

SUPPLEMENTARY MATERIALS

Table S1 (PATIENTS' CHARACTERISTICS 1)

Variable	Category	Freq. (n)	Percent (%)	Cumulative (%)
Sex	Male	17	39.53	39.53
	Female	26	60.47	100.0
Thyroid surgery	Yes	43	100.0	100.0
Somatic RET mutation (n=9)	No	8	88.89	88.89
	Yes	1	11.11	100.0
MEN2A (n=11)	No	8	72.73	72.73
	Yes	3	27.27	100.0
MEN2B (n=11)	No	10	90.91	90.91
	Yes	1	9.09	100.0
FDG-PET	Negative/not performed	40	93.02	93.02
	Positive	3	6.98	100.0
Gallium68-PET	Negative/not performed	43	100.0	100.0
DOPA-PET	Negative/not performed	35	81.4	81.4
	Positive	8	18.6	100.0
Last follow-up Status	Cured	26	60.47	60.47
	Not cured	17	39.53	100.0
Metastasis at Last Follow-up	No	36	83.72	83.72
	Yes	7	16.28	100.0
Systemic Therapy	No	39	90.7	90.7
	Yes	4	9.3	100.0

Table S2 (PATIENTS' CHARACTERISTICS 2)

Variable	Category	Freq. (n)	Percent (%)	Cumulative (%)
Tumor Type	Only medullary cancer	30	69.77	69.77
	Double tumors	13	30.23	100.0
Stage at diagnosis	I	26	60.47	60.47
	II	2	4.65	65.12
	III	3	6.98	72.09
	IVA	10	23.26	95.35
	IVC	2	4.65	100.0
T stage	T1a	25	58.14	58.14
	T1b	10	23.26	81.4
	T2	3	6.98	88.37
	T3a	3	6.98	95.35
	T4a	2	4.65	100.0
N stage	N0	29	67.44	67.44
	N1a	4	9.3	76.74
	N1b	10	23.26	100.0
M stage	M0	41	95.35	95.35
	M1	2	4.65	100.0
Extrathyroid extension	No	40	93.02	93.02
	Yes	3	6.98	100.0
Vascular invasion	No	27	62.79	62.79
	Yes	16	37.21	100.0
Perineural invasion	No	41	95.35	95.35
	Yes	2	4.65	100.0
Encapsulated neoplasm	No	41	95.35	95.35
	Yes	2	4.65	100.0

Capsular infiltration	No	41	95.35	95.35
	Yes	2	4.65	100.0
Surgical margins	Negative	41	95.35	95.35
	Positive	2	4.65	100.0
Multifocality	No	22	51.16	51.16
	Yes	21	48.84	100.0

Table S3 (PATIENTS' CHARACTERISTICS 3)

Variable	Mean	Std. dev.	Variance	Skewness	Kurtosis
Age at diagnosis (years)	54.34884	15.29221	233.8516	-0.0308773	2.028669
Primary tumor size (mm)	11.51628	9.62645	92.66854	2.024632	7.578509
Pre-surgery Calcitonin (pg/ml)	1737.293	6532.515	42700000.0	5.70827	35.48947
Post-surgery Calcitonin (pg/ml)	212.4198	718.4437	516161.3	3.95343	17.40085
Last follow-up Calcitonin (pg/ml)	185.2802	607.7949	369414.6	4.105559	19.13593
Last follow-up CEA (ng/ml)	37.48907	139.7096	19518.76	4.833083	26.55489
Disease-free survival (months)	49.1	62.91174	3957.887	2.095722	6.106124

Progression-free survival (months) (n=3)	48.66667	66.15386	4376.333	0.7025652	1.5
Mean Follow-up duration (months)	52.46512	65.35629	4271.445	1.973686	5.509953

Table S4 (PATIENTS' CHARACTERISTICS 4)

Variable	Category	Freq. (n)	Percent (%)	Cumulative (%)
Hypertension (n=42)	No	27	64.29	64.29
	Yes	15	35.71	100.0
Diabetes (n=42)	No	37	88.1	88.1
	Yes	5	11.9	100.0
Osteopenia/Osteoporosis (n=42)	No	36	85.71	85.71
	Yes	6	14.29	100.0
Other Non-Thyroid Neoplasms (n=42)	No	35	83.33	83.33
	Yes	7	16.67	100.0
Pheochromocytoma (n=42)	No	38	90.48	90.48
	Yes	4	9.52	100.0
Hyperparathyroidism (n=42)	No	38	90.48	90.48
	Yes	4	9.52	100.0
Dyslipidemia	No	29	67.44	67.44
	Yes	14	32.56	100.0

Table S5 (COMORBIDITIES Vs OUTCOME)

	Cured	Not cured	TOTAL	TEST (p-value)
Pheochromocytoma N (%)				
No	24 (96.0%)	14 (82.4%)	38 (90.5%)	0.139
Yes	1 (4.0%)	3 (17.6%)	4 (9.5%)	
Hyperparathyroidism N (%)				
No	24 (96.0%)	14 (82.4%)	38 (90.5%)	0.139
Yes	1 (4.0%)	3 (17.6%)	4 (9.5%)	
Dyslipidemia N (%)				
No	16 (61.5%)	13 (76.5%)	29 (67.4%)	0.307
Yes	10 (38.5%)	4 (23.5%)	14 (32.6%)	
Hypertension N (%)				
No	17 (68.0%)	10 (58.8%)	27 (64.3%)	0.542
Yes	8 (32.0%)	7 (41.2%)	15 (35.7%)	
Diabetes N (%)				
No	21 (84.0%)	16 (94.1%)	37 (88.1%)	0.320
Yes	4 (16.0%)	1 (5.9%)	5 (11.9%)	
Osteopenia/Osteoporosis N (%)				
No	23 (92.0%)	13 (76.5%)	36 (85.7%)	0.158
Yes	2 (8.0%)	4 (23.5%)	6 (14.3%)	
Other Non-Thyroid Neoplasms N (%)				
No	21 (84.0%)	14 (82.4%)	35 (83.3%)	0.888
Yes	4 (16.0%)	3 (17.6%)	7 (16.7%)	

Table S6 (TUMOR TYPE)

	PURE MTC	DOUBLE TUMORS	TOTAL	TEST (p-value)
Number of patients N (%)	30 (69.8 %)	13 (30.2 %)	43 (100 %)	
Sex N (%)				
M	12 (40.0 %);	5 (38.5 %);	17 (39.5 %);	0.925
F	18 (60.0 %)	8 (61.5 %)	26 (60.5 %)	
Age at diagnosis (yrs) Mean (SD)	53.033 (15.446)	57.385 (15.086)	54.349 (15.292)	0.398
Stage at Diagnosis N (%)				
I	18 (60.0 %);	8 (61.5 %);	26 (60.5 %);	0.869
II	1 (3.3 %);	1 (7.7 %);	2 (4.7 %);	
III	2 (6.7 %);	1 (7.7 %);	3 (7.0 %);	
IVa	7 (23.3 %);	3 (23.1 %);	10 (23.3 %);	
IVb	0 (0.0%);	0 (0.0%);	0 (0.0%);	
IVc	2 (6.7 %)	0 (0 %)	2 (4.7 %)	
Primary-tumour size (mm) Mean (SD)	11.690 (10.717)	11.115 (6.820)	11.516 (9.626)	0.860
Extrathyroid Extension N (%)				
No	28 (93.3 %);	12 (92.3 %);	40 (93.0 %);	0.903
Yes	2 (6.7 %)	1 (7.7 %)	3 (7.0 %)	
Vascular Invasion N (%)				
No	17 (56.7 %);	10 (76.9 %);	27 (62.8 %);	0.207
Yes	13 (43.3 %)	3 (23.1 %)	16 (37.2 %)	
Perineural Invasion N (%)				
No	28 (93.3 %);	13 (100 %);	41 (95.3 %);	0.340
Yes	2 (6.7 %)	0 (0 %)	2 (4.7 %)	

Encapsulated neoplasm N (%)				
No	28 (93.3 %);	13 (100 %);	41 (95.3 %);	0.340
Yes	2 (6.7 %)	0 (0 %)	2 (4.7 %)	
Capsular infiltration N (%)				
No	28 (93.3 %);	13 (100 %);	41 (95.3 %);	0.340
Yes	2 (6.7 %)	0 (0 %)	2 (4.7 %)	
Positive surgical margins N (%)				
No	28 (93.3 %);	13 (100 %);	41 (95.3 %);	0.340
Yes	2 (6.7 %)	0 (0 %)	2 (4.7 %)	
Multifocality				
N (%)				
No	20 (66.7 %);	2 (15.4 %);	22 (51.2 %);	0.002
Yes	10 (33.3 %)	11 (84.6 %)	21 (48.8 %)	
Ki-67 index				
N (%)				
0-3%	26 (86.7 %);	12 (92.3 %);	38 (88.4 %);	0.772
>3%	4 (13.3 %);	1 (7.7 %);	5 (11.6%);	
SSTR2 expression N (%)				
Negative	28 (93.3 %);	9 (69.2 %);	37 (86.0 %);	0.036
Positive	2 (6.7 %)	4 (30.8 %)	6 (14.0 %)	
INSM1 expression N (%)				
Negative	5 (16.7 %);	1 (7.7 %);	6 (14.0 %);	0.435
Positive	25 (83.3 %)	12 (92.3 %)	37 (86.0 %)	
Pre-surgery calcitonin (pg/ml)				
Mean (SD)	2 358.237 (7 771.791)	304.346 (448.672)	1 737.293 (6 532.515)	0.350
Post-surgery calcitonin (pg/ml)				
Mean (SD)	296.450 (850.384)	18.504 (23.553)	212.420 (718.444)	0.249
Last FU calcitonin (pg/ml)				
Mean (SD)	260.533 (717.964)	11.619 (19.907)	185.280 (607.795)	0.222
Last FU CEA (ng/ml)				
Mean (SD)	52.700 (165.754)	2.386 (2.442)	37.489 (139.710)	0.283

Disease-free survival (mo)	56.037	34.692	49.100	0.321
Mean (SD)	(68.437)	(48.806)	(62.912)	
Not cured at last FU				
N (%)	12 (40.0 %)	3 (23.1 %)	15 (34.9 %)	0.285
Metastasis at last FU				
N (%)	7 (23.3 %)	0 (0 %)	7 (16.3 %)	0.057

Figure SA

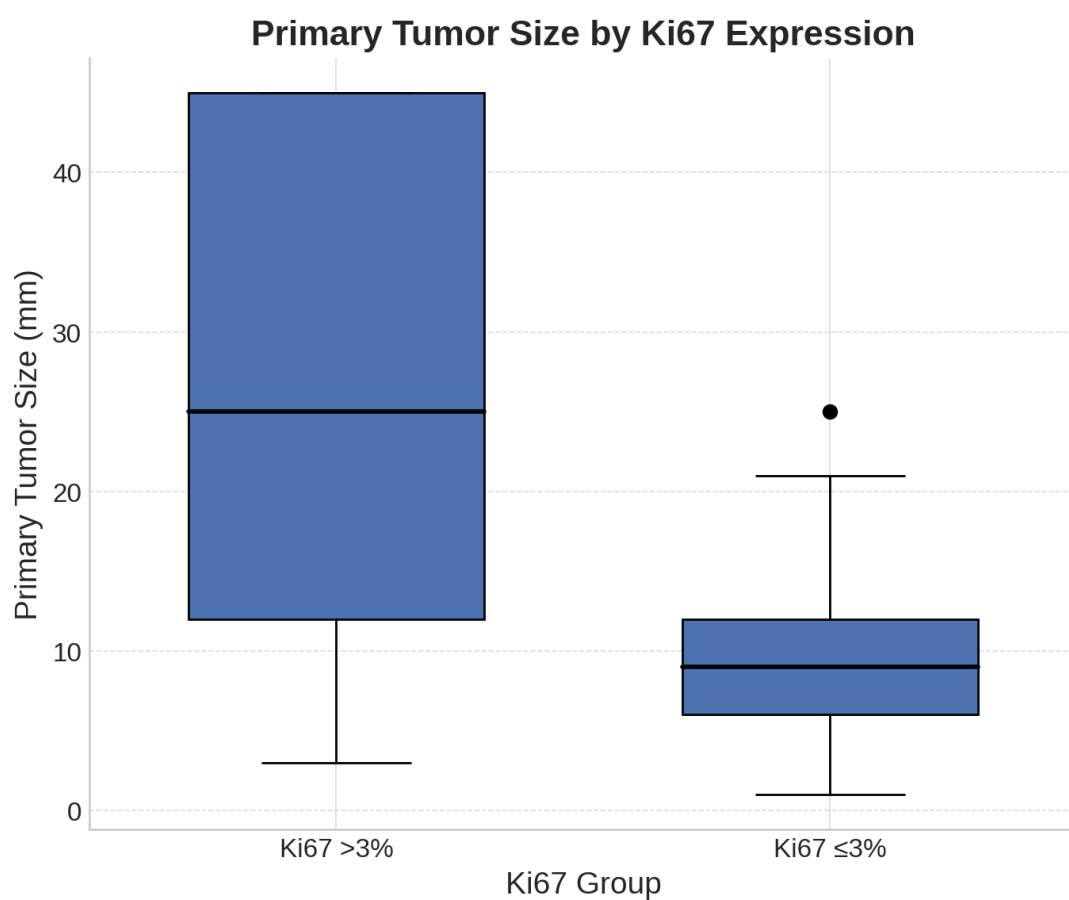


Figure SB

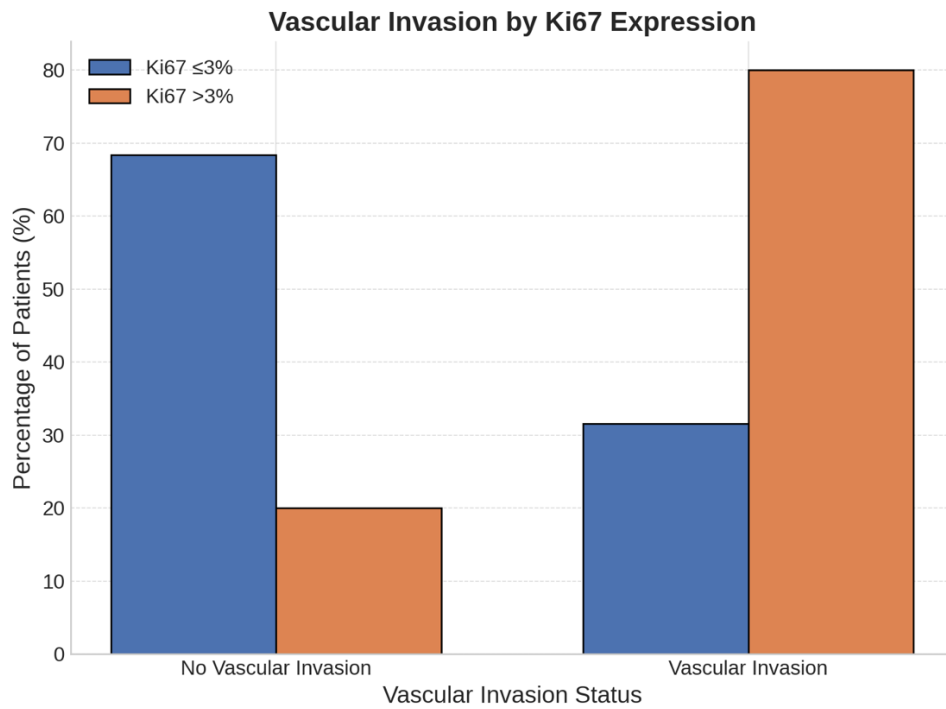


Figure SC

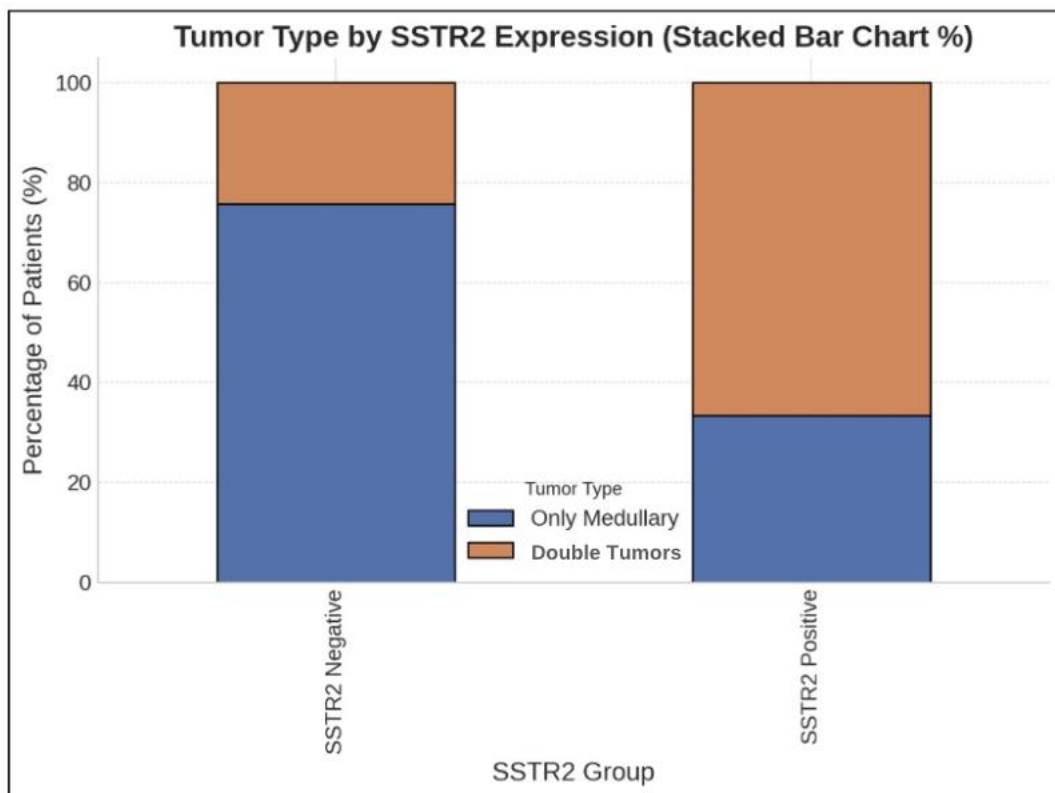


Figure SD

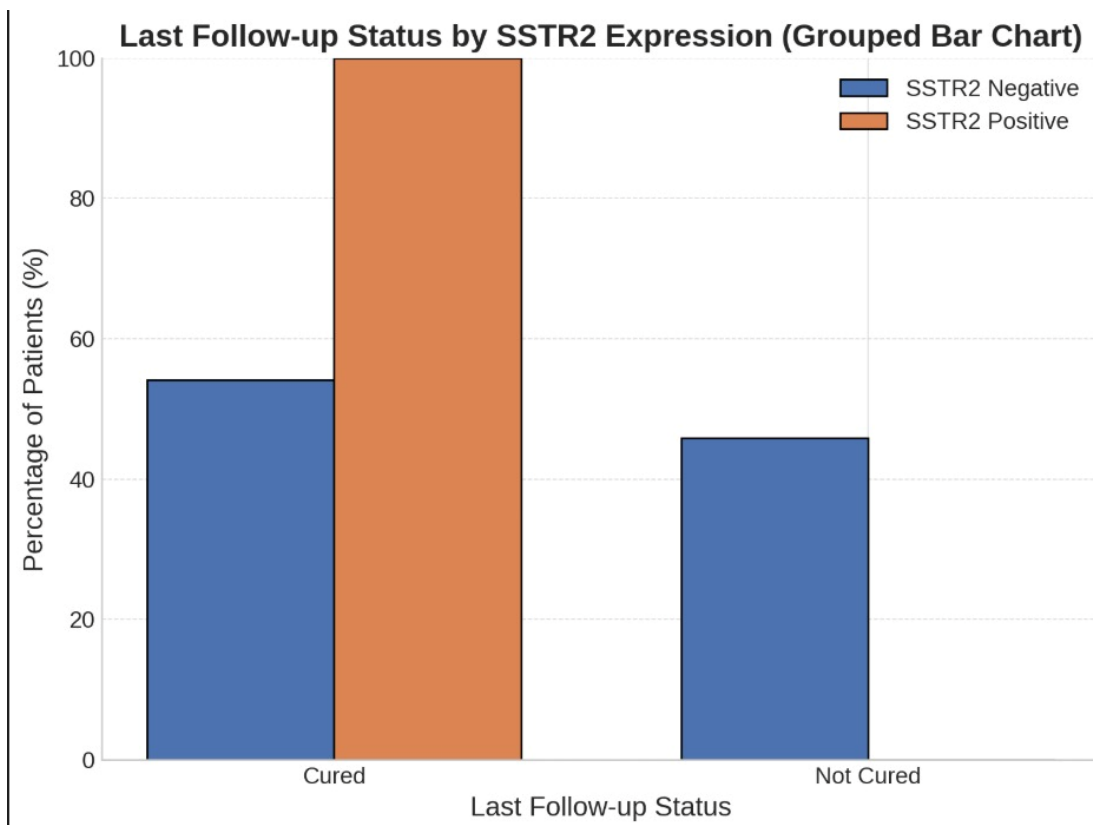


Figure SE

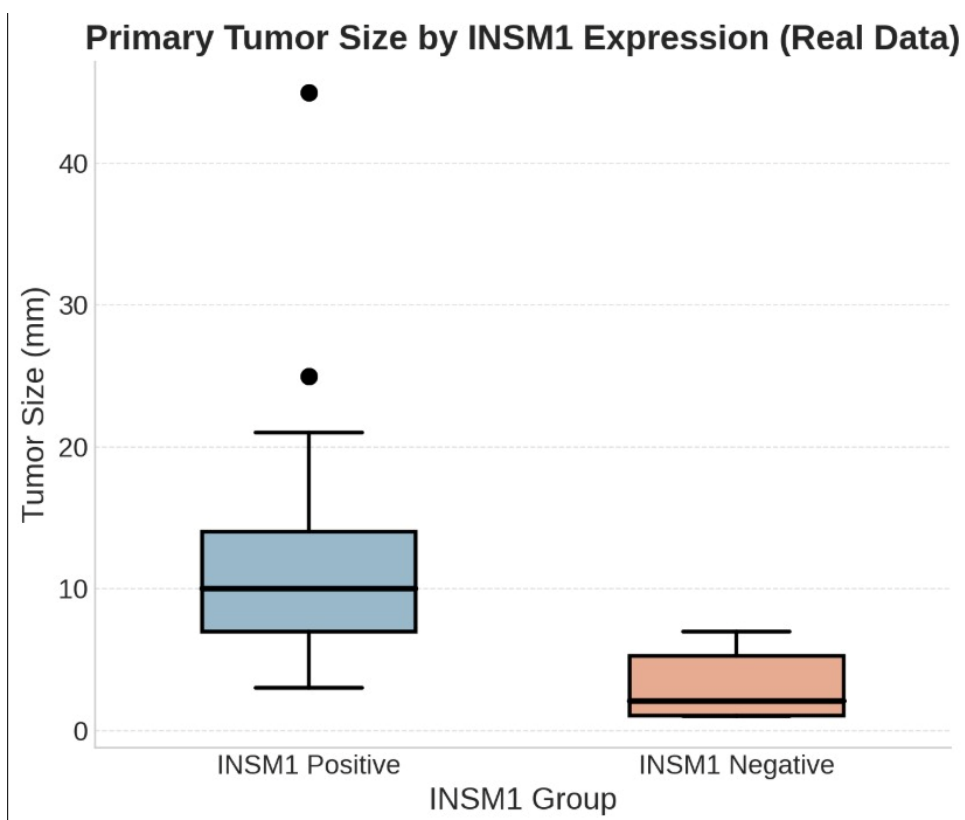


Figure SF

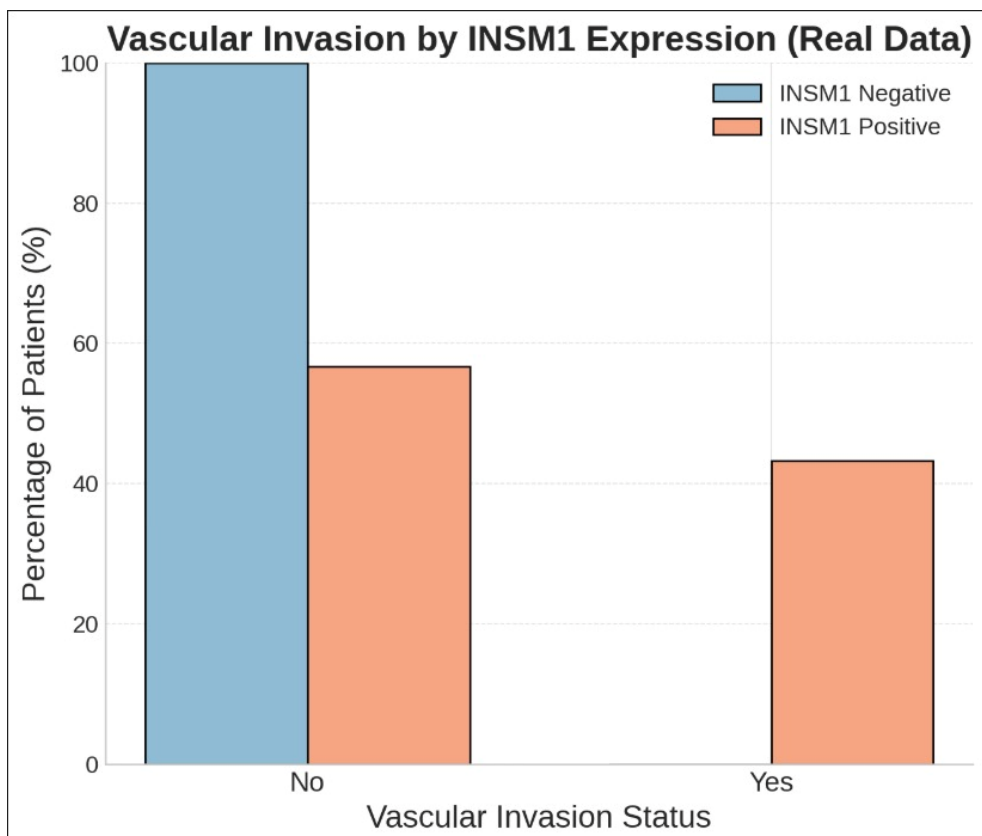


Figure SG

