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Update on Treatments for Sinonasal Undifferentiated Carcinoma

2022 Multidisciplinary Cancer Update

October 28th, 2022

Disclosures

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- None

Epidemiology

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- Squamous cell carcinoma 50%
- Adenocarcinoma 13%
- Mucosal melanoma 7%
- Esthesioneuroblastoma 6%
- Adenoid cystic carcinoma 6%
- Sinonasal undifferentiated carcinoma 3%
- Others 15%

Epidemiology

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- **Sinonasal undifferentiated carcinoma 3%**
- Others 15%

Epidemiology

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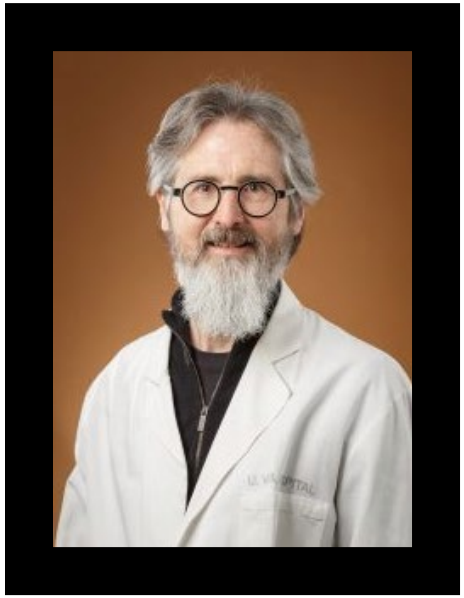
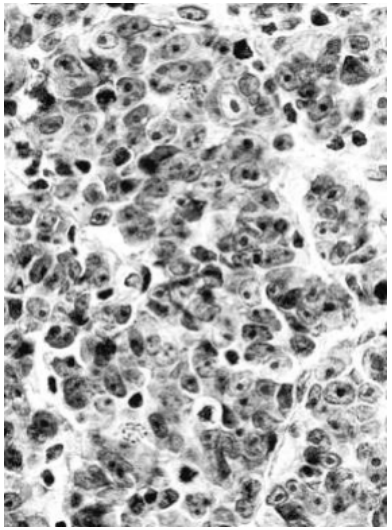
- First described as a unique entity by Dr. Frierson at UVA in 1986
  - Report of 8 cases
  - More aggressive than ONB

Sinonasal Undifferentiated Carcinoma

An Aggressive Neoplasm Derived from Schneiderian Epithelium and Distinct from Olfactory Neuroblastoma

Henry F. Frierson, Jr., M.D., Stacey E. Mills, M.D., Robert E. Fechner, M.D., Jerome B. Taxy, M.D., and Paul A. Levine, M.D.





Epidemiology

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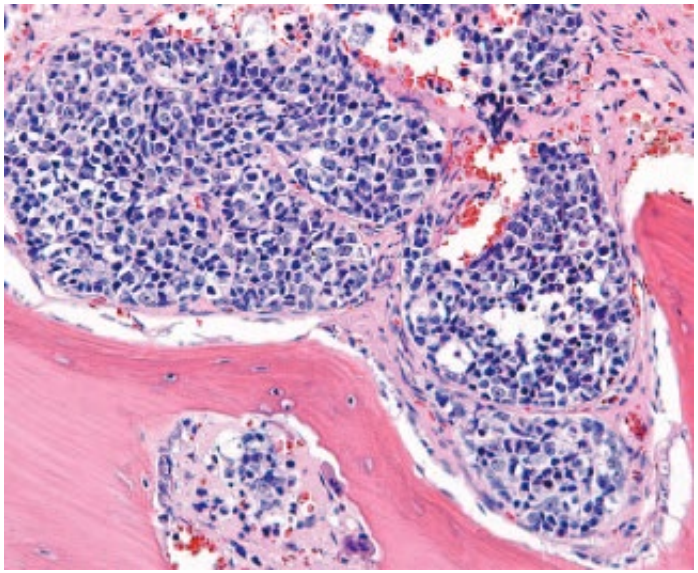
- Arises from Schneiderian epithelium
  - Lack glandular or squamous differentiation
- Strong staining for:
  - Keratin (pancytokeratin (AE1/AE3), CK7, OSCAR, CAM5.2)



Epidemiology

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- SNUC
  - 3-5% sinonasal carcinomas
  - Male predominance
    - 2.3:1
  - Ave age 60
    - 20-90

Chambers KJ, et al. Incidence and survival patterns of sinonasal undifferentiated carcinoma in the United States. J Neurol Surg B Skull Base. 2015 Mar;76(2):94-100.

Epidemiology

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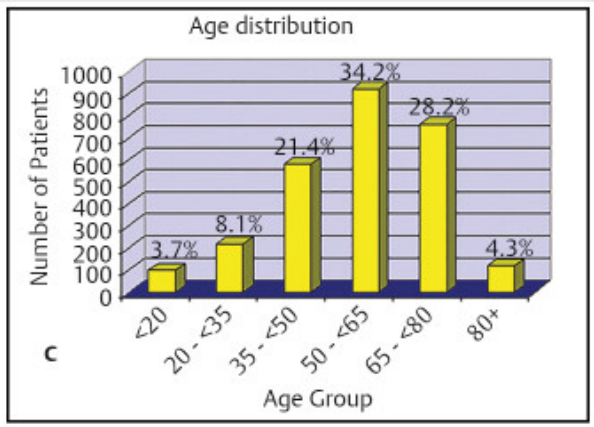
- Rapid onset
  - Nasal obstruction, epistaxis, proptosis, pain, CN deficit
- Location
  - Nasal cavity (38%), ethmoid (23%), maxillary (15%)
- Prognosis
  - SEER database (318 SNUCs)
    - 5 year survival 34.9%
    - 10 year survival 31.3%
    - Median 22.1 months



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Management

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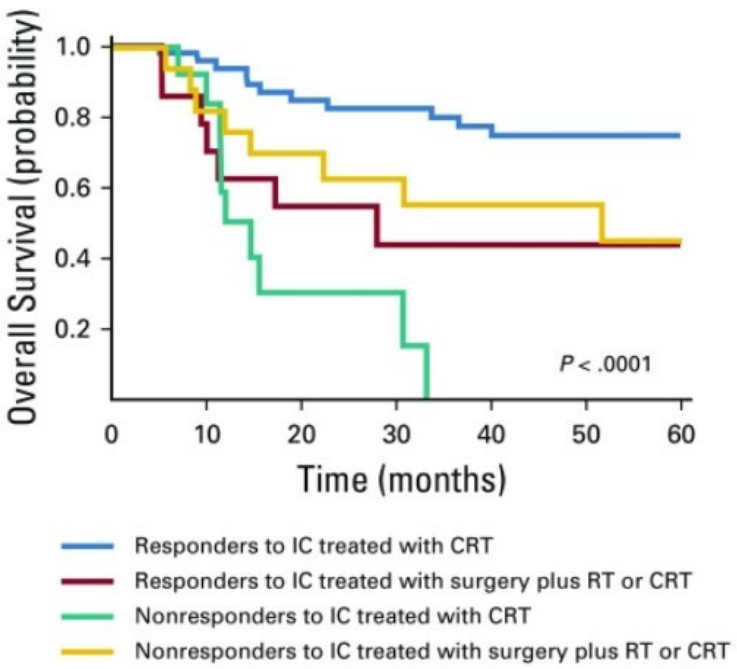
- Multimodality therapy
- Induction chemotherapy
  - Considered for extensive disease with goal of tumor shrinkage
  - Based on response, consider surgery + XRT vs definitive CR
- Surgery
  - If resectable with minimal morbidity and negative margins

original report

Induction Chemotherapy Response as a Guide for Treatment Optimization in Sinonasal Undifferentiated Carcinoma

Moran Amit, MD, PhD[1,2]; Ahmed S. Abdelmeguid, MD[2]; Teemaranawich Watcherporn, MD[2]; Hideaki Takahashi, MD, PhD[2]; Samantha Tam, MD[2]; Diana Bell, MD[2]; Renata Ferrarotto, MD[2]; Bonnie Glisson, MD[2]; Michael E. Kupferman, MD[2]; Dianna B. Roberts, PhD[2]; Shirley Y. Su[2]; Shaan M. Raza, MD[2]; Franco DeMonte, MD[2]; and Ehab Y. Hanna, MD[2]



Amit M, Abdelmeguid AS, et al. Induction Chemotherapy Response as a Guide for Treatment Optimization in Sinonasal Undifferentiated Carcinoma. J Clin Oncol. 2019 Feb 20;37(6):504-512

Management

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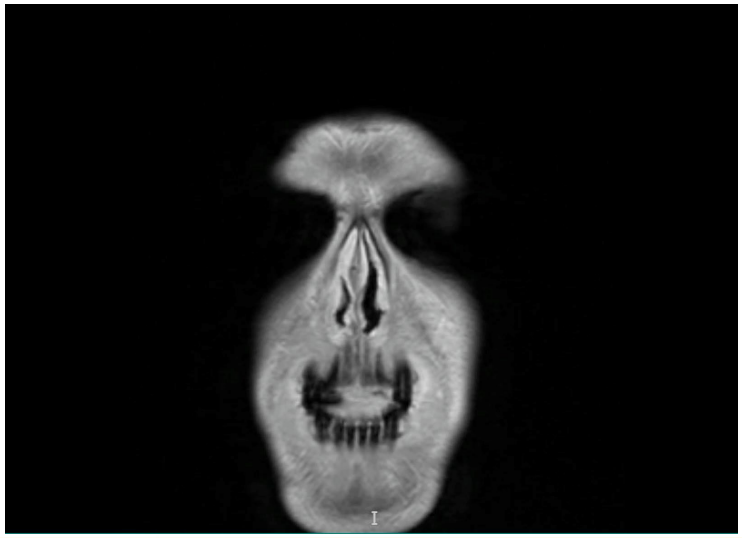
- Non responder



- Responder

SMARCB1/INI-1

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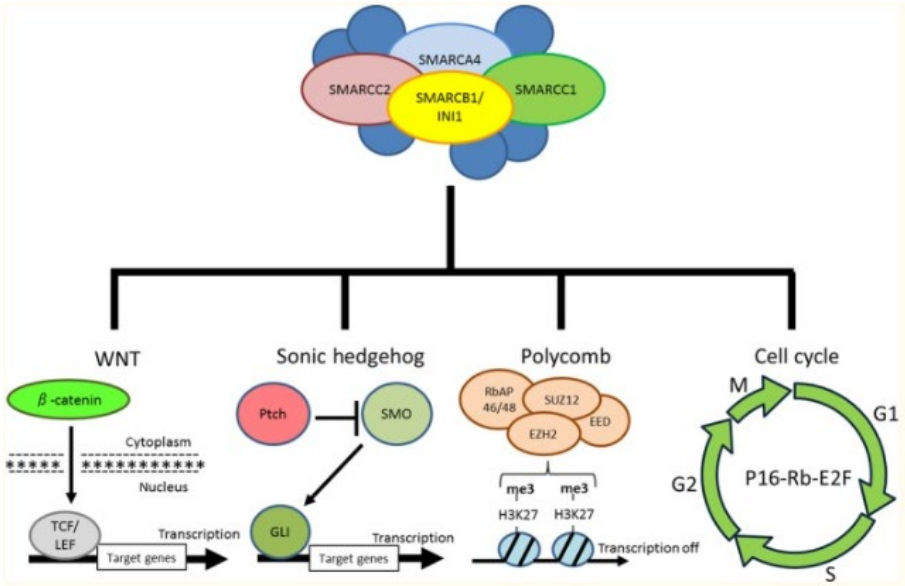
- SMARCB1 gene on chromosome 22q11.3
- Encodes protein involved in regulation of gene expression
- Involved with tumor suppression
- First noted in 1998 to be deficient in rhabdoid tumors



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SMARCB1/INI-1

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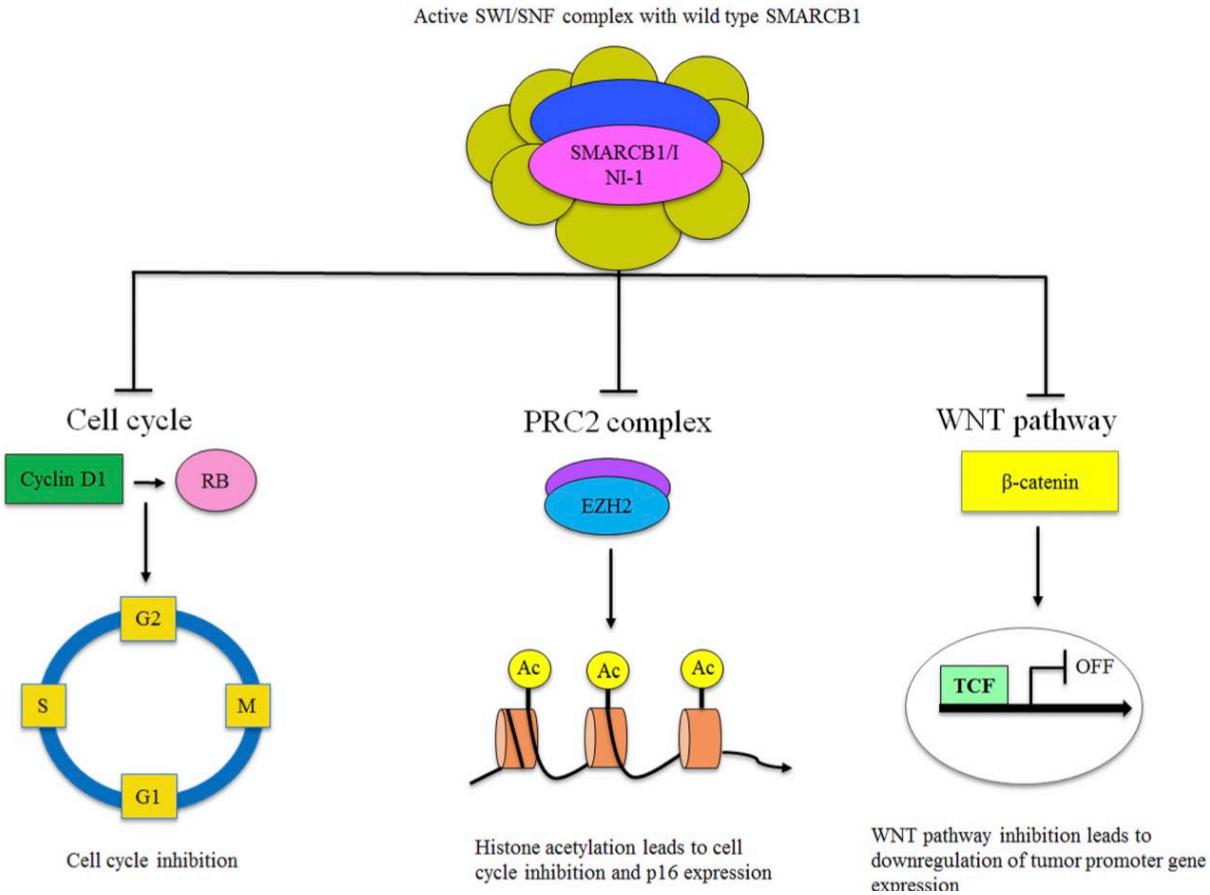

Shaverdashvili K, et al. INI-1 (SMARCB1)-Deficient Undifferentiated Sinonasal Carcinoma: Novel Paradigm of Molecular Testing in the Diagnosis and Management of Sinonasal Malignancies. Oncologist. 2020 Sep;25(9):738-744.

INI-1 Deficient SNUC

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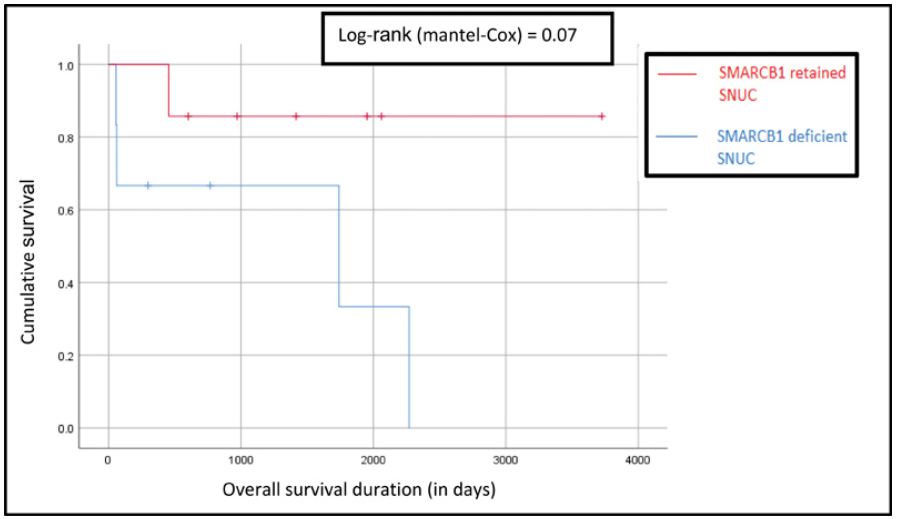
- 14 patients SNUC
- IH staining
  - Six INI-1 deficient
- INI-1 deficient tumors showed
  - Poorer OS (28.8 mo), & DFS (10.62 mo)
  - Higher recurrence



C Chitguppi, et al. Loss of *SMARCB1* Expression Confers Poor Prognosis to Sinonasal Undifferentiated Carcinoma. J Neurol Surg B Skull Base. 2020 Dec;81(6):610-619.

SMARCB1/INI-1

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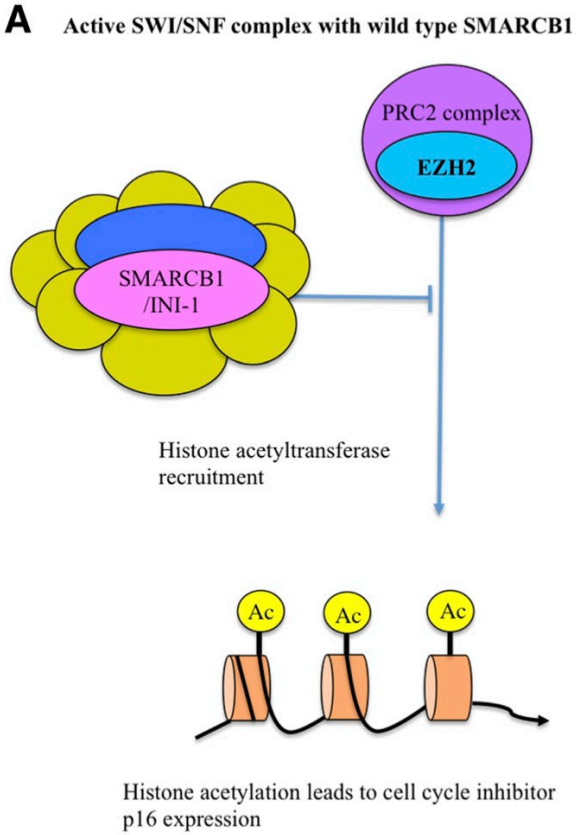

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INI-1 Deficient SNUC

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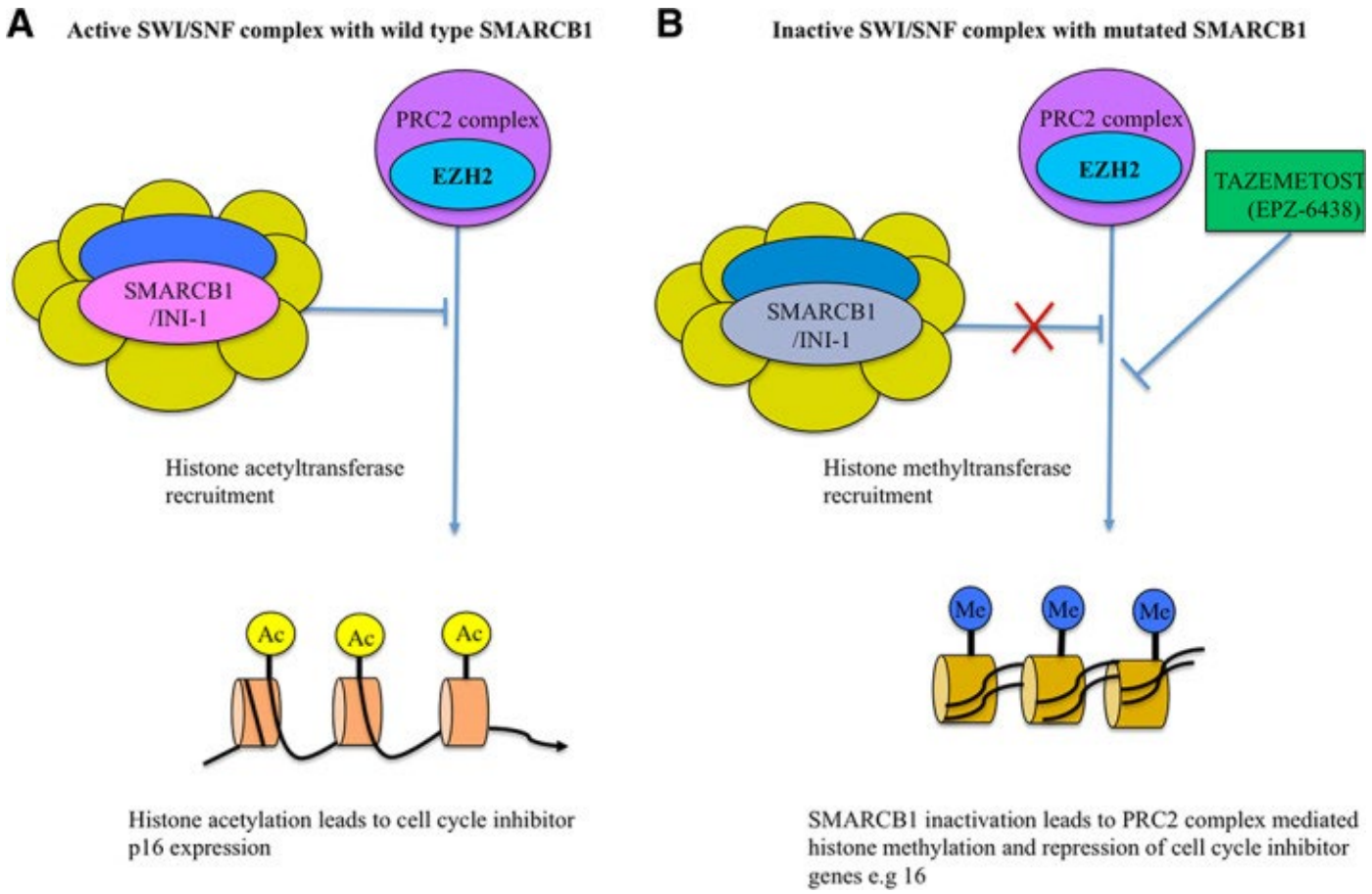

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Tazemetostat

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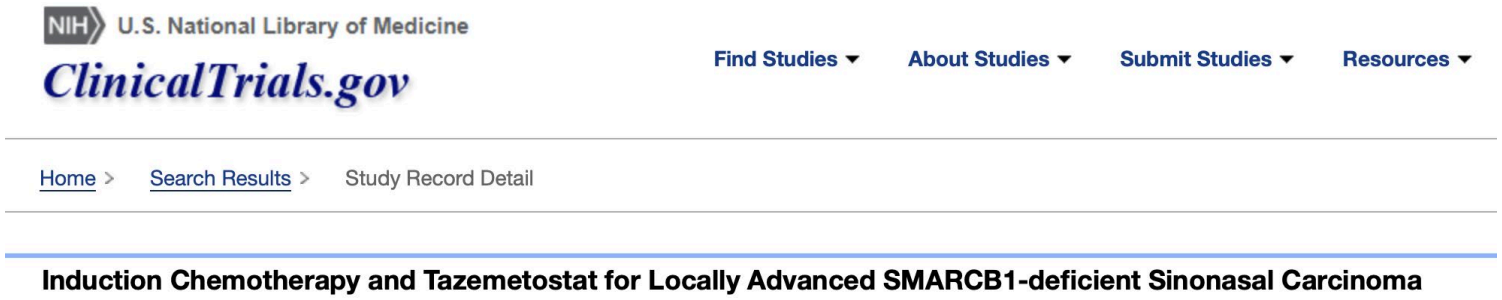
- Selective EZH2 inhibitor



- Phase II study
  - INI deficient SNUC
  - TPF+Tazmetostat
    - Surgery vs CRT+Tazmetostat

Conclusions

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- Multidisciplinary management key
- Pathology, medical/radiation oncology, surgical oncology needs to be discussed
- IC may be prognostic indicator in unresectable disease
  - Organ preservation
- Limited by retrospective nature of studies
- Responders do better than non-responders
  - Molecular analysis

Questions?

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- Thank you

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