

## INTRODUCTION

- Five-year survival rates of SNUC over the past decade reveal widely variable rates ranging from 6 to 75%. This suggests that SNUC likely represent a heterogeneous group of tumors with varying prognosis.
- Loss of SMARCB1 (INI-1, BAF47 or hSNF5), a tumor suppressor gene, is a genetic recently described genetic aberration in various undifferentiated sinonasal and extra sinonasal which appears to confer poor prognosis.
- The objectives of this study were first, to examine the differential expression of SMARCB1 in the SNUC population and, second, to analyze whether this differential expression is associated with different survival outcomes.

## METHODS

- All cases of SNUC that were diagnosed between 2007 and 2018 at a single tertiary care center were identified and their formalin-fixed, paraffin-embedded specimens were retrieved.
- Immunohistochemistry (IHC) was performed using the SMARCB1 (INI1) antibody (MRQ-27, 1:50, Zytomed).
- Cases were divided into two subgroups based on SMARCB1 staining – SMARCB1-retained SNUC (SR-SNUC) and SMARCB1-deficient SNUC (SD-SNUC) (Fig 1).
- Statistical analysis: Kaplan–Meier methods were used to estimate survival durations. A two-tailed P value of 0.05 was considered statistically significant. It was performed using SPSS software, v.25 (IBM, NY).

## RESULTS

### SMARCB1 nuclear expression by IHC:

- Fourteen patients were included in the study out of which forty-three percent (n=6) were SD-SNUC. Mean surveillance duration was 41.97±35.61 months.

### Overall demographics:

- 64% of patients were male and 79% were within the 5<sup>th</sup> and 7<sup>th</sup> decade. 50% showed bilateral sinonasal tract involvement, 79% had skull base invasion and 93% had orbital invasion. More than two-thirds of patients (71%) presented with TNM stage IV disease.

### Comparison of SD-SNUC and SR-SNUC:

- Pre-treatment (clinical and pathological) and treatment related variables were found to be comparable (p>0.05; Tables 1-3). However, post-treatment outcomes were significantly different between the two groups.
- SD-SNUC had both higher recurrence (75% vs. 17%) and higher mortality rates (67% vs. 14%) (Cox Hazard rate: 8.562; p=0.05).
- Pattern of recurrence was distinct too. SR-SNUC developed local recurrence alone (n=1), while SD-SNUC developed all three pattern - local (n=1), regional (n=1) and metastasis (n=1). Metastasis was noted in adrenal, portocaval and mediastinal lymph nodes.
- Mean overall survival (53.2 ± 37.5 vs. 28.8 ± 31.15 months) and disease free survival (43.7 ± 40.97 vs. 10.62 ± 10.26 months) durations were longer for SR-SNUC. Additionally, 5-year survival probabilities were worse for SD-SNUC (0.33 vs. 0.85). Kaplan Meier survival curves were significantly worse for SD-SNUC (Fig 2)

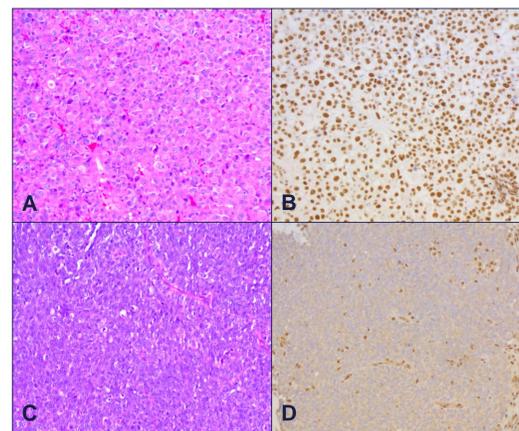


Figure 1: SR-SNUC (H and E 20x): Squamoid morphology, abundant eosinophilic cytoplasm and distinct cell borders (A); IHC shows strong nuclear staining (B).

SD-SNUC (H and E 20x): Basaloid morphology with high nuclear to cytoplasmic ratio (C); IHC shows absent SMARCB1 nuclear expression in tumor cells with retained staining of background non-neoplastic cells (D).

Table 1: Comparison of pre-treatment clinical variables

Variable	Details	P value
Age	Mean, SD	0.59
Gender	Males vs. Females	1.00
Race	Caucasian, Asian, African American	0.74
Smoking history	Ever vs. Never	1.00
Alcohol history	Ever vs. Never	1.00
Charlson comorbidity Index	Score 2 to 4	0.99
ECOG functional status	Score 0 to 2	0.99
Primary site	Nasal cavity and PNS	0.08
Laterality	Unilateral vs. Bilateral	0.59
Orbital involvement	Present vs. Absent	1.00
Skull base involvement	Present vs. Absent	0.20
TNM staging	Based on AJCC TNM staging	1.00

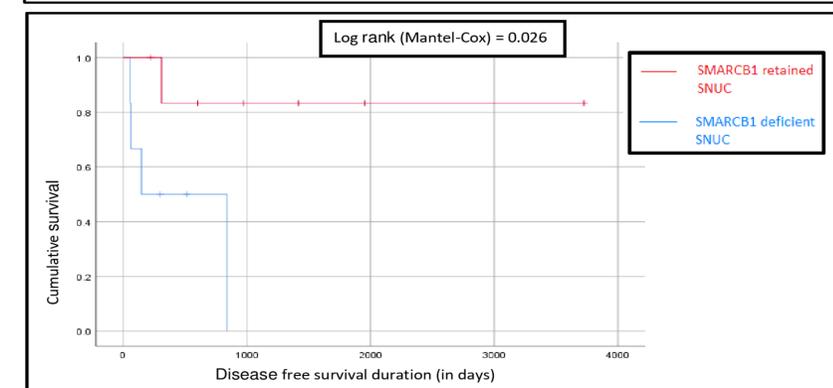
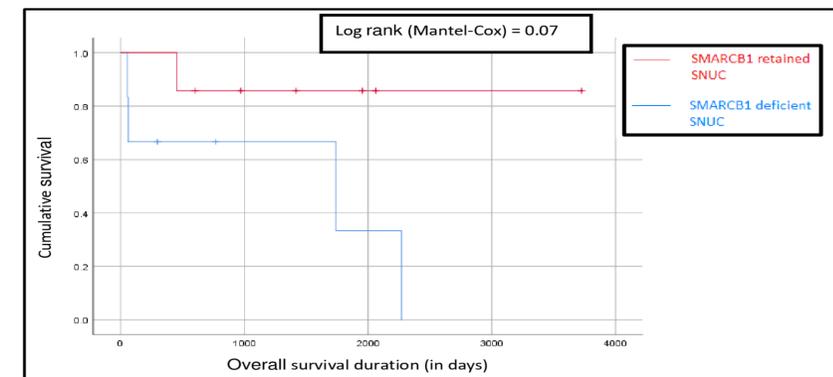
Table 2: Comparison of pre-treatment pathological variables

Variable	Details	P value
Growth pattern	Trabecular, Sheet-like, Papillary	0.74
Cytomorphology	Basaloid, Squamoid, Plasmacytoid	1.00
Necrosis	Present vs. Absent	0.30
Mitotic count	Mean, SD	0.60
Pancytokeratin	Present vs. Absent	0.99
Synaptophysin	Present vs. Absent	1.00
Chromogranin	Present vs. Absent	1.00
S-100	Present vs. Absent	1.00
P16	Present vs. Absent	0.60

Table 3: Comparison of treatment-related variables

Variable	Details	P value
Treatment lag (in days)	Duration from diagnosis to treatment	0.46
Modality	Surgical vs. Non-surgical	0.10
Approach	Endoscopic vs. Open	0.46
Oncological clearance	Positive vs. Negative margins	0.21
Total radiation dose	Mean, SD	0.43
Interruption during radiotherapy	Unplanned delays in treatment	0.05

Figure 2: Comparison of Kaplan Meier survival curves for overall and disease free survival between SR-SNUC and SD-SNUC



## LIMITATIONS

- Retrospective study design including incomplete and inconsistent data in medical records.
- Low sample size, owing to rarity of the tumor is also recognized.

## CONCLUSIONS

- SNUC represent a heterogeneous group of undifferentiated sinonasal malignancies.
- This study demonstrates that tumors with and without SMARCB1 expression by IHC have marked differences in survival and therefore may represent distinct clinical entities.
- We propose that SMARCB1 expression may represent a viable option to subtype morphologically undifferentiated sinonasal tumors in an effort to develop more individualized treatment protocols.

## REFERENCES

- Agaimy A, Hartmann A, Antonescu CR, et al. SMARCB1 (INI-1)-deficient Sinonasal Carcinoma: A Series of 39 Cases Expanding the Morphologic and Clinicopathologic Spectrum of a Recently Described Entity. Am J Surg Pathol. 2017;41(4):458-471.
- Morand GB, Anderegg N, Vital D, et al. Outcome by treatment modality in sinonasal undifferentiated carcinoma (SNUC): A case-series, systematic review and meta-analysis. Oral Oncol. 2017;75:28-34.