

Table S1. Clinical trial schedule/visit plan

Day	Pre-screening	Baseline T 0	1	2	3	4	5	6	7	8	9	10 or EOT	30	90	180
Check inclusion and exclusion criteria	X (check)	x													
Clarification, obtaining the declaration of consent		X													
Pregnancy test if necessary ¹		X													
Randomization		X													
Demographics ²		X													
SOFA score		X			X		X		X			X			
APACHE/CFS		X													
Extended-CardioVasc-SOFA-Sub-Score		X	X	X	X	X	X	X	X	X	X	X			
Concomitant diseases		X													
Concomitant medication ³							X								
Microbiological results						X									
Physiological parameters ⁴		X													
Serology herpes viruses ⁵		X													
Renal replacement procedures		X	X	X	X	X	X	X	X	X	X	X			
Immune status		X													
Laboratory values ⁶		X			X		X		X			X			
Acyclovir administration (intervention group only).							X								
Delirium/Coma (CAM-ICU / RASS)		X	X	X	X	X	X	X	X	X	X	X			
Vasopressor		X	X	X	X	X	X	X	X	X	X	X	X		
Ventilation		X	X	X	X	X	X	X	X	X	X	X	X		
Length of stay Hospital/ICU													X	X	X
Whereabouts													X	X	X
Survival status													X	X	X
EQ5D-5L												X	X (±48h)	X (±48h)	X (±48h)
Questionnaire ethical aspects (once) ⁷												X	X	X	X
HSV-1 PCR blood		X										X			
HSV-1 PCR respiratory ⁸												X			
(S)AEs ⁹							X								
Study protocol deviations															X

¹ Blood or urine (only in women with childbearing potential)² Age, gender, height, weight³ Interferon, intrathecal methotrexate, theophylline, zidovudine, ciclosporin, nephrotoxic agents, probenecid, valacyclovir, famciclovir/penciclovir, brivudine, cidofovir, foscarnet, ganciclovir, valganciclovir, other viral agents.⁴ Blood pressure, heart rate, body temperature, urine output⁵ Herpes simplex 1 (HSV-1) IgG/IgM, Varicella Zoster (VZV) IgG/IgM, Cytomegalovirus (CMV) IgG/IgM⁶ on **day 0 and 3**: sodium, potassium, creatinine, GFR - according to Cockcroft -Gault, bilirubin, ALAT (GPT), lactate, CRP, PCT, hematocrit, leukocytes, platelets, ferritin, IL6, **day 5 and 7**: Sodium, potassium, creatinine, GFR - according to Cockcroft -Gault, bilirubin, ALAT (GPT), lactate, CRP, PCT, hematocrit, leukocytes, platelets and **on day 10**: creatinine, GFR - according to Cockcroft -Gault, bilirubin, ALAT (GPT), lactate, CRP, PCT, leukocytes, platelets, ferritin.⁷ One time between day 10/EOT and day 180 (depending on when the patient can adequately respond).⁸ or tracheobronchial secretion or pharyngeal lavage water (depending on clinical diagnostics)⁹ If the patient is discharged from the ICU before day 10, then the (S)AE recording ends with this day.