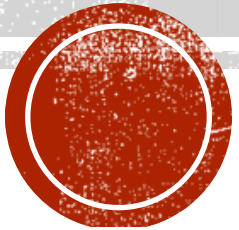
CASE 2019-1

Gestrich C, Jajosky A, Sadri N, Couce M, Cohen M



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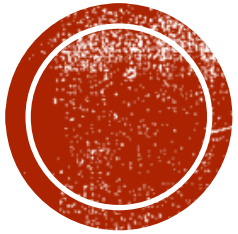
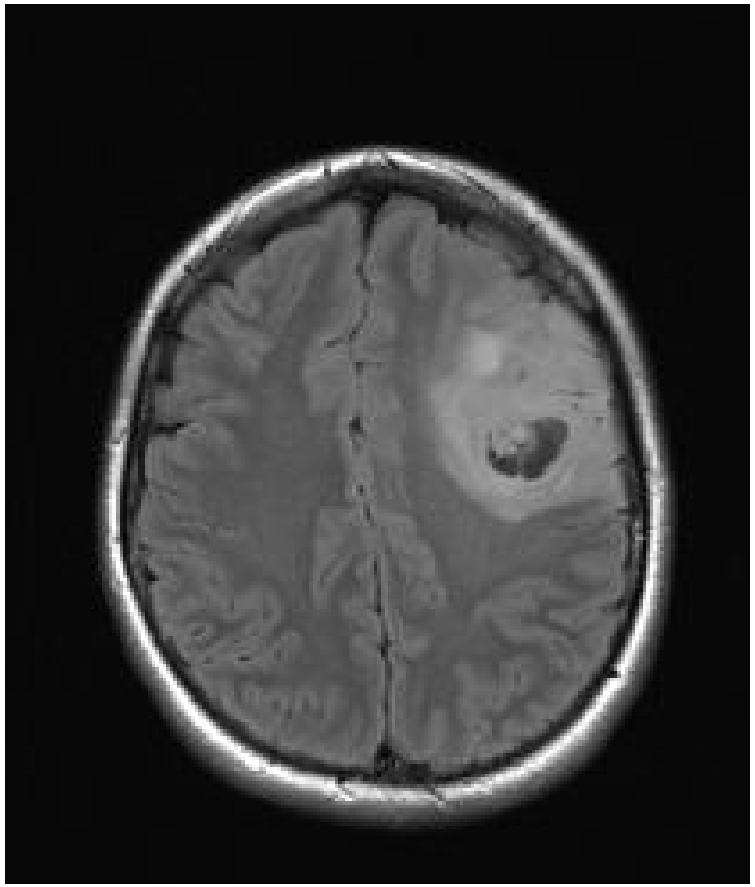
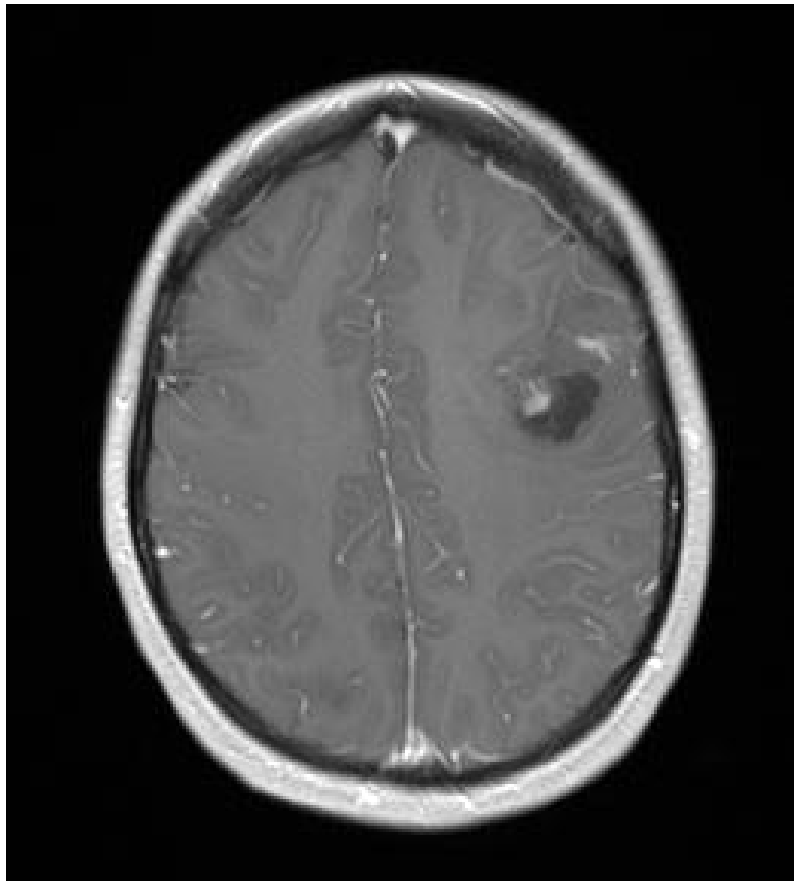


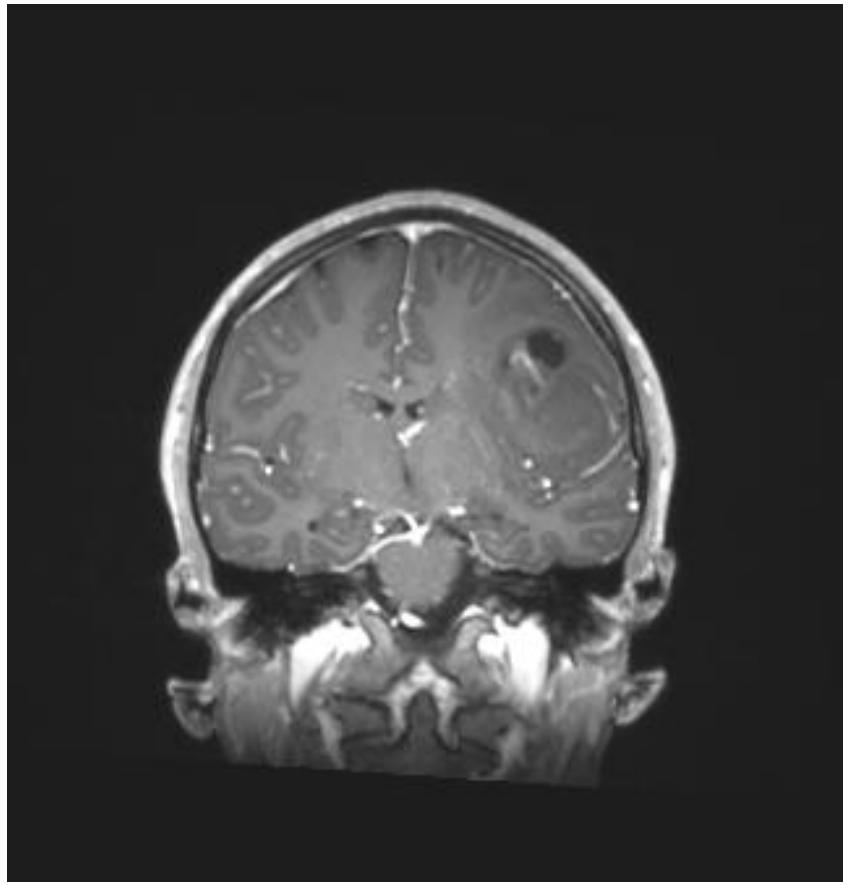
DISCLOSURE

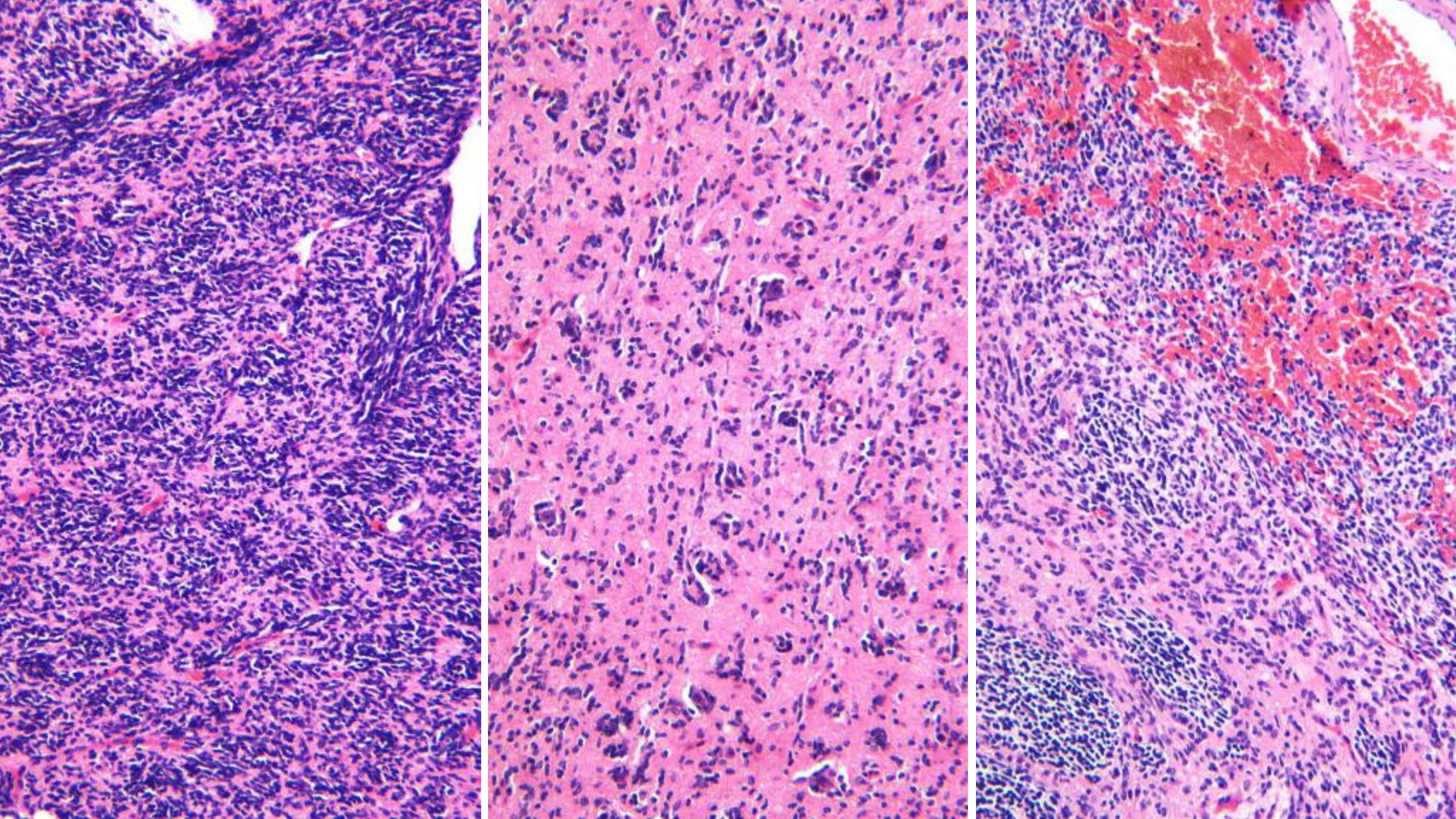
Unfortunately, none of the contributors have financial relationships to disclose.

22 YEAR OLD FEMALE WITH NEW ONSET SEIZURES









POINTS FOR DISCUSSION

1. Differential diagnosis
2. Diagnostic work-up
3. Prognosis

DIFFERENTIAL DIAGNOSIS

- Oligodendroglioma
- Ependymoma
- Astrocytoma
- Primitive neuroectodermal tumor

DIAGNOSTIC WORK-UP

- Immunohistochemistry
  - Positive: GFAP (weak), ATRX
  - Negative: IDH1-R132H, Olig2, synaptophysin, neurofilament, p53 (wild-type pattern)
  - Ki-67: 10% to >50%
- FISH
  - Negative for 1p/19q

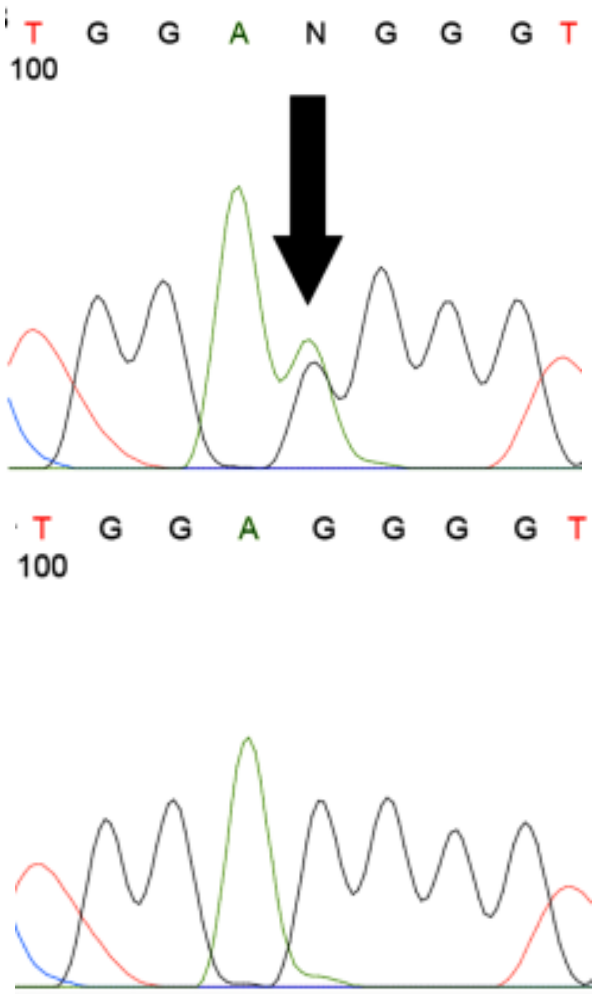
- Molecular (Oncomine Comprehensive Assay v3)
  - *H3F3A* G34R c.103G>A, VAF = 30%
  - *TERT* c.146C>T, VAF = 30%
  - *MYCN* c.131C>T, VAF = 10%
  - No *IDH* 1 or 2 mutations

Final Diagnosis:

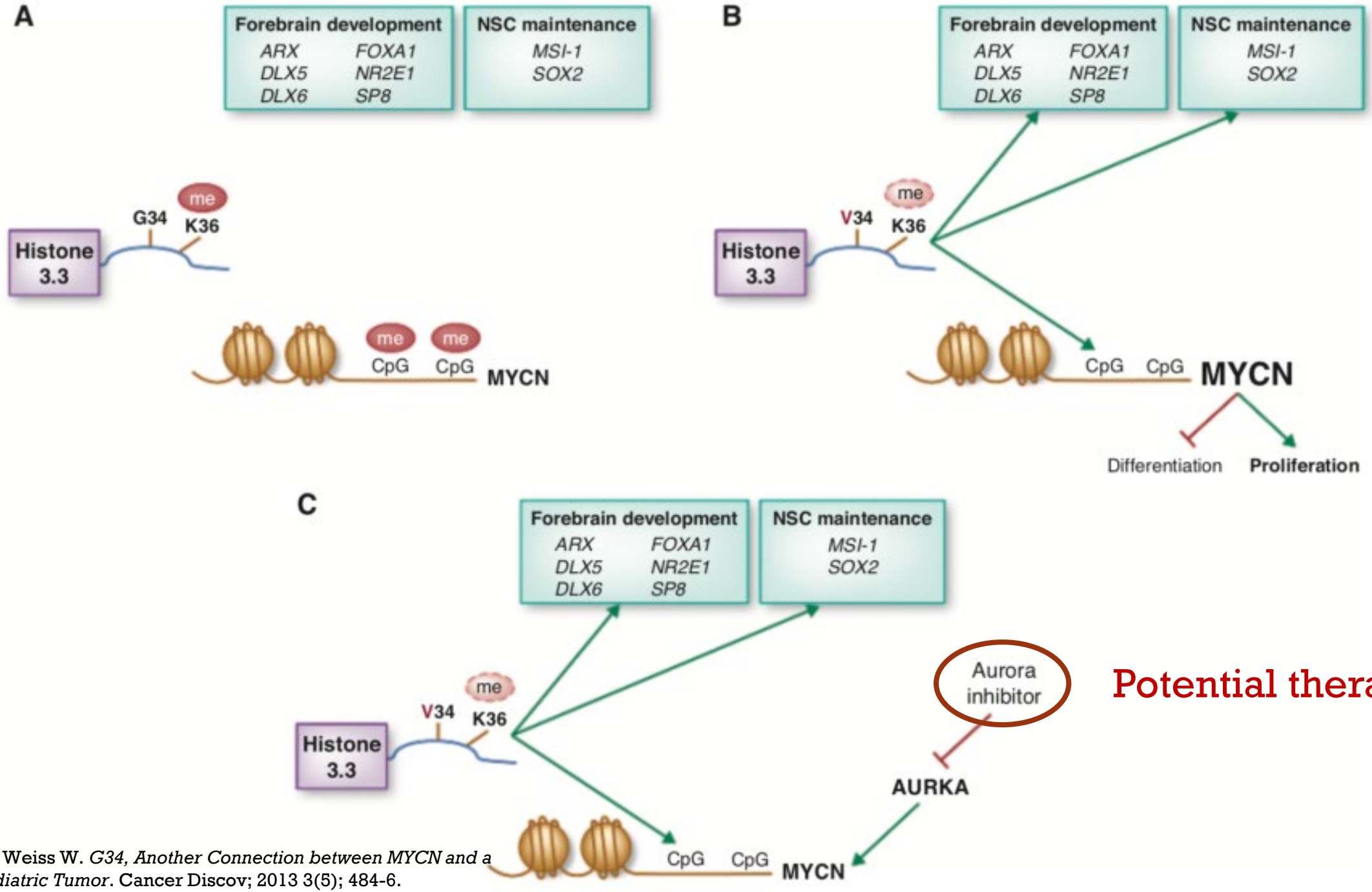
Diffuse astrocytic glioma, IDH wild-type, with molecular features of glioblastoma (WHO Grade IV)

H3F3A G34R MUTATION

- Involves critical amino acids within the N-terminal tail of the histone H3 variants, H3.3 and H3.1
- Affects gene transcription by altering chromatin accessibility
- Tumors have expression profiles resembling embryonic and early fetal stages of neocortical and striatal development, which may explain "PNET-like" histologic features



Yoshimoto K, et al. Prevalence and clinicopathological features of H3.3 G34-mutant high-grade gliomas: a retrospective study of 411 consecutive glioma cases in a single institution. Brain Tumor Pathol. 2017 Jul;34(3):103-112.



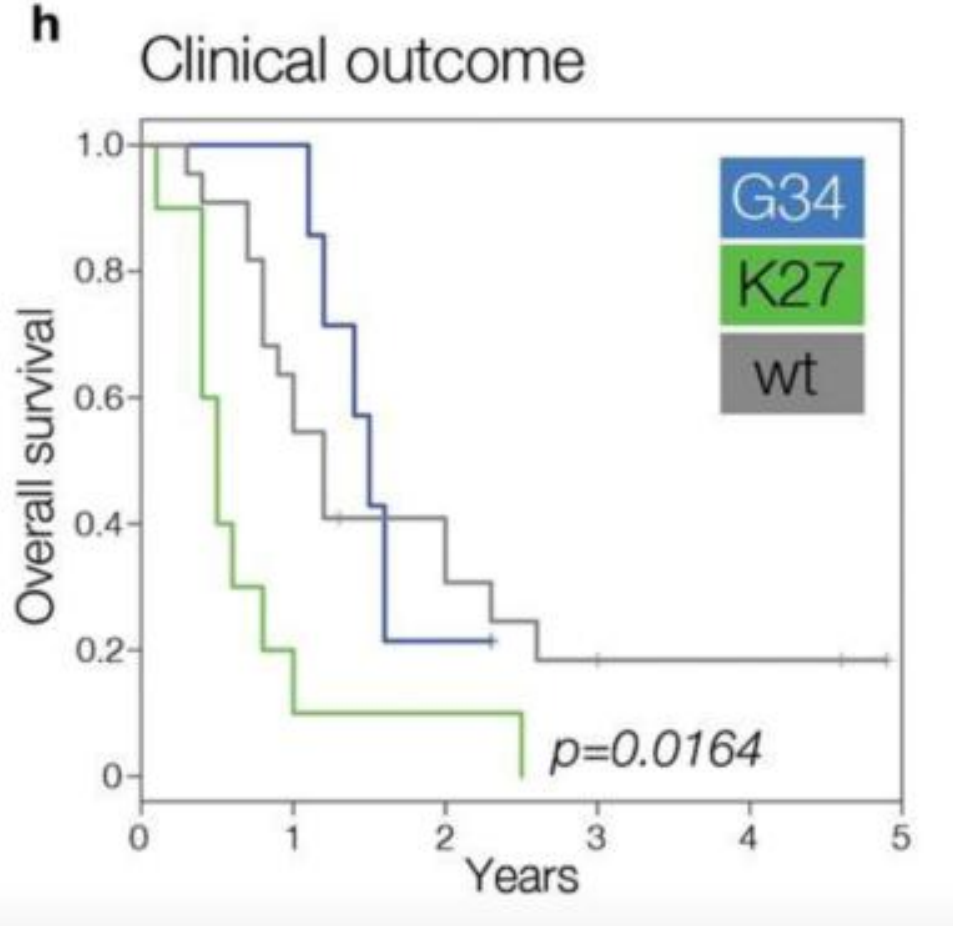
Potential therapy?

Huang M and Weiss W. *G34, Another Connection between MYCN and a Pediatric Tumor*. Cancer Discov; 2013 3(5); 484-6.

PROGNOSIS FOR THIS PATIENT?

- Better than *H3F3A* K27M mutant diffuse gliomas
- *TERT* mutation - reduced overall survival in absence of *IDH* mutation

- At 4 month follow-up (status post chemotherapy and proton therapy), patient is doing well with no recurrence



Bjerke L, Mackay A, Nandhabalan M, et al. Histone H3.3. mutations drive pediatric glioblastoma through upregulation of MYCN. *Cancer Discov*. 2013;3(5):512–519. doi:10.1158/2159-8290.CD-12-0426

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