## **SUPPLEMENTAL DATA**

**Supplementary figure 1** Survival according to uptake intensity on [18F]FET PET (TBRmax).



TBRmax – maximum tumor-to-brain-ratio, IDH – isocitrate dehydrogenase, TERT – telomerase reverse transcriptase

**Supplementary figure 2** Survival of CNS WHO 2021 Grade 4 glioma according to [18F]GE180 uptake


Supplementary table 1 [18F]GE180 PET SUVmax and survival outcome according to number of recurrence

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| All recurrent glioma cases | SUVmax (median (range)) | P-value | PRS (median; months) | P-value | TTF (median; months) | P-value |
| All diagnoses (n=88) First recurrence (n=46) Second recurrence (n=25) Third or later recurrence (n=17) | 1.68 (0.59-4.36)1.60 (0.59-3.34)1.65 (0.61-3.82)2.15 (0.72-4.36) | 0.159 | 27.931.436.914.0 | 0.532 | **8.7****11.8****9.9****5.3** | **0.001** |
| All IDH-wildtype (n=42) First recurrence (n=28) Second recurrence (n=11) Third or later recurrence (n=3) | **1.89 (0.85-3.83)****1.67 (0.85-3.34)****2.01 (1.40-3.08)****2.82 (2.32-3.83)** | **0.024** | 10.610.68.215.0 | 0.504 | 6.15.26.15.3 | 0.291 |
| All IDH-mutant (46) First recurrence (n=18) Second recurrence (n=14) Third or later recurrence (n=14) | 1.60 (0.59-4.36)1.46 (0.59-2.76)1.23 (0.61-3.82)1.98 (0.72-4.36) | 0.296 | 36.941.636.913.5 | 0.055 | **18.4****29.3****Not reached****5.7** | **<0.001** |

SUVmax – maximum standardized uptake value, IDH – isocitrate dehydrogenase

Supplementary table 2 [18F]GE180 TBRmax in the examined patient population.

|  |  |  |
| --- | --- | --- |
| All recurrent gliomas | TBRmax(median (range)) | P-value |
| Overall (n=88) | 3.87 (1.45-13.63) |  |
| Male (n=56)Female (n=32) | 4.35 (1.59-8.36)3.28 (1.45-13.63) | 0.100 |
| CNS WHO 2021 grade 2 (n=8)CNS WHO 2021 grade 3 (n=28)CNS WHO 2021 grade 4 (n=52) | **2.15 (1.73-4.15)****3.16 (1.45-13.63)****4.44 (2.13-8.15)** | **0.022** |
| IDH-mutant (n=46)IDH-wildtype (n=42) | 3.80 (1.45-13.63)4.39 (2.13-8.15) | 0.291 |
| IDH mut. -1p/19 codel (n=28)IDH mut. +1p/19 codel (n=18) | 4.06 (1.59-8.36)2.75 (1.45-3.63) | 0.457 |
| IDH wt, TERT wildtype (n=5)IDH wt, TERT mutant (n=22) | 3.20 (3.07-8.15)4.44 (2.58-7.21) | 0.633 |
| IDH wt, MGMT methylated (n=19)IDH wt, MGMT unmethylated (n=22) | 4.51 (2.13-8.15)3.66 (2.13-8.15) | 0.132 |
| Low-affinity binding status (n=7)Medium-affinity binding status (n=27)High-affinity binding status (n=44) | 6.56 (1.78-7.73)3.95 (1.59-7.00)3.65 (1.45-8.36) | 0.105 |

*TBRmax*  – *maximum tumor-to-background-ratio, CNS WHO 2021* – *World Health Organization Classification of Tumors of the Central Nervous System, IDH* – *isocitrate dehydrogenase, TERT* – *telomerase reverse transcriptase*

Supplementary table 3 Treatment regimens in patients with lower or higher than median [18F]GE180 TBRmax

|  |  |  |  |
| --- | --- | --- | --- |
|  | TBRmax ≤ median (n; %) | TBRmax > median (n; %) | P-value |
| IDH-wildtype (n=42)Radio-and chemotherapyRadiotherapy onlyChemotherapy onlyExperimental/othersNo tumor-specific therapy | 21 (100)6 (28.6)8 (38.1)4 (19.0)0 (0.0)3 (14.3) | 21 (100)6 (28.6)7 (33.3)6 (28.6)2 (9.5)0 (0.0) | 0.243 |
| IDH-mutant (n=46)Radio-and chemotherapyRadiotherapy onlyChemotherapy onlyExperimental/others | 24 (100)8 (33.3)12 (50.0)4 (16.7)0 (0.0) | 22 (100)6 (27.3)7 (31.8)8 (36.4)1 (4.3) | 0.278 |

TBRmax  – maximum tumor-to-background-ratio, IDH – isocitrate dehydrogenase

Supplementary table 4 Survival of recurrent glioma patient groups according to [18F]GE180 TBRmax.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| All recurrent glioma cases | PRS (median; months) | P-value | TTF (median; months) | P-value |
| All diagnoses (n=88)TBRmax ≤ 3.87 (n=44)TBRmax > 3.87 (n=44) | 27.941.617.5 | 0.051 | 8.710.58.2 | 0.130 |
| All IDH-wildtype (n=42)TBRmax ≤ 4.39 (n=21)TBRmax > 4.39 (n=21) | 10.611.88.2 | 0.150 | 6.15.46.8 | 0.331 |
| All IDH-mutant (46)TBRmax ≤ 3.80 (n=24)TBRmax > 3.80 (n=22) | 36.941.627.9 | 0.158 | **18.4****32.2****11.4** | **0.039** |
| All astrocytoma, IDH-mutant (28) TBRmax ≤ 4.06 (14)TBRmax > 4.06 (14) | 27.936.927.9 | 0. 597 | **11.7****32.2****8.7** | **0.037** |
| Astrocytoma WHO 2021 grade 3, IDH mutant (17)TBRmax ≤ 3.80 (9)TBRmax > 3.80 (8) | **36.9****36.9****13.1** | **0.037** | 11.714.52.7 | 0.215 |
| All low-grade (2 or 3) astrocytoma, IDH-mutant (18) TBRmax ≤ 3.36 (9)TBRmax > 3.36 (9) | **36.9****36.9****13.1** | **0.003** | 14.532.26.2 | 0.063 |
| All oligodendroglioma, IDH-mutant and 1p/19q codeleted (18)TBRmax ≤ 2.75 (9)TBRmax > 2.75 (9) | Not reached Not reached Not reached | 0.464 | Not reachedNot reached18.4 | 0.130 |

*TBRmax*  – maximum tumor-to-background-ratio*, IDH – isocitrate dehydrogenase; PRS – post recurrence survival; TTF – time to treatment failure*

Supplementary table 5 Characteristics of high and low [18F]GE180 TBRmax groups.

|  |  |  |  |
| --- | --- | --- | --- |
|  | TBRmax ≤ median (n; % or median; range) | TBRmax > median (n; % or median; range) | P-value |
| IDH-wildtype (n=42)Male / female sexMGMT methylated / unmeth. (n=41)TERT wildtype / mutant (n=27)Age [18F]FET TBRmax (n=35)[18F]FET tumor volume ( n=35)T2 volumeContrast volume | 21 (50.0)13 / 8 (31.0 / 19.0)8 / 12 (19.5 / 29.3)3 / 10 (11.1 / 37.0)56.5 (32.3-70.0)3.02 (1.55-3.79)9.54 (0.0-76.66)50.30 (0.0-198.10)3.54 (.27-66.20) | 21 (50.0)16 / 5 (38.1/69.0)11 / 10 (26.8 / 24.4)2 / 12 (7.4 / 44.4)54.6 (30.8-70.2)3.35 (2.47-5.28)27.18 (7.68-124.75)80.10 (24.20-337.3)18.50 (0.0-85.6) | 0.3170.4270.5570.560**0.008**0.0740.054**0.006** |
| IDH-mutant (n=46)Male / female sexCNS WHO 2021 grade 2 / 3 / 4MGMT methylated / unmeth.TERT wildtype / mutant (n=28)Age[18F]FET TBRmax (n=42)[18F]FET tumor volume (n=42)T2 volumeContrast volume | 24 (52.2)12 / 12(25.0 / 25.0)7 / 16 / 1 (15.2 / 34.8 / 2.2)21 / 3 (45.7 / 6.5)9 / 6 (32.1 / 21.4)47.6 (23.6-66.2)2.51 (1.21-5.64)5.14 (0.0-172.04)51.30 (12.40-226.50)0.07 (0.0-20.80) | 22 (47.8)15 / 7 (32.6 / 15.2)1 / 12 / 9 (2.2 / 26.1 / 19.6)17 / 5 (37.0 / 10.9)10 / 3 (35.7 / 10.7)40.5 (29.1-71.9)3.79 (2.88-7.49)33.08 (1.67-120.69)60.40 (9.13-253.90)11.50 (0.0-61.2) | 0.211**0.003**0.3610.3390.511**0.001****0.029**0.499**<0.001** |
| Astro, IDH mut., grade 3 (n=17)Male / female sexMGMT methylated / unmeth.Age[18F]FET TBRmax[18F]FET tumor volumeT2 volumeContrast volume | 97 / 2 (41.2 / 11.8)7 / 2 (41.2 / 11.8)42.3 (29.9-56.3)2.01 (1.56-5.64)3.21 (0.00-172.04)31.6 (12.40-226.50)0.00 (0.00-6.09) | 86 / 2 (35.3 / 11.8)5 / 3 (29.4 / 17.6)37.7 (30.4-57.6)3.79 (3.08-5.86)71.96 (11.44-120.69)63.50 (39.10-110.10)18.55 (6.63-61.20) | 0.8930.4900.321**0.019**0.2090.654**0.005** |

TBRmax  – maximum tumor-to-background-ratio, IDH – isocitrate dehydrogenase, TERT – telomerase reverse transcriptase, [18F]FET – [18F]Fluoroethyltyrosine, TBRmax – maximum tumor-to-brain-ratio, CNS WHO 2021-World Health Organization Classification of Tumors of the Central Nervous System