|  |  |  |
| --- | --- | --- |
|  | **Anaplastic Astrocytoma (AA)** | **Glioblastoma (GBM)** |
| **Variable** | **Radiotherapy****N=20** | **Neoadjuvant TMZ****N=21** |  **Radiotherapy****N=52** | **Neoadjuvant TMZ****N=51** |
| **Concomitant TMZ** | 13 (65.0) | 16 (76.2) | 36 (69.2) | 27 (52.9) |
| **Age years, median (range)** | 47.5 (27-60) | 45 (28-57) | 53 (25-60) | 56 (24-60) |
| **Gender, n (%)** |  |  |  |  |
| Male | 15 (75.0) | 11 (52.4) | 33 (63.5) | 30 (58.8) |
| Female | 5 (25.0) | 10 (47.6) | 19 (36.5) | 21 (41.2) |
| **WHO Performance status n (%)** |  |  |  |  |
| 0-1  | 19 (95.0) | 21 (100) | 47 (90.4) | 46 (90.2) |
| 2 | 1 (5.0) | 0 (0) | 5 (9.6) | 5 (9.8) |
| **Surgery type, n (%)** |  |  |  |  |
| Complete | 5 (25.0) | 6 (28.6) | 18 (34.6) | 24 (47.1) |
| Partial | 10 (50.0) | 11 (52.4) | 28 (53.9) | 21 (41.2) |
| Biopsy | 5 (25.0) | 4 (19.0) | 5 (9.6) | 4 (7.8) |
| Not reported | 0 (0.0) | 0 (0.0) | 1 (1.9) | 2 (3.9) |
| **Baseline steroids, n (%)** |  |  |  |  |
| Yes  | 7 (35.0) | 9 (42.9) | 17 (32.7) | 15 (29.4) |
| No | 13 (65.0) | 12 (57.1) | 35 (67.3) | 34 (66.7) |
| Not reported | 0 (0.0) | 0 (0.0) | 0 (0.0) | 2 (3.9) |
| **Molecular markers, n (%)** | **N=15** | **N=16** | **N=44** | **N=37** |
| Concomitant TMZ | 11 (73.3) | 13 (81.2) | 32 (72.7) | 20 (54.1) |
| IDH1 mut/wt  | 6/9 (40.0/60.0) | 11/5 (68.7/31.3) | 3/41 (6.8/93.2) | 0/37 (0.0/100.0) |
| 1p/19q codeletion/noncodel | 1/13 (6.7/86.6) 1 mb (6.7) | 0/15 (0.0/93.7) 1 mb (6.3) | 1/42 (2.3/95.4)1 mb (2.3) | 0/36 (0/97.3) 1 mb (2.7) |
| MGMT promotoramethylated/unmethylated | 10/3(66.7/20.0)2 mb (13.3) | 14/2 (87.5/12.5) | 24/19(54.5/43.2) 1 mb (2.3) | 24/11(64.9/29.7)2 mb (5.4) |

**Table 1. Patient characteristics and molecular markers** per diagnosis and randomization

1 patient with AA and 1 patient with GBM, randomized to radiotherapy, were both IDH1 mutated and 1p/19q codeleted

aCut-off for MGMT methylation ≥9%

bm= missing

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Randomization** | **Diagnosis** | **Age** | **Surgery** | **IDH1** | **1p/19q** | **ATRXa** | **P53a** | **MGMT promotor** | **Survival months** |
| NeoTMZ | AA | 32 | biop | mut | - | loss | posb | meth | 33.9 |
| NeoTMZ | AA | 34 | comp | mut | - | loss | pos | meth | 95.1 |
| SRT | AA | 27 | part | mut | uc | loss | pos | N/Ae | 35.2 |
| NeoTMZ | AA | 35 | part | mut | - | loss | pos | meth | f103.4 |
| SRT | AA | 29 | comp | mut | - | loss | pos | N/Ae | f97.6 |
| NeoTMZ | AA | 28 | part | mut | - | loss | - | meth | 51.5 |
| NeoTMZ | AA | 44 | part | mut | - | + | pos | meth | f96.1 |
| NeoTMZ | AA | 37 | part | mut | - | N/Ad | N/Ad | meth | f95.8 |
| NeoTMZ | AA | 38 | comp | mut | uc | + | pos | meth | f95.1 |
| SRT | AA | 32 | comp | mut | - | + | pos | meth | 23.4 |
| NeoTMZ | AA | 51 | part | mut | - | loss | - | unmeth | f93.2 |
| SRT | AA | 60 | comp | mut | codel | + | - | meth | 48.8 |
| NeoTMZ | AA | 49 | part | mut | - | + | pos | meth | f90.4 |
| NeoTMZc | AA | 46 | part | mut | - | loss | pos | meth | f89.6 |
| SRTc | AA | 39 | part | mut | - | loss | pos | meth | f86.7 |
| SRTc | AA | 38 | part | mut | - | + | pos | meth | f77.0 |
| NeoTMZc | AA | 35 | part | mut | - | loss | pos | meth | 44.7 |
| NeoTMZ | AA | 57 | biop | wt | - | + | pos | meth | 20.6 |
| SRT | AA | 32 | part | wt | - | loss | pos | meth | 82.0 |
| SRT | AA | 56 | part | wt | - | + | - | unmeth | 16.1 |
| SRT | AA | 47 | part | wt | - | + | pos | unmeth | 4.5 |
| NeoTMZ | AA | 51 | comp | wt | - | loss | - | meth | 20.6 |
| SRT | AA | 56 | comp | wt | - | loss | pos | meth | 44.5 |
| NeoTMZ | AA | 51 | part | wt | - | loss | pos | meth | 81.2 |
| SRT | AA | 38 | part | wt | - | + | pos | unmeth | 19.3 |
| SRT | AA | 41 | part | wt | - | + | - | meth | 17.3 |
| SRT | AA | 51 | biop | wt | - | loss | pos | meth | 42.8 |
| NeoTMZ | AA | 35 | comp | wt | - | loss | pos | unmeth | 70.7 |
| SRT | AA | 40 | comp | wt | - | + | - | meth | f81.1 |
| NeoTMZ | AA | 45 | part | wt | - | + | pos | meth | 57.0 |
| SRT | AA | 55 | part | wt | - | + | - | meth | 22.7 |
| SRT | GBM | 52 | biop | mut | codel |  + | -  | meth | 30.5 |
| SRT | GBM | 41 | comp | mut | - |  + |  pos | meth | f102.4 |
| SRT | GBM | 56 | comp | mut | - |  + |  pos | meth | 46.2 |
| NeoTMZ | GBM | 57 | part | wt | - |   |   | meth | 17.7 |
| NeoTMZ | GBM | 39 | comp | wt | - |   |   | meth | 20.4 |
| SRT | GBM | 48 | part | wt | - |   |   | meth | f129.3 |
| NeoTMZ | GBM | 59 | comp | wt | - |   |   | meth | 21.1 |
| NeoTMZ | GBM | 53 | comp | wt | - |   |   | unmeth | 9.0 |
| SRT | GBM | 59 | part | wt | - |   |   | meth | 20.3 |
| SRT | GBM | 59 | part | wt | - |   |   | meth | 3.7 |
| NeoTMZ | GBM | 45 | comp | wt | - |   |   | meth | 6.5 |
| SRT | GBM | 53 | comp | wt | - |   |   | meth | 107.7 |
| NeoTMZ | GBM | 58 | part | wt | - |   |   | unmeth | 8.6 |
| SRT | GBM | 41 | part | wt | - |   |   | unmeth | 11.1 |
| SRT | GBM | 59 | part | wt | - |   |   | meth | 38.4 |
| NeoTMZ | GBM | 58 | part | wt | - |   |   | unmeth | 11.0 |
| NeoTMZ | GBM | 30 | comp | wt | - |   |   | meth | 11.1 |
| SRT | GBM | 56 | comp | wt | - |   |   | meth | 22.9 |
| NeoTMZ | GBM | 36 | comp | wt | - |   |   | meth | 41.3 |
| SRT | GBM | 59 | part | wt | - |   |   | unmeth | 0.5 |
| SRT | GBM | 59 | comp | wt | - |   |   | meth | 24.1 |
| NeoTMZ | GBM | 56 | comp | wt | - |   |   | meth | 7.0 |
| SRT | GBM | 41 | part | wt | - |   |   | unmeth | 8.7 |
| NeoTMZ | GBM | 58 | part | wt | - |   |   | meth | 1.9 |
| SRT | GBM | 54 | part | wt | - |   |   | unmeth | 5.6 |
| NeoTMZ | GBM | 54 | part | wt | - |   |   | unmeth | 17.2 |
| SRT | GBM | 58 | part | wt | - |   |   | unmeth | 19.6 |
| NeoTMZ | GBM | 54 | part | wt | - |   |   | unmeth | 1.7 |
| SRT | GBM | 45 | part | wt | - |   |   | unmeth | 13.6 |
| NeoTMZ | GBM | 56 | part | wt | - |   |   | meth | 12.0 |
| NeoTMZ | GBM | 54 | comp | wt | - |   |   | meth | 20.2 |
| SRT | GBM | 59 | comp | wt | - |   |   | meth | 48.3 |
| NeoTMZ | GBM | 55 | comp | wt | - |   |   | meth | 9.1 |
| SRT | GBM | 58 | comp | wt | - |   |   | unmeth | 9.3 |
| NeoTMZ | GBM | 51 | comp | wt | - |   |   | unmeth | 13.7 |
| SRT | GBM | 60 | comp | wt | - |   |   | meth | 39.6 |
| NeoTMZ | GBM | 59 | comp | wt | - |   |   | meth | 50.9 |
| SRT | GBM | 40 | part | wt | - |   |   | meth | 12.5 |
| NeoTMZ | GBM | 58 | comp | wt | - |   |   | meth | f102.4 |
| SRT | GBM | 47 | part | wt | - |   |   | meth | 17.3 |
| SRT | GBM | 48 | part | wt | - |   |   | meth | 28.8 |
| NeoTMZ | GBM | 57 | part | wt | - |   |   | meth | 20.0 |
| NeoTMZ | GBM | 54 | comp | wt | - |   |   | meth | 53.3 |
| SRT | GBM | 58 | part | wt | - |   |   | unmeth | 18.1 |
| SRT | GBM | 58 | comp | wt | - |   |   | meth | 16.7 |
| SRT | GBM | 25 | part | wt | - |   |   | meth | 92.9 |
| NeoTMZ | GBM | 60 | comp | wt | N/A |   |   | N/Ae | 15.3 |
| NeoTMZ | GBM | 24 | biop | wt | - |   |   | N/Ae | 0.5 |
| SRT | GBM | 48 | part | wt | - |   |   | unmeth | 22.1 |
| NeoTMZ | GBM | 57 | comp | wt | - |   |   | unmeth | 10.0 |
| SRT | GBM | 60 | comp | wt | - |   |   | unmeth | 25.6 |
| NeoTMZ | GBM | 56 | comp | wt | - |   |   | unmeth | 20.8 |
| SRT | GBM | 58 | comp | wt | - |   |   | unmeth | 27.6 |
| SRT | GBM | 51 | comp | wt | - |   |   | unmeth | 50.0 |
| NeoTMZ | GBM | 56 | comp | wt | - |   |   | meth | 4.8 |
| NeoTMZ | GBM | 53 | comp | wt | - |   |   | unmeth | 8.0 |
| SRT | GBM | 52 | part | wt | - |   |   | meth | 21.3 |
| NeoTMZ | GBM | 55 | comp | wt | - |   |   | unmeth | 8.3 |
| SRT | GBM | 52 | part | wt | - |   |   | unmeth | 14.7 |
| SRT | GBM | 56 | part | wt | - |   |   | meth | 42.9 |
| NeoTMZ | GBM | 47 | part | wt | - |   |   | meth | 14.6 |
| SRT | GBM | 37 | part | wt | - |   |   | meth | f87.3 |
| SRT | GBM | 50 | part | wt | - |   |   | unmeth | 11.7 |
| NeoTMZ | GBM | 55 | part | wt | - |   |   | meth | 15.7 |
| SRT | GBM | 59 | comp | wt | - |   |   | unmeth | 20.3 |
| SRT | GBM | 52 | biop | wt | uc |   |   | N/Ae | 10.0 |
| SRT | GBM | 58 | part | wt | - |   |   | unmeth | 11.1 |
| NeoTMZ | GBM | 58 | part | wt | - |   |   | meth | 16.0 |
| NeoTMZ | GBM | 49 | part | wt | - |   |   | meth | 20.8 |
| SRT | GBM | 53 | biop | wt | - |   |   | unmeth | 18.2 |
| SRT | GBM | 44 | part | wt | - |   |   | meth | 6.5 |
| NeoTMZ | GBM | 60 | part | wt | - |   |   | unmeth | 17.7 |
| NeoTMZ | GBM | 45 | comp | wt | - |   |   | meth | 12.2 |
| SRT | GBM | 50 | part | wt | - |   |   | meth | 15.6 |
| NeoTMZ | GBM | 53 | part | wt | - |   |   | meth | 16.2 |
| SRT | GBM | 59 | part | wt | - |   |   | unmeth | 4.3 |
| NeoTMZ | GBM | 59 | part | wt | - |   |   | meth | 35.0 |
| SRT | GBM | 50 | comp | wt | - |   |   | unmeth | f72.4 |
| NeoTMZ | GBM | 59 | part | wt | - |   |   | meth | 26.1 |
| SRT | GBM | 38 | comp | wt | - |   |   | meth | 16.1 |
| SRT | GBM | 52 | part | wt | - |   |   | meth | 14.3 |

**Table 2. Diagnosis, prognostic factors, molecular markers and survival**NeoTMZ: Neoadjuvant treatmentSRT: Standard radiotherapyap53 and ATRX immunostaining reported for those included as AA and IDH1 mutated GBMbpos=immunostaining indicating p53 mutation **c**Previous low grade gliomadNo TMA available eNo DNA availablefalive at follow-up 1st of March 2014N/A: no tissue availableAge reported in yearsSurgery: comp=complete, part=partial, biop= biopsyuc: uncountable |

 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **Number of patients** | **Number of events (%)** | **Hazard ratio** | **95% Confidence Interval** | **p-value** |
| **Age** |  |  |  |  |  |
|  <50 years | 51 | 36 (70.6) | 1.00 | - | - |
|  ≥50 years | 91 | 86 (94.5) | 1.29 | 0.81-2.05 | 0.28 |
| **Gender** |  |  |  |  |  |
|  Women | 54 | 44 (81.5) | 1.00 | - | - |
|  Men | 88 | 78 (88.6) | 1.42 | 0.96-2.10 | 0.077 |
| **WHO Performance status** |  |  |  |  |  |
|  0-1 | 132 | 112 (84.8) | 1.00 | - | - |
|  2 | 10 | 10 (100.0) | 1.61 | 0.80-3.24 | 0.18 |
| **Type of surgery** |  |  |  |  |  |
|  Biopsy | 18 | 18 (100.0) | 1.00 | - | - |
|  Partial resection | 70 | 58 (82.9) | 0.46 | 0.24-0.88 | 0.019 |
|  Complete resection | 53 | 45 (84.9) | 0.34 | 0.17-0.67 | 0.0018 |
|  Resection unknown | 1 | 1 (100.0) | 2.00 | 0.25-16.28 | 0.52 |
| **Steroids at baselinea** |  |  |  |  |  |
|  No | 94 | 78 (83.0) | 1.00 | - | - |
|  Yes | 48 | 44 (91.7) | 1.50 | 0.98-2.30 | 0.059 |
| **Diagnosis at inclusion** |  |  |  |  |  |
|  Anaplastic astrocytoma | 41 | 27 (65.9) | 1.00 | - | - |
|  Glioblastoma | 101 | 95 (94.1) | 3.35 | 2.00-5.62 | <0.001 |
| **Treatment arm** |  |  |  |  |  |
|  Radiotherapy | 72 | 64 (88.9) | 1.00 | - | - |
|  Neoadjuvant TMZ | 70 | 58 (82.9) | 1.17 | 0.81-1.70 | 0.40 |

**Table 3a. Multivariate cox regression for baseline patient characteristics and treatment arm** (n=142a)  aFor 2 patients steroids at baseline is not reported and these patients are excluded from the analysis

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **Number of patients** | **Number of events (%)** | **Hazard ratio** | **95% Confidence Interval** | **p-value** |
| **Age** |  |  |  |  |  |
|  <50 years | 40 | 28 (70.0) | 1.00 | - | - |
|  ≥50 years | 67 | 64 (95.5) | 1.09 | 0.64-1.87 | 0.75 |
| **Gender** |  |  |  |  |  |
|  Women | 42 | 35 (83.3) | 1.00 | - | - |
|  Men | 65 | 57 (87.7) | 1.21 | 0.78-1.87 | 0.40 |
| **WHO Performance Status** |  |  |  |  |  |
|  0-1 | 100 | 85 (85.0) | 1.00 | - | - |
|  2 | 7 | 7 (100.0) | 1.42 | 0.59-3.41 | 0.44 |
| **Type of surgery** |  |  |  |  |  |
|  Biopsy | 5 | 5 (100.0) | 1.00 | - | - |
|  Partial resection | 60 | 50 (83.3) | 0.88 | 0.30-2.56 | 0.81 |
|  Complete resection | 42 | 37 (88.1) | 0.59 | 0.19-1.81 | 0.36 |
| **Steroids at baseline** |  |  |  |  |  |
|  No | 76 | 64 (84.2) | 1.00 | - | - |
|  Yes | 31 | 28 (90.3) | 1.74 | 1.02-2.96 | 0.041 |
| **Diagnosis at inclusion** |  |  |  |  |  |
|  Anaplastic astrocytoma | 29 | 19 (65.5) | 1.00 | - | - |
|  Glioblastoma | 78 | 73 (93.6) | 1.92 | 1.00-3.70 | 0.050 |
| **Treatment arm** |  |  |  |  |  |
|  Radiotherapy | 56 | 49 (87.5) | 1.00 | - | - |
|  Neoadjuvant TMZ | 51 | 43 (84.3) | 1.54 | 0.98-2.43 | 0.063 |
| **MGMT Methylated** |  |  |  |  |  |
|  No (<9%) | 35 | 33 (94.3) | 1.00 | - | - |
|  Yes (≥9%) | 72 | 59 (81.9) | 0.52 | 0.33-0.83 | 0.0054 |
| **IDH mutated** |  |  |  |  |  |
| No | 89 | 84 (94.4) | 1.00 | - | - |
| Yes | 18 | 8 (44.4) | 0.23 | 0.10-0.56 | 0.0012 |

**Table 3b. Multivariate Cox regression analysis of patients with MGMT and IDH status determined** (n=107)

|  |
| --- |
| **Grade 3-5 Adverse Events** |
|  | **Grade 3** | **Grade 4** | **Grade 5** | **Serious** |
| Seizuresa | 6b | 0 | 0 | 3 |
| Rash/Urticaria | 2 | 0 | 0 | 0 |
| Infection/Fever | 5 | 0 | 0 | 1 |
| Abdominal pain | 1 | 0 | 0 | 1 |
| Syncope | 1 | 0 | 0 | 0 |
| Breathing problems | 0 | 0 | 1c | 1 |
| Psychosisd | 1 | 0 | 0 | 0 |
| Thromboembolic event | 3 | 1 | 1 | 4 |
| Hydrocephalus | 1 | 0 | 0 | 1 |
| Intracranial hemorrhage | 0 | 0 | 1 | 1 |
| Breast cancera | 0 | 0 | 1 | 1 |
| Elevated ALTe | 2 | 0 | 0 | 0 |
| Elevated GT | 1 | 0 | 0 | 0 |
| Pancytopenia | 0 | 1 | 0 | 1 |
| Myelodysplastic Syndrome/ Aplastic Anemia | 0 | 0 | 2 | 2 |

|  |
| --- |
| **Table 4.** **Adverse events all patients:** Patient may have had several AE:s of the same type, highest grade per patient reportedaAll patients, except for 1 with seizures and 1 with breast cancer, received TMZ either neoadjuvant and/or concomitant with radiotherapybFor 1 patient seizures grade 2 is rated serious due to hospitalization, for 1 patient grade of seizures is not reportedcPatient progressed early and received TMZ instead of allocated treatment, which was standard RTdSteroid inducedeFor 1 patient unrelated to study treatment |
|  |