|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Neutropenic patients****n=58** |  | **p value** |  |
|  | **Grade I****n=42** | **Grade II****n=14** | **Grade III -IV\*****n=2** | **p value****I Vs II** | **p value****I Vs III-IV** | **p value****II Vs III-IV** |
| **Patients characteristics****At baseline** |  |  |  |  |  |  |
|  **Demographic** |  |  |  |  |  |  |
| Age, mean (mean±SD)ⱡ | 55.3 ± 14.1 | 61.2 ± 10.6 | 82.5 ±4.9 | 0.276 | 0.02 | 0.04 |
| Female gender, N (%) | 33 (78.6) | 12 (85.7) | 2 (100.0) | 0.711 | 1.000 | 0.131 |
| Total follow-up (months), median (range) | 18 (6-48) | 18 (6-48) | 12 (6-18) | 0.811 | 0.279 | 0.292 |
| Time after RA diagnosis, median (range)¶ | 12 (0-108) | 12 (0-120) | 6 (0 – 12) | 0.947 | 0.272 | 0.374 |
| Smoking, N (%) | 5 (11.9) | 1 (7.1) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Alcohol consumption, N (%) | 30 (71.4) | 9 (64.2) | 1 (50.0) | 0.740 | 0.509 | 1.000 |
| **Laboratory** |  |  |  |  |  |  |
| Anaemiaa, N (%) | 3/39 (7.7) | 3 (21.4) | 1 (50.0) | 0.158 | 0.175 | 0.450 |
| Thrombocytopeniab, N (%) | 0/39 (0.0) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Leukopeniac, N (%) | 1/39 (2.6) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Lymphopeniad, N (%) | 1/39 (2.6) | 2 (14.2) | 1 (50.0) | 0.167 | 0.096 | 0.350 |
| Neutropeniae, N (%) | 3/39 (7.7) | 1 (7.1) | 1 (50.0) | 1.000 | 0.187 | 0.242 |
| Neutrophils, (mean±SD) (X109/L) | 3.94±1.54 | 5.15±3.42 | 3.70±3.96 | 0.291 | 0.841 | 0.595 |
| RF positive, N (%) | 19/24 (79.2) | 7/10 (70.0) | 1/2 (50.0) | 0.667 | 0.415 | 1.000 |
| Anti-CCP positive, N (%) | 27/36 (75.0) | 7/10 (70.0) | 1/2 (50.0) | 0.706 | 0.462 | 1.000 |
| Baseline DAS28 (mean±SD) | 4.69±1.53 | 4.54±1.24 | 7.20±0.51 | 0.645 | 0.018 | 0.026 |
| **Patients characteristics****through – out disease** |  |  |  |  |  |  |
| **Laboratory** |  |  |  |  |  |  |
| Anemiaa, N (%) | 16 (38.1) | 8 (57.1) | 1 (50.0) | 0.218 | 1.000 | 1.000 |
| Thrombocytopeniab, N (%) | 1 (2.4) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Leukopeniac, N (%) | 30 (71.4) | 10 (71.4) | 1 (50.0) | 1.000 | 1.000 | 1.000 |
| Lymphopeniad, N (%) | 6 (14.3) | 6 (42.9) | 1 (50.0) | 0.052 | 0.284 | 1.000 |
| **Treatment** |  |  |  |  |  |  |
| Methotrexate, N (%) | 38 (90.5) | 13 (92.9) | 1 (50.0) | 1.000 | 0.217 | 0.242 |
| Sulfasalazine, N (%) | 23 (54.8) | 9 (64.2) | 1 (50.0) | 0.756 | 1.000 | 1.000 |
| Hydroxychloroquine, N (%) | 21 (50.0) | 10 (71.4) | 0 (0.0) | 0.220 | 0.489 | 0.125 |
| Leflunomide, N (%) | 2 (4.8) | 1 (7.1) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Azathioprine, N (%) | 1 (2.4) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Prednisone po, N (%) | 3 (7.1) | 1 (7.1) | 0 (0.0) | 0.562 | 1.000 | 1.000 |
| Corticosteroids IM, N (%) | 35 (83.3) | 12 (85.7) | 1 (50.0) | 1.000 | 0.334 | 0.350 |
| Anti-TNF, N (%) | 3 (7.1) | 2 (14.3) | 0 (0.0) | 0.590 | 1.000 | 1.000 |
| Abatacept, N (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Tocilizumab, N (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| Rituximab, N (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1.000 | 1.000 | 1.000 |
| **Outcomes** |  |  |  |  |  |  |
| Infections, incidence rate (95% CI)# | 5.07 (1.63 – 11.83) | 2.92 (0.04 – 16.27) | NA | 1.000 | NA | NA |

**Supplementary Table 2:** Baseline and through-out disease characteristics. Comparison between patients developed different grades of neutropenia. For grade of neutropenia definition, see patients and methods. \*patients who developed grade III and grade IV neutropenia were analyzed as one group. ⱡ Age at the time of RA diagnosis, ¶: time from the diagnosis of RA to the first episode of neutropenia. a. Hb<135 g/L for men and Hb<120 g/L for women, b. platelets<100×10^9/L, c. white blood cells: <4.0X109/L, d. lymphocytes: <1.0 X 109/L, e: neutrophils<2.0 X 109/L, §: Therapy with methotrexate, sulfasalazine and hydroxychloroquine. #: Incidence rate is expressed as events per 1000 month-persons, N: number of patients, IM: Intramuscular, NA: Not applicable because of the limited number of cases, CI: confidence intervals