SUPPLEMENTAL DATA

Gene therapy enhances chemotherapy tolerance and efficacy in glioblastoma patients

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SUPPLEMENTAL TABLES

Supplemental Table 1. Chemotherapy-associated myelosuppression in longest treated case patient

GBM Patient	Cycle No.	Days ANC ≤500/µl (Nadir)	Days ANC ≤100/µl (Nadir)	Days Platelets ≤25,000/µl (Nadir)	Days Platelets ≤10,000/µl (Nadir)	Grade 4 Non-Hematologic Toxicity Observed
Case 1	1	-	-	-	-	-
	2	1 (140)[A]	-	-	-	-
	3[B]	3 (310)	-	7 (16,000)	-	-
	4	-	-	-	-	-
	5	-	-	-	-	-
	6	-	-	-	-	-
	7	-	-	-	-	-
	8	-	-	-	-	-
	9	-	-	-	-	-

[A] Required intervention: for neutropenia, G-CSF administration; for thrombocytopenia, transfusion.

[B] TMZ dose-escalated cycle (590 mg/m^2)

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Supplemental Table 2. Gene modified cell manufacturing and infused cell product data

GBM Patient	$CD34^+$ Content After Enrichment (%)	Cell Viability Following Gene Transfer (%)	Colony-forming Efficiency Following Gene Transfer[A] (%)	Gene Transfer Efficiency in Colony-forming Units (%)	Total Cell Dose Infused (per kg body weight)	Total Colony-forming Units Infused (per kg body weight)[B]	Total Gene-Modified Colony-forming Units Infused (per kg body weight)[C]
Case 1	96.3	96.0	2.6	70.6	8.9×10^6	2.30×10^5	1.60×10^5
Case 2	94.8	100.0	13.5	79.0	21.9×10^6	2.95×10^6	2.33×10^6
Case 3	94.1	100.0	21.6	74.0	7.5×10^6	1.62×10^6	1.20×10^6
Case 4	96.5	98.5	20.1	90.6[D]	3.8×10^6	7.64×10^5	6.92×10^5
Case 5	96.7	96.9	27.0	53.4	9.9×10^6	2.67×10^6	1.43×10^6
Case 6	95.1	94.3	8.9	41.1	5.2×10^6	4.62×10^5	1.90×10^5
Case 7	97.9	97.0	22.4	47.7	4.4×10^6	9.86×10^5	4.70×10^5

[A] Per 100,000 cells plated.

[B] Calculated by multiplying the colony-forming efficiency by the total cell dose infused.

[C] Calculated by multiplying the gene transfer efficiency in colony-forming units by the total colony-forming units infused.

[D] Abnormal negative controls (blank methylcellulose from the same plate) indicate an artificially high level of gene transfer in this patient.

Supplemental Table 3. Biomathematical modeling characteristics used to match case and control patients

GBM Patient	*D* mm^2/yr	ρ yr^{-1}	V mm/day	EOR	Age/RPAClass/ Gender	KPS at diagnosis	MGMT Promoter Status	Initial Treatment	No. Adjuvant TMZ cycles	OS (days)
Case 1	14.3	176.5	1.5E-01	GTR	57/IV/M	100	Unmethylated	RT[A]	9[C]	1720*
Control 1A	8.1	100.7	3.5E-02	GTR	76/IV/M	80	Unmethylated	RT[B]	3[D]	381
Control 1B	5.2	178.4	1.7E-01	GTR	53/IV/M	90	ID	RT[B]/TMZ	3[E]	343
Case 2	17.31	25.3	1.1E-01	STR	52/IV/F	100	Unmethylated	RT[A]	3[F]	555
Control 2	12.2	15.4	3.1E-02	STR	57/IV/M	90	Unmethylated	RT[B]/TMZ	4[F]	481
Case 3	126.4	133.2	4.5E-01	GTR	53/IV/M	90	Unmethylated	RT[A]	4[F]	705
Control 3	98.0	154.3	2.6E-01	GTR	66/IV/M	100	Methylated	RT[A]/TMZ	22[E]	1406[G]
Case 4	119	177	6.6E-01	GTR	64/IV/F	90	Unmethylated	RT[A]	2[F]	412
Control 4	181.2	98.5	1.5E-01	GTR	74/V/M	80	Unmethylated	RT[A]/TMZ	8[E]	525

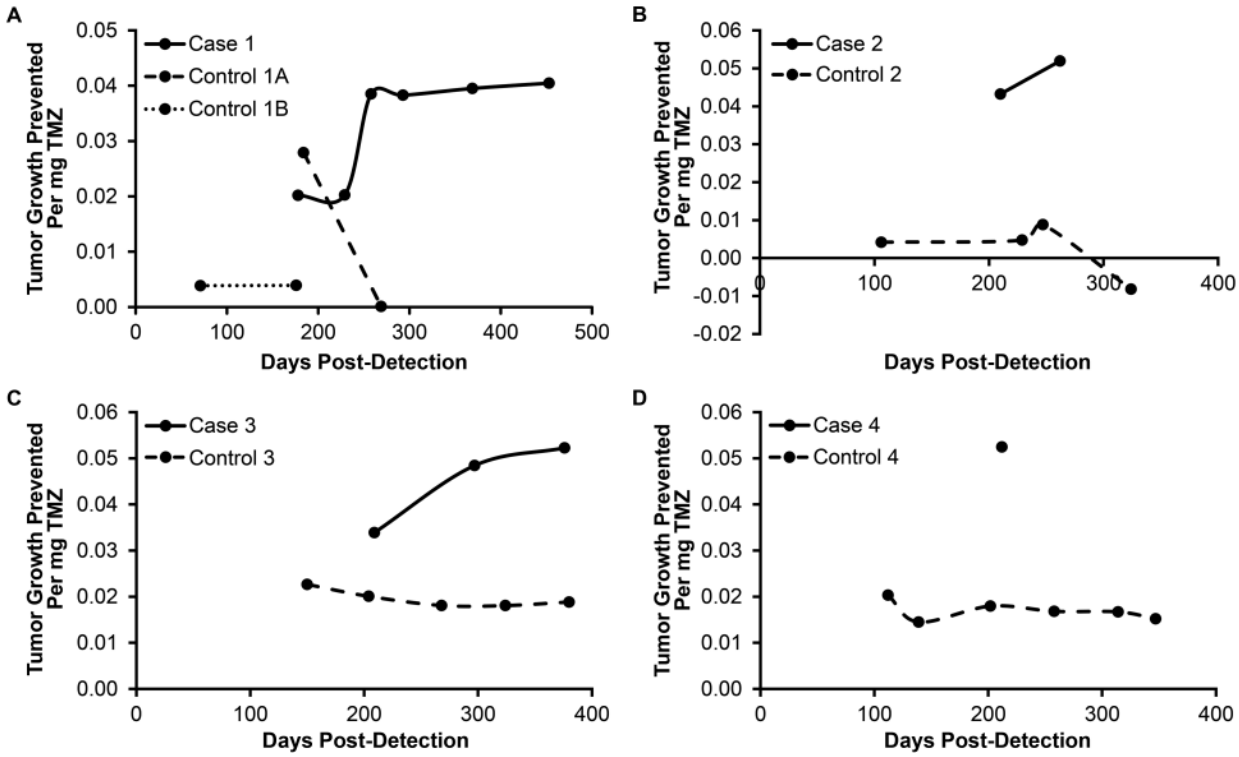
D: Diffusion rate of tumor determined by the model; P: Proliferation value determined by the model; V: Velocity of tumor growth determined by the model; ID: Indeterminate, sample was tested but result could not be obtained for unknown reasons.

Initial Treatment RT dosing: [A] 60 Gy, [B] 61.2 Gy

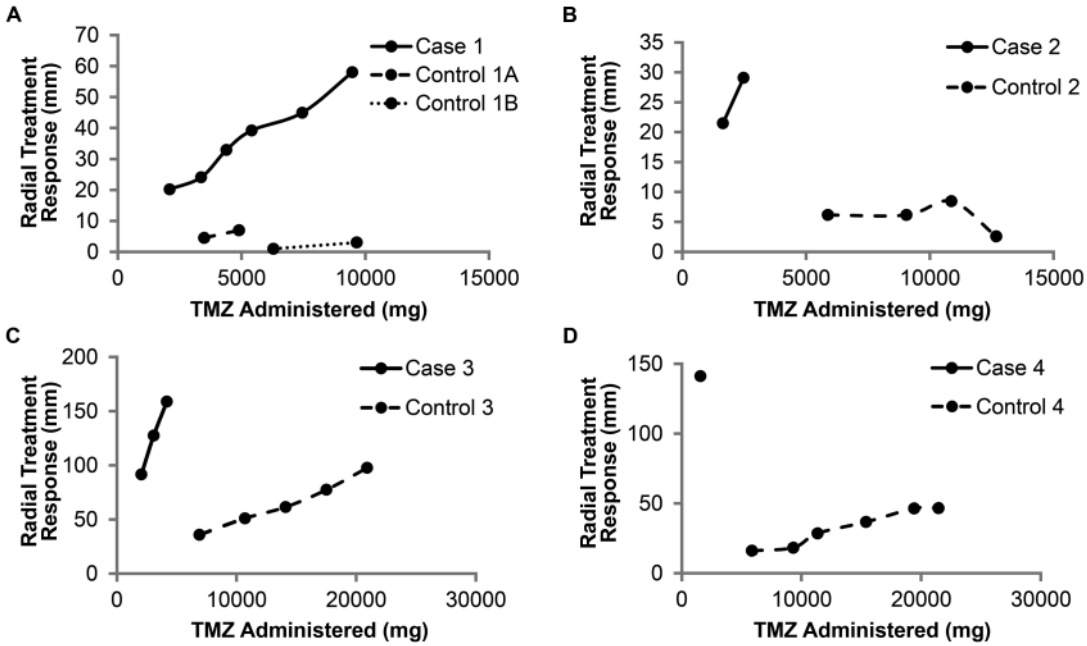
No. Adjuvant TMZ cycles dosing range: [C] 472-590 mg/m^2, [D] 125-200 mg/m^2, [E] 150-200 mg/m^2, [F] 472 mg/m^2

[G] Censored data

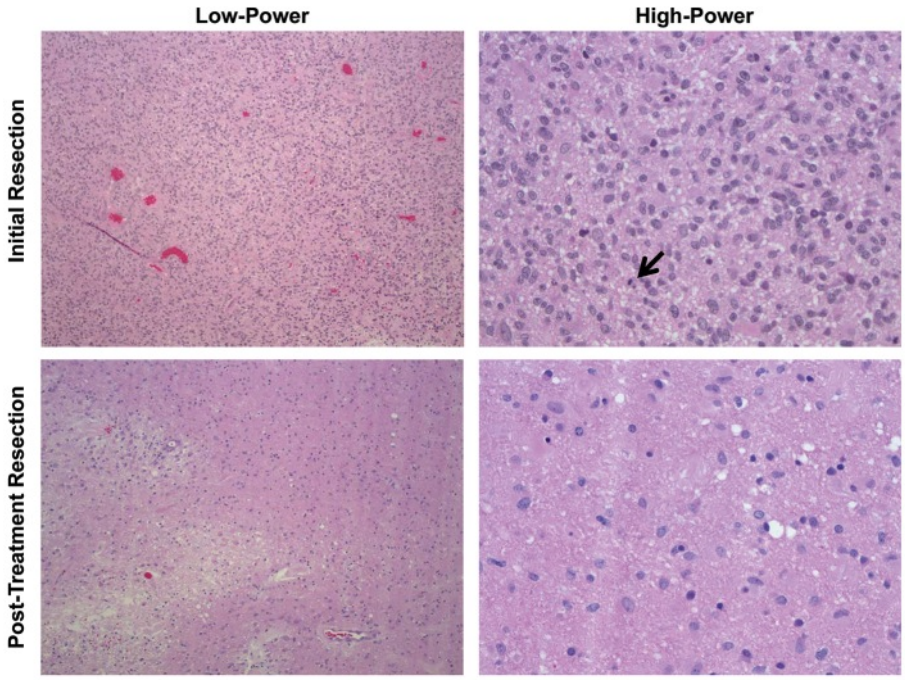
SUPPLEMENTAL FIGURES



Supplemental Figure 1. Trends in days gained per mg TMZ determined for each study patient and matched control. Each panel compares the study patient (solid black line) and matched control patients (dashed black line) observed days gained per mg TMZ dosed at each response evaluation. The x-axis represents the number of days since first MRI scan of tumor detection and the y-axis represents the days gained per mg of TMZ dosed, where the connecting dashed line between the markers is for illustrative purposes and not to imply a continuous state of dose delivery. Study patients in panels **A**, **B**, and **C** demonstrated cumulative increases in days gained per mg of TMZ with each cycle of TMZ dosed. The single dip in panel **A**, case patient 1 represents pseudoprogression (confirmed by tissue pathology). Control patients in panels **A**, **B**, and **D** have decreasing or stable trends in days gained, while control patient 3 (panel **C**), who displayed a better prognosis methylated MGMT promoter in tumor cells, experienced undulating days gained per mg TMZ.



Supplemental Figure 2. Trends in radial treatment response per mg TMZ determined for each study patient and matched control. Each panel compares the study patient (solid black line) and matched control patients (dashed black line) observed radial treatment response, or mm of anticipated tumor growth that were prevented, per mg TMZ dosed at each response evaluation. The x-axis represents the number of days since first MRI scan of tumor detection and the y-axis represents the mm of tumor growth prevented based on predicted, untreated tumor growth per mg of TMZ dosed, where the connecting dashed line between the markers is for illustrative purposes and not to imply a continuous state of dose delivery. All but one patient (control patient 2, panel **B**) displayed increased radial treatment response per mg of TMZ administered. However, case patients displayed more significant radial treatment responses at equal (case patient 1) or lower (case patients 2, 3 and 4) cumulative TMZ doses.



Supplemental Figure 3. Histopathologic comparison of resection tissues from case patient 1. Representative micrographs of hematoxylin and eosin stained sections of resection tissue from the initial craniotomy and subsequent post-treatment craniotomy. **Initial resection:** Low-power view of glioblastoma with hypercellularity and microvascular proliferation. High-power view showing cells with enlarged hyperchromatic pleomorphic nuclei and indiscernible cytoplasm; high-power includes a mitotic figure (black arrow). **Post-treatment resection:** Low-power view of astrocytoma-like lesion demonstrating significantly reduced cellularity and necrosis (left edge) without pseudopalisading of surrounding neoplastic cells. High-power view with no evidence for mitotic figures. Low-power images were captured under a 100× original magnification; high-power images were captured under a 400× original magnification.