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**Aggressive treatment and survival outcomes in NUT midline carcinoma (NMC) of the head and neck (HN).**

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**Abstract**

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**Background:** NMC is a rare subtype of squamous cancer defined by rearrangement of the *NUT* gene. NMC is typically found in the thorax, although ~20% of cases arise in the HN. NMC is almost uniformly fatal. We report on a cohort of patients (pts) with HN NMC to identify disease characteristics, treatment and outcomes. **Methods:** A clinical database was established using demographic and outcomes data available on all known cases of HN NMC obtained from the International NMC Registry ([www.NMCRegistry.org](http://www.NMCRegistry.org)). Clinicopathologic variables were assessed for 40 pts, the largest cohort of HN NMC studied to date. Outcome data from 31 patients treated from 1990-2013 were available for survival analyses. **Results:** HN NMC incidence has increased annually since 2010. Median age was 21.9 years (range 0.1-81.7), male: female (%) was 45:55, sinonasal origin was 50%, and the *BRD4-NUT* fusion was found in 82%. At diagnosis, 36% had regional node metastases and 15% had distant metastases. Initial treatment was upfront surgery (S) +/- adjuvant chemoradiation (CRT) or adjuvant radiation (RT) (48%), upfront RT +/- chemotherapy (C) (21%), or upfront C +/- S or RT (31%). Median progression-free survival (PFS) was 7.2 months (range 6.3-8.7). Median overall survival (OS) was 9.8 months (range 6.6-15.6). The 2-year PFS was 27% (95% CI, 9-44). The 2-year OS was 31% (95% CI, 13-50). Upfront S +/- post-operative CRT or RT, and S with negative margins were significant predictors of improved PFS and OS. Initial RT or C, type of C regimen, and *NUT* translocation type were not significantly associated with improved outcome. **Conclusions:** HN NMC portends a poor prognosis. Aggressive initial surgical resection with or without post-operative CRT or RT may be associated with enhanced survival. C or RT alone is inadequate, and the development of targeted therapies is now underway.

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**PFS and OS by treatment.**

Treatment		n	2-year PFS (95% CI)	P value	2-year OS (95% CI)	P value
<b>Initial upfront strategy</b>	S +/- CRT or RT	14*	55 (26-85)	0.01	55 (26-85)	0.01
	RT +/- C	6	0		0	
	C +/- S or RT	8	0		14 (1-27)	
<b>Extent of surgical resection</b>	None	13	0	0.03	8 (0-24)	0.03
	Debulking	4	33 (0-88)		33 (0-88)	
	Gross total	6	40 (0-84)		40 (0-84)	
	Complete with negative margins	5	75 (32-100)		75 (32-100)	

\* 12/14 had S then CRT, 1/14 had S then RT.

Abstract presentation from the 2014 ASCO Annual Meeting

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