SUPPLEMENTAL TABLES AND FIGURES

Supplemental Table 1

SD-101 Dose	1 mg (n=10)		2 mg (n=3)		4 mg (n=3)		8 mg (n=13)		Total (n=29)		
Grade	1/2	3	1/2	3	1/2	3	1/2	3	1/2	3	ALL
Anemia	0	0	1(33)	0	0	0	1(8)	0	2(7)	0	2(7)
Anxiety	1(10)	0	0	0	0	0	1(8)	0	2(7)	0	2(7)
Back Pain	0	0	1(33)	0	1(33)	0	0	0	2(7)	0	2(7)
Constipation	1(10)	0	0	0	0	0	1(8)	0	2(7)	0	2(7)
Flu-like Illness	0	0	0	0	0	0	2(15)	0	2(7)	0	2(7)
Hyperbilirubinemia	0	0	1(33)	0	1(33)	0	0	0	2(7)	0	2(7)
Hyperhidrosis (Sweating)	0	0	1(33)	0	0	0	1(8)	0	2(7)	0	2(7)
Injection Site Pain	0	0	0	0	0	0	2(15)	0	2(7)	0	2(7)
Injection Site Rash	1(10)	0	0	0	0	0	1(8)	0	2(7)	0	2(7)
Rash	2(20)	0	0	0	0	0	0	0	2(7)	0	2(7)
Abdominal Discomfort	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Abdominal Pain	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Abdominal Pain Upper	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Arthralgia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
AST increase	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Asthenia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Blood Calcium Decrease	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Blood Chloride Increase	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Chest Discomfort	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Cold Sweat	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Confusion	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Cough	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Dizziness	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
DNA Antibody Positive	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Dry Eye	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Dysgeusia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Eosinophil Count Decrease	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Erythema	0	0	0	0	1(33)	0	0	0	1(3)	0	1(3)
Exercise Tolerance Decrease	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Eye Irritation	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
GGT Increase	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Herpes Virus Infection	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Hot Flash	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
hyperglycemia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Hypotension	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Increased Viscosity of Bronchial Secretion	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Injection Site Discoloration	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Leukopenia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Lymphadenopathy Increase	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Lymphocyte Count Decrease	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Lymphocyte Count Increase	0	0	0	0	1(33)	0	0	0	1(3)	0	1(3)
Maculo-Papular Rash	0	0	0	0	1(33)	0	0	0	1(3)	0	1(3)
Medial Tibial Stress Syndrome	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Menstruation Irregular	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Muscle Spasms	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Neck Pain	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Oral Hypoesthesia	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Oral Paraesthesia	1(10)	0	0	0	0	0	0	0	1(3)	0	1(3)
Peripheral Swelling of Lower Extremities	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Pleuritic Pain	0	0	0	0	1(33)	0	0	0	1(3)	0	1(3)
Presyncope	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Skin hyperpigmentation	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Sneezing	1	0	0	0	0	0	0	0	1(3)	0	1(3)
Stomatitis	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Tachycardia	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)
Total Protein Decrease	0	0	1(33)	0	0	0	0	0	1(3)	0	1(3)
Urinary Incontinence	0	0	0	0	0	0	1(8)	0	1(3)	0	1(3)

Supplemental Table 1: Uncommon Drug-related Adverse Events

Drug-related adverse events that occurred in less than 10% of patients

Supplemental Table 2

Tumor Subtype	Initial Tumor Burden (sum of cross products sum of cm x cm)	Stage	FLIPI	Flu-like Symptom (Highest Grade)	Best Overall Response	Best Distant Response
FOLLICULAR	133.64	STAGE IV	2	1	-23	-21
FOLLICULAR	19.22	STAGE IV	2	3	-41	-38
FOLLICULAR	24.77	STAGE IV	3	3	-21	-18
FOLLICULAR	27.77	STAGE III	1	3	-37	-8
FOLLICULAR	6.73	STAGE III	1	2	-22	-3
FOLLICULAR	9.21	STAGE III	2	2	-72	-53
FOLLICULAR	25.5	STAGE IV	2	2	-20	-19
MARGINAL ZONE	26.88	STAGE III	N/A	3	-48	-29
FOLLICULAR	23.74	STAGE IV	2	3	-1	13
FOLLICULAR	23.59	STAGE IV	3	3	-17	14
FOLLICULAR	8.38	STAGE IV	2	2	-70	-61
FOLLICULAR	18.59	STAGE IV	2	2	-25	-16
FOLLICULAR	18.19	STAGE III	3	2	-53	-49
MARGINAL ZONE	30.88	STAGE IV	N/A	2	-12	-5
MARGINAL ZONE	38.18	STAGE IV	N/A	2	30	25
CUTANEOUS	3.68	STAGE IV	N/A	2	-82	-61
FOLLICULAR	6.55	STAGE IV	1	3	-50	-5
MARGINAL ZONE	7.11	STAGE II	N/A	2	-2	-3
SLL	34.41	STAGE IV	N/A	1	-19	-14
FOLLICULAR	30.32	STAGE IV	3	1	-59	-52
FOLLICULAR	19.89	STAGE IV	3	1	-59	-56
FOLLICULAR	8.03	STAGE IV	2	2	-17	-28
CLL	21.48	STAGE IV	N/A	2	-13	-13
FOLLICULAR	19.91	STAGE IV	2	2	3	7
FOLLICULAR	12.44	STAGE III	3	2	-73	-67
FOLLICULAR	79.72	STAGE IV	2	2	5	45
SLL	72.05	STAGE IV	N/A	2	-28	-20
FOLLICULAR	21.91	STAGE II	2	1	-45	-21
FOLLICULAR	12.43	STAGE II	0	2	-45	-39

Supplemental Table 2: Initial Tumor Burden, Stage, FLIPI, and the Grade of Flu-like symptoms do not correlate to the best overall or distant response.

The initial tumor burden, stage, follicular lymphoma international prognostic index (for those patients with FL), nor the development of the flu-like symptoms (malaise, chills, headache, fatigue, and fever) during therapy correlated with either overall or distant response.

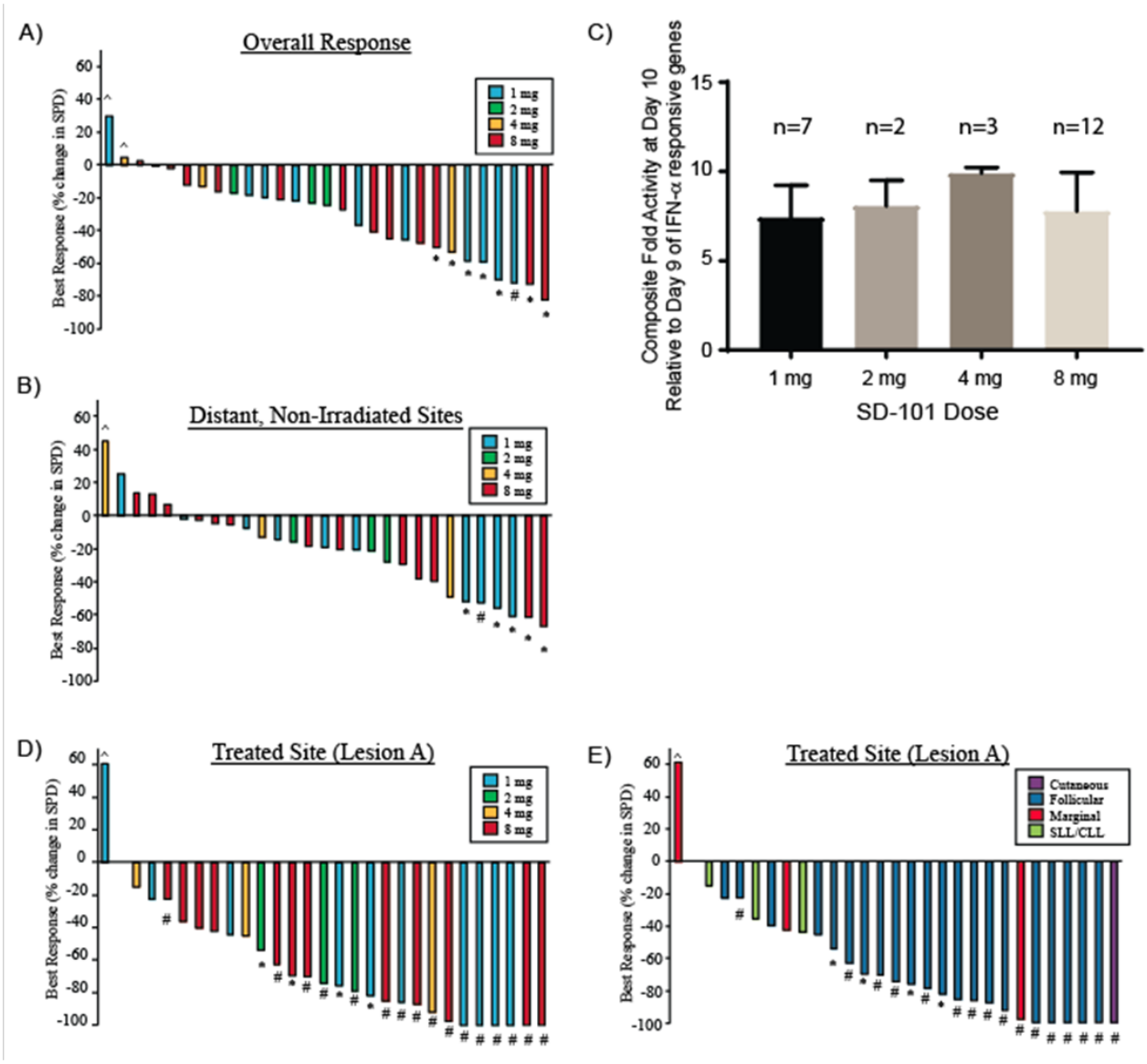
Supplemental Table 3

		Time (hrs)					
Cohort (Dose)	**Subject ID**	**0**	**1**	**2**	**4**	**6**	**24**
1 (1 mg)	Patient #1	BLOQ	29.40	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #2	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #3	27.3	35.6	BLOQ	25.3	BLOQ	29.0
2 (2 mg)	Patient #4	BLOQ	BLOQ	26.7	BLOQ	BLOQ	BLOQ
	Patient #5	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #6	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ	BLOQ
3 (4 mg)	Patient #7	BLOQ	58.8	BLOQ	BLOQ	28.4	BLOQ
	Patient #8	BLOQ	52.9	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #9	BLOQ	50.7	BLOQ	BLOQ	BLOQ	BLOQ
4 (8 mg)	Patient #10	BLOQ	99.8	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #11	BLOQ	139	BLOQ	BLOQ	BLOQ	BLOQ
	Patient #13	BLOQ	BLOQ	57.5	BLOQ	BLOQ	BLOQ

Supplemental Table 3: Concentration of SD-101 in plasma samples before and after the second intratumoral administration

The concentration (in ng/ml) of SD-101 was measured in the plasma at baseline, 1, 2, 4, 6, and 24 hours after treatment. BLOQ = below the limit of quantitation, which was 25 ng/mL except for samples from patients 6, 8, and 13, where the LLOQ was 50 ng/mL, and samples from patient 11 where the LLOQ was 100 ng/mL.

Supplemental Figure 1

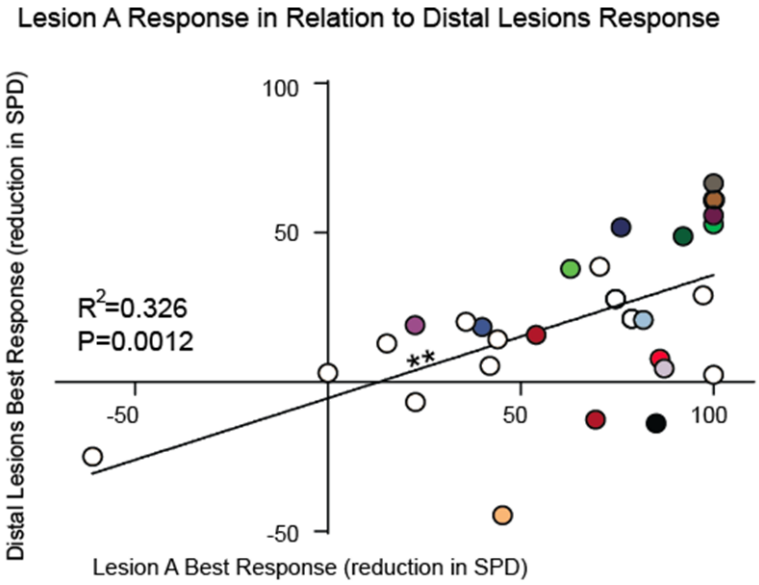


Supplemental Figure 1. SD-101 and low-dose radiation induces clinical responses in patients with indolent lymphoma independent of SD-101 dose.

Waterfall plot showing the best overall change in the sum of the product of the diameters in all target lesions (A), or distal sites (B) by dose. Relative fold activity ± SEM of the expression of IFN-alpha regulated genes at Day 10, 24 hours after injection with SD-101. Fold activity represents a composite score of the geometric mean of the fold activity of 4 IFN-regulated genes (GBP-1, ISG-54, MCP-1, and MxB) relative to baseline (Day 9) for each subject followed by calculating the arithmetic mean of the geometric means within each cohort. The number of

patients included for each dose level are shown. (C) Waterfall plot showing the best overall change in the sum of the product of the diameters in the treated site by dose (D) and lymphoma subtype (E). Patients achieving a partial response (*), complete response (#), or progression (^) by the Revised 2007 International Working Group criteria are shown.

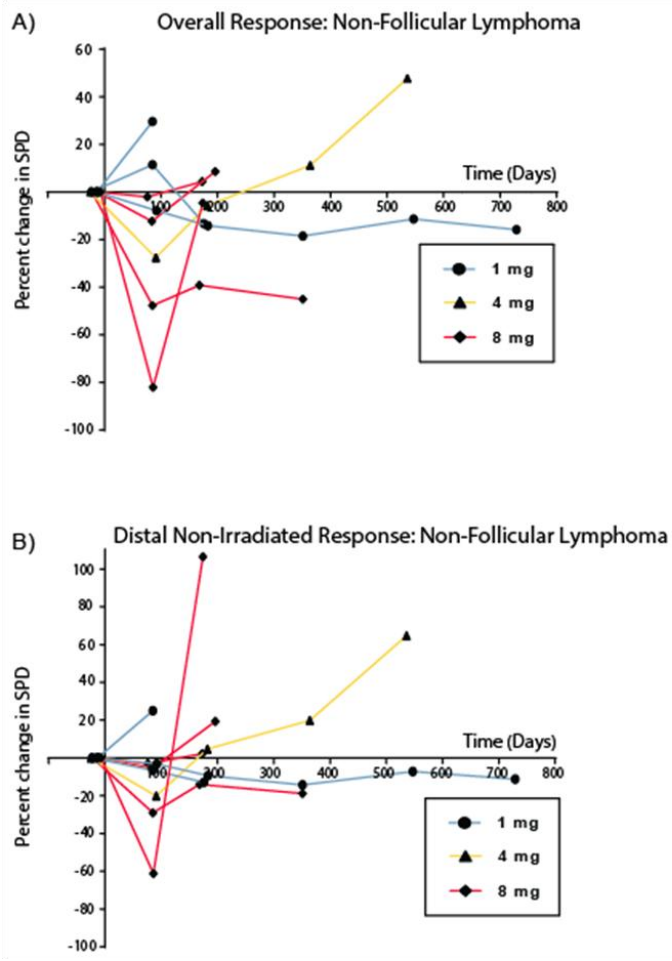
Supplemental Figure 2



Supplemental Figure 2: Lesion A tumor response correlates with Distal Lesion response

The best overall reduction of the treated site, Lesion A, positively correlated to the best overall reduction of the distal lesions as measured by the sum of the product of the diameters by linear regression analysis (p=0.0012). Patient, who have samples available for the immune response analysis, are tracked by a specific color.

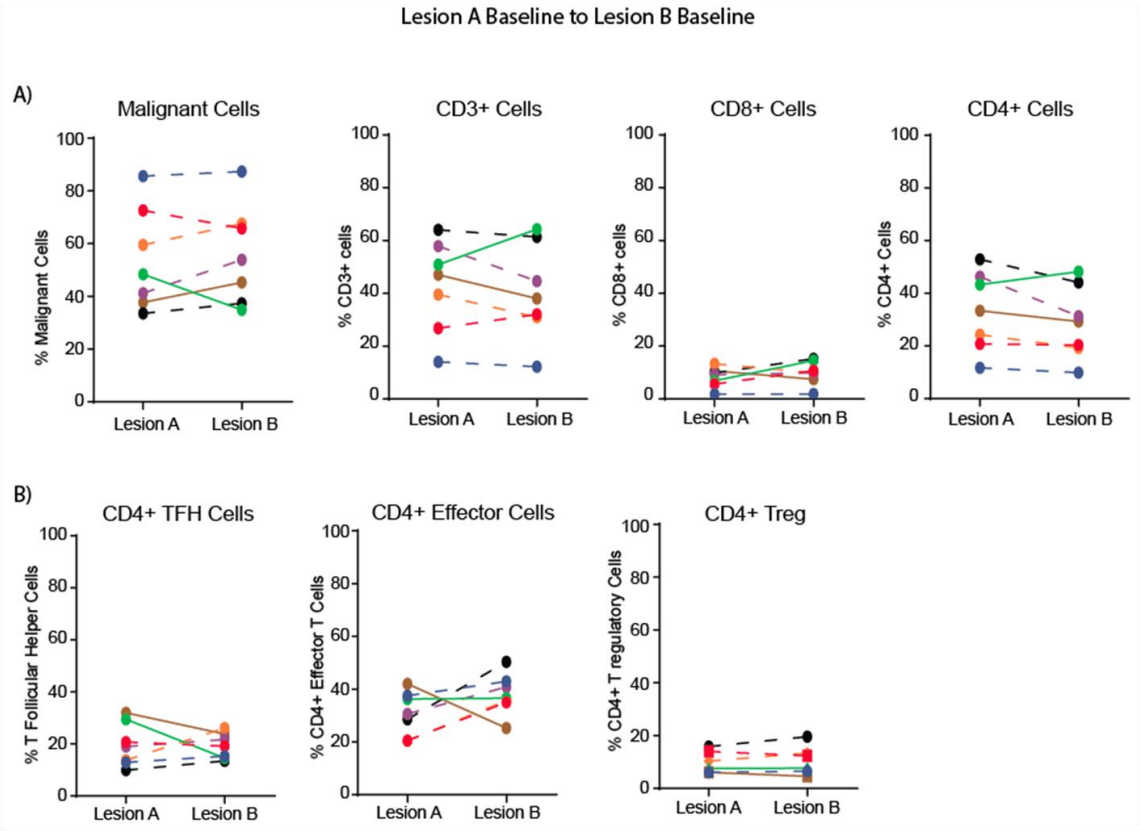
Supplemental Figure 3



Supplemental Figure 3: Spider plots for patients with non-Follicular Lymphoma subtypes after treatment with SD-101 and low-dose radiation

Spider plots showing the change in the sum of the product of the diameters in all lesions (A) or distal sites (excluding Lesion A) (B) in non-Follicular lymphoma subtypes by SD-101 dose .

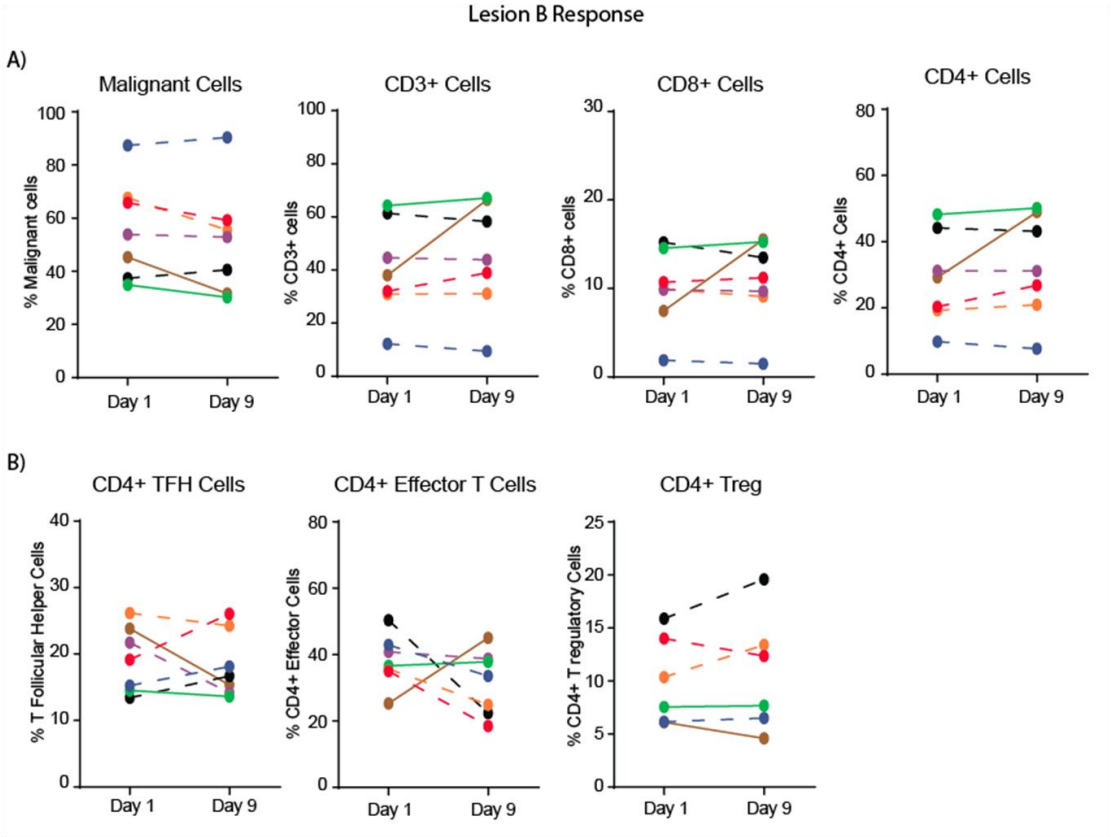
Supplemental Figure 4



Supplemental Figure 4: Intratumoral immune cell composition is similar between different tumor sites within each patient.

We evaluated the percentage of intratumoral malignant cells, CD3+ cells, CD8+ T-cells, CD4+ T-cells, and CD4+ subsets including TFH cells, Treg cells, and CD4+ effector cells were evaluated prior to treatment in Lesion A and Lesion B in 7 patients who had FNA samples available for analysis. Each patient is tracked by a specific color and patients achieving at least an overall partial response are connected by solid lines and those who did not by dashed lines.

Supplemental Figure 5



Supplemental Figure 5: Treatment Induced Immune Cell Changes in Distal Lesions Malignant cells, CD3+ cells, CD8+ T-cells, and CD4+ T-cells were evaluated pre- (Day 1) and post-treatment (Day 9) from an uninjected, distal lesion. As a percentage of all cells, the percent of intratumoral malignant cells, CD3+, CD8+, and CD4+ T-cells were not significantly different when evaluated by paired t-test. (A) As a percentage of CD3+ T-cells, the CD4+ TFH cells, effector cells, and Tregs were not significantly different when evaluated by paired t-test. (B) Each patient is tracked by a specific color and patients achieving at least an overall partial response are connected by solid lines and those who did not by dashed lines.