

Appendix 1

Figure 1 - Flowchart with overall population, best supportive care and systemic treatment groups.
Abbreviations: BSC, best supportive care; SGC, salivary group cancer; ST, systemic treatment.

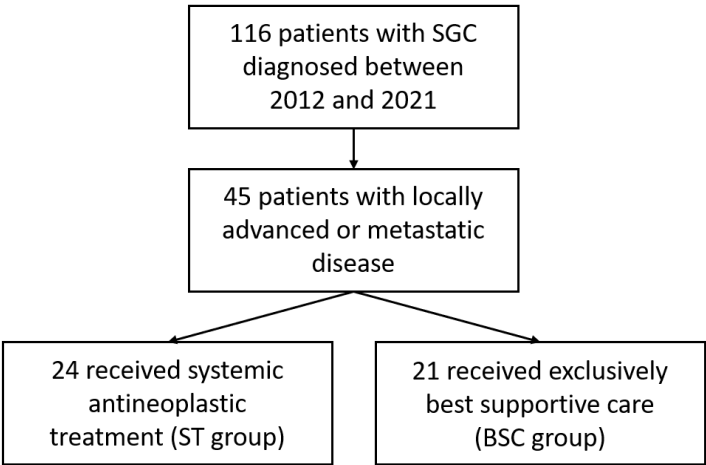


Table 1 - Crude and adjusted hazard ratios and 95% confidence intervals for death for the comparison between patients with locally advanced or metastatic disease and submitted to systemic therapy (reference) with those submitted to best supportive care calculated using Cox regression, according to demographic and clinical characteristics. Abbreviations: HR, Hazard Ratio; 95% CI, 95% Confidence Interval; ^a Age (continuous), ^b Age (continuous) and stage (II, III, IVA, IVB and IVC), ^c According to AJCC 8th Edition

	Crude-HR	Age-adjusted HR ^a	Age- and stage-adjusted HR ^b
All	4.09 (2.04 - 8.21)	5.41 (2.33 - 12.55)	6.10 (2.54 - 14.67)
Age at diagnosis (years)			
<55	5.50 (0.49 - 62.08)	--	--
55-64	9.10 (0.81 - 102.53)	--	--
>64	4.63 (1.79 - 11.94)	--	--
Sex			
Male	3.30 (1.38 - 7.88)	4.96 (1.88 - 13.10)	5.62 (2.00 - 15.78)
Female	5.10 (1.52 - 17.16)	4.57 (0.65 - 32.33)	20.77 (0.53 - 811.04)
Cancer stage at diagnosis ^c			
II-III	--	--	--
IV	4.01 (1.74 - 9.22)	6.44 (2.33 - 17.78)	--
Primary tumor site			
Parotid gland	4.24 (1.96 - 9.18)	5.45 (2.21 - 13.43)	5.92 (2.31 - 15.17)
Submandibular gland	--	--	--
Sublingual gland	1.67 (0.29 - 9.64)	2.43 (0.16 - 36.54)	--
Previous curative-intent treatment			
Yes	2.72 (1.05 - 7.02)	3.13 (0.86 - 11.40)	4.07 (0.89 - 18.66)
No	5.32 (1.17 - 24.27)	8.44 (1.57 - 45.43)	9.98 (1.71 - 58.18)
Recurrence			
Yes	2.57 (0.93 - 7.06)	2.63 (0.54 - 12.76)	4.32 (0.55 - 33.88)
No	4.79 (1.32 - 17.40)	6.11 (1.52 - 24.57)	8.12 (1.79 - 36.89)

Table 2 - Metastatic disease characteristics.

	Best Supportive Care (N=21)	Systemic therapy (N=24)
Metastases site, n (%)		
Bone	6 (29)	9 (38)
Lung	4 (19)	12 (50)
Liver	3 (14)	5 (21)
Non-locoregional lymph nodes	3 (14)	10 (42)
Brain	2 (10)	2 (8)
Pancreas	1 (5)	0 (0)
Stomach	1 (5)	0 (0)
Suprarenal	0 (0)	2 (8)
Pleura	0 (0)	1 (4)
Skin	0 (0)	1 (4)
Number of metastases sites, n (%)		
0	9 (43)	2 (8)
1	8 (38)	7 (29)
2	0 (0)	10 (42)
3	4 (19)	5 (21)

Table 3 - Tumor characteristics. Abbreviations: AR, androgen receptor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NGS, next-generation sequencing. Note: Some patients presented more than one targetable genetic alteration.

	Systemic therapy (N=24)
Tumor Characteristic, n (%)	
AR (IHC)	
Available samples	12 (50)
Positive	9 (38)
Negative	3 (13)
HER2 (IHC)	
Available samples	11 (46)
Positive	0 (0)
Negative	11 (100)
NGS	
Available samples	11 (46)
Targetable genetic alteration[‡]	
HRAS mutation	3 (13)
PIK3CA mutation	3 (13)
ATM mutation	2 (8)
FGFR3-TACC3 fusion	1 (4)
NOTCH1 mutation	1 (4)
CDKN2A mutation	1 (4)
Others genetic alteration	
Splice site alteration AR-V7 in the AR gene	2 (8)
At least one targetable genetic alteration	8 (33)