

Supplementary Table 5. Kaplan-Meier Univariate Analysis of (RP)FS and Time to develop aDTC/RR-DTC in eDTC Cohort (N=98)

Parameters	N	(RP)FS			Time to develop aDTC/RR-DTC		
		Median (95%CI)	Hazard Ratio (95%CI)	Log-rank p-value	Median (95%CI)	Hazard Ratio (95%CI)	Log-rank p-value
<b>General variables</b>							
Age at diagnosis, years							
>=45 [ref.]	76	2.4 (1.8 - 3.0)			2.3 (1.5 - 2.9)		
<45	22	2.8 (1.2 - 5.3)	0.841 (0.505 - 1.343)	0.4863	2.3 (1.2 - 3.9)	0.932 (0.560 - 1.486)	0.7769
>=55 [ref.]	56	2.3 (1.5 - 3.0)			2.2 (1.3 - 3.0)		
<55	42	2.6 (1.4 - 3.9)	0.867 (0.573 - 1.299)	0.4912	2.3 (1.4 - 3.4)	0.936 (0.619 - 1.401)	0.7488
Gender							
Female [ref.]	61	2.8 (1.8 - 3.9)			2.8 (1.8 - 3.9)		
Male	37	2.2 (1.3 - 3.0)	1.467 (0.957 - 2.223)	0.0722	1.9 (1.3 - 2.4)	1.675 (1.086 - 2.554)	0.0167 *
<b>Variables of initial diagnosis and first treatment</b>							
Histology							
Papillary [ref.]	58	2.6 (1.8 - 4.5)			2.4 (1.8 - 3.7)		
Follicular	13	1.3 (0.9 - 7.7)	0.981 (0.506 - 1.764)	0.6357	1.3 (0.9 - 7.6)	0.979 (0.505 - 1.761)	0.6810
Hürthel	16	2.5 (1.1 - 3.9)	1.333 (0.733 - 2.297)		2.0 (0.9 - 3.9)	1.360 (0.749 - 2.336)	
Others	11	2.3 (0.9 - 4.7)	1.380 (0.681 - 2.547)		2.3 (0.9 - 4.7)	1.266 (0.626 - 2.331)	
Surgical outcome							
R2 [ref.]	1	0.1 (NE - NE)			0.1 (NE - NE)		
R0/R1	90	2.3 (1.8 - 3.0)	0.022 (0.002 - 0.463)	<0.0001 *	2.3 (1.8 - 2.9)	0.021 (0.002 - 0.453)	<0.0001 *
Others <sup>(1)</sup>	7	3.7 (0.1 - 13.0)	0.012 (0.001 - 0.271)		1.7 (0.1 - 3.7)	0.018 (0.002 - 0.415)	
Surgical extension							
Thyroidectomy total [ref.]	67	2.3 (1.8 - 3.3)			2.3 (1.5 - 3.0)		

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Thyroidectomy partial + others <sup>(2)</sup>	31	2.7 (1.0 - 4.7)	1.098 (0.705 - 1.675)	0.6695	1.9 (1.0 - 3.9)	1.181 (0.758 - 1.802)	0.4501
Disease extension							
Locoregional [ref.]	10	1.7 (0.1 - 3.4)			1.7 (0.1 - 3.4)		
Metastatic	88	2.4 (1.8 - 3.4)	0.531 (0.285 - 1.102)	0.0591	2.3 (1.8 - 2.9)	0.571 (0.307 - 1.183)	0.0949
Ablative RAI +/- local therapies							
Yes [ref.]	93	2.3 (1.8 - 2.9)			2.2 (1.7 - 2.8)		
No	5	9.0 (0.1 - 14.4)	0.488 (0.171 - 1.094)	0.1142	9.0 (0.1 - 14.4)	0.469 (0.164 - 1.056)	0.0961
RAI Refractoriness at initial diagnosis							
No [ref.]	97	2.4 (1.8 - 3.3)			2.3 (1.8 - 2.9)		
Yes	1	0.1 (NE - NE)	47.9 (2.232 - 500.92)	<0.0001 *	0.1 (NE - NE)	47.9 (2.232 - 500.92)	<0.0001 *
RAI cumulative dose							
>=600 mCi [ref.]	5	8.4 (3.9 - 13.0)			5.3 (1.7 - 9.3)		
<600 mCi	87	2.2 (1.4 - 2.7)	2.257 (1.007 - 6.445)	0.0384 *	2.1 (1.3 - 2.6)	1.446 (0.648 - 4.118)	0.1300
No RAI treatment <sup>(3)</sup>	5	9.0 (0.1 - 14.4)	0.940 (0.260 - 3.396)		9.0 (0.1 - 14.4)	0.612 (0.168 - 2.228)	
RAI with Sensitizing agent at first instance							
No [ref.]	71	2.4 (1.9 - 3.4)			2.3 (1.8 - 2.9)		
Yes	18	0.9 (0.6 - 2.2)	2.404 (1.364 - 4.042)	0.0010 *	0.9 (0.6 - 1.9)	2.232 (1.269 - 3.744)	0.0027 *
RAI Response at First Instance. ATA criteria <sup>(4)</sup>							
Excellent [ref.]	13	5.8 (1.8 - 11.1)			5.8 (1.8 - 10.7)		
Biochemical Incomplete + Indeterminate	38	2.5 (1.8 - 3.4)	2.365 (1.203 - 5.103)	0.0014 *	2.5 (1.8 - 3.4)	2.366 (1.200 - 5.121)	0.0010 *
Structural Incomplete	40	1.2 (0.9 - 2.4)	3.489 (1.778 - 7.515)		1.1 (0.9 - 2.1)	3.572 (1.818 - 7.701)	

**Initial Clinical and Treatment Patterns of Advanced Differentiated Thyroid Cancer. ERUDIT Study.**

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Parameters	N	(RP)FS			Time to develop aDTC/RR-DTC		
		Median (95%CI)	Hazard Ratio (95%CI)	Log-rank p-value	Median (95%CI)	Hazard Ratio (95%CI)	Log-rank p-value
RAI-scan positivity after initial <sup>(5)</sup> RAI treatment							
No [ref.]	19	5.8 (2.4 - 9.2)			4.8 (2.2 - 8.1)		
Yes	53	1.8 (1.2 - 2.6)	2.737 (1.577 - 5.015)	0.0004 *	1.8 (1.0 - 2.5)	2.347 (1.366 - 4.240)	0.0023 *

(1) Resection of other lesions such as adenopathy or metastasis. (2): Lobectomies and Lymphadenectomies + others; RAI, Radioactive Iodine (I-131). (3) Patients that did not receive RAI treatment because were not susceptible of receive it (either clinically not required or no-RAI uptake). (4): Haugen et al., 2016 (1). (5): Refers to 6-12 months follow-up post-treatment scans in patients that could have received surgery ± RAI as first therapeutic approach (Types 1, 3, and 4). [ref.]: Reference category. R0: Microscopic complete resection. R1: Macroscopic resection with microscopic residual tumour. R2: Gross macroscopic residual tumour. (RP)FS: Relapse/Progression-free survival (a composite variable to describe the time elapsed from reception of upfront or initial diagnosis until death, relapse into aDTC in patients who were initially free of disease, in the cohort of patients originally diagnosed with early disease, or structural progression into aDTC in patients who had initial residual disease, respectively). CI: Confidence interval. NE: Non-Estimable. (\*): Statistically significant (p<0.05).