give empirical topical + oral antiviral coverage if I were to start topical NSAIDs while results ar	Please select one

9. From Delphi 1, a significant proportion of experts (>60%) will use cycloplegics/mydriatics in a case of HSV/VZV viral AU. However, consensus was not reached as some experts felt it was not required and a small minority (6.5-10%) worry about permanent mydriasis. In view of the results, what do you think is a GOOD GENERAL GUIDELINE regarding the use of cycloplegics and mydriatics in HSV/VZV viral AU

HSV/VZV	Please select one
I am comfortable with routine use of cycloplegics/mydriatics in cases of HSV/VZV viral AU	
I will consider using cycloplegics/mydriatics in cases of HSV/VZV viral AU if necessary (patient has significant AC inflammation, pain etc although this might be rare)	
I will not use cycloplegics/mydriatics as I worry about the possibilty of permanent mydriasis	

- **<u>Follow-up and complication</u>**

1. From Delphi 1, consensus amongst experts is if there is active corneal invovlement of a HSV/VZV viral AU patient, topical antivirals should be added. Other recommendations that did not reach consensus include: titration of topical steroids to the activity/type of keratitis, starting of oral antivirals and referral to a cornea specialist for co-management. As a general guideline, is it APPROPRIATE TO CONSIDER the following:

Starting oral antiviral therapy if not already on for the HSV/VZV viral AU		Yes or No (check boxes, can select more than 1)
Titrating topical steroids to the viral keratitis (i.e. decrease if there is epithelial keratitis but increase if there is stromal keratitis)		Yes or No (check boxes, can select more than 1)
Referral to a cornea specialist for co-manage		Yes or No (check boxes, can select more than 1)