**Supplementary table 1. Clinical responses after bortezomib treatment**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
| **Bortezomib treatment** |  |  |  |  |  |
| Disease onset to initiation of bortezomib(days) | 269 | 364 | 144 | 151 | 143 |
| CGI-S at initiation of bortezomib | 6 | 6 | 6 | 6 | 6 |
| Bortezomib regimen | Twice-weeklya | Twice-weekly | Twice-weekly | Twice-weekly | Once-weeklyb |
| Number of cycles of bortezomib | 3 | 2 | 2.5c | 3 | 6d |
| Number of cycles of CyBorD | N/A | 2 | 1.5 | N/A | First and third week |
| **Clinical responses** |  |  |  |  |  |
| Major clinical symptoms at the time of bortezomib initiation | Vegetative state, oromandibular dyskinesia, stereotypic limb movement, abnormal posture, autonomic instability, and central hypoventilation | Vegetative state, oromandibular dyskinesia, stereotypic limb movement, rigidity, central hypoventilation and sympathetic paroxysmal hyperactivity | Vegetative state, stereotypic limb movement, rigidity, abnormal posture | Vegetative state, oromandibular dyskinesia, stereotypic limb movement, rigidity, sympathetic paroxysmal hyperactivity | Vegetative state, oromandibular dyskinesia, stereotypic limb movement |
| Clinical improvement after 2 cycles of bortezomib | Improved to minimally consciousness state (pursuit eye movement and blink eyes following command), decreased movement symptoms, and some improvement in breathing | Decreased movement symptoms and improved autonomic instability | Improved to minimally consciousness state (pursuit eye movement and localize noxious stimuli), and decreased movement symptoms | Decreased movement symptoms and improved autonomic instability | Improved to minimal consciousness state (gestural and verbal responses, intelligible verbalization, and some purposeful movements) and decreased movement symptomse |
| Initial antibody titer in serum at admission | 1:640 | 1:1280 | 1:160 | Not checked | Not checked |
| Initial antibody titer in CSF at admission | Not checked | 1:640 | 1:160 | 1:320 | Not checked |
| Change in serum antibody titerbefore and after two cycles of bortezomib | 1:640 → 1:1280 | 1:640→ 1:640 | 1:160→ 1:160 | 1:1280 → 1:640 | Not checked |
| Change in CSF antibody titer before and after two cycles of bortezomib | 1:80 → 1:80 | 1:160 → 1:160 | 1:320 → 1:160 | 1:160 → 1:80 | Not checked |
| Clinical improvement at 6 month | More improved awareness and cognitive functions (some purposeful movements and gestural responses, follow simple commands, simple, but intelligible verbalization, and emotional response such as smiling in more consistent manner), stabilized spontaneous breathing and removal of tracheostomy tube | Improved to minimally consciousness state (some purposeful movements and vocalization), more decreased movement symptoms, and stabilized spontaneous breathing | More improved awareness and cognitive functions (follow simple commands, gestural responses, simple, but intelligible verbalization, and emotional response such as smiling in inconsistent manner) | Still no definite sign of minimally conscious state but more decreased movement symptoms | N/A |
| CGI-I after bortezomib treatment | 2 | 3 | 3 | 3 | 3 |
| Change in mRS at last follow-up | 5 → 5 | 5 → 5 | 5 → 5 | 5 → 5 | 5 → 5 |
| Follow-up period (since initiation of bortezomib therapy) (months) | 8 | 8 | 8 | 8 | 2 |
| Follow-up period (since disease onset) (months) | 17 | 20 | 13 | 13 | 7 |
| **Adverse Events** |  |  |  |  |  |
| During bortezomib treatment | Anemia (Gr 2), andileus (Gr 2) | Anemia (Gr 2) | Pneumonia (Gr 3), Febrile neutropenia (Gr 3), and anemia (Gr2) | Neutropenia (Gr 1) and anemia (Gr1) |  |
| During CyBorD treatment |  | Febrile neutropenia (Gr 3), leukopenia (Gr 2) |  | Pneumonia (Gr 3) | Neutropenia (Gr 4), anemia (Gr4), diarrhea (Gr 2) |

CGI-S=clinical global impression-severity scale; CyBorD=weekly cyclophosphamide, bortezomib, and dexamethasone (regimen described in methods section); CSF=cerebrospinal fluid; CGI-I=clinical global impression-improvement scale; N/A=not applicable; mRS=modified Rankin Scale; Gr=grade

aBortezomib administration on days 1, 4, 8, 11 in 21-day cycle (regimen described in methods section)

bBortezomib administration once a week (regimen described in methods section)

cEscalated to CyBorD regimen after two doses of bortezomib during the third cycle

dIncluding two CyBorD treatment at first and third week

eEvaluated after 6 weekly administrations of bortezomib

**Supplementary Table 2**. Clinical characteristics and outcome of the control population

|  |  |  |  |
| --- | --- | --- | --- |
|  | Control patient 1 | Control patient 3 | Control patient 4 |
| Age (years) | 44 | 35 | 25 |
| Sex | M | F | F |
| Presenting symptoms | Psy, Sp, Mm, Sz, Mv, C, A, HV | Psy, Sp, Mm, Sz, Mv, C, A, Hv | Psy, Sp, Sz, Mv, C, A, HV |
| CSF initial | Normal | Pleocytosis (37/µL), elevated protein (51.1 mg/dL) | Pleocytosis (140/µL) |
| Brain MRI | No significant focal lesion | Increased T2 signal of bilateral hippocampus | Increased T2 signal at bilateral cerebral sulci and subtle leptomeningeal enhancementin the perimeduallry/prepontine surface |
| EEG | Generalized theta to delta slowing | Generalized delta slowing | Generalized delta slowing |
| Tumor |  | Ovarian teratoma (surgically removed) | Ovarian teratoma (surgically removed) |
| Duration of disease onset to initiation of first-line immunotherapy(days) | 44 | 27 | 11 |
| First-line agents | IVIg | MP, IVIg, PLEX (2 sessions) | IVIg |
| Duration of disease onset to initiation of second-line immunotherapy (days) | 47 | 50 | 18 |
| Second-line agents | RTX, CYC (7 cycles) | RTX, CYC (2 cycles) | RTX, CYC (1 cycle) |
| Duration of disease onset to initiation of tocilizumab (days) | Not used. | 331 | 46 |
| Number of cycles of TCZ |  | 4 | 10 |
| Other treatments | Cyclosporin A, mycophenolate mofetil | IL2 (3 cycles) | IL2 (4 cycles), mycophenolate mofetil |
| Major clinical symptoms at 3 months after rituximab treatment | Comatose, oromandibular dyskinesia, stereotypic limb movement, and seizure | Comatose, oromandibular dyskinesia, stereotypic limb movement, abnormal posture, autonomic instability, and central hypoventilation | Comatose,oromandibular dyskinesia, stereotypic limb movement, autonomic instability, and central hypoventilation |
| mRS at 1 year after onset | 5 (minimally conscious state) | 5 (vegetative state) | 3 |
| mRS at 18 month after onset | 4 | 5 (minimally conscious state) | 2 |
| mRS at last-follow-up | 4 | 4 | 2 |
| Follow-up, month | 27 | 25 | 18 |

Psy=psychiatric symptoms; Sp=speech dysfunction; Mm=memory dysfunction; Sz=seizures; Mv=movement disorder, C=consciousness decrement; A=autonomic dysfunction, HV=central hypoventilation; CSF=cerebrospinal fluid; MRI=magnetic resonance imaging; EEG=electroencephalography; IVIg=intravenous immunoglobulin; MP=methylprednisolone; PLEX=plasmapheresis; RTX=rituximab; CYC=cyclophosphamide; TCZ=tocilizumab; IL2=low-dose interleukin-2; mRS=modified Rankin Scale