Figure 1

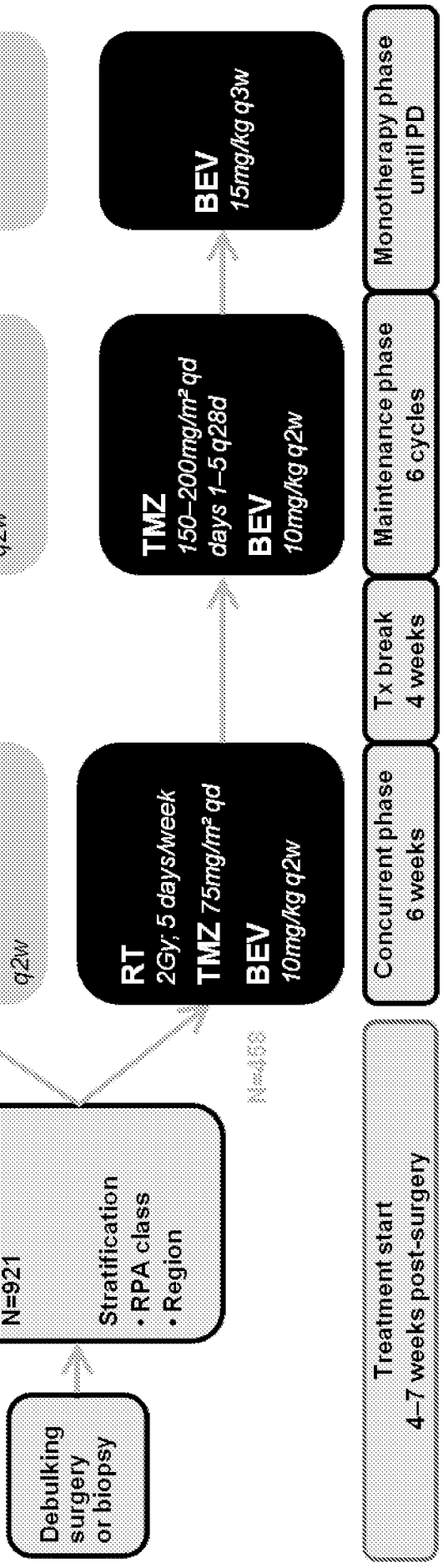

Debulking surgery or biopsy
Randomization N=921
Stratification
• RPA class
• Region
N=463
N=458
RT 2Gy; 5 days/week
TMZ 75mg/m² qd
Placebo q2w
TMZ 150–200mg/m² qd days 1–5 q28d
Placebo q2w
Placebo q3w
RT 2Gy; 5 days/week
TMZ 75mg/m² qd
BEV 10mg/kg q2w
TMZ 150–200mg/m² qd days 1–5 q28d
BEV 10mg/kg q2w
BEV 15mg/kg q3w
Treatment start 4–7 weeks post-surgery
Concurrent phase 6 weeks
Tx break 4 weeks
Maintenance phase 6 cycles
Monotherapy phase until PD

Figure 2A

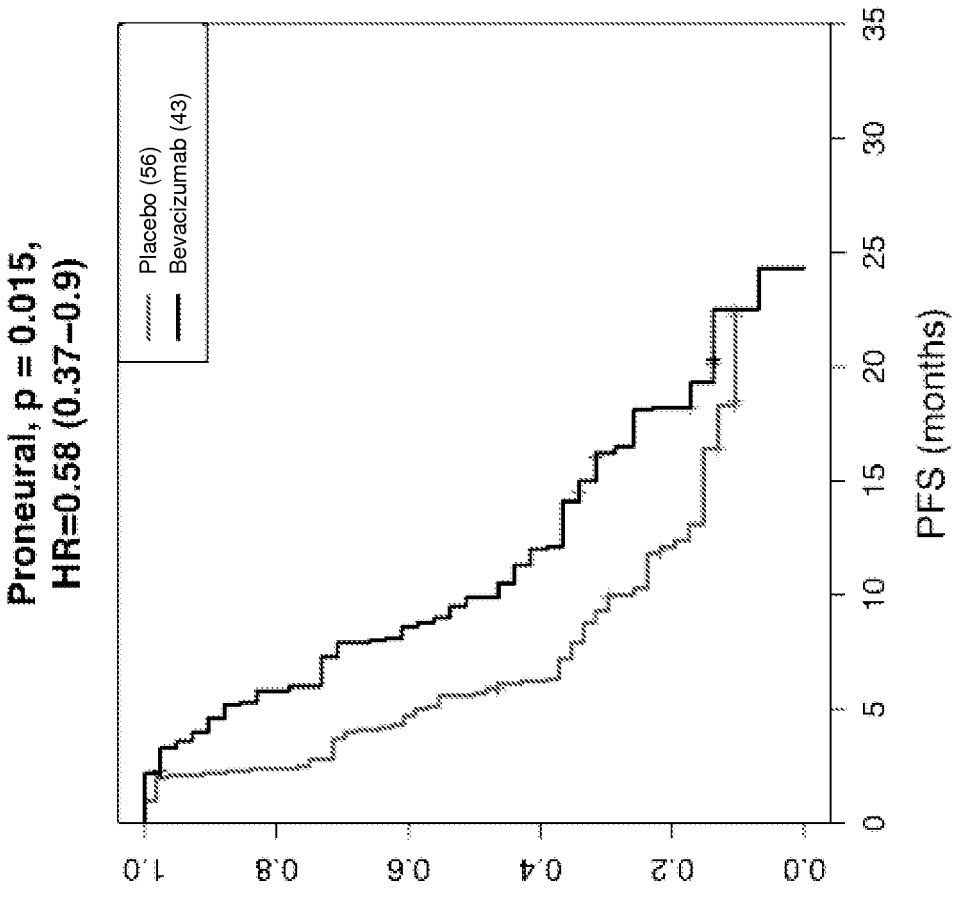

Proneural, p = 0.015,
HR=0.58 (0.37–0.9)
Placebo (56)
Bevacizumab (43)
0.0
0.2
0.4
0.6
0.8
1.0
0
5
10
15
20
25
30
35
PFS (months)

Figure 2B

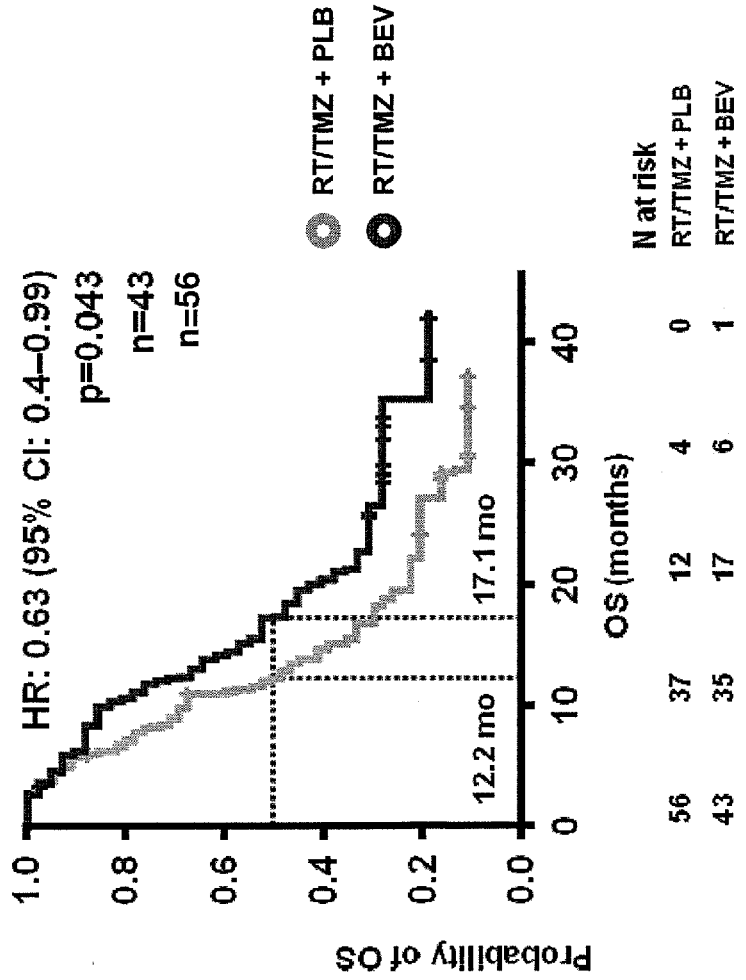

HR: 0.63 (95% CI: 0.4–0.99)
p=0.043
n=43
n=56
RT/TMZ + PLB
RT/TMZ + BEV
12.2 mo
17.1 mo
Probability of OS
OS (months)
N at risk
RT/TMZ + PLB
RT/TMZ + BEV
56 37 12 4 0
43 35 17 6 1

Figure 3

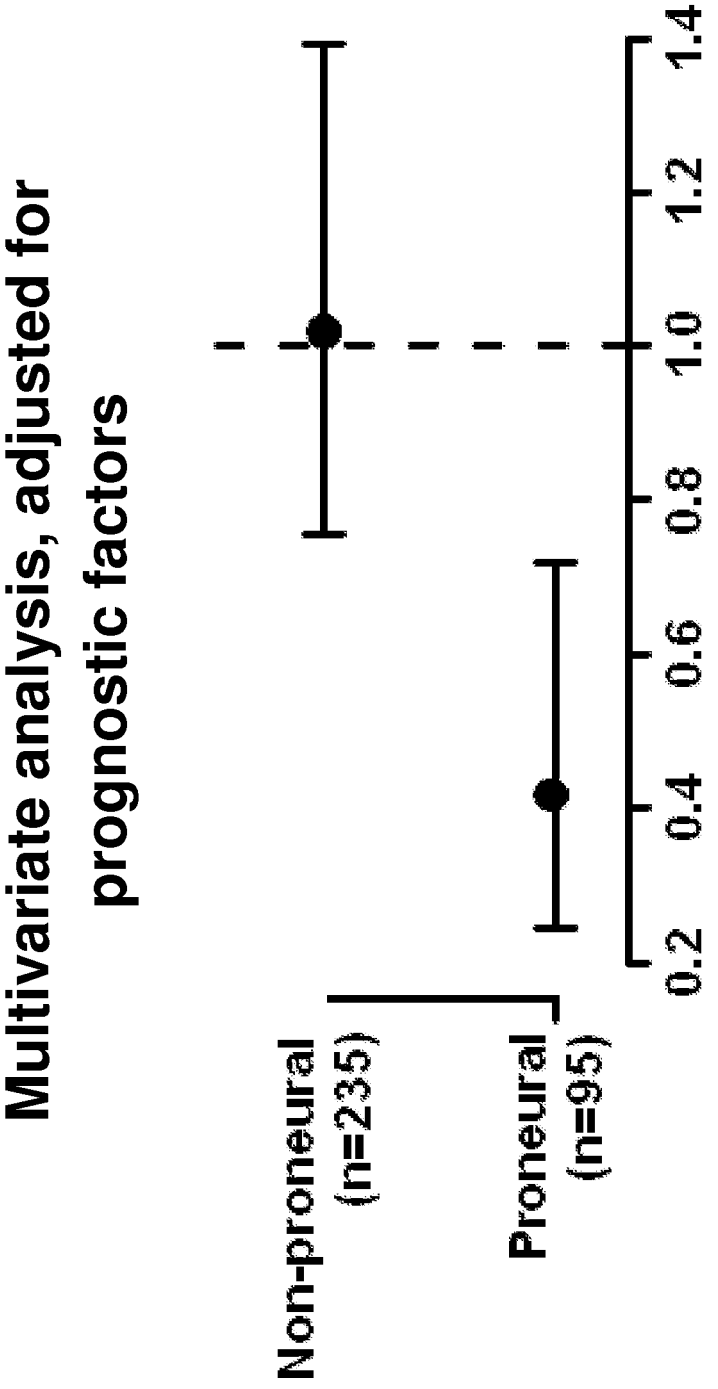

Multivariate analysis, adjusted for prognostic factors
Non-proneural (n=235)
Proneural (n=95)
0.2
0.4
0.6
0.8
1.0
1.2
1.4

Figure 4A

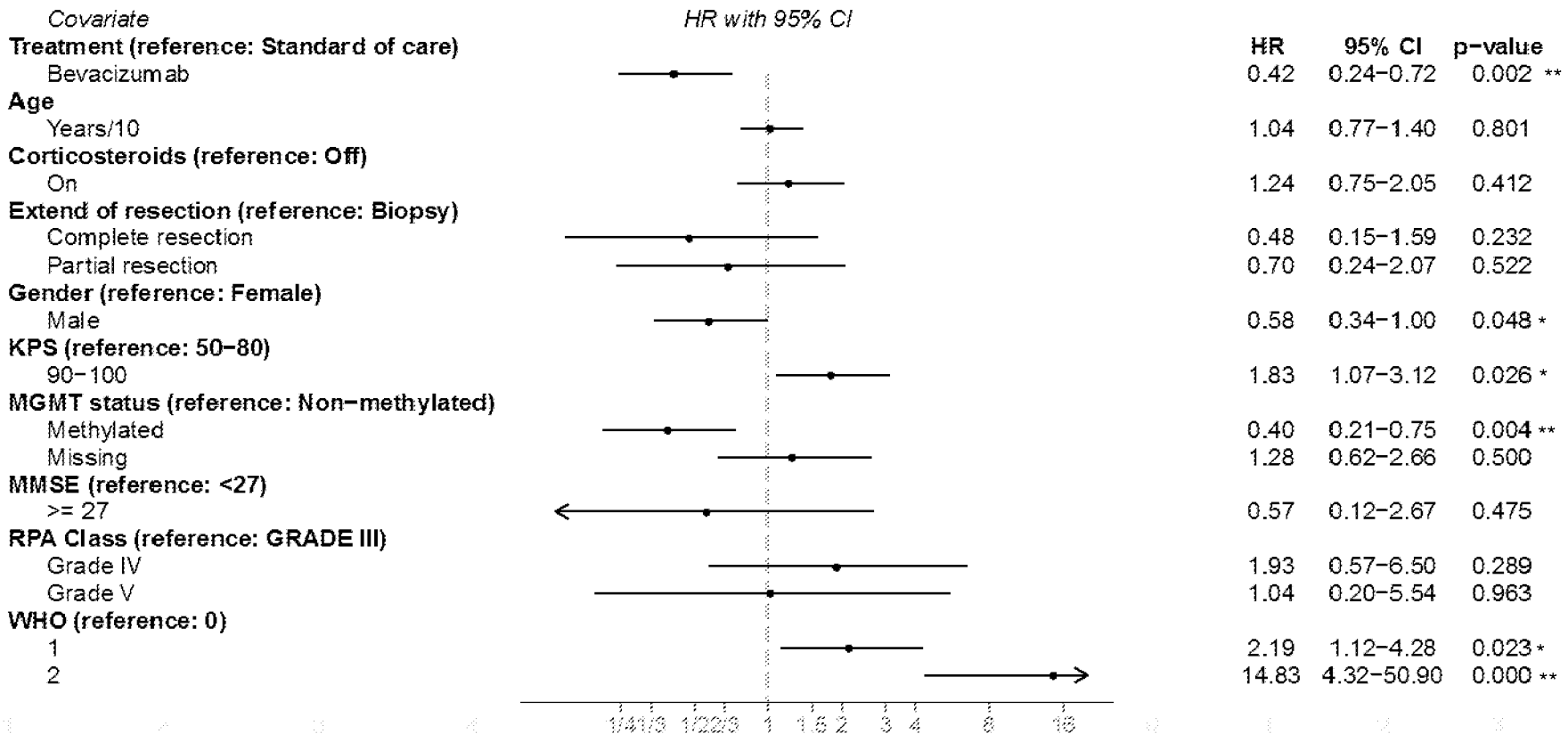

Covariate
HR with 95% CI
Treatment (reference: Standard of care)
Bevacizumab
Age
Years/10
Corticosteroids (reference: Off)
On
Extend of resection (reference: Biopsy)
Complete resection
Partial resection
Gender (reference: Female)
Male
KPS (reference: 50-80)
90-100
MGMT status (reference: Non-methylated)
Methylated
Missing
MMSE (reference: <27)
>= 27
RPA Class (reference: GRADE III)
Grade IV
Grade V
WHO (reference: 0)
1
2
1/4 1/3 1/2 2/3 1 1.5 2 3 4 6 15
HR 95% CI p-value
0.42 0.24-0.72 0.002 **
1.04 0.77-1.40 0.801
1.24 0.75-2.05 0.412
0.48 0.15-1.59 0.232
0.70 0.24-2.07 0.522
0.58 0.34-1.00 0.048 *
1.83 1.07-3.12 0.026 *
0.40 0.21-0.75 0.004 **
1.28 0.62-2.66 0.500
0.57 0.12-2.67 0.475
1.93 0.57-6.50 0.289
1.04 0.20-5.54 0.963
2.19 1.12-4.28 0.023 *
14.83 4.32-50.90 0.000 **

Figure 4B

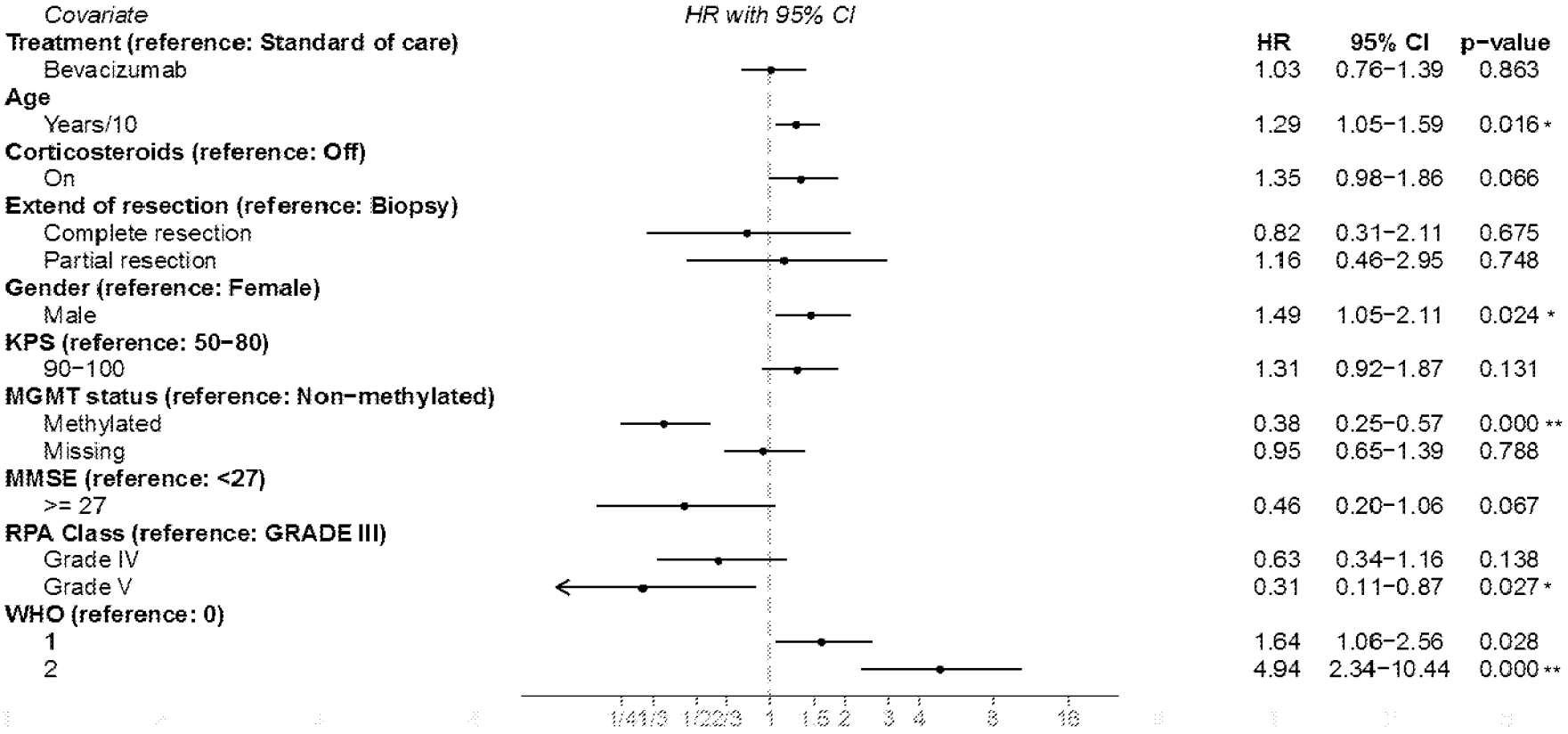

Covariate
HR with 95% CI
Treatment (reference: Standard of care)
Bevacizumab
Age
Years/10
Corticosteroids (reference: Off)
On
Extend of resection (reference: Biopsy)
Complete resection
Partial resection
Gender (reference: Female)
Male
KPS (reference: 50−80)
90−100
MGMT status (reference: Non−methylated)
Methylated
Missing
MMSE (reference: <27)
>= 27
RPA Class (reference: GRADE III)
Grade IV
Grade V
WHO (reference: 0)
1
2
1/4 1/3 1/2 2/3 1 1.5 2 3 4 8 16
HR 95% CI p−value
1.03 0.76−1.39 0.863
1.29 1.05−1.59 0.016 *
1.35 0.98−1.86 0.066
0.82 0.31−2.11 0.675
1.16 0.46−2.95 0.748
1.49 1.05−2.11 0.024 *
1.31 0.92−1.87 0.131
0.38 0.25−0.57 0.000 **
0.95 0.65−1.39 0.788
0.46 0.20−1.06 0.067
0.63 0.34−1.16 0.138
0.31 0.11−0.87 0.027 *
1.64 1.06−2.56 0.028
4.94 2.34−10.44 0.000 **

Figure 5A

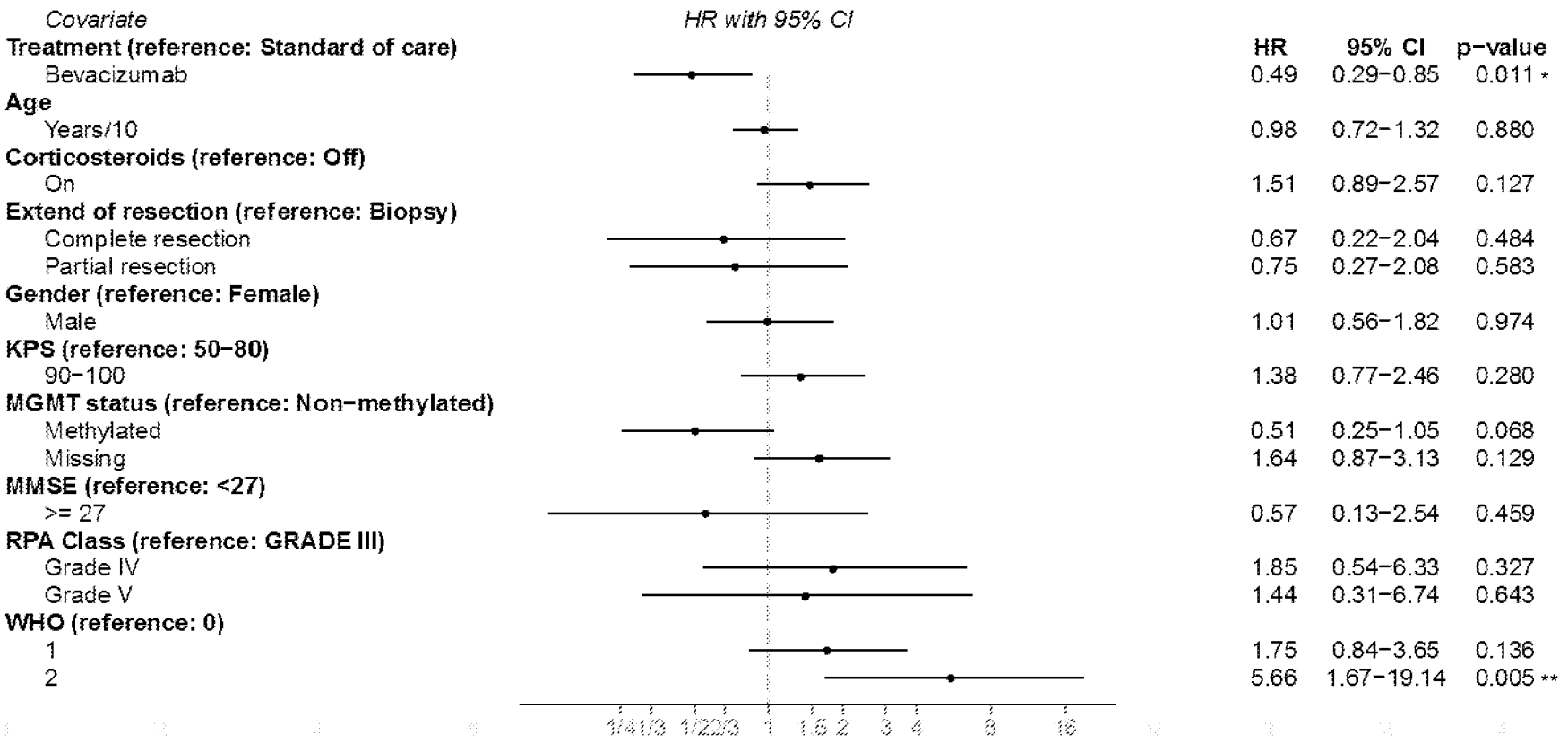
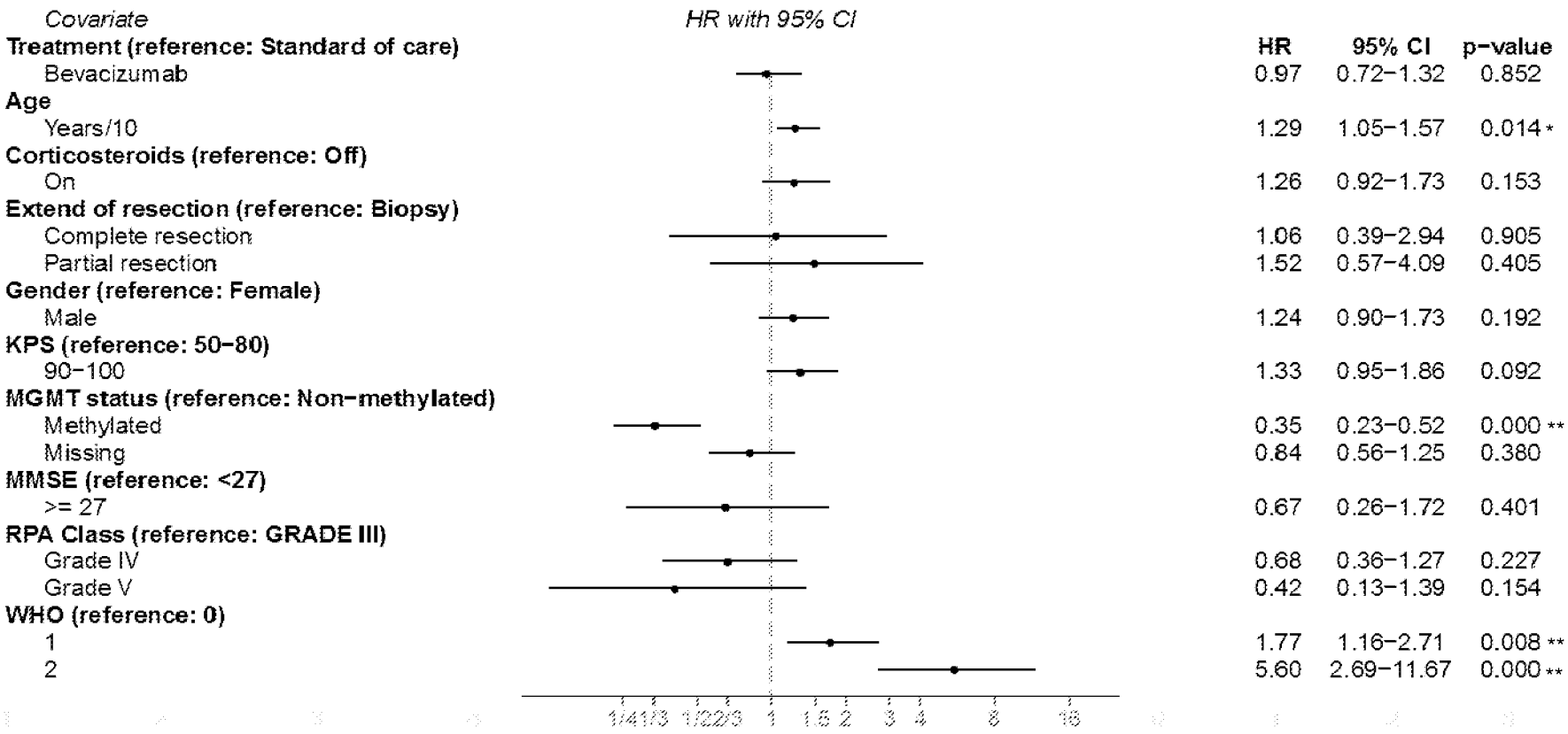

Covariate
HR with 95% CI
HR
95% CI
p-value
Treatment (reference: Standard of care)
Bevacizumab 0.49 0.29−0.85 0.011 *
Age
Years/10 0.98 0.72−1.32 0.880
Corticosteroids (reference: Off)
On 1.51 0.89−2.57 0.127
Extend of resection (reference: Biopsy)
Complete resection 0.67 0.22−2.04 0.484
Partial resection 0.75 0.27−2.08 0.583
Gender (reference: Female)
Male 1.01 0.56−1.82 0.974
KPS (reference: 50−80)
90−100 1.38 0.77−2.46 0.280
MGMT status (reference: Non−methylated)
Methylated 0.51 0.25−1.05 0.068
Missing 1.64 0.87−3.13 0.129
MMSE (reference: <27)
>= 27 0.57 0.13−2.54 0.459
RPA Class (reference: GRADE III)
Grade IV 1.85 0.54−6.33 0.327
Grade V 1.44 0.31−6.74 0.643
WHO (reference: 0)
1 1.75 0.84−3.65 0.136
2 5.66 1.67−19.14 0.005 **
1/4 1/3 1/2 2/3 1 1.5 2 3 4 8 16

Figure 5B


Covariate
HR with 95% CI
HR
95% CI
p-value
Treatment (reference: Standard of care)
Bevacizumab 0.97 0.72−1.32 0.852
Age
Years/10 1.29 1.05−1.57 0.014 *
Corticosteroids (reference: Off)
On 1.26 0.92−1.73 0.153
Extend of resection (reference: Biopsy)
Complete resection 1.06 0.39−2.94 0.905
Partial resection 1.52 0.57−4.09 0.405
Gender (reference: Female)
Male 1.24 0.90−1.73 0.192
KPS (reference: 50−80)
90−100 1.33 0.95−1.86 0.092
MGMT status (reference: Non−methylated)
Methylated 0.35 0.23−0.52 0.000 **
Missing 0.84 0.56−1.25 0.380
MMSE (reference: <27)
>= 27 0.67 0.26−1.72 0.401
RPA Class (reference: GRADE III)
Grade IV 0.68 0.36−1.27 0.227
Grade V 0.42 0.13−1.39 0.154
WHO (reference: 0)
1 1.77 1.16−2.71 0.008 **
2 5.60 2.69−11.67 0.000 **
1/4 1/3 1/2 2/3 1 1.5 2 3 4 8 16