## Online-Only Tables

### eTable 1

### Summary of clinical findings and diagnostic investigations for patients with prion disease. (NA indicates data not available)

| Diagnosis [a] | Mean DDA RRC [b] | Result [c] | Codon 129 Genotype [d] | MRC Rating Scale [e] | Clinical Features | EEG [f] | MRI [g] | 14.3.3 [h] | S100B [i] | RT QuIC [J] |
|---|---|---|---|---|---|---|---|---|---|---|
| sCJD | 0.14 | NEG | MM | 10 | Personality Change, Left Hemisensory Extinction, Ataxia, Myoclonus, Rapid Cognitive Decline | Slow | Basal Ganglia signal change, Cortical Ribboning | Positive | Raised (0.97) | Positive |
| sCJD | 0.15 | NEG | VV | 0 | Personality Change, Ataxia, Insomnia, Neuromyotonia, Rapid Cognitive Decline, Supranuclear Gaze Palsy, Myoclonus | Slow | NA | Positive | Raised (4.5) | Positive |
| vCJD | 0.17 | NEG | MM | 10 | Lower Limb Pain, Rapid Cognitive Decline, Ataxia, Depression, Psychosis | Slow | Pulvinar Sign | Negative | NA | NA |
| vCJD | 0.17 | NEG | MM | 11 | Acral Paraesthesia, Rapid Cognitive Decline, Ataxia, Dysarthria, Weight Loss, Myoclonus, Auditory & Visual Hallucinations | Slow with sharp waves bilaterally | Pulvinar Sign | Negative | Raised (1.03) | NA |
| sCJD | 0.20 | NEG | MM | 1 | Rapid Cognitive Decline, Complex Partial Seizures, Visual Hallucinations, Myoclonus | Slow | Caudate signal change, Cortical Ribboning | Negative | Raised (0.55) | NA |
| sCJD | 0.20 | NEG | MV | 2 | Ataxia, Rapid Cognitive Decline, Visual Hallucinations, Myoclonus | Slow | Basal Ganglia signal change, Cortical Ribboning | Positive | Raised (0.57) | NA |

| Diagnosis [a] | Mean DDA RRC [b] | Result [c] | Codon 129 Genotype [d] | MRC Rating Scale [e] | Clinical Features | EEG [f] | MRI [g] | 14.3.3 [h] | S100B [i] | RT QuIC [J] |
|---|---|---|---|---|---|---|---|---|---|---|
| sCJD | 0.22 | NEG | VV | 0 | Ataxia, Myoclonus, Dysarthria, Apraxia, Rapid Cognitive Decline, Chorea | Slow | Basal Ganliga signal change, Cortical Ribboning, Cerebellar Atrophy | Positive | Raised (2.3) | NA |
| vCJD | 0.23 | NEG | MM | NA | Right Lower Limb Pain, Spasticity, Ataxia, Dysarthria, Frontality | NA | Pulvinar Sign | Positive | Raised (1.39) | NA |
| vCJD | 0.28 | NEG | MM | NA | Personality Change, Ataxia, Dysarthria, Weight Loss, Myoclonus, Chorea | Slow | Thalamic signal change | Negative | NA | NA |
| sCJD | 0.29 | NEG | VV | 2 | Diplopia, Cortical Blindness, Ataxia, Alien Limb, Myoclonus, Rapid Cognitive Decline | Slow | Thalamic signal change, Cortical Ribboning | Positive | Raised (>2) | NA |
| sCJD | 0.29 | NEG | VV | 9 | Rapid Cognitive Decline, Ataxia, Myoclonus, Dysphasia | Slow | Basal Ganglia signal change, Cortical Ribboning | Positive | Raised | NA |
| sCJD | 0.33 | NEG | MM | 0 | Lower Limb Pain, Ataxia, Rapid Cognitive Decline, Visuospatial Deficits, Myoclonus | Periodic Sharp Wave Complexes | Basal Ganglia change, Cortical Ribboning | Positive | Raised (2.93) | NA |
| vCJD | 0.35 | NEG | MM | NA | Lower Limb Allodynia, Spastic Paraplegia, Ataxia, Depression, Personality Change, Rapid Cognitive Decline | Normal | Thalamus | NA | NA | NA |
| vCJD | 0.39 | NEG | MM | 7 | Ataxia, Personality Change, Rapid Cognitive Decline, Chorea | Low Amplitude & Slow | Pulvinar Sign | Positive | Raised (0.85) | NA |

| Diagnosis [a] | Mean DDA RRC [b] | Result [c] | Codon 129 Genotype [d] | MRC Rating Scale [e] | Clinical Features | EEG [f] | MRI [g] | 14.3.3 [h] | S100B [i] | RT QuIC [J] |
|---|---|---|---|---|---|---|---|---|---|---|
| vCJD | 0.44 | NEG | MM | 3 | Personality Change, Ataxia, Rapid Cognitive Decline, Myoclonus | Slow | Pulvinar Sign | Negative | Raised (0.71) | NA |
| sCJD | 0.48 | NEG | MM | 0 | Metamorphopsia, Oscillopsia, Ataxia, Rapid Cognitive Decline, Myoclonus | Periodic Sharp Wave Complexes | Right frontal arteriovenous malformation, caudate signal change, cortical ribboning | Positive | Raised (2.32) | Positive |
| IPD (P102L) | 0.49 | NEG | MV | 10 | Ataxia, Lower Limb Allodynia, Dysarthria, Spasticity, Sensorimotor Axonopathy, Visual Hallucinations, Cognitive Decline | Normal | Normal | NA | NA | NA |
| vCJD | 0.49 | NEG | MM | 6 | Depression, Personality Change, Ataxia, Rapid Cognitive Decline, Visual Hallucinations | Slow | Pulvinar Sign | NA | NA | NA |
| sCJD | 0.49 | NEG | MM | 3 | Aphasia, Limb Apraxia, Gait Ataxia, Akinetic Mutism | NA | Basal Ganglia changes | Negative | Raised (0.69) | Negative |
| vCJD | 0.50 | NEG | MM | 14 | Personality Change, Dysarthria, Ataxia, Rapid Cognitive Decline | Slow | Pulvinar Sign | NA | NA | NA |
| vCJD | 0.60 | NEG | MM | 7 | Personality Change, Depression, Ataxia, Rapid Cognitive Decline, Visual Hallucinations, Lower Limb Sensory Symptoms | Slowing over temporal regions | Pulvinar Sign | NA | NA | NA |
| vCJD | 0.65 | NEG | NA | NA | NA | NA | NA | NA | NA | NA |

| Diagnosis [a] | Mean DDA RRC [b] | Result [c] | Codon 129 Genotype [d] | MRC Rating Scale [e] | Clinical Features | EEG [f] | MRI [g] | 14.3.3 [h] | S100B [i] | RT QuIC [J] |
|---|---|---|---|---|---|---|---|---|---|---|
| vCJD | 0.67 | NEG | MM | 5 | Depression, Personality Change, Ataxia, Dysphagia, Rapid Cognitive Decline | Slow | Pulvinar Sign, Basal Ganglia high signal | Negative | Raised (0.54) | NA |
| sCJD | 0.88 | NEG | MM | 0 | Alien Limb, Dysphasia, Visual Hallucinations, Rapid Cognitive Decline | Periodic Sharp Wave Complexes | Basal Ganglia signal change, Cortical Ribboning | Positive | Raised (3.93) | Negative |
| sCJD | 1.16 | NEG | MM | 4 | Rapid Cognitive Decline, Personality Change, Ataxia, Myoclonus | Periodic Sharp Wave Complexes | Right Putamen high signal | Positive | Raised (1.27) | NA |
| IPD (5-OPRI) | 1.25 | NEG | MM | NA | Episodic Memory Problems, Ataxia, Apraxia, Frontal Lobe Dysfunction | NA | NA | NA | NA | NA |
| sCJD | 1.56 | POS | MM | 1 | Obsessions, Paranoia, Ataxia, Insomnia, Visual Hallucinations, Rapid Cognitive Decline | Periodic Sharp Wave Complexes | Basal Ganglia high signal, Cortical Ribboning | Positive | Raised (2.62) | Positive |
| iCJD (Growth Hormone) | 1.70 | NEG | MV | NA | Gait Ataxia, Sensory Symptoms In Feet, Myoclonus, Insomnia, Nystagmus | Slow | Normal | Borderline | Raised (1.35) | NA |
| sCJD | 1.94 | POS | VV | 1 | Ataxia, Rapid Cognitive Decline, Dysphasia, Sweet Tooth | Periodic Sharp Wave Complexes | Cortical Ribboning (Left Frontal) | Positive | Raised (1.04) | NA |
| sCJD | 2.54 | POS | MM | 1 | Oscillopsia, Visual Hallucinations, Cortical Blindness, Ataxia, Rapid Cognitive Decline, Myoclonus | Periodic Sharp Wave Complexes | Basal Ganglia high signal & Cortical Ribboning | Positive | Raised (2.59) | NA |

| Diagnosis [a] | Mean DDA RRC [b] | Result [c] | Codon 129 Genotype [d] | MRC Rating Scale [e] | Clinical Features | EEG [f] | MRI [g] | 14.3.3 [h] | S100B [i] | RT QuIC [J] |
|---|---|---|---|---|---|---|---|---|---|---|
| sCJD | 2.89 | POS | VV | 7 | Rapid Cognitive Decline, Personality Change, Gait Apraxia, Visual Hallucinations, Myoclonus | Slow | Basal Ganglia high signal, Thalamic high signal & Cortical Ribboning | Positive | Raised (1.37) | Positive |
| iCJD (Growth Hormone) | 3.42 | POS | MV | NA | Gait Ataxia, Episodic Memory Loss, Dysarthria, Myoclonus | NA | Normal | NA | NA | NA |
| sCJD | 3.72 | POS | VV | 1 | Rapid Cognitive Decline, Ataxia, Dysphasia, Myoclonus | Low Amplitude & Slow | Basal Ganglia high signal | Positive | Raised (>4) | NA |
| vCJD | 4.22 | POS | MM | 8 | NA | NA | NA | NA | NA | NA |
| sCJD | 5.38 | POS | MV | 10 | Rapid Cognitive Decline (Visuospatial and Dysphasia), Akinetic Mutism | Slow | Cortical Ribboning | Positive | Raised (0.86) | NA |
| sCJD | 6.29 | POS | MV | 6 | Personality Change, Depression, Right Upper & Lower Limb Weakness & Sensory Symptoms, Dysphasia, Ataxia, Rapid Cognitive Decline, Visual Hallucinations, Myoclonus | Slow | NA | Weak Positive | Raised (1.7) | NA |
| sCJD | 7.04 | POS | VV | 1 | Dysautonomia, Chorea, Rapid Cognitive Decline, Ataxia, Myoclonus | Slow | Basal Ganglia high signal, Thalamic high signal & Cortical Ribboning | Positive | Raised (4.13) | Positive |

**Footnotes**

[a] **Diagnosis :** *sCJD - sporadic Creutzfeldt-Jakob Disease*, *vCJD variant Creutzfeldt-Jakob Disease*, *iCJD iatrogenic Creautzfeldt-Jakob Disease*, *IPD Inherited Prion Disease*, *P102L point mutation with proline to leucine substitution on position 102 of the prion protein gene (PRNP), 5-OPRI 5 Octapeptide Repeat Insertion in the prion protein gene*.

[b] **Mean DDA RRC :** *the mean ratio relative to cut-off of two independent assays (for details see Materials and Methods).*

[c] **Result :** *determination by DDA of positive (POS) for prion disease or unaffected (NEG) by DDA (for details see Materials and Methods).*

[d] **Codon 129 Genotype :** *Polymorphism at codon 129 of the PRNP gene encoding either methionine homozygous MM, valine homozygous VV or methionine valine heterozygous MV.*

[e] **MRC Rating Scale :** *The Medical Research Council prion disease rating scale: a new outcome measure for prion disease therapeutic trials developed and validated using systematic observational studies (Thompson et al, Brain 2013 136:1116-1127).*

[f] **EEG :** *Electroencephalogram (EEG) findings in sCJD vary between diffuse slowing to more characteristic generalised periodic sharp wave complexes in sCJD depending on the stage of disease (Zerr et al, Brain 2009 132:2659-2668).*

[g] **MRI :** *Magnetic Resonance Imaging (MRI) findings in brains of patients with sCJD characteristically show high signal abnormalities in the caudate nucleus and putamen or at least two cortical regions either in diffusion-weighted imaging (DWI) or fluid-attenuated inversion recovery (FLAIR) sequences; the thalami of vCJD patient classically return higher signal than the basal ganglia, known as the "Pulvinar Sign" (Zerr et al, Brain 2009 132:2659-2668).*

[h] **14-3-3 :** *14.3.3 is an intracellular neuronal protein that is detectable via immunoassay in the cerebrospinal fluid (CSF) of patients where there is rapid and widespread neuronal destruction. It has a sensitivity of >90% in sCJD and 40% in vCJD; but a low specificity of 70 – 80% (Zerr et al, Brain 2009 132:2659-2668).*

[i] **S100B :** *A glial protein quantifiably in CSF and elevated (≥ 0.41ng/L) in approximately 90% of sCJD patients. It is also raised in other destructive diseases of the central nervous system.*

[j] **RT QuIC :** *Real-Time Quaking Induced Conversion, an experimental in vitro amplification method for detecting prion infection in CSF, with sensitivity and specificity for sCJD reported as 89% and 99% respectively. (McGuire et al, Annals of Neurology 2012 72:278-285).*