**Figure: Schematic diagram of study design**

- Admission, baseline data, CT scan, lumbar puncture for CSF, start of treatment with acyclovir
- Proof of diagnosis by CSF analysis for detection of HSV-DNA with PCR assay
- Selection of patients with respect to the inclusion and exclusion criteria
- Randomization

| Day 0 of study | **Experimental group:** Treatment with adjuvant dexamethasone  
Aciclovir: 10mg/kg BW acyclovir (intravenously, 1 hour infusion) every 8 hours for 14 days  
Dosage adaptation in case of decreased creatinine clearance  
Dexamethasone 40 mg intravenously every 24 hours for 4 days. | **Control group:** Treatment with placebo  
Aciclovir: 10mg/kg BW acyclovir (intravenously, 1 hour infusion) every 8 hours for 14 days  
Dosage adaptation in case of decreased creatinine clearance  
Placebo identical in appearance to dexamethasone infusion every 24 hours for 4 days. |
| --- | --- | --- |
| Day 0 | • Neurological examination, GCS, pre-encephalitis Barthel Index, pre-encephalitis mRS, Neuropsychological test, seizures.  
• Cranial MRI-scan as soon as possible after positive HSV in CSF, at the latest 48 hours after initiation of study medication (Dexamethasone/Placebo). |  |
| Discharge at the latest Day 30 | • Physical and neurological examinations. | • Physical and neurological examinations, mRS, GOS, Barthel index, seizures. |
| 6 months after randomization | • Physical, neurological and neuropsychological examinations, mRS, GOS, quality of life (EuroQol 5D), Barthel-Index, seizures.  
• Cranial MRI-scan. |  |
| 12 months after randomization | • Physical and neurological examinations, mRS, GOS, quality of life (EuroQol 5D), Barthel-Index, seizures. |  |