**Appendix**

**Indications for the use of rituximab**

*Minor relapse*: minor relapses were defined as those episodes of disease activity requiring an increase in therapy with new onset of a Birmingham Vasculitis Activity Score (BVAS) item.

*Major relapse*: Major relapses were those with life- or organ-threatening manifestations as assessed by BVAS.

*Maintenance*: Rituximab was used to maintain a remission state.

*Refractory disease*: Refractory disease was defined as persistent disease activity despite a full course of first-line immunosuppressive and steroid treatment.

*Steroid sparing*: In patients on a persistent decent dose of steroids, rituximab was initiated to reduce the average daily steroid dose.

*1st line therapy*: Rituximab was used alongside steroids for the induction of remission in immunosuppression-naïve patients.

**Common Terminology Criteria for Adverse Events v4.0 (CTCAE)**

CTCAE represents a descriptive terminology which can be used to systematically report adverse events (AE). For a clinical purpose and for the conduction of trials (observational or prospective), a given grading (severity) scale is provided for each AE term, which can help to differentiate the impact of diverse treatment strategies on the occurrence of mild to severe/life-threatening complications. In general, the grading (severity) scale is outlined below [[1](#_ENREF_1)]:

|  |  |
| --- | --- |
| Grade 1 | Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. |
| Grade 2 | Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental Activities of Daily Living. |
| Grade 3 | Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care Activities of Daily Living. |
| Grade 4 | Life-threatening consequences; urgent intervention indicated. |
| Grade 5 | Death related to AE. |

As an example for infectious complications, the grading (severity) scale for urinary tract infections including the particular definition is given below. Definition: A disorder characterized by an infectious process involving the urinary tract, most commonly the bladder and the urethra [1]. Abbreviations used: AE (adverse event), IV (intravenous), UTI (urinary tract infection).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| AE | 1 | 2 | 3 | 4 | 5 |
| UTI | - | Localized; local intervention indicated (e.g., topical antibiotic, antifungal, or antiviral) | IV antibiotic, antifungal, or antiviral intervention indicated; radiologic or operative intervention indicated | Life-threatening consequences; urgent intervention indicated | Death |

References

1. Institute NC. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. 2009.