Supplemental Table 1

Characteristic	Unmatched cohort (n = 1177)	No GLP-1 RA (n = 1106)	GLP-1 RA (n = 71)	p-value	Matched cohort (n = 629)	No GLP-1 RA (n = 560)	GLP-1 RA (n = 69)	p-value
Mean age (± SD)	68.76 ± 8.37	68.90 ± 8.43	66.56 ± 7.03	**0.02**	67±8.06	67.02±8.19	66.83 ± 6.95	0.84
Sex				0.46				0.69
Male	517 (43.9%)	489 (44.2%)	28 (39.4%)		262 (41.65%)	235 (41.96%)	27 (39.13%)	
Female	660 (56.1%)	617 (55.8%)	43 (60.6%)		367 (58.35%)	325 (58.04%)	42 (60.87%)	
Race				0.29				0.69
White	1068 (90.7%)	1006 (91%)	62 (87.3%)		556 (88.39%)	496 (88.57%)	60 (86.96%)	
Non-White	109 (9.3%)	100 (9%)	9 (12.7%)		73 (11.61%)	64 (11.43%)	9 (13.04%)	
Smoking status				1				1.00
Non-smoker	82 (7%)	77 (7%)	5 (7%)		40 (6.36%)	36 (6.43%)	4 (5.8%)	
smoker	1095 (93%)	1029 (93%)	66 (93%)		589 (93.64%)	524 (93.57%)	65 (94.20%)	
Mean BMI (± SD)	30.93 ± 5.03	30.66 ± 4.81	35.07± 6.42	**0.001**	33.33±5.06	33.18±4.98	34.53±5.55	0.059
Clinical stage				0.41				0.88
I	970 (82.4%)	908 (82.1%)	62 (87.3%)		477 (75.83%)	425 (75.89%)	52 (75.36%)	
II	193 (16.4%)	184 (16.6%)	9 (12.7%)		152 (24.17%)	135 (24.11%)	17 (24.64%)	
III	14 (1.2%)	14 (1.3%)	0					
Histology				0.97				0.99
Adenocarcinoma	669 (56.8%)	628 (56.8%)	41 (57.7%)		376 (59.78%)	336 (60%)	40 (57.97%)	
Squamous cell carcinoma	345 (29.3%)	325 (29.4%)	20 (28.2%)		166 (26.39%)	147 (26.25%)	19 (27.54%)	
Other	163 (13.8%)	153 (13.8%)	10 (14.1%)		87 (13.83%)	77 (13.75%)	10 (14.49%)	

Supplemental Table 1. Patient characteristics of the Clinical Cohort A. Patient demographics (age, sex, race, smoking status, BMI) and disease/treatment characteristics (stage, histology) are given as mean/count and standard deviation (SD)/percentage. Overall distributions and group distributions, when split into GLP-1 RA users vs. nonusers, are provided. Group distributions of the full unmatched cohort and the post-propensity score matched cohort were compared using an independent t-test for continuous variables and chi-square tests for all other variables. P-value < 0.05 was considered statistically significant.

BMI: body mass index.

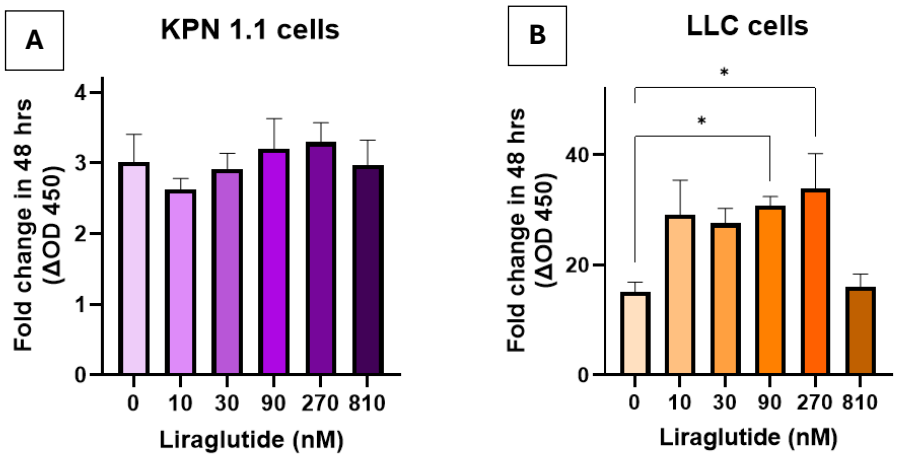
Supplemental Table 2

Characteristic	Unmatched cohort (n = 300)	No GLP-1 RA (n = 290)	GLP-1 RA (n = 10)	p-value	Matched cohort (n = 89)	No GLP-1 RA (n = 79)	GLP-1 RA (n = 10)	p-value
Mean age (± SD)	65.76 ± 9.28	65.97 ± 9.30	59.5 ± 6.32	**0.03**	60.39 ± 8.44	60.51 ± 8.70	59.50 ± 6.33	0.71
Sex				1				1
Male	149 (49.7%)	144 (49.7%)	5 (50%)		45 (50.56%)	40 (50.63%)	5 (5%)	
Female	151 (50.3%)	146 (50.3%)	5 (50%)		44 (49.44%)	39 (49.37%)	5 (5%)	
Race*				0.49				1
White	271 (90.3%)	263 (90.7%)	8 (80%)		72 (80.90%)	64 (81.01%)	8 (80%)	
Non-White	28 (9.3%)	26 (9%)	2 (20%)		17 (19.10%)	15 (18.99%)	2 (20%)	
Smoking status				0.67				0.87
current smoker	123 (41%)	118 (41.7%)	5 (50%)		42 (47.19%)	37 (46.84%)	5 (50%)	
former smoker	161 (53.7%)	156 (53.8%)	5 (50%)		45 (50.56%)	40 (50.63%)	5 (50%)	
never smoker	16 (5.3%)	16 (5.5%)	0		2 (2.25%)	2 (2.53%)	00	
Diabetes Mellitus								
Yes	83 (27.5%)	73 (25.17)	10 (100%)		25 (28.09%)	15 (18.99%)	10 (100%)	
No	217 (72.4%)	217 (84.83%)	0 (0%)		64 (71.91%)	64 (71.91%)	0 (0%)	
Mean BMI (± SD)	30.37 ± 4.9	30.35 ± 4.9	31.2 ± 4.05	0.53	30.50 ± 4.49	30.41± 4.55	31.20± 4.05	0.409
Histology				0.27				0.93
Adenocarcinoma	180 (60%)	176 (60.7%)	4 (40%)		40 (44.94%)	36 (45.57%)	4 (40%)	
Squamous cell carcinoma	83 (27.7%)	78 (26.9%)	5 (50%)		40 (44.94%)	35 (44.30%)	4 (50%)	
Other	37 (12.3%)	36 (12.4%)	1 (10%)		9 (10.11%)	8 (10.13%)	1 (10%)	
Stage				0.45				1.00
III	64 (21.3%)	61 (21%)	3 (30%)		25 (28.09%)	22 (27.85%)	3 (30%)	
IV	236 (78.7%)	229 (79%)	7 (70%)		64 (71.91%)	57 (72.15%)	7 (70%)	
Mode of therapy				0.75				0.75
Immunotherapy	158 (52.7%)	152 (52.4%)	6 (60%)		42 (47.19%)	38 (48.10%)	4 (40%)	
Chemo-immunotherapy	142 (47.3%)	138 (47.6%)	4 (40%)		47 (52.81%)	41 (51.90%)	6 (60%)	
PDL1 expression				0.5				0.15
<1	69 (26.6%)	67 (26.9%)	2 (20%)		22 (27.8%)	20 (29%)	2 (20%)	
1-50	81 (31.3%)	79 (31.7%)	2 (20%)		31 (39.2%)	29 (42%)	2 (20%)	
>50	109 (42.1%)	103 (41.4%)	6 (60%)		26 (32.9%)	20 (29%)	6 (60%)	

Supplemental Table 2: Patient characteristics of the clinical cohort B. Patient demographics (age, sex, race, smoking status, BMI) and disease/treatment characteristics (histology, first-line regimen, PD-1 expression, T2DM status) are given as mean/count and standard deviation (SD)/percentage. Overall distributions as well as group distributions when split into GLP-1 RA vs. not on GLP-1 RA are provided. Group distributions of the full unmatched cohort and the post-propensity score matched cohort were compared using an independent t-test for age and chi-square tests for all other variables. P-value < 0.05 was considered statistically significant

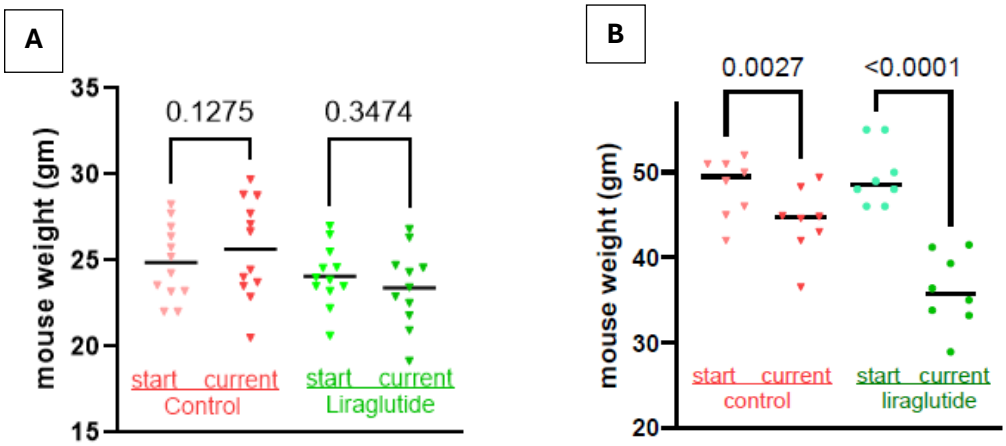
*ICI = Immune checkpoint inhibitor, BMI = Body mass index, T2DM = Type 2 Diabetes mellitus

Supplemental Figure 1



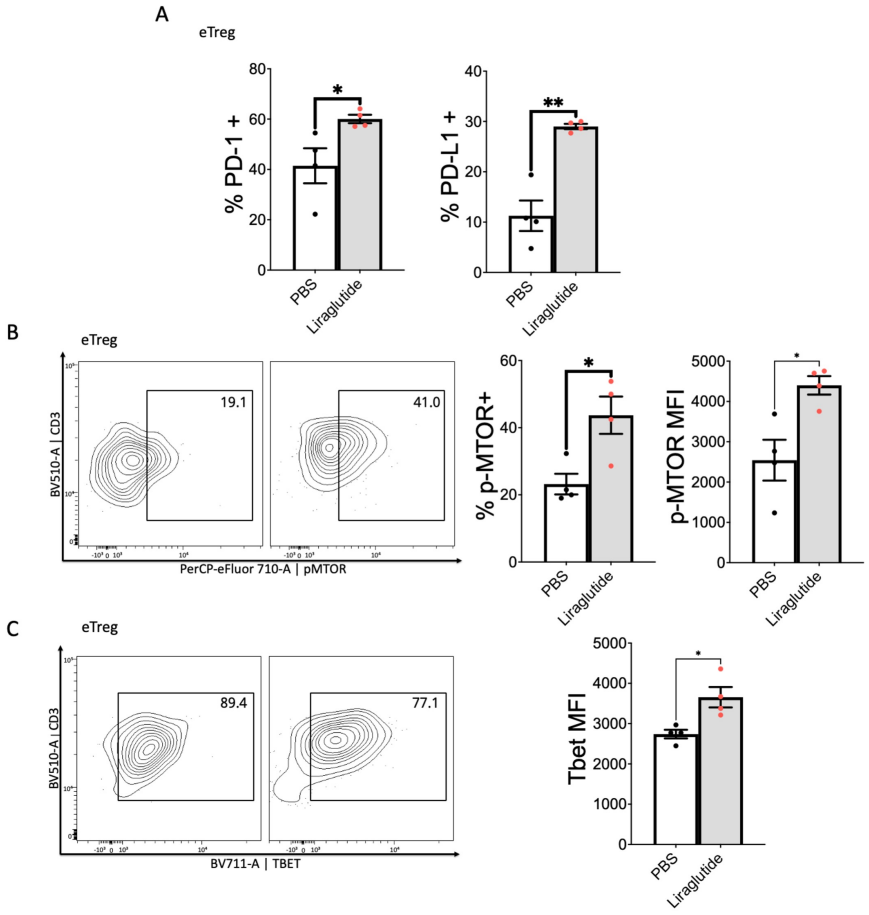
Supplemental Figure 1. Effects of liraglutide on in vitro tumor cell proliferation. The indicated cell lines were grown in vitro and subjected to the CCK-8 proliferation assay in the presence of various liraglutide concentrations. Shown are mean proliferation values +/-SD for the KPN1.1 **(A)** and LLC cell lines **(B)** from one of two independent experiments**.** *P<0.05 by t test.

Supplemental Figure 2



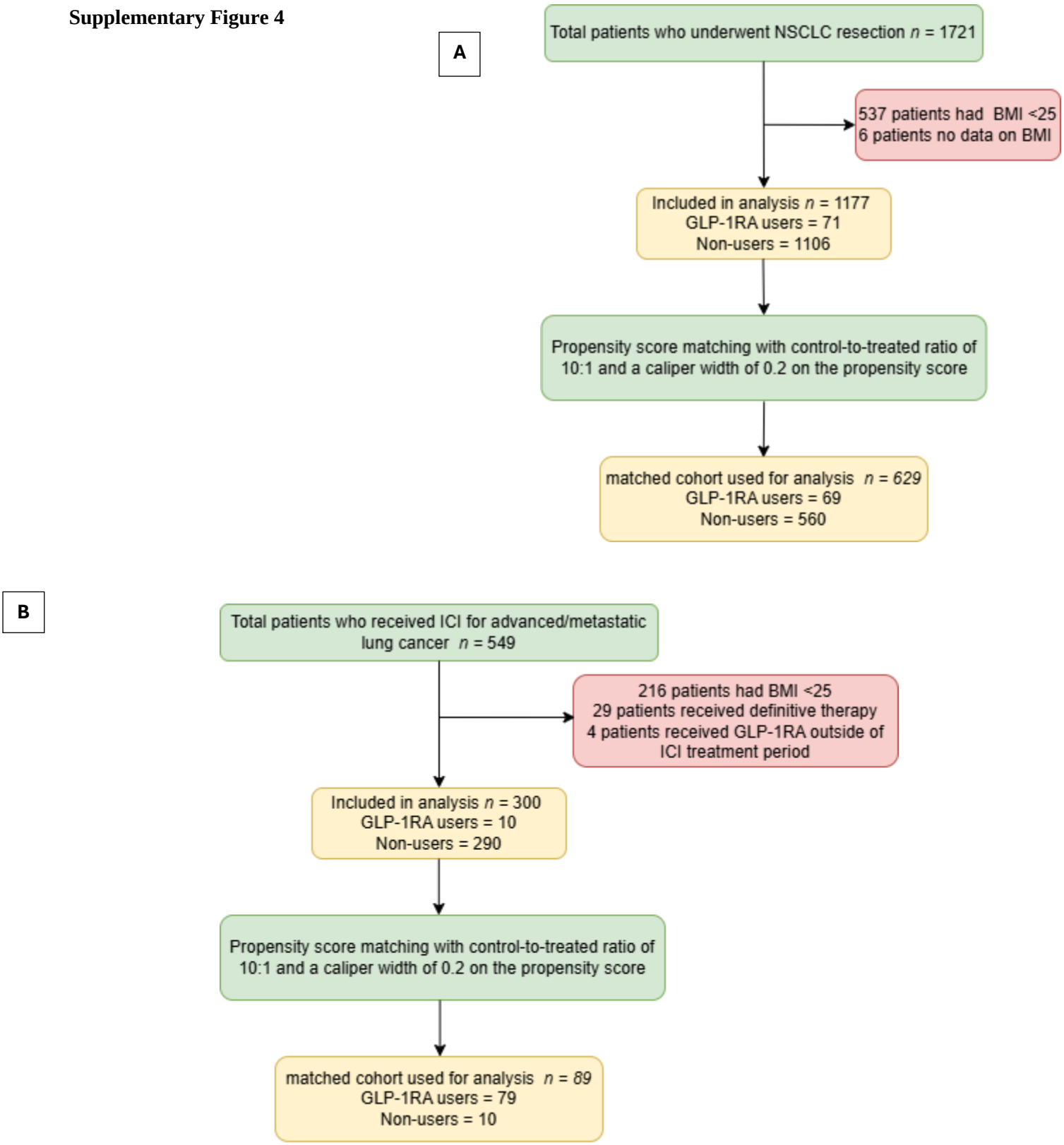
Supplemental Figure 2. Weight change in tumor-bearing mice treated with liraglutide or a PBS control. Obese C57BL/6 mice were challenged with s.c. KPN1.1 tumors and treated with liraglutide or PBS as described in Figure 2. Control mice had slight weight gain in normal-weight mice while liraglutide reduced the weight. Liraglutide-treated obese mice with higher weight loss than the control mice, as mice in both groups experienced significant weight loss **(A, B).** Numbers represent the P values for the indicated comparisons (t test).

Supplementary Figure 3



Supplemental Figure 3. Characterizing the impact of GLP-1Ra treatment on tumor-infiltrating Treg populations and phenotypes. Tumor tissues were recovered from the mice described in Figure 3, and, after enzymatic and mechanical digestion, single-cell suspensions were generated. Immunostaining followed by spectral flow cytometry analysis revealed the effects of liraglutide on Treg cells. Shown are the mean +/-SEM results from one of two independent experiments and representative flow plots (n=5 per group/trial). *p < 0.05, ***<0.01 by t test.

Supplementary Figure 4



Supplemental Figure 4. Flowchart showing the Patient Cohort Selection. This flowchart illustrates the process of patient selection and analysis within both the retrospective clinical cohorts. It details the number of patients assessed at each stage, including initial screening, application of inclusion/exclusion criteria, and final inclusion in the study.