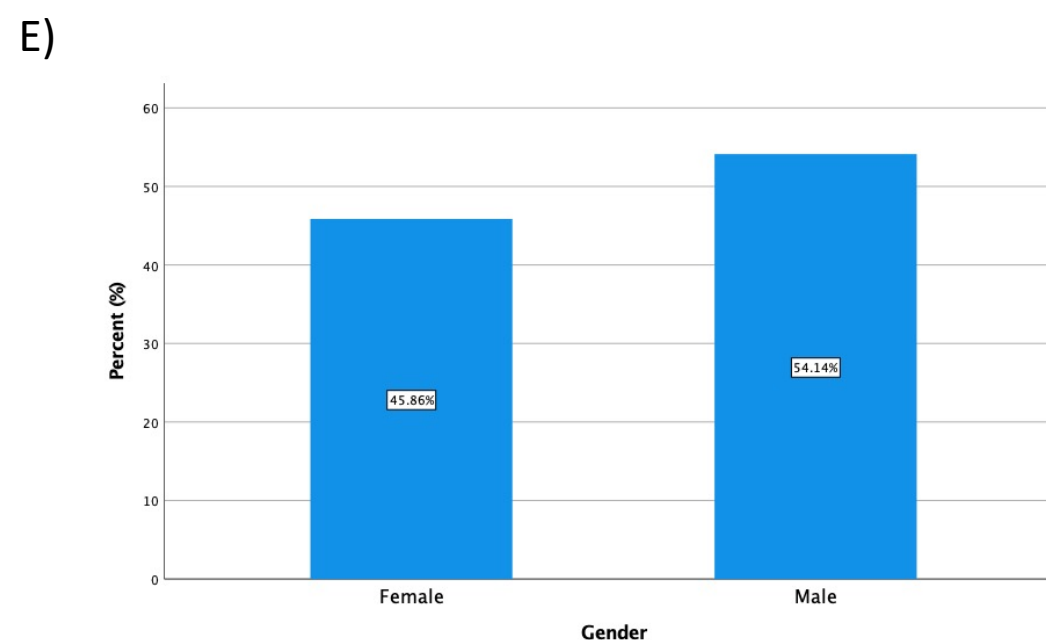
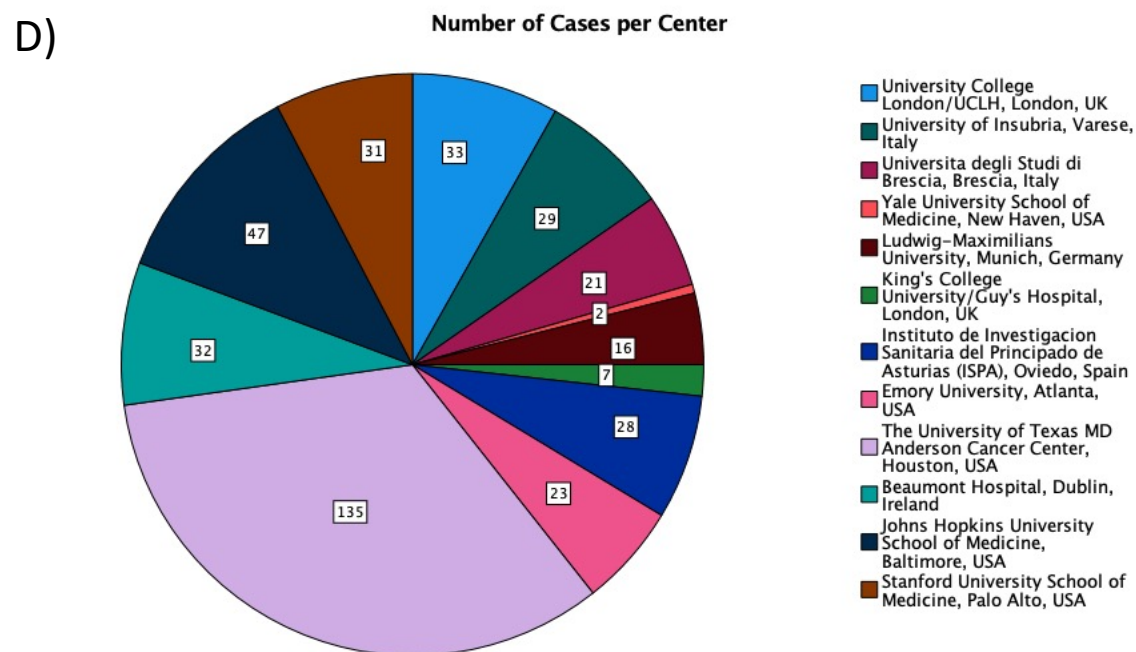
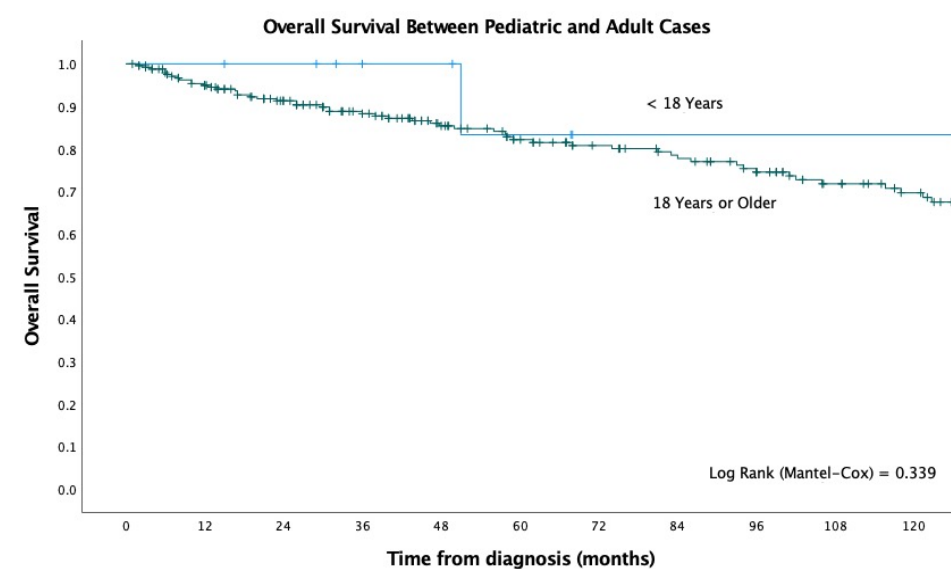
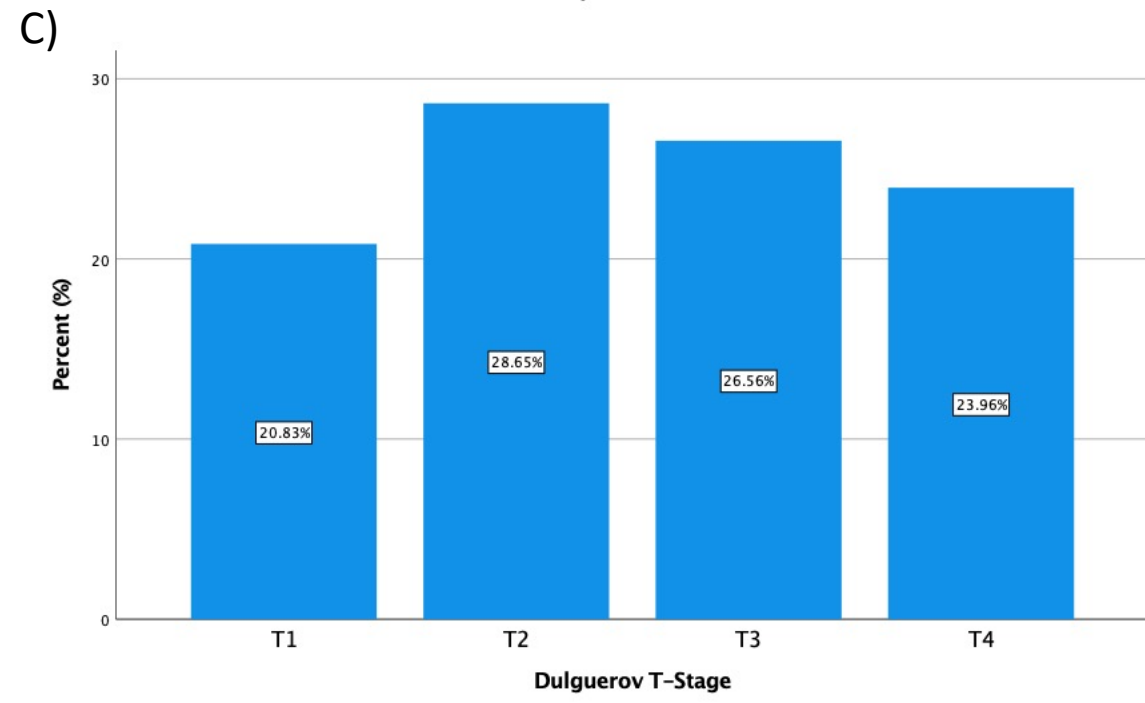
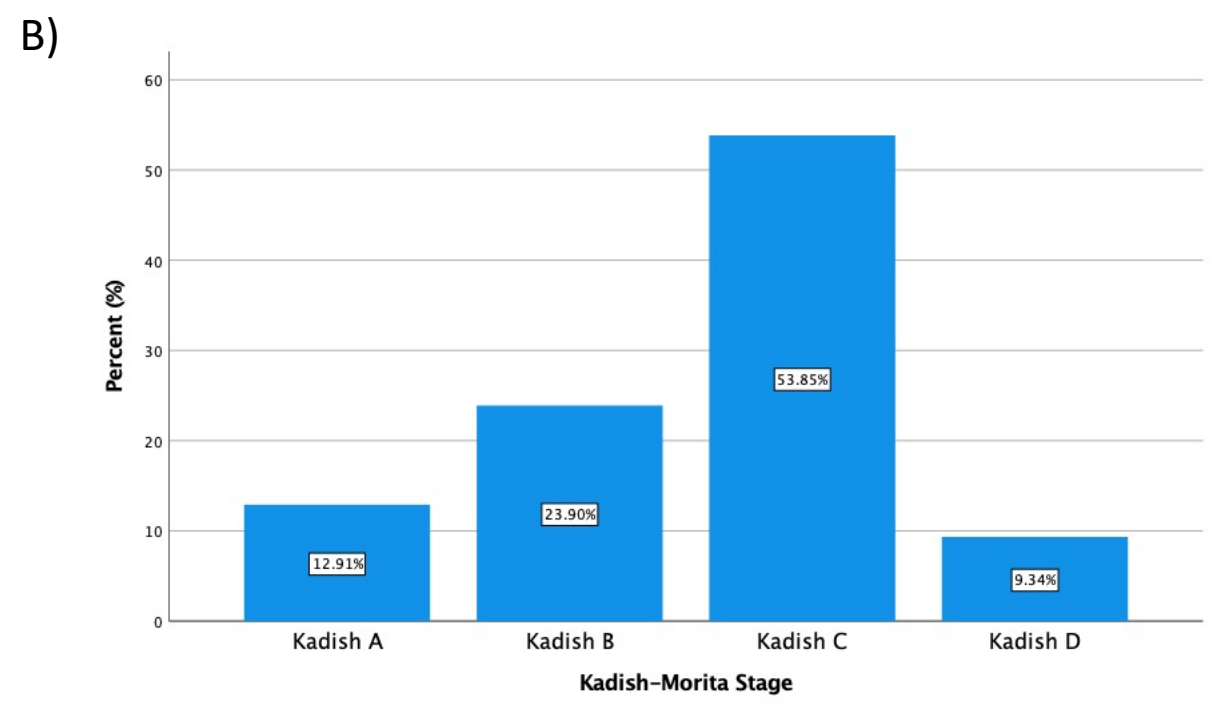
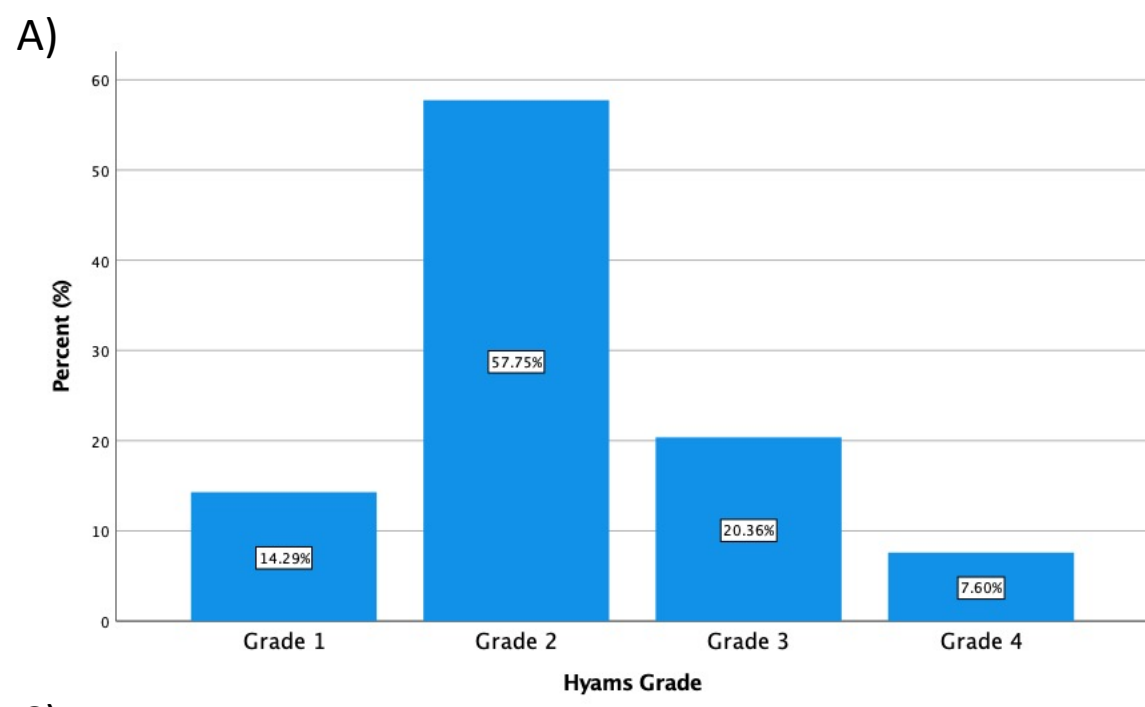


C) Clinical Characteristics of Pediatric and Adult Cases

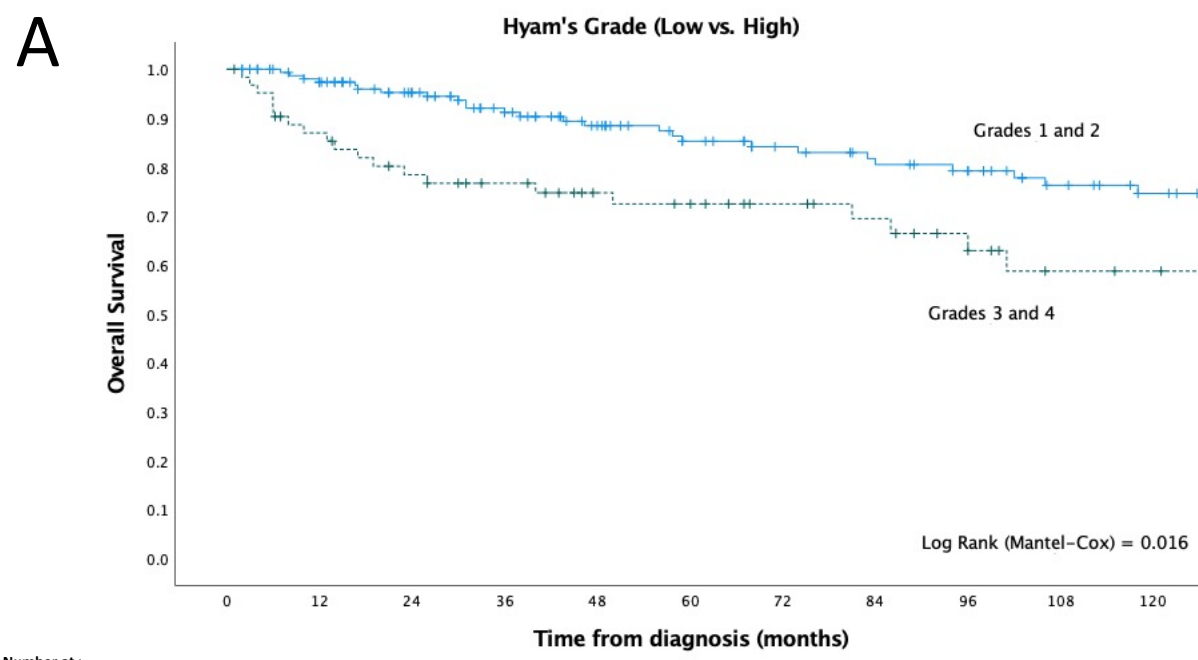
	Age < 18 Years (n=11)		Age >= 18 Years (n=262)		p-value
	N	%	N	%	
Gender					0.759
Male	5	45.5	143	54.6	
Female	6	54.5	119	45.4	
Hyam's Grade					0.076
1	4	50.0	38	16.9	
2	3	37.5	122	54.2	
3	0	0.0	46	20.4	
4	1	12.5	19	8.4	
Missing	3		37		
Kadish-Morita Stage					0.058
A	0	0.0	26	10.9	
B	0	0.0	56	23.5	
C	8	88.9	134	56.3	
D	1	11.1	22	9.2	
Missing	2		24		
Dulguerov T-Stage					0.105
T1	0	0.0	34	23.6	
T2	0	0.0	44	30.6	
T3	2	50.0	36	25.0	
T4	2	50.0	30	20.8	
Missing	8		118		
Bony Skull Base Involvement					1.000
No	2	22.2	55	27.9	
Yes	7	77.8	142	72.1	
Missing	3		65		
Dural Infiltration					0.739
No	4	44.4	98	52.7	
Yes	5	55.6	88	47.3	
Missing	3		76		
Intracranial Involvement					0.059
No	0	0.0	66	49.6	
Yes	5	100.0	67	50.4	
Missing	7		129		
Orbital Involvement					0.051
No	2	40.0	109	82.0	
Yes	3	60.0	24	18.0	
Missing	6		129		



Supplemental Figure 1. A) Bar graph representing tumour status at presentation for all cases; B) histograms of the age distribution in all cases and in primary cases only, demonstrating a unimodal distribution C) Clinical characteristics of pediatric and adult cases and overall survival curve demonstrating similar outcome between the two subgroups. D) Pie chart illustrating distribution of cases by center. E) Bar graph presenting gender distribution for all cases.

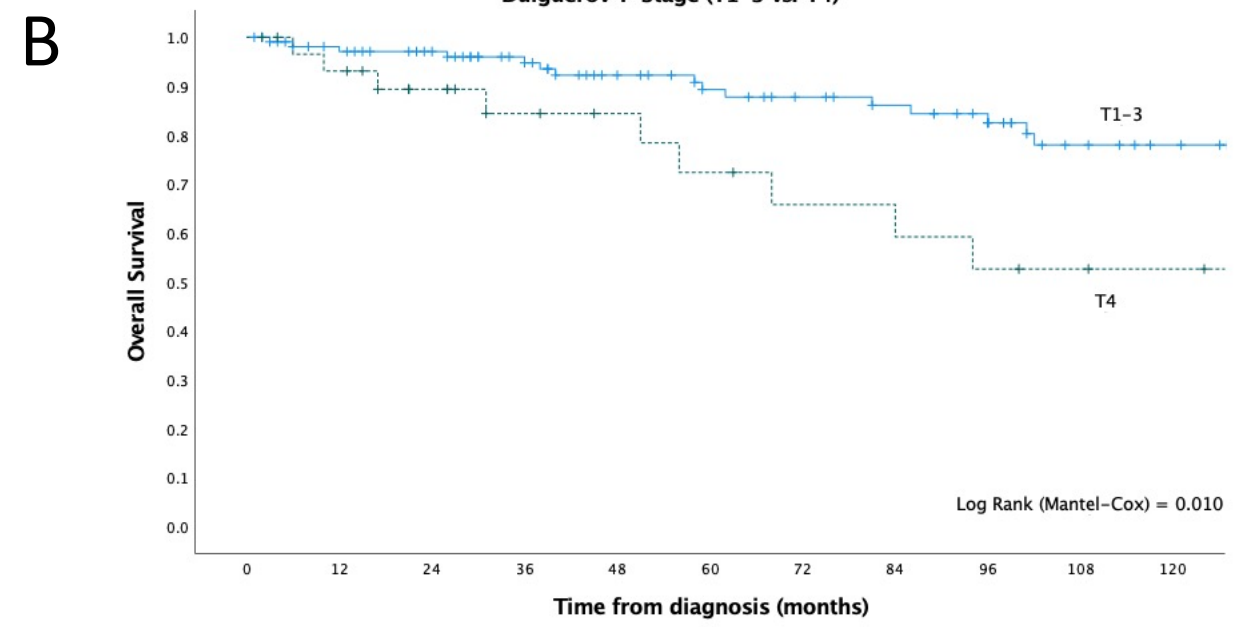


Supplemental Figure 2. A) – C) Bar graphs illustrating percentage of cases for each stage/grade group for each of Hyams Grade, Kadish-Morita Stage and Dulguerov T-Stage.



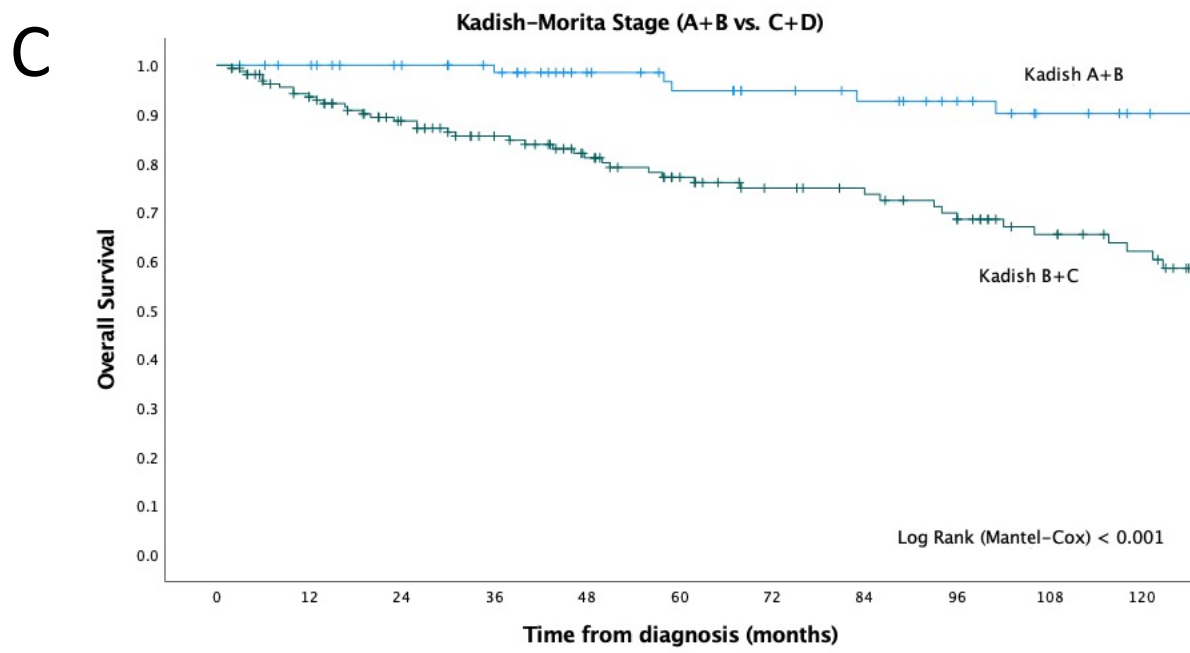
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Grades 1 and 2 (n = 161)	161	145	126	106	91	79	71	65	59	50	44
Grades 3 and 4 (n = 63)	63	52	45	40	33	31	26	23	17	13	12



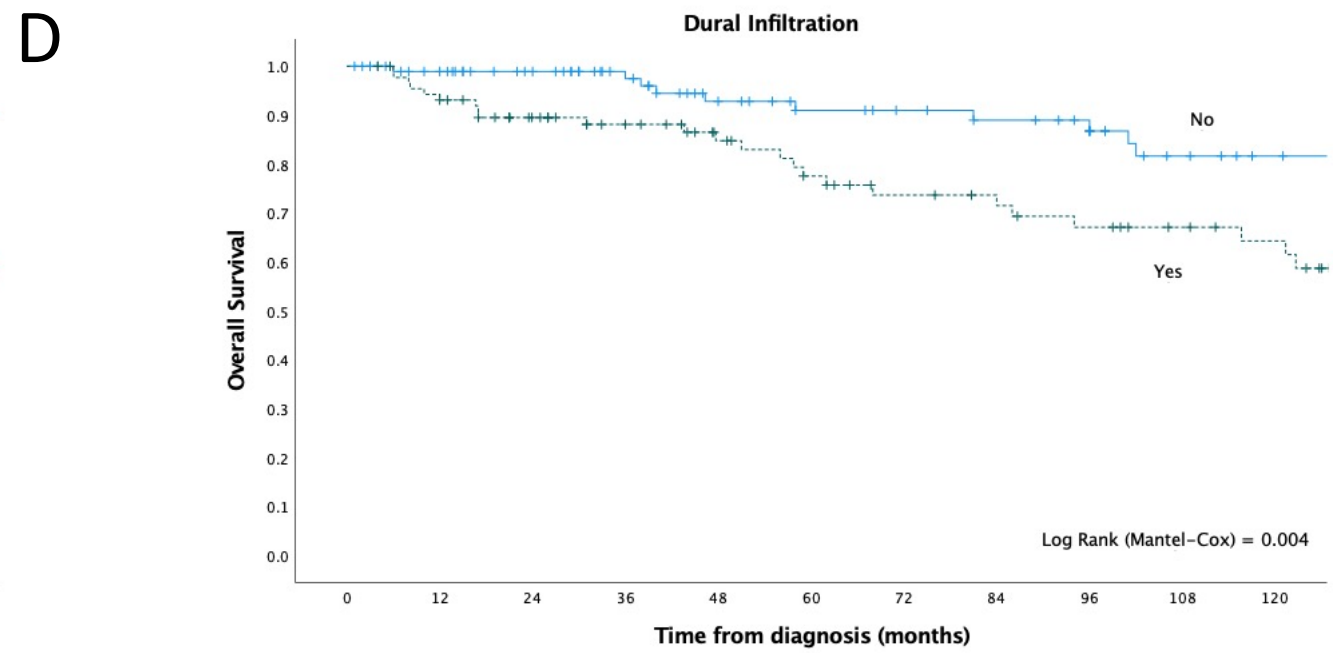
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
T1-3 (n = 108)	108	97	89	77	66	59	54	50	41	32	28
T4 (n = 31)	31	27	21	16	14	12	10	9	8	7	6



Number at risk

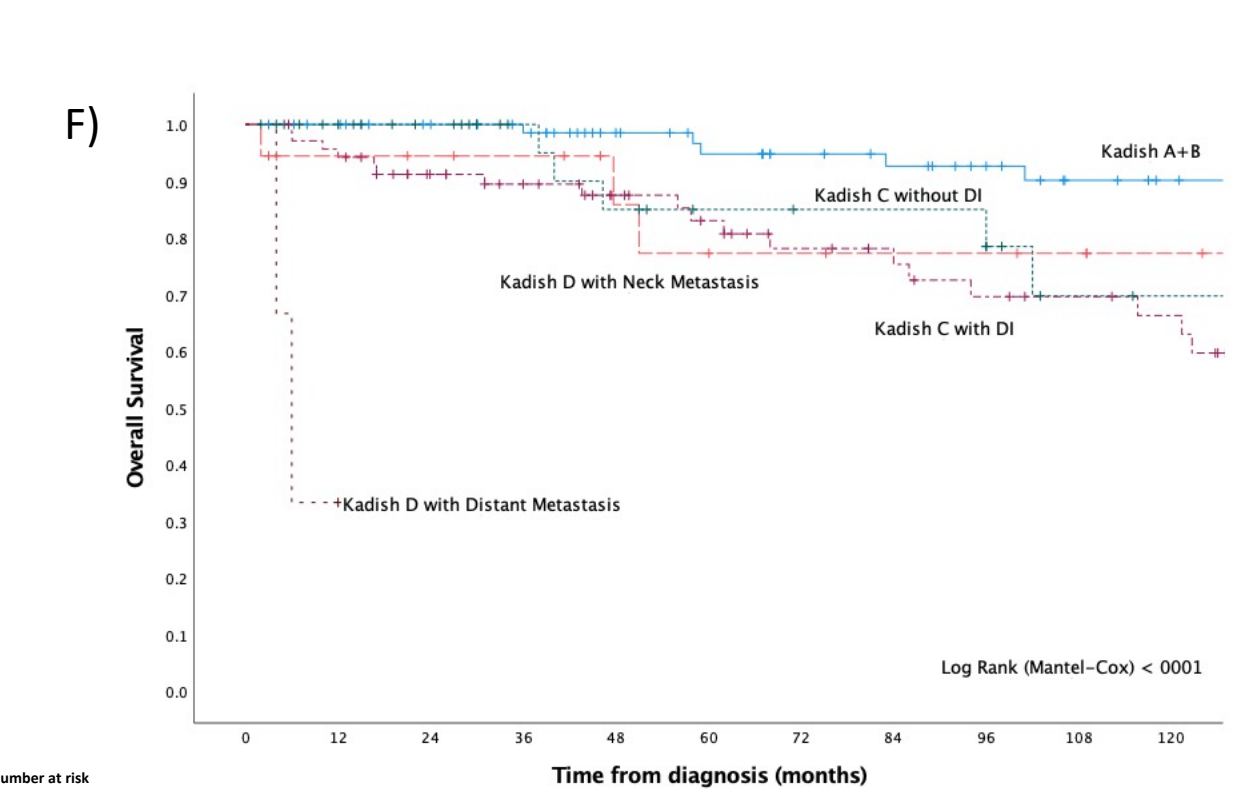
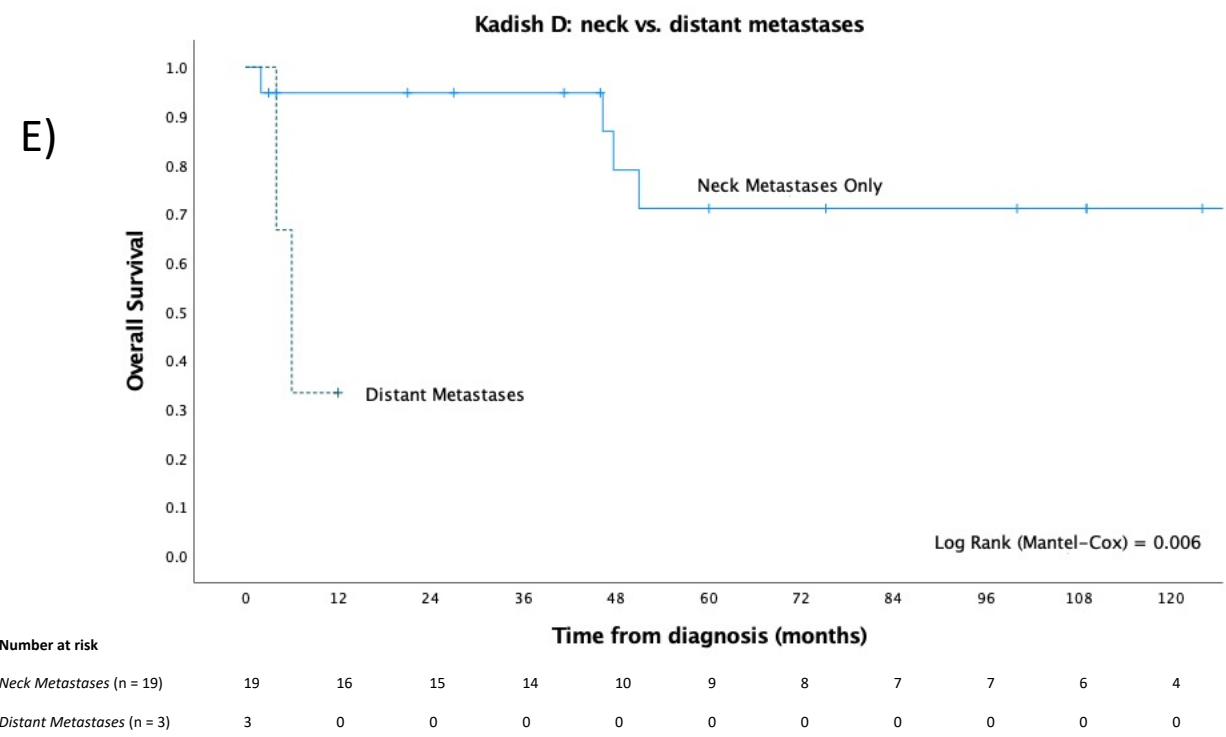
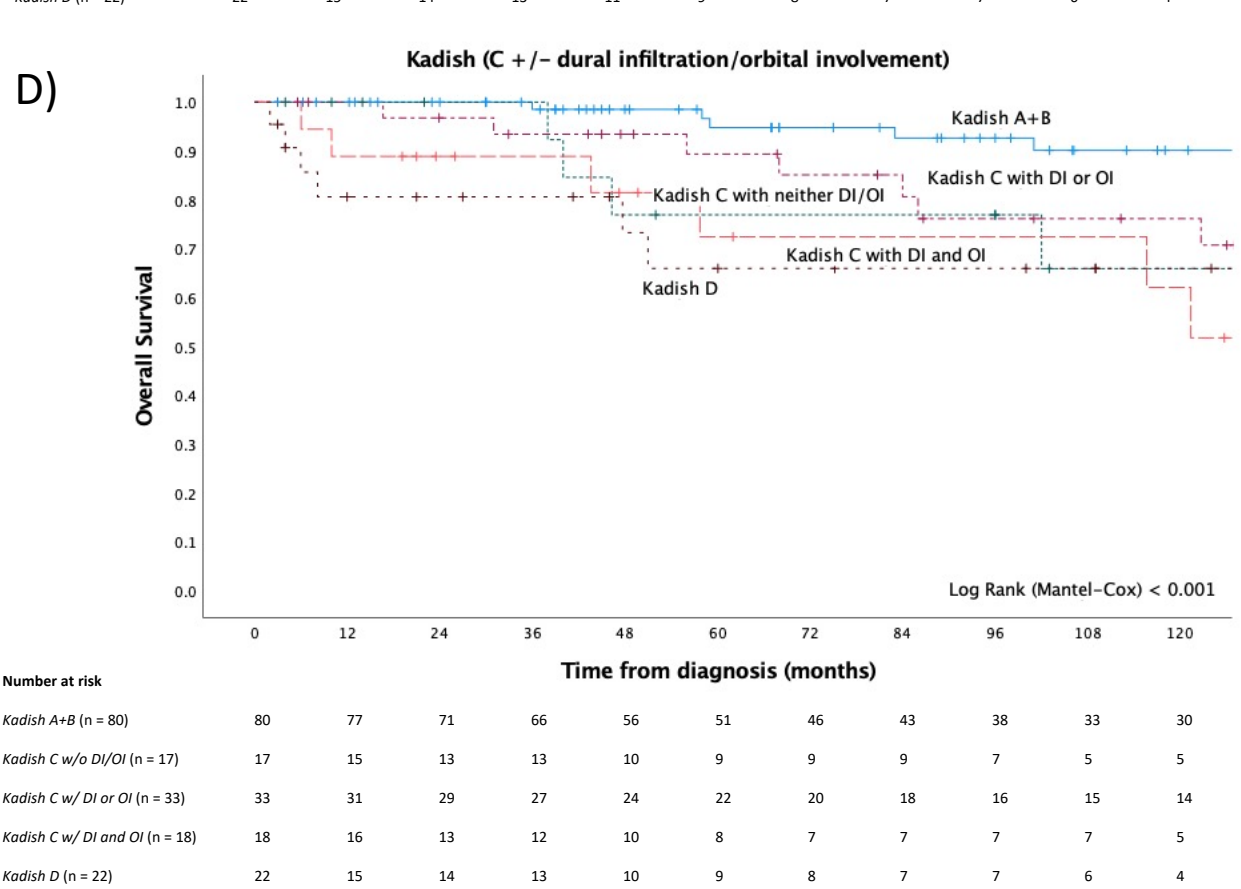
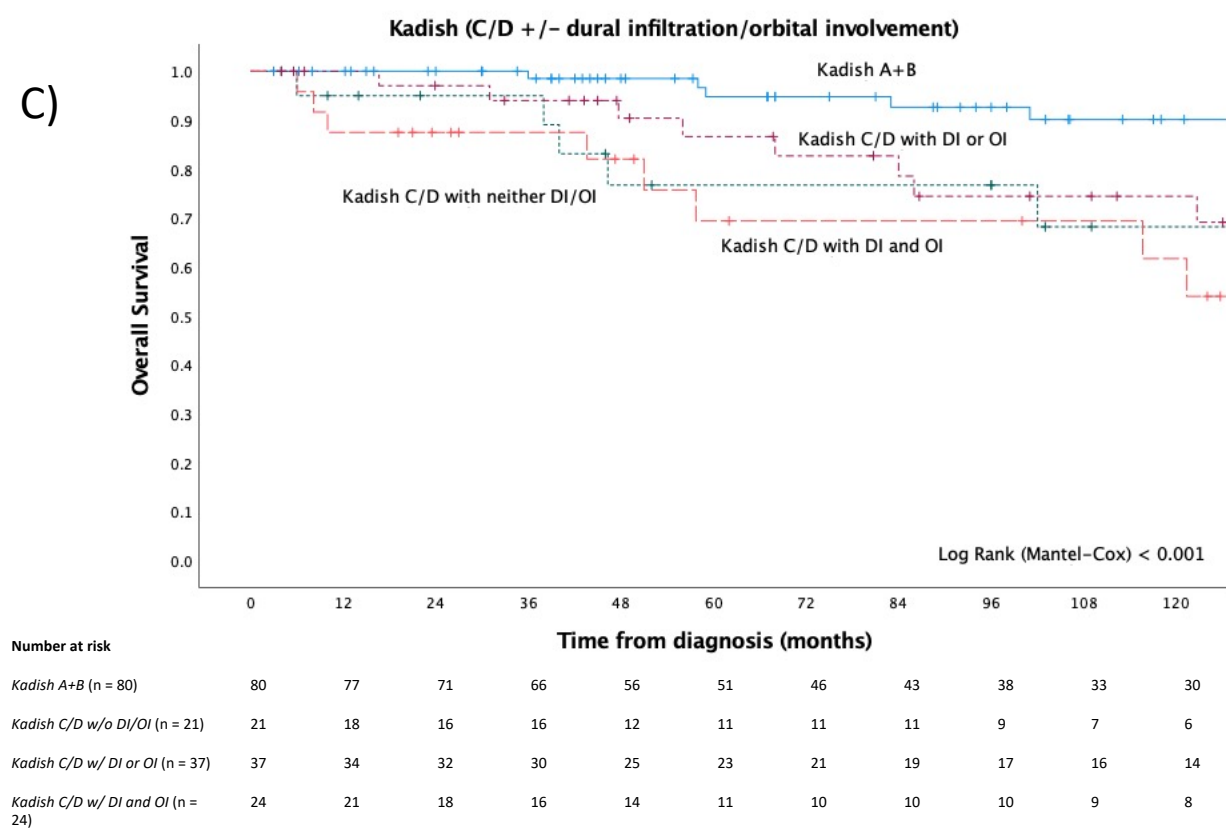
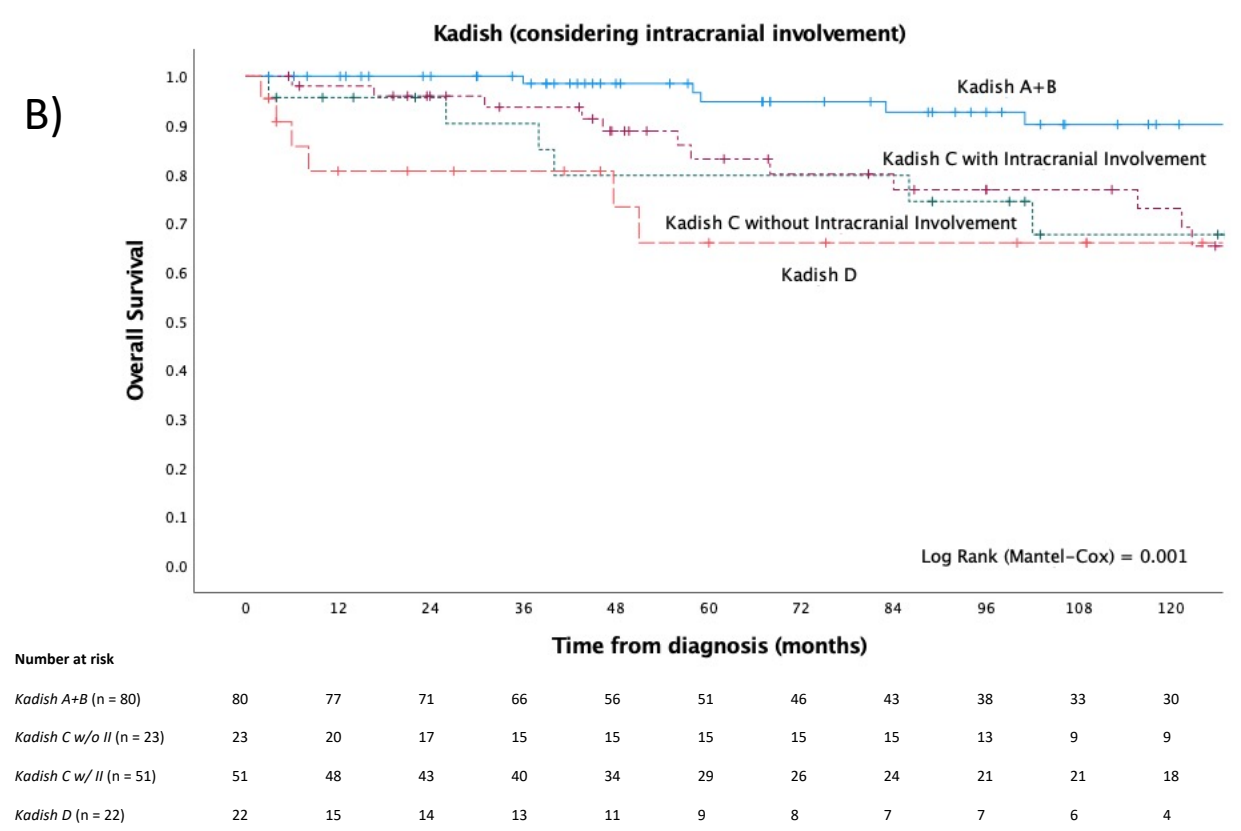
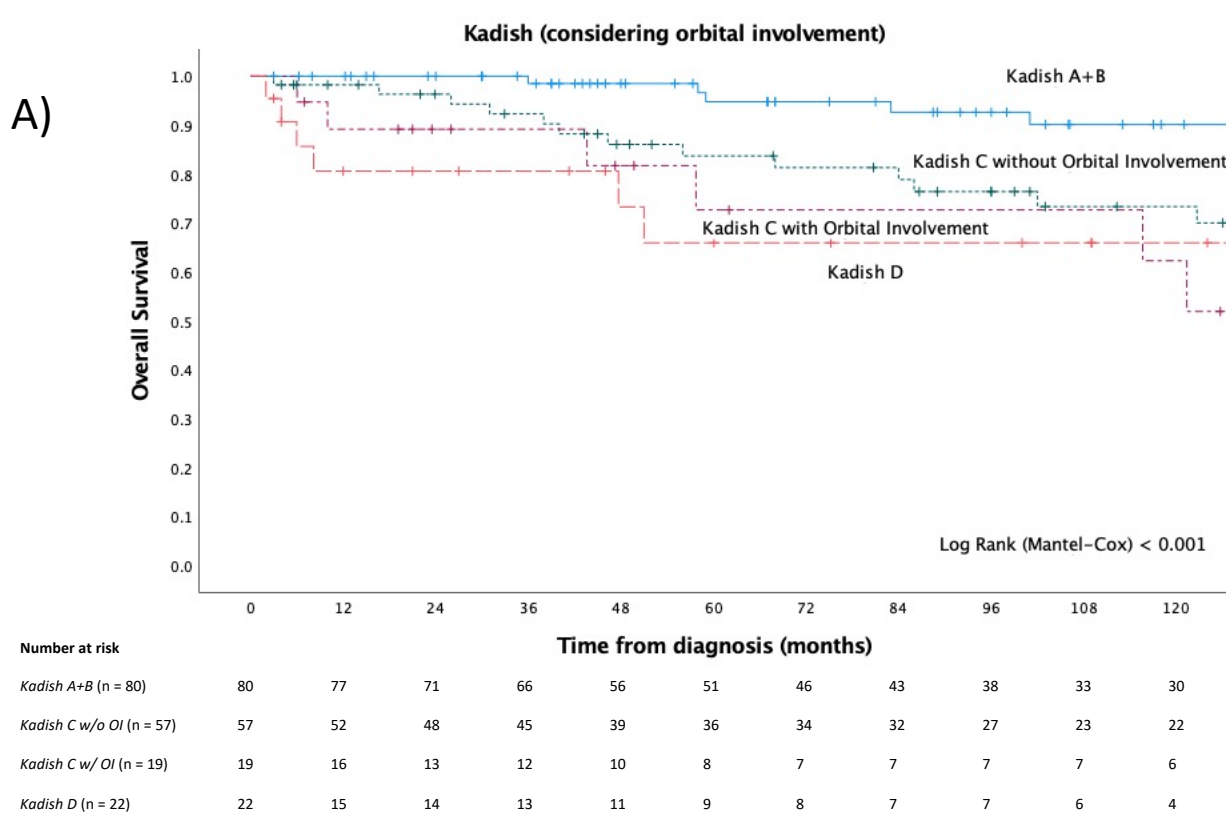
	0	12	24	36	48	60	72	84	96	108	120
Kadish A+B (n = 80)	80	77	71	66	56	51	46	43	38	33	30
Kadish C+D (n = 161)	161	139	118	101	86	73	63	59	51	42	36



Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Dural Infiltration (n = 89)	89	80	68	58	49	42	36	33	30	26	23
None (n = 99)	99	88	78	67	55	49	46	43	36	30	26

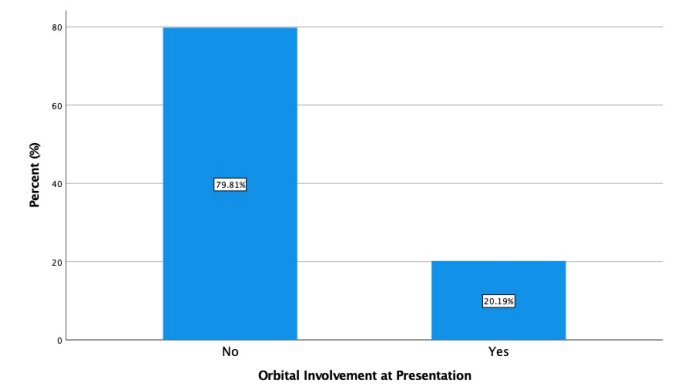
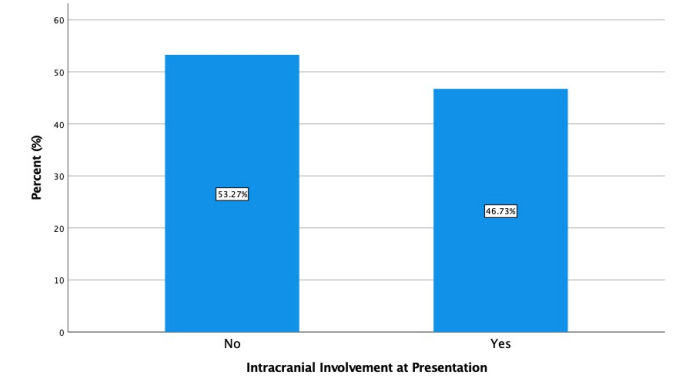
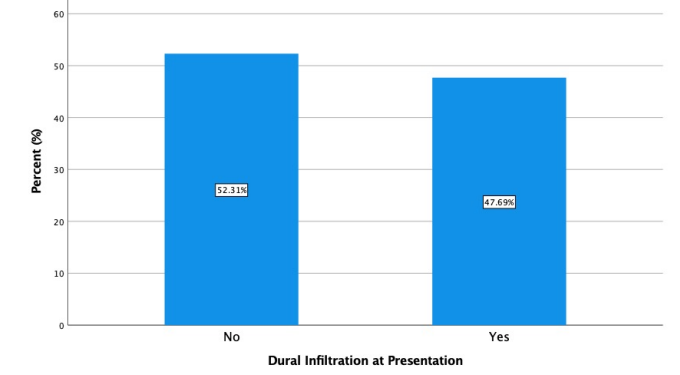
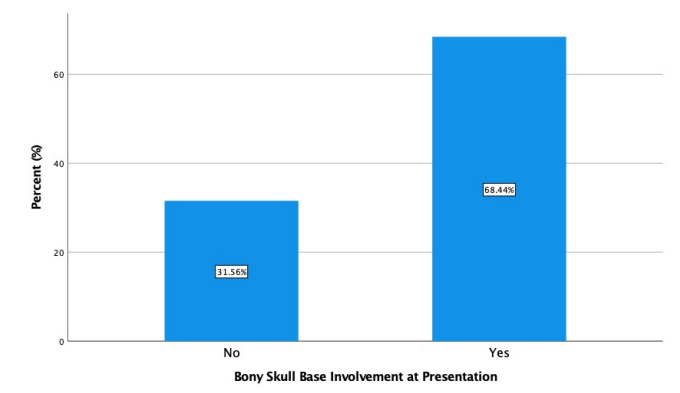
Supplemental Figure 3. A) – C) Additional Kaplan-Meier survival analyses of Dulguerov T-stage dichotomized into T1-3 vs. T4 and Kadish-Morita stage dichotomized into A+B vs. C+D, respectively; D) Kaplan-Meier survival analysis of dural infiltration.



Supplemental Figure 3. Additional Kaplan Meier survival analyses of A)-B) Kadish A+B, Kadish C stratified into those presenting with or without orbital involvement or intracranial involvement, respectively, and Kadish D; C) Kadish A+B, Kadish C/D stratified into those presenting without either of dural infiltration or orbital involvement, those presenting with one or the other or those presenting with both, D) Kadish A+B, Kadish C stratified into those presenting without either of dural infiltration or orbital involvement, those presenting with one or the other or those presenting with both, and Kadish D, E) Kadish D cases presenting with either neck metastases only or with distant metastases; F) Kadish A+B, Kadish C stratified by presentation with or without dural infiltration, Kadish D stratified by neck or distant metastases.

A)

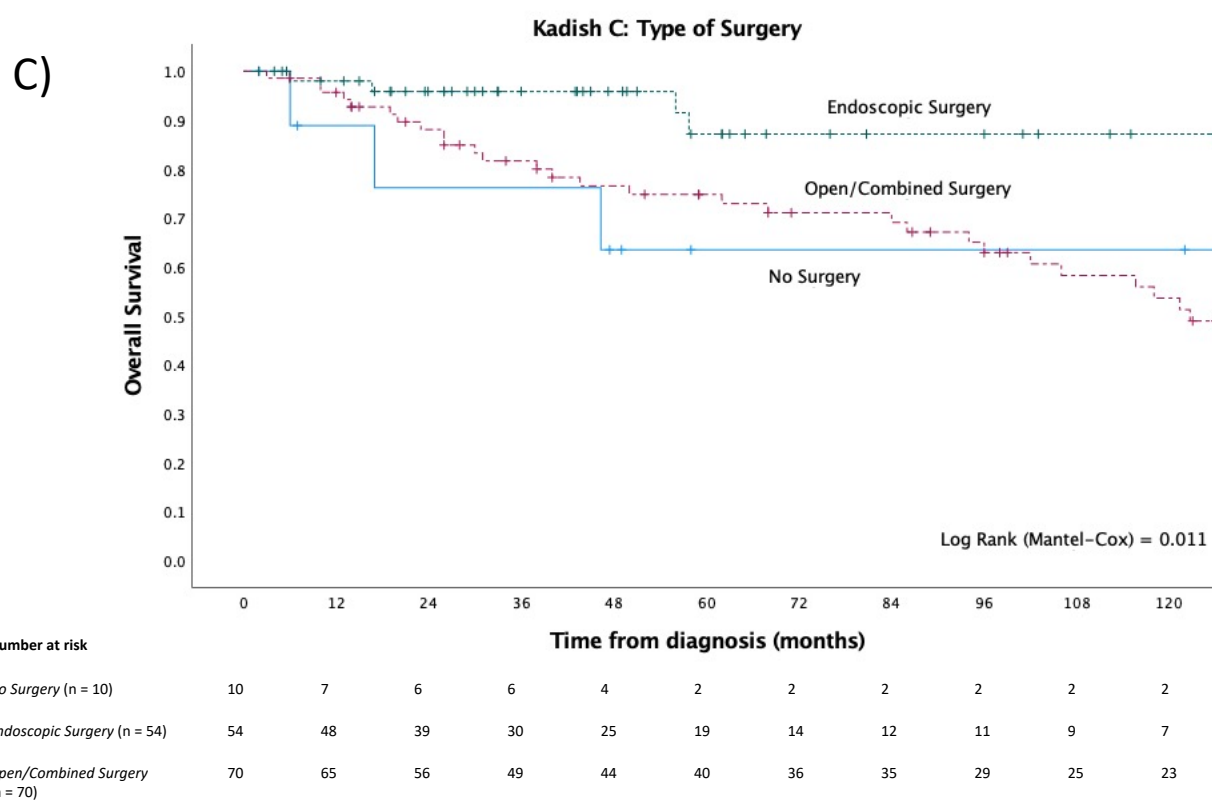
	Kadish A		Kadish B		Kadish C		Kadish D	
	n	%	n	%	n	%	n	%
Bony Skull Base Involvement								
Yes	5	21.7	19	43.2	105	92.9	16	84.2
No	18	78.3	25	56.8	8	7.1	3	15.8
Dural Infiltration								
Yes	0	0.0	3	9.4	71	65.7	13	72.2
No	22	100.0	29	90.6	37	34.3	5	27.8
Intracranial Involvement								
Yes	0	0.0	3	11.1	51	68.9	12	66.7
No	8	100.0	24	88.9	23	31.1	6	33.3
Orbital Involvement								
Yes	0	0.0	0	0.0	19	25.0	6	35.3
No	8	100.0	27	100.0	57	74.0	11	64.7



B)

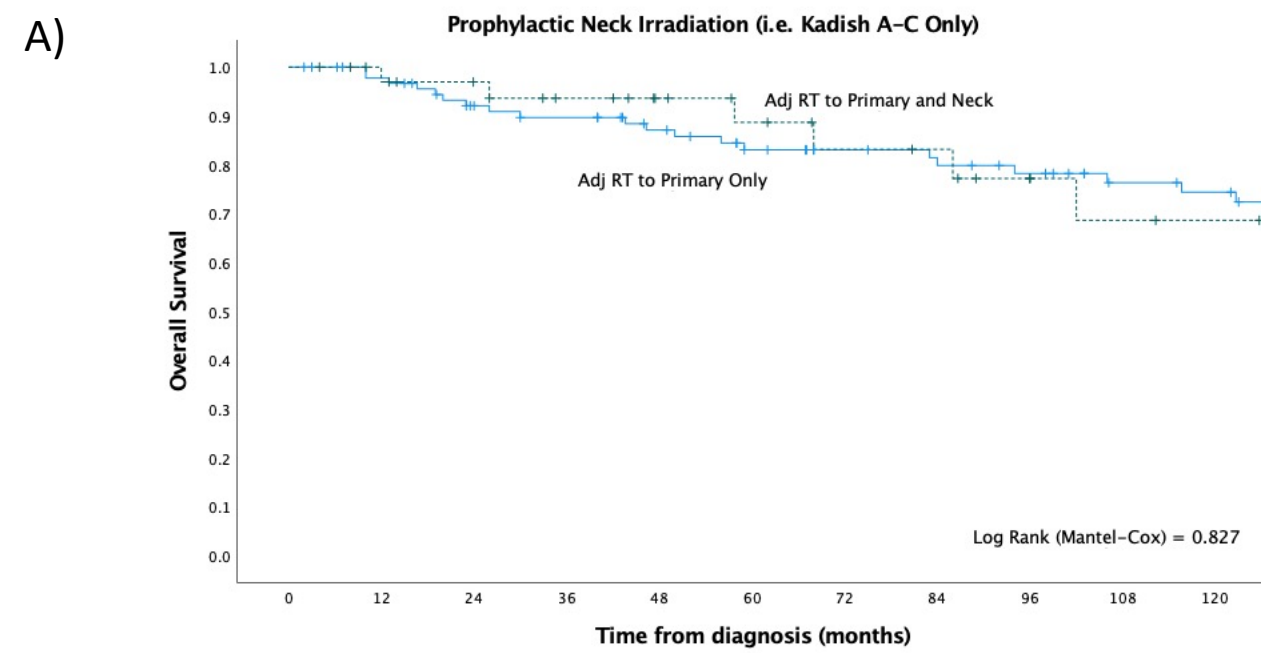
		Induction Chemotherapy			
		No	Yes	Total	
Kadish-Morita Stage	Kadish A	18	1	19	$p = 0.054$
	Kadish B	50	4	54	
	Kadish C	99	13	112	
	Kadish D	11	10	21	
	Total	178	28	206	
	Kadish A+B	68	5	73	
	Kadish C+D	110	23	133	
Total	178	28	206		
Dural Infiltration	Yes	61	16	77	$p = 0.050$
	No	76	8	84	
	Total	137	24	161	

*Fisher's Exact Test, 2-sided



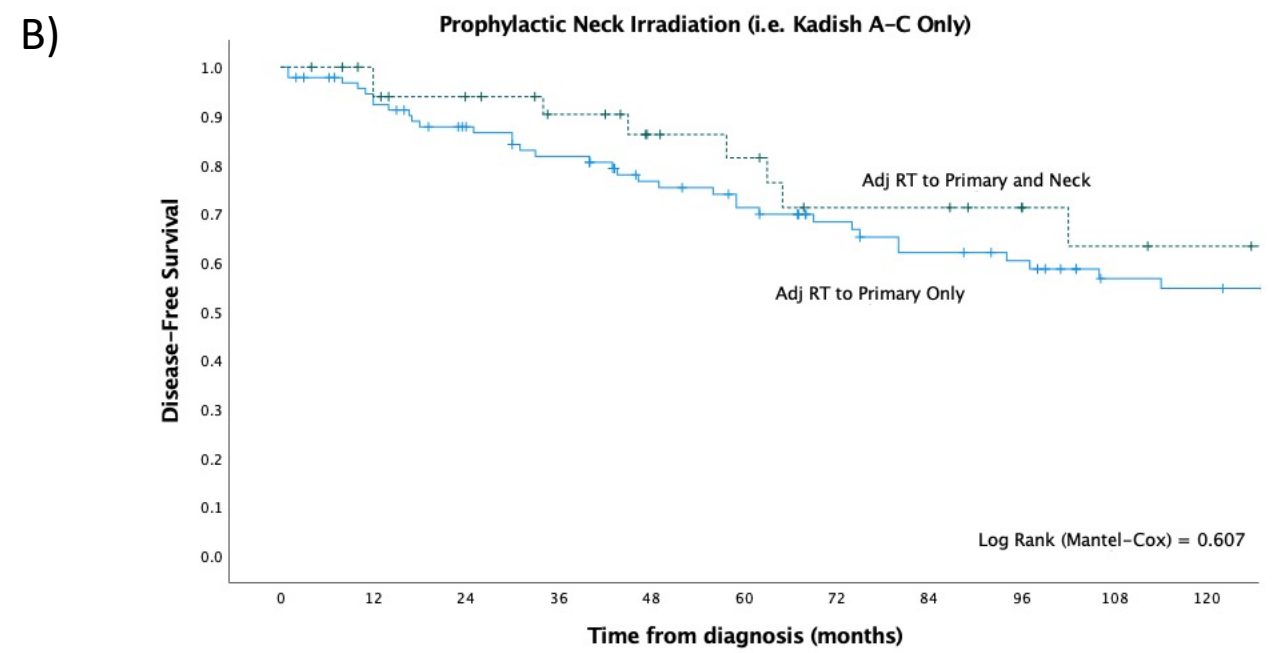
		Surgical Approach		
		No Surgery (n=10)	Endoscopic (n=56)	Open/Combined (n=70)
Bony Skull Base Involvement	No (n=8)	12.5%	62.5%	25.0%
	Yes (n=102)	4.9%	48.0%	47.1%
Dural Infiltration	No (n=36)	5.6%	52.8%	41.7%
	Yes (n=69)	5.8%	50.7%	43.5%
Dural Resection	No (n=18)	5.6%	55.6%	38.9%
	Yes (n=90)	0.0%	48.9%	41.1%
Intracranial Involvement	No (n=22)	0.0%	27.3%	72.7%
	Yes (n=51)	9.8%	43.1%	47.1%
Orbital Involvement	No (n=56)	3.6%	35.7%	60.7%
	Yes (n=19)	15.8%	42.1%	42.1%
Adjuvant Radiotherapy	No (n=13)	15.4%	30.8%	53.8%
	Yes (n=121)	6.6%	43.0%	50.4%

Supplemental Figure 4. A) Prevalence of bony skull base involvement, dural infiltration, intracranial involvement and orbital involvement by Kadish stage and accompanying bar graph of overall prevalence for primary cases. B) Numbers of patients who received induction chemotherapy based on Kadish-Morita stage and presence of dural infiltration at presentation; C) Kaplan-Meier overall survival analysis of surgical approach in Kadish C cases only with corresponding table of clinical characteristics.



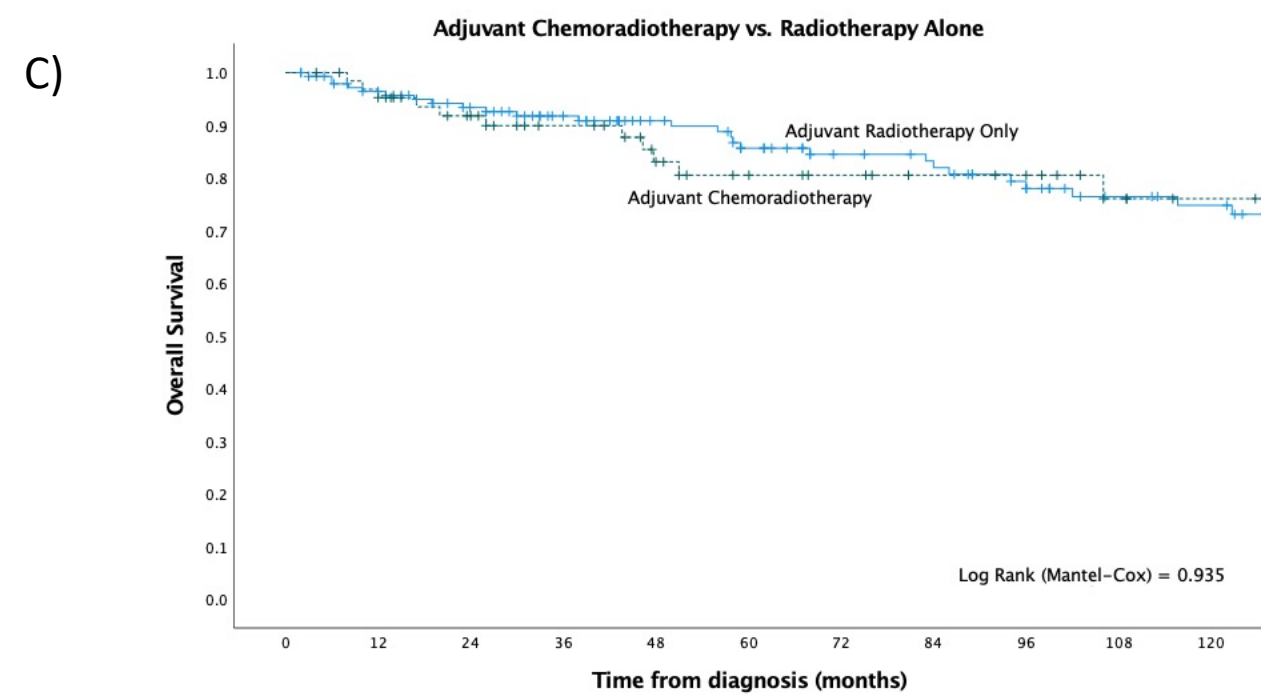
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Adj RT to Primary and Neck (n = 36)	36	32	29	25	21	18	15	14	9	8	7
Adj RT to Primary Only (n = 94)	94	88	77	74	67	59	53	50	47	40	38



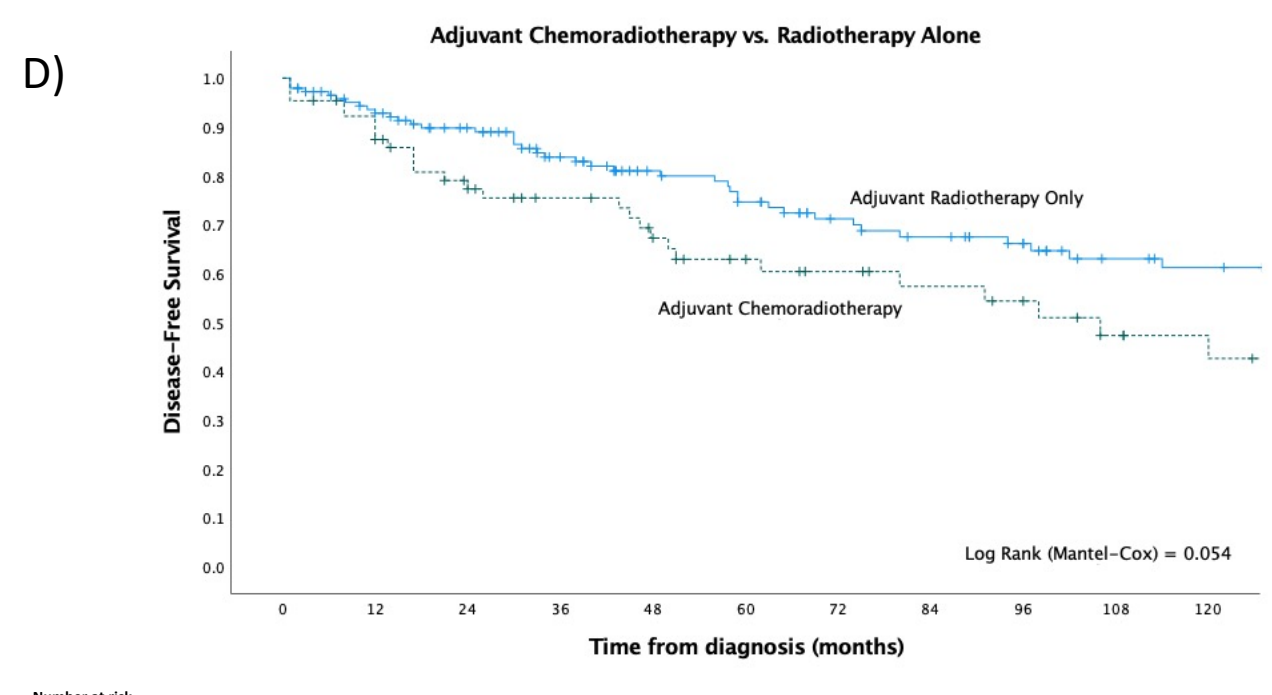
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Adj RT to Primary and Neck (n = 36)	36	31	28	24	19	17	13	13	9	8	7
Adj RT to Primary Only (n = 94)	94	83	73	67	58	52	44	39	36	28	27



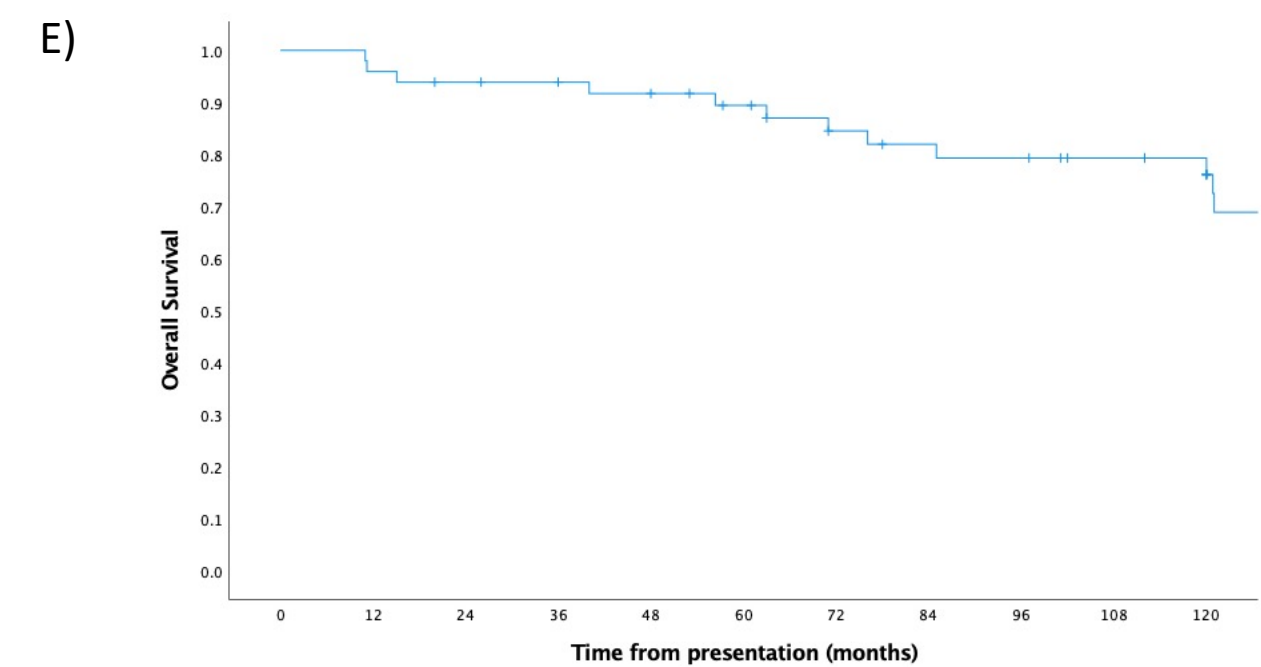
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Adj. RT Only (n = 145)	145	131	117	102	89	79	69	65	55	48	45
Adj. CRT (n = 65)	65	59	50	43	34	29	26	23	21	16	13



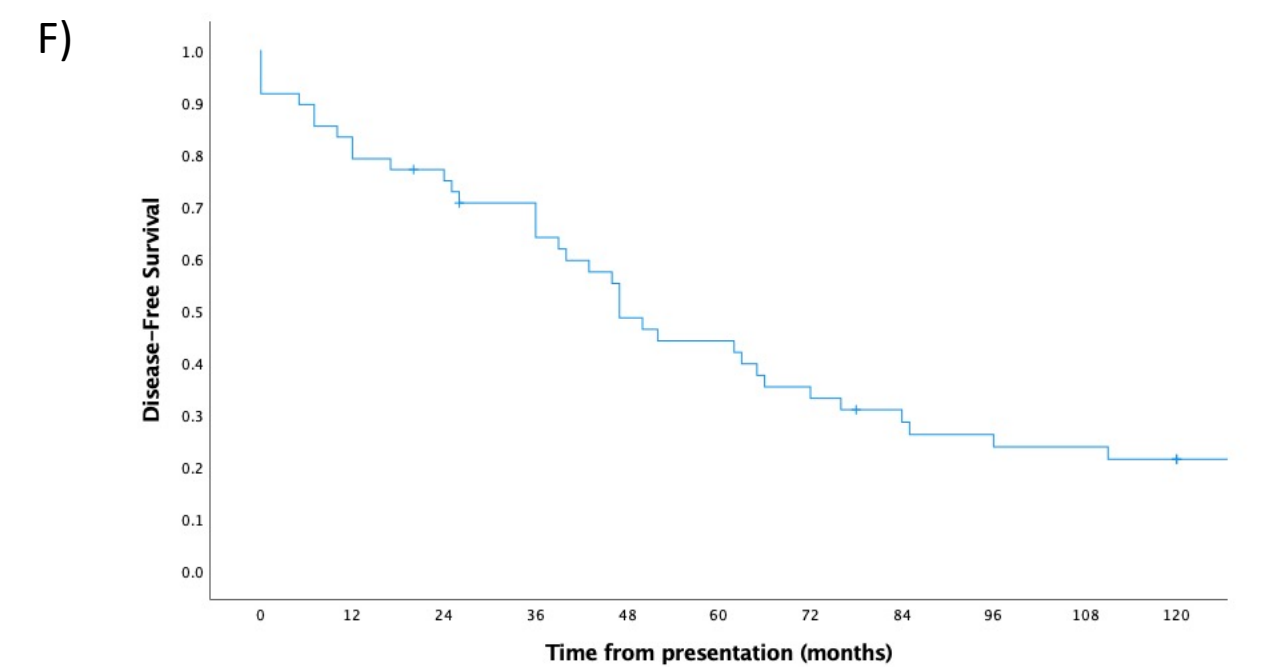
Number at risk

	0	12	24	36	48	60	72	84	96	108	120
Adj. RT Only (n = 144)	144	125	111	92	77	69	58	53	45	37	34
Adj. CRT (n = 65)	65	54	43	38	31	26	22	19	16	12	9



Number of Events

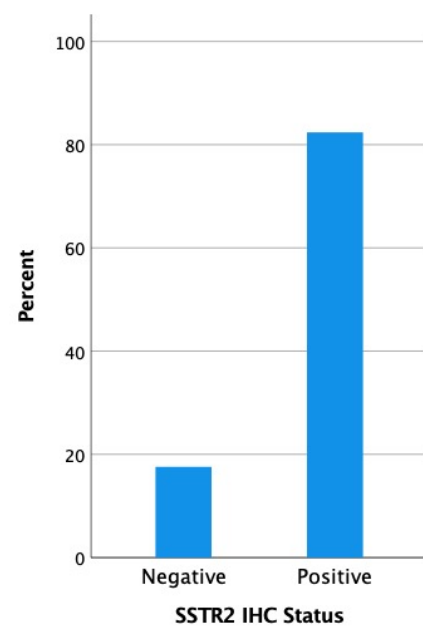
	0	12	24	36	48	60	72	84	96	108	120
Number of Events	0	2	3	3	4	5	7	8	9	9	10
Number at Risk	49	47	45	43	41	38	33	31	30	27	21



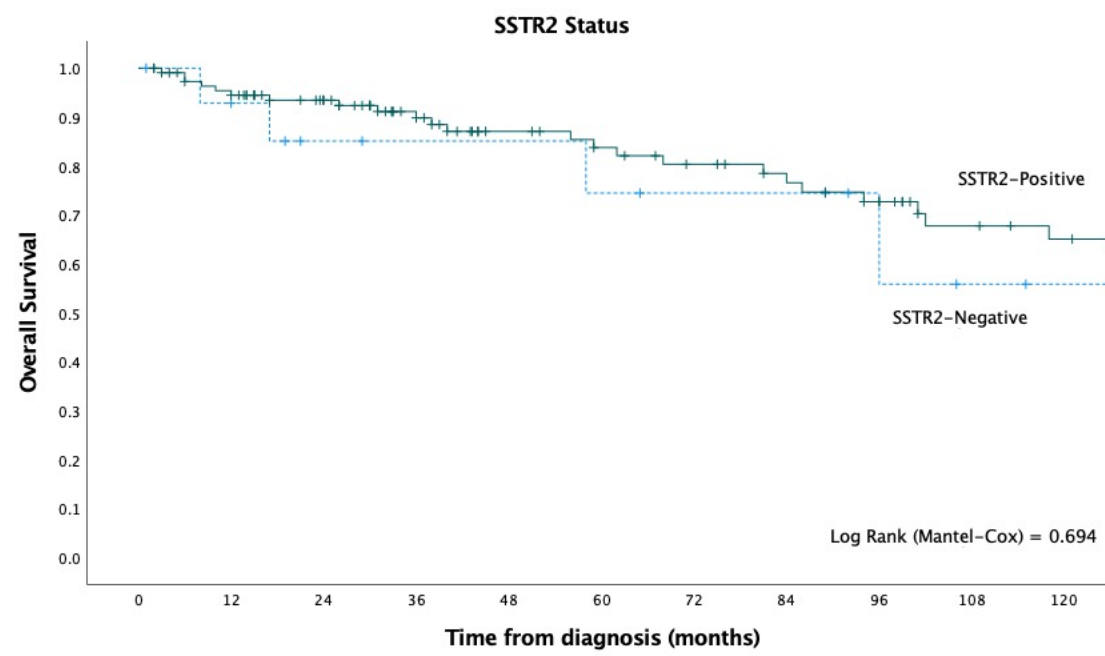
Number of Events

	0	12	24	36	48	60	72	84	96	108	120
Number of Events	0	10	12	17	24	26	31	33	35	35	36
Number at Risk	48	38	35	29	22	20	15	12	10	10	7

Supplemental Figure 5. Additional Kaplan-Meier survival analyses of A)-B) overall and disease-free survival between those who receive prophylactic neck irradiation (i.e. Kadish A-C cases only) and those who do not, respectively; C)-D) overall and disease-free survival comparing adjuvant chemoradiotherapy and radiotherapy only); E)-F) overall and disease-free survival of first recurrences at presentation.



Supplemental Figure 6: Expression data on SSTR2 in ONB. 82.4% of the cohort, for which immunohistochemical staining for SSTR2 were available, were positive for the biomarker.



Number at risk	0	12	24	36	48	60	72	84	96	108	120
<i>SSTR2-Negative</i> (n = 15)	15	12	9	8	8	7	6	6	3	2	1
<i>SSTR2-Positive</i> (n = 114)	114	101	86	67	55	50	45	40	34	27	24

Supplemental Figure 7. Kaplan-Meier survival curve of SSTR2 status

Dulguerov modified-TNM Staging System

Tumour

T1	Tumour involving nasal cavity and/or paranasal sinuses (excluding the sphenoid), sparing the most superior ethmoidal cells
T2	Tumour involving the nasal cavity and/or paranasal sinuses (including the sphenoid), with extension to or erosion of the cribriform plate
T3	Tumour extending into the orbit or protruding into the anterior cranial fossa, without dural invasion
T4	Tumour involving the brain

Node

N0	No cervical lymph node metastasis
N1	Any form of cervical lymph node metastasis

Metastasis

M0	No metastasis
M1	Distant metastasis

Kadish Staging System

A	Confined to the nasal cavity
B	Involvement of one or more paranasal sinuses
C	Extension beyond the nasal cavity and paranasal sinuses involving cribriform lamina, skull base, orbit or intracranial cavity
D	Regional lymph node or distant metastasis

		U.K.		U.S.A.					Europe				
		UCL/UCLH, London	Guy's and St. Thomas', London	MD Anderson Cancer Center, Houston, TX	Stanford University, Palo Alto, CA	Johns Hopkins University, Baltimore, MD	Emory University, Atlanta, GA	Yale University, New Haven, CT	University of Insubria, Varese, Italy	Universita degli Studi di Brescia, Italy	Instituto de ISPA, Oviedo, Spain	Beaumont Hospital, Dublin, Ireland	Ludwig- Maximilians University, Munich, Germany
Total		33	7	135	31	47	23	2	29	21	28	32	16
Sex	Male	16	2	83	13	28	13	1	11	11	11	20	7
	Female	17	5	52	18	19	8	1	18	10	15	12	8
	Missing	0	0	0	0	0	2	0	0	0	2	0	1
Hyam's Grade	1	8	1	2	0	8	2	0	6	0	12	8	0
	2	15	2	82	12	23	15	0	16	11	4	10	0
	3	4	0	17	3	11	1	0	7	9	5	10	0
	4	4	1	10	0	5	0	0	0	1	0	4	0
	Missing	2	3	24	16	0	5	2	0	0	7	0	16
Kadish-Morita Stage	A	9	2	18	2	4	1	0	5	1	0	0	5
	B	7	0	36	7	4	5	0	7	10	1	10	0
	C	10	5	57	14	34	12	2	16	10	6	20	10
	D	2	0	12	8	5	4	0	1	0	0	2	0
	Missing	5	0	12	0	0	1	0	0	0	21	0	1
Dulguerov T-Stage	T1	10	2	0	4	8	0	0	6	5	5	0	0
	T2	11	0	0	5	13	7	0	9	5	5	0	0
	T3	1	4	0	6	12	10	0	7	7	4	0	0
	T4	4	1	0	15	10	5	0	7	4	0	0	0
	Missing	7	0	135	1	4	1	2	0	0	14	32	16
Dural Infiltration	Yes	10	1	52	15	18	5	1	11	8	4	0	0
	No	20	6	16	17	18	16	1	18	13	11	0	0
	Missing	3	0	67	0	11	2	0	0	0	13	32	16
Bony Skull Base Involvement	Yes	22	5	68	24	28	18	2	19	16	4	0	0
	No	8	2	46	7	12	3	0	10	4	3	0	0
	Missing	3	0	21	0	7	21	0	0	1	21	32	16
Intracranial Involvement	Yes	0	0	65	12	11	9	0	0	0	3	0	0
	No	0	0	49	19	29	12	0	0	0	5	0	0
	Missing	33	7	21	0	7	2	2	29	21	20	32	16
Orbital Involvement	Yes	0	0	29	6	3	4	0	0	0	1	0	0
	No	0	0	83	25	39	17	0	0	0	6	0	0
	Missing	33	7	23	0	5	2	2	29	21	21	32	16

Supplemental Table 2. Clinical information for all cases, at presentation, by centre.

	Total n		n	%
Sex	273	Female	125	45.8
		Male	148	54.2
SSTR2 Status	142	Positive	117	82.4
		Negative	25	17.6
Hyams Grade	235	1	43	18.3
		2	126	53.6
		3	46	19.6
		4	20	8.5
Kadish-Morita Stage	247	A	26	10.5
		B	56	22.7
		C	142	57.5
		D	23	9.3
Dulguerov T-Stage	148	T1	34	23.0
		T2	44	29.7
		T3	38	25.7
		T4	32	21.6
Type of Surgery	238	None	16	6.7
		Endoscopic	120	50.4
		Open	85	35.7
		Combined	15	6.3
		Neck Dissection Only	1	0.4
		Debulking Only	1	0.4
Adjuvant Treatment	112	None	31	12.7
		Radiotherapy only	146	59.8
		Chemotherapy only	2	0.8
		Chemoradiotherapy	65	26.6
Induction Chemotherapy	213	No	183	85.9
		Yes	30	14.1
Recurrence Site	222	No Recurrence	158	71.2
		Local	29	13.1
		Cervical nodal metastasis	16	7.2
		Parotid	3	1.4
		Intracranial	8	3.6
		Locoregional	2	0.9
		Distant	6	2.7

Supplemental Table 3. Clinicopathological characteristics and treatment details of primary cases (i.e. no previous treatment).

	SSTR2 Status				p-value
	Negative		Positive		
	n	%	n	%	
Sex					0.073
Female	16	66.7	53	45.3	
Male	8	33.3	64	54.7	
Age					0.163
<65	22	91.7	90	76.9	
>65	2	8.3	27	23.1	
Hyams Grade					0.003
Grade 1	6	28.6	20	18.7	
Grade 2	4	19.0	62	57.9	
Grade 3	6	28.6	19	17.8	
Grade 4	5	23.8	6	5.6	
Kadish-Morita Stage					0.807
Kadish A	3	23.1	18	16.4	
Kadish B	1	7.7	18	16.4	
Kadish C	8	61.5	68	61.8	
Kadish D	1	7.7	6	5.5	
Dulguerov T-Stage					0.162
T1	8	42.1	20	20.6	
T2	6	31.6	27	27.8	
T3	3	15.8	30	30.9	
T4	2	10.5	20	20.6	
Dural Infiltration					0.630
No	13	65.0	61	58.7	
Yes	7	35.0	43	41.3	
Bony Skull Base Involvement					0.529
No	5	35.7	28	26.7	
Yes	9	64.3	77	73.3	
Intracranial Involvement					0.678
No	4	66.7	27	52.9	
Yes	2	33.3	24	47.1	
Orbital Involvement					1.000
No	5	100.0	45	84.9	
Yes	0	0.0	8	15.1	

Supplemental Table 4. Clinicopathological characteristics of SSTR2-positive and negative primary tumours.