Supplementary file 3. Delphi round-two questions for TITAN CMV study

Questions for Delphi - Round 2 for The Infectious Uveitis Treatment Algorithm Network (TITAN) study – CMV related viral AU

In the case of an immunocompetent otherwise healthy individual with purely CMV anterior uveitis (based on clinical presentation and SUN guidelines) and no history/clinical signs of previous episodes (i.e. corneal scars, glaucomatous optic neuropathy) or active corneal involvement

Diagnosis and Investigations to guide treatment

Q1.

From Delphi 1, consesus was reached that a unilateral, hypertensive AU without synechiae and engorged iris vessels is specific for CMV related viral AU.

Corneal oedema, various forms of KPs and diffuse iris atrophy were found to be useful to some experts but not others. No consensus was achieved on their specificity towards diagnosing CMV related viral AU

What ADDITIONAL clinical signs will you consider CRITICAL to assist you in making a better diagnosis of CMV related viral AU at the first presentation of the patient above?

Corneal oedema

○ Yes ○ No ○ Decline to answer

Comments:

Diffuse KPs

○ Yes ○ No ○ Decline to answer

Comments:

Stellate KPs

○ Yes ○ No ○ Decline to answer

Comments:

Granulomatous KPs

○ Yes ○ No ○ Decline to answer

Comments:

Diffuse iris atrophy

○ Yes ○ No ○ Decline to answer

Comments:

Q2.

From Delphi 1, consesus was reached that an aqueous tap was important to perform if you suspect CMV related viral AU. The experts do it often or all the time.

Will you consider CMV serology IgM and IgG as an IMPORTANT ADJUNCT and under what circumstances?

- ○ I will perform serology together with an aqueous tap
- ○ I will perform serology only if aqueous tap is negative
- ○ I do not perform serology as an aqueous tap is sufficient for me
- ○ Decline to answer

Comments:

Q3.

From Delphi 1, in the current practice of the experts, CMV related viral AU is currently diagnosed 50% of the time solely on clinical features (IQR 10-70%) and 50% with clinical features and a positive lab test (IQR 25-95%).

Consensus by experts however reveals an aqueous tap should be done often or all the time in the diagnosis of CMV related viral AU.

Will you ALWAYS consider performing an aqueous tap to diagnose a suspected CMV related viral AU UNLESS THERE ARE SPECIAL CIRCUMSTANCES ?

I will always perform an aqeous tap in a suspected case of CMV related viral AU

○ Yes ○ No ○ Decline to answer

Comments:

I will prefer to rely on clinical features solely still unless I am unsure of the diagnosis

○ Yes ○ No ○ Decline to answer

Comments:

Q4.

From Delphi 1, consensus is that the ophthalmologist should be responsible for monitoring blood investigations (FBC/CBC; UECr; LFT) for the patient while on systemic antiviral therapy.

The commonest response (mode) for the frequency of all the blood investigations (FBC/CEC; UECr; LFT) is 4 times a year or more. However consensus cannot be achieved because there were significant portion of experts performing these investigations at a lower frequency especially for LFTs

What do you think will be a RELIABLE GENERAL GUIDE to the frequency of blood investigations for patients maintained on systemic antiviral therapy in light of this?

I will repeat the blood investigations (FBC/CBC; UECr; LFT) at least 2 -4 times per year

○ Yes ○ No ○ Decline to answer

Comments:

I will repeat LFTs at a lower frequency as it is less crucial than the other 2 investigations - at least twice a year

○ Yes ○ No ○ Decline to answer

Comments:

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Treatment - General

Q1.

From Delphi 1, 68% of experts only rely on PCR/GWC for diagnosis and subsequently treatment plans (dosages, frequency, response) are based on clinical response.

Only 30% of experts repeat the PCR/GWC to guide their subsequent treatment plans.

In a STRAIGHTFORWARD CASE of CMV related viral AU where the patient is responding well to treatment, will you still ROUTINELY REPEAT the PCR/GWC?

- ○ No, I will monitor this patient clinically without further investigations i.e. PCR/GWC
- ○ Yes, I prefer to routinely repeat the PCR/GWC to guide my treatment plan
- ○ Decline to answer

Comments:

Q2.

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 CMV related viral AU.

A significant propotion of experts (61%) also require resolution of corneal oedema as a clinical treatment endpoint.

Do you feel it is NECESSARY for corneal oedema to resolve as a clinical treatment endpoint?

- ☐ Yes, if corneal oedema persist despite no intraocular inflammation and normal IOP, I will continue to treat the patient
- ☐ No, corneal edema sometimes may lag behind the other clinical signs such as IOP, cells, KPs, flare which are more sensitive
- ☐ No, corneal edema sometimes may persist because of corneal decompensation (despite it being the first episode)

Comments:

Q3.

From Delphi 1, 58% of experts will alter their management if the CMV related viral AU presents more as a chronic AU as opposed to episodic hypertensive flares.

More than half of these experts prefer to start the patient on long term oral antivirals +/- topical anti-inflammatory drops.

How will you alter your treatment plan for the treatment of a CMV related viral AU that appears to be chronic?

- ○ Start long term maintenance antiviral +/- anti-inflammatory therapy

- ○ Aggressively attempt to treat to quiescent and taper off
- ○ Decline to answer

Comments:

Treatment - Antiviral

Q1.

From Delphi 1, 85% of experts will start antiviral therapy for CMV related viral AU (as per above case scenario) but there is significant variation in the route of administration.

Half of these experts use only topical antiviral - mainly ganciclovir gel 0.15%

Half will use both topical and oral valganciclovir.

How do you decide if the patient requires systemic antiviral therapy ?

I routinely use both topical and systemic forms of ganciclovir once I confirm the diagnosis of CMV related viral AU even if it is the FIRST PRESENTATION

○ Yes ○ No ○ Decline to answer

Comments:

I only add systemic forms of ganciclovir for severe / prolonged / atypical cases of CMV related viral AU

○ Yes ○ No ○ Decline to answer

Comments:

No, I only use topical forms of ganciclovir regardless of clinical variation in the CMV related viral AU

○ Yes ○ No ○ Decline to answer

Comments:

Q2.

From Delphi 1, the most common dosage and duration for **initial antiviral therapy** for CMV related viral AU if used is:

Ganciclovir gel 0.15% TDS - QDS for 1 month;
PO Valganciclovir 900mg BD for 2-3 weeks

Do you agree that this will be a GOOD GENERAL GUIDELINE for initial antiviral therapy for CMV related viral AU?

- ○ Yes, I agree with both topical and systemic dosage and duration
- ○ No, I agree with only the topical dosage and duration
- ○ No, I agree with only the systemic dosage and duration
- ○ No, I disagree with both
- ○ Decline to answer

Comments:

Q3.

From Delphi 1, the most common dosage and duration for **maintenance antiviral therapy** for CMV related viral AU if used is:

Ganciclovir gel 0.15% BD 3-12 months;
PO Valganciclovir 450mg OD or BD for 3-12 months

Do you agree that this will be a GOOD GENERAL GUIDELINE for maintenance antiviral therapy for CMV related viral AU?

- ○ Yes, I agree with both topical and systemic dosage and duration
- ○ No, I agree with only the topical dosage and duration
- ○ No, I agree with only the systemic dosage and duration
- ○ No, I disagree with both
- ○ Decline to answer

Comments:

Treatment - Anti-inflammatory / IOP

Q1.

From Delphi 1, consensus was achieved on **NOT** starting topical steroids without antiviral coverage in a case of CMV related viral AU.

However, 66% of experts are willing to start topical NSAIDs without antiviral coverage i.e. while aqueous tap results are pending / empirical treatment

Will you be comfortable starting topical NSAIDs without antiviral coverage for a case you suspect is CMV related viral AU?

- ○ Yes, I am comfortable to start topical NSAIDs
- ○ No, I will not do so
- ○ Decline to answer

Comments:

Q2.

From Delphi 1, consensus was topical steroids is the preferred choice over topical NSAIDs when it comes to topical anti-inflammatory therapy (95% vs 4%) if no contraindications

Prednisolone Acetate 1% was the commonest drug used by the experts as first line (61%)

IF YOU HAD TO USE a topical steroid, please select your first choice assuming no contraindications?

- ○ Fluorometholone

- ○ Loteprednol
- ○ Prednisolone Acetate 0.12%
- ○ Prednisolone Acetate 1%
- ○ Dexamethasone 0.1%
- ○ Decline to answer

Comments:

Q3.

From Delphi 1, the experts felt that only topical steroids should be used with antiviral coverage for CMV related viral AU for **initial therapy**. Systemic steroids have no role.

The typical dosage and duration for initial topical steroids is at least QDS for 1-2 weeks, increasing depending on severity of inflammation.

Do you agree that this will be a GOOD GENERAL GUIDELINE for initial topic steroid therapy for CMV related viral AU?

○ Yes ○ No ○ Decline to answer

Comments:

Q4.

From Delphi 1, the experts felt that only topical steroids should be used with antiviral coverage for CMV related viral AU for **maintenance therapy**. Systemic steroids have no role.

The typical duration of maintenance topical steroid therapy is 3-12 months without recurrence and involves a very slow taper

Do you agree that this will be a GOOD GENERAL GUIDELINE for maintenance topic steroid therapy for CMV related viral AU?

○ Yes ○ No ○ Decline to answer

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Follow up and Complications affecting treatment

Q1.

From Delphi 1, >50% of experts will consider long term antiviral therapy (topical +/- systemic) for patients with 2 recurrences or more in a year:

As a general guideline, is it APPROPRIATE TO CONSIDER long term antiviral therapy (topical +/- systemic) if patients have at least 2 episodes of flare in a year

- [ ] I will consider long term topical antiviral therapy
- [ ] I will consider long term systemic antiviral therapy
- [ ] I will consider long term topical and systemic antiviral therapy
- [ ] No, I will not consider long term antiviral therapy
- [ ] Decline to answer

Comments:

Q2.

From Delphi 1, >50% of experts will consider long term topical steroid therapy for patients with 3 recurrences or more in a year:

As a general guideline, is it APPROPRIATE TO CONSIDER long term topical steroid therapy if patients have at least 3 episodes of flare in a year

- [ ] I will consider long term topical steroid therapy
- [ ] No, I will not consider long term steroid therapy
- [ ] Decline to answer

Comments:

Q3.

From Delphi 1, 64% of experts treat recurrences of CMV related viral AU "shortly after stopping therapy" by restarting initial dosages (both antiviral and anti-inflammatory medication) and opt for a longer taper. Consider a patient having a flare of CMV related viral AU in the 4th to 6th months after stopping therapy for example.

If there is recurrence shortly after stopping therapy, will this be a reasonable therapeutic approach you will adopt?

- ○ Yes
- ○ No
- ○ Decline to answer

Comments:

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