|                                    | Relationship between   | Severity           | Outcome             | Impact on NTZ treament                  |  |
|------------------------------------|------------------------|--------------------|---------------------|---|--|
|                                    | SAEs and NTZ treatment |                    |                     |   |  |
|                                    |                        |                    | recovered           |   |  |
| Multiple sclerosis                 | unrelated              | severe             | with sequelae       | no action taken                         |  |
|                                    | unrelated              | severe             | not recovered       | stopped temporarily                     |  |
|                                    | unrelated              | moderate           | recovered           | stopped temporarily                     |  |
|                                    | unrelated              | moderate           | recovered           | stopped temporarily                     |  |
|                                    | unrelated              | moderate           | recovered           | withdrawn                               |  |
|                                    |                        |                    | recovered           |   |  |
|                                    | unrelated              | moderate           | with sequelae       | no action taken                         |  |
| relapses                           | unrelated              | mild               | recovered           | no action taken                         |  |
| (N = 14)                           |                        |                    | recovered           |   |  |
| (14 – 14)                          | unrelated              | mild               | with sequelae       | stopped permanently                     |  |
|                                    | unrelated              | mild               | not recovered       | stopped temporarily                     |  |
|                                    | unrelated              | unknown            | recovered           | no action taken                         |  |
|                                    | unrelated              | unknown            | recovered           | no action taken                         |  |
|                                    | unrelated              | unknown            | recovered           | no action taken                         |  |
|                                    |                        |                    | recovered           |   |  |
|                                    | unrelated              | unknown            | with sequelae       | no action taken                         |  |
|                                    | unknown                | unknown            | unknown             | stopped temporarily                     |  |
| Cardiac disorders<br>(N = 5)       | related                | severe             | recovered           | stopped permanently                     |  |
|                                    | related                | severe             | recovered           | stopped permanently                     |  |
|                                    | unrelated              | severe             | recovered           | stopped permanently                     |  |
|                                    |                        |                    | recovered           |   |  |
| (11 3)                             | unrelated              | severe             | with sequelae       | no action taken                         |  |
|                                    |                        |                    | recovered           |   |  |
|                                    | unrelated              | severe             | with sequelae       | no action taken                         |  |
| Infections<br>(N = 2)              | unrelated              | unknown            | not recovered       | stopped permanently                     |  |
|                                    |                        |                    | recovered           |   |  |
|                                    | unknown                | moderate           | with sequelae       | stopped temporarily                     |  |
| Neurological disorders             | related                | unknown            | not recovered       | withdrawn                               |  |
| (N = 3)                            | unrelated              | mild               | not recovered       | stopped permanently                     |  |
|                                    | unknown                | unknown            | recovered           | stopped permanently                     |  |
|                                    | related                | severe             | not recovered       | stopped permanently                     |  |
| <b>PML</b> (N = 3)                 | related                | moderate           | not recovered       | stopped permanently                     |  |
|                                    |                        |                    | recovered           |   |  |
|                                    | related                | unknown            | with sequelae       | stopped permanently                     |  |
| Immune reconstitution              | undated.               | unknown            | recovered           | stonned normanistic                     |  |
| inflammatory syndrome              | related<br>related     |                    | with sequelae       | stopped permanently                     |  |
| (N = 3)                            |                        | unknown            | not recovered       | stopped permanently                     |  |
| Allowsia neastions                 | unknown                | unknown            | not recovered       | stopped permanently                     |  |
| Allergic reactions<br>(N = 2)      | related<br>unknown     | severe             | recovered           | stopped permanently                     |  |
|                                    |                        | severe             | not recovered       | stopped permanently stopped temporarily |  |
| Neoplasms                          | unknown                | severe<br>unknown  |                     | stopped temporarily stopped permanently |  |
| (N = 2)                            | unknown<br>unknown     | unknown            | recovered recovered | · · · · · · · · · · · · · · · · · · ·   |  |
| Pregnancy complications            | unknown                | unknown            | unknown             | no action taken                         |  |
| (N = 2)<br>Progression of multiple | related                |                    | not recovered       | withdrawn withdrawn                     |  |
| sclerosis (N = 2)                  | unrelated              | severe             | recovered           |   |  |
| Acute renal failure (N = 1)        | unrelated              | unknown<br>unknown |                     | no action taken                         |  |
| Autonomic dysfunction              | umeiateu               | unknown            | not recovered       | stopped permanently                     |  |
| (N = 1)                            | related                | moderate           | recovered           | stopped permanently                     |  |
| Depressive symptom                 | relateu                | mouerate           | recovered           | stopped permanently                     |  |
| aggravated (N = 1)                 | unrelated              | moderate           | not recovered       | no action taken                         |  |
| Femoral neck fracture              | unrelated              | severe             | recovered           | no action taken                         |  |
| remoral neck fracture              | umeiateu               | severe             | recovered           | 110 activil takeli                      |  |

| (N = 1)                   |           |         | with sequelae |                     |
|---------------------------|-----------|---------|---------------|---------------------|
| Hypoxic brain damage      |           |         |               |                     |
| (N = 1)                   | unrelated | severe  | fatal         | stopped permanently |
| Postoperative bleeding    |           |         |               |                     |
| (N = 1)                   | unrelated | severe  | recovered     | stopped permanently |
| Retinal detachment        |           |         | recovered     |                     |
| (N = 1)                   | unknown   | unknown | with sequelae | no action taken     |
| Sinus tachycardia (N = 1) |           |         | recovered     |                     |
|                           | unrelated | severe  | with sequelae | no action taken     |