AANP 2022
Diagnostic Slide Session (10)

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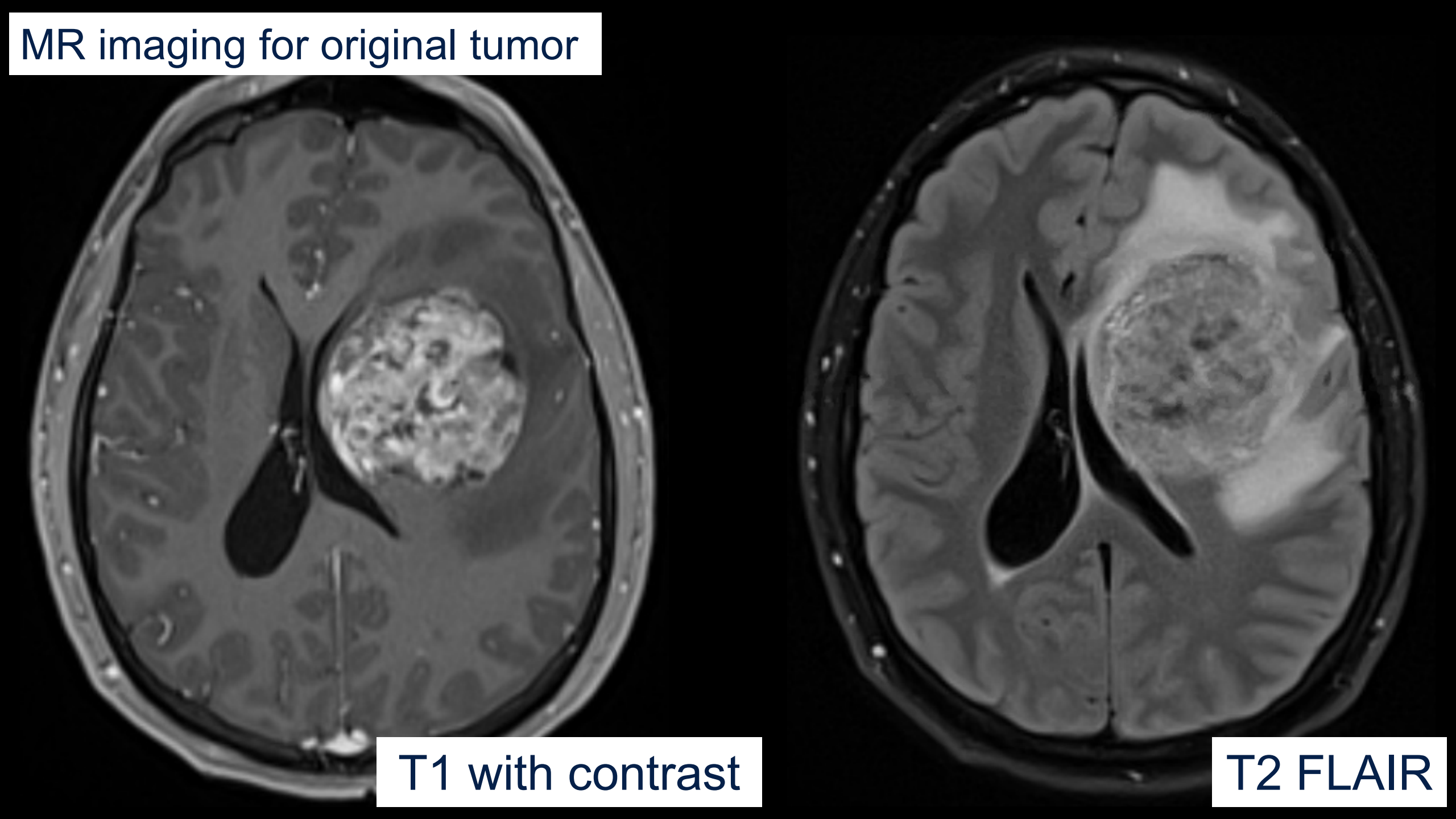
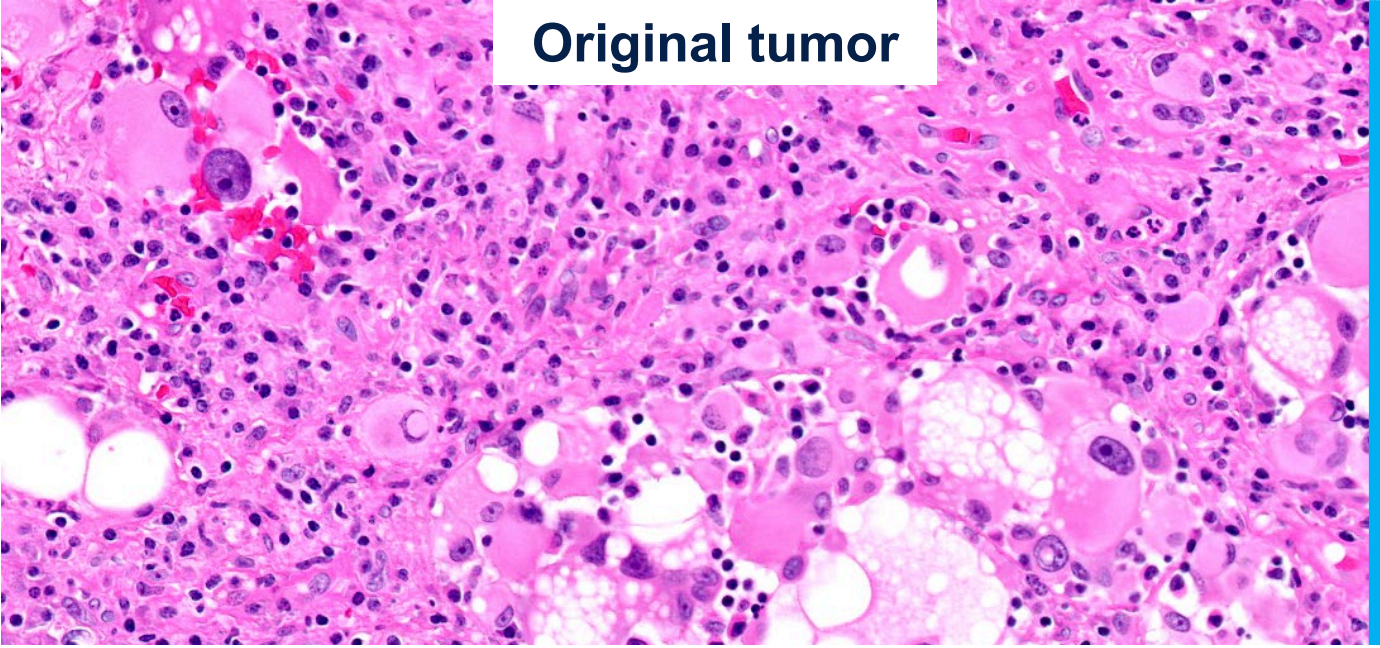
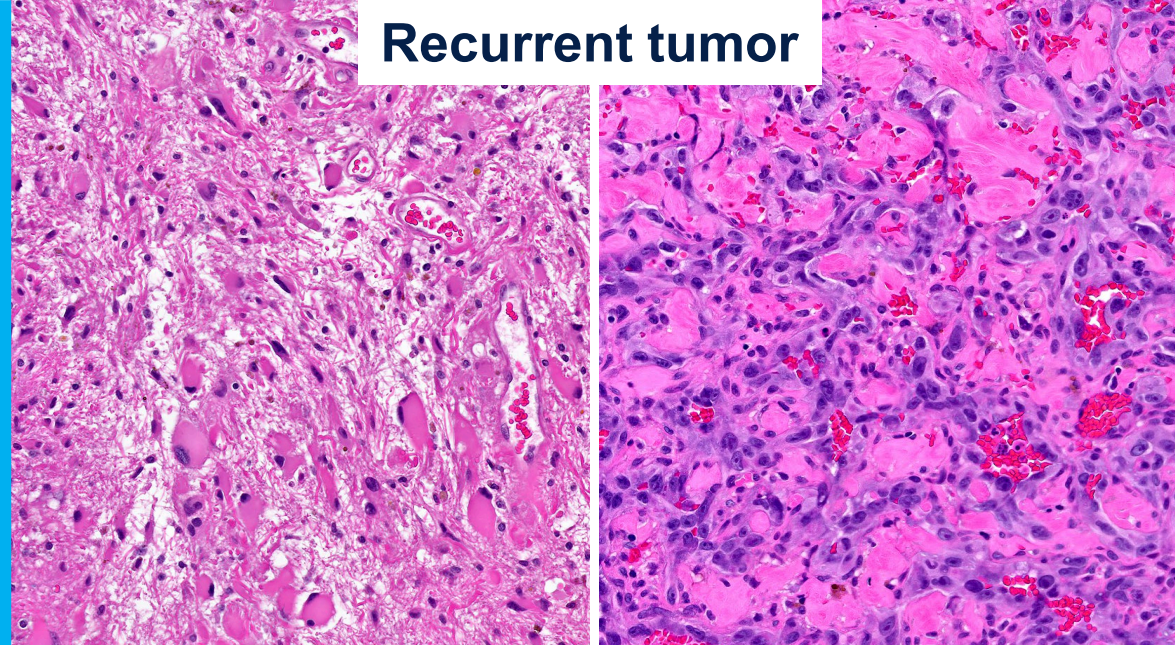
UCSF

Clinical Presentation

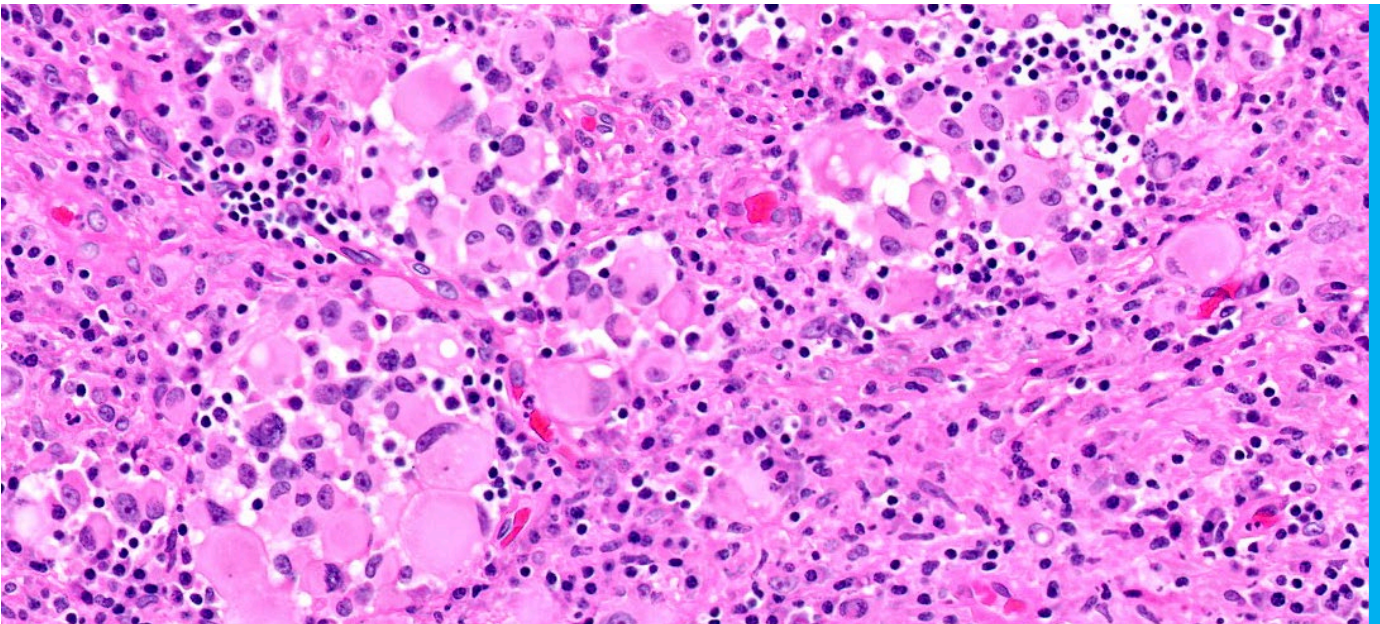
- The patient is a 23-year-old man who presented with progressively-worsening headache, nausea, vomiting, facial and upper extremity weakness (age at presentation 21 years).
- Imaging showed a left frontal contrast-enhancing mass.

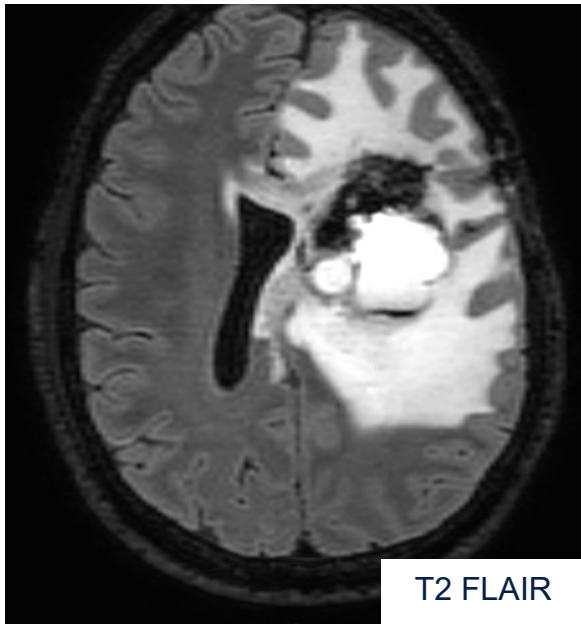

MR imaging for original tumor
T1 with contrast
T2 FLAIR

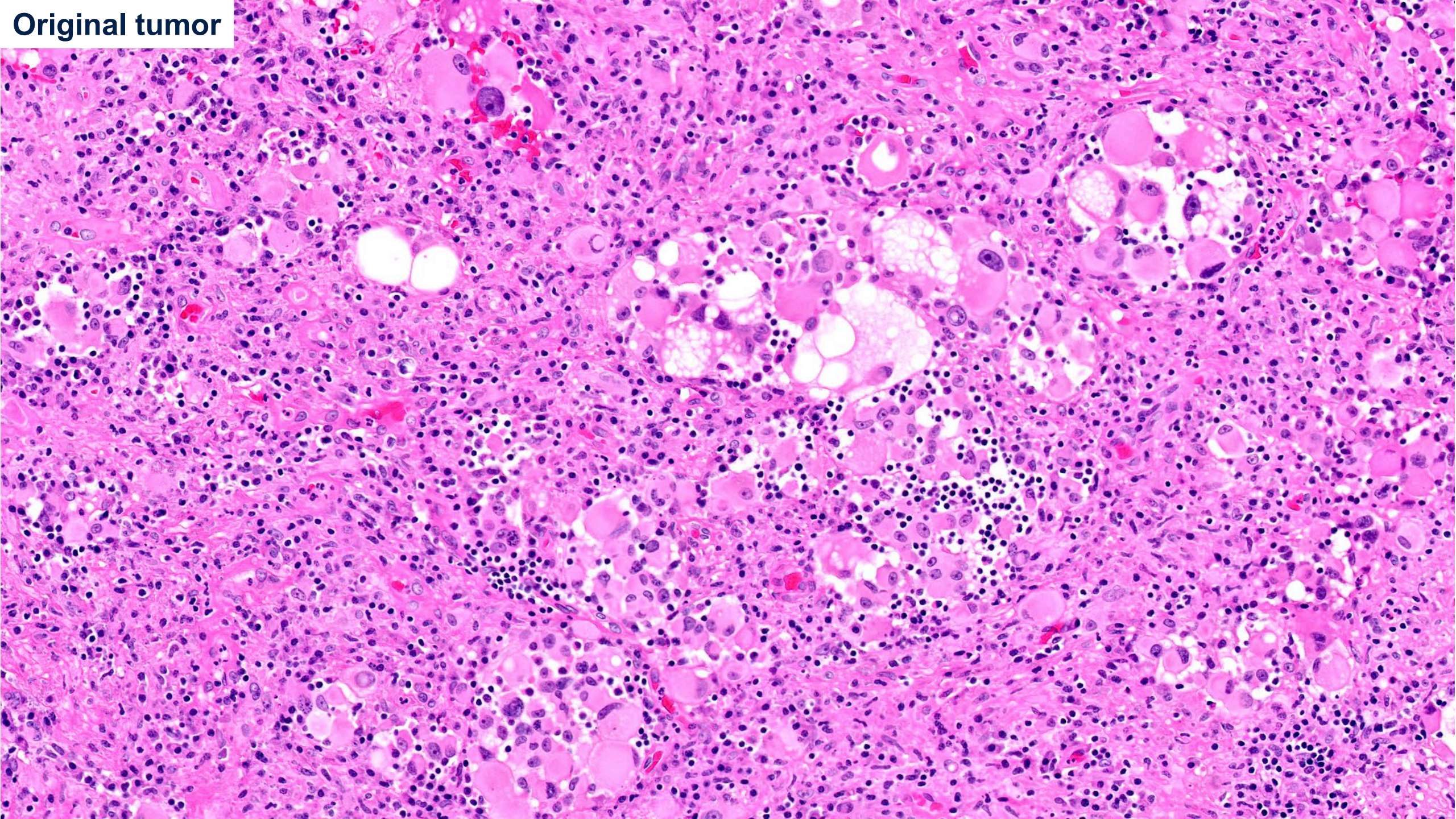


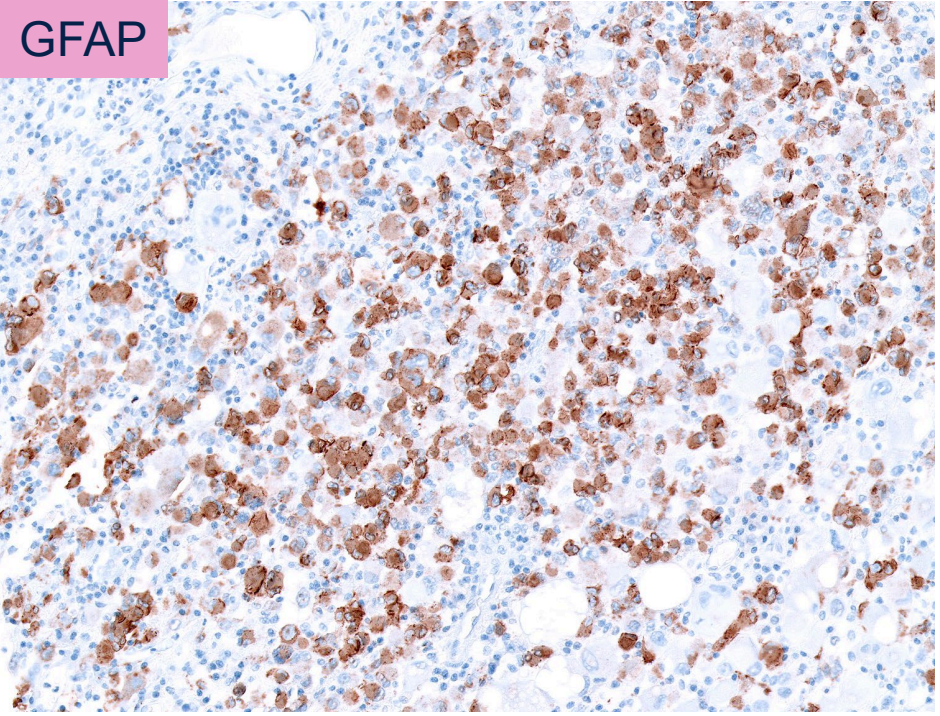


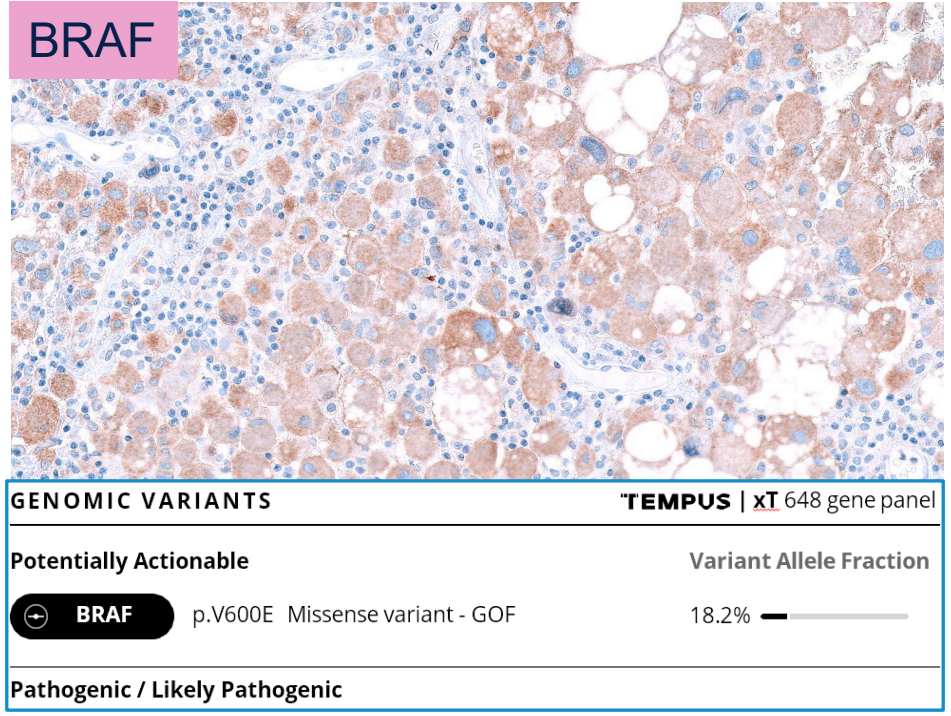
Discussion and differential diagnosis?






Original tumor



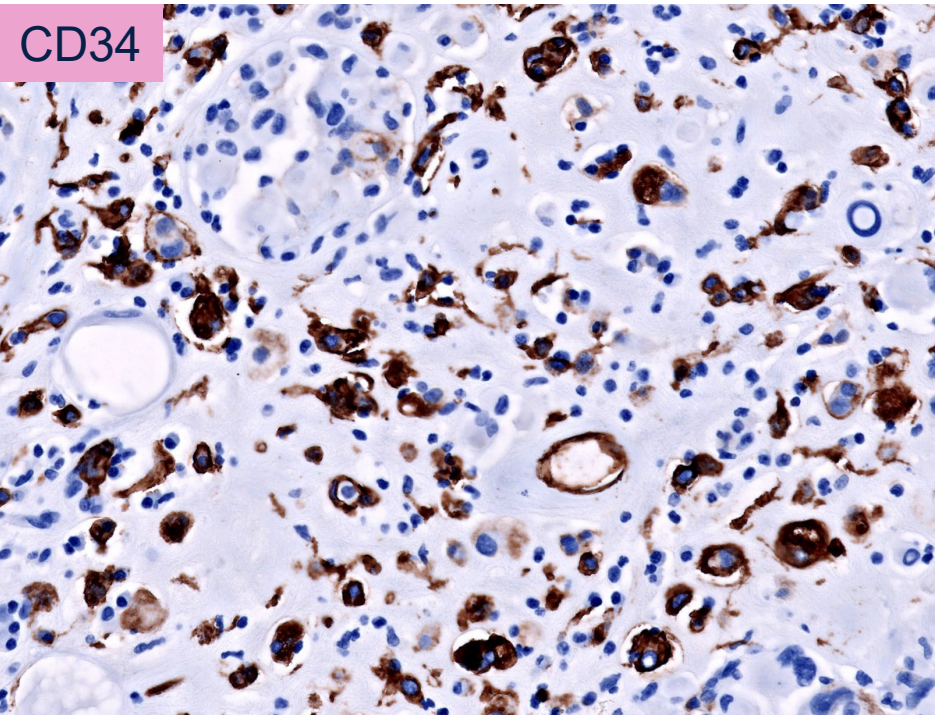


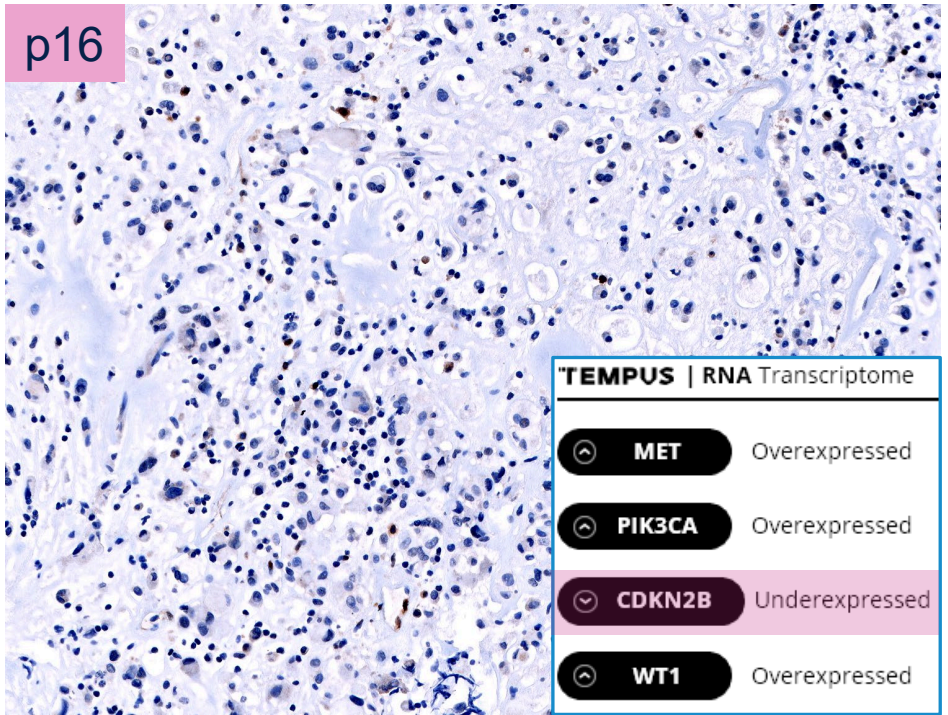
GENOMIC VARIANTS — TEMPUS | xT 648 gene panel

Potentially Actionable — Variant Allele Fraction

BRAF p.V600E Missense variant - GOF 18.2%

Pathogenic / Likely Pathogenic





TEMPUS | RNA Transcriptome

MET	Overexpressed
PIK3CA	Overexpressed
CDKN2B	Underexpressed
WT1	Overexpressed

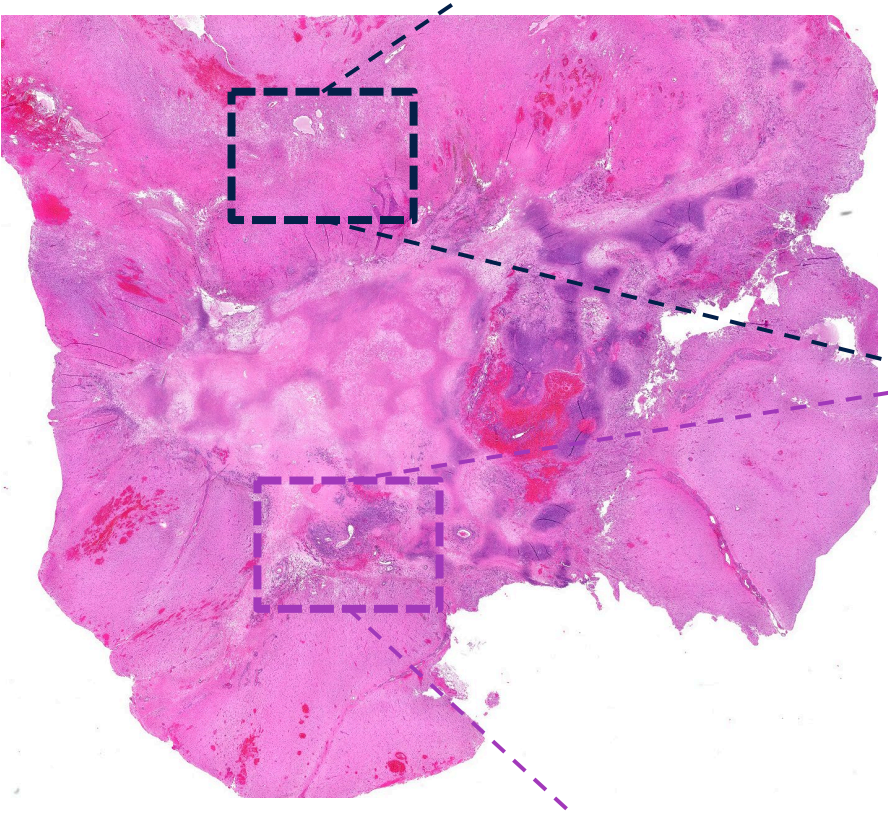
Diagnosis: PXA, WHO grade 3

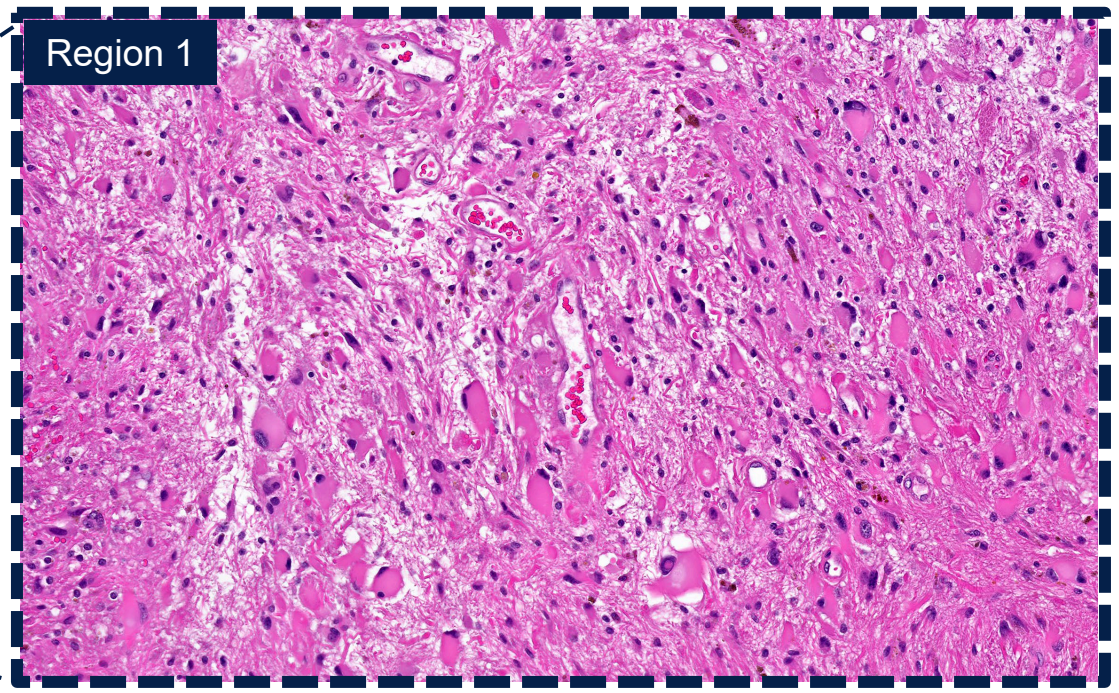
Original tumor

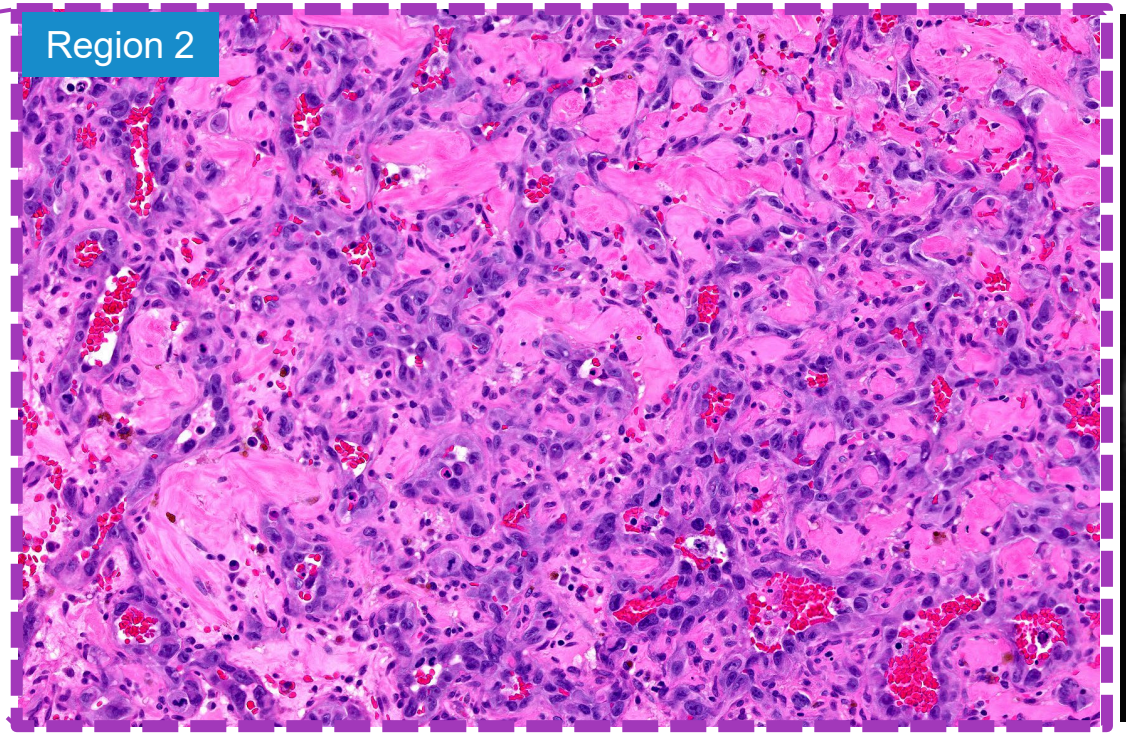
Clinical Follow-up

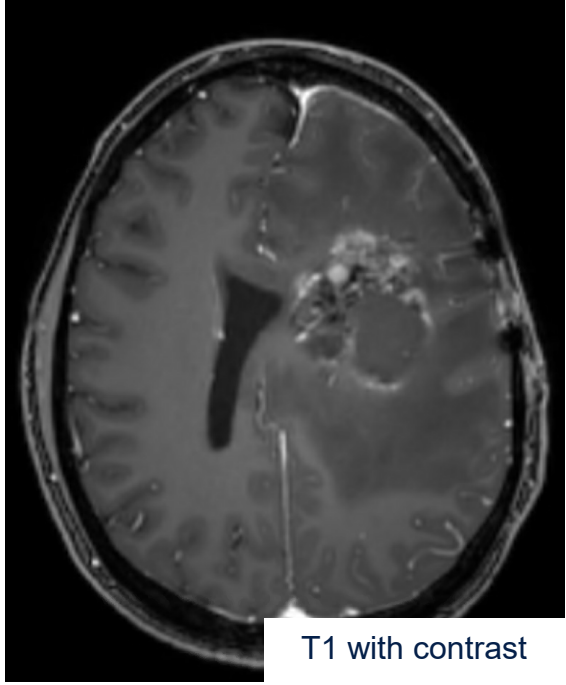
- Following the initial resection, he was treated with dabrafenib (BRAF inhibitor), trametinib (MEK inhibitor), and radiotherapy (5940 cGy in 33 fractions).
- Surveillance imaging (1 year later) demonstrated tumor recurrence and serial progression, he eventually underwent re-resection (2 years later).
- Intraoperatively, the tumor had solid and cystic components.

Recurrence 2 years after original surgery

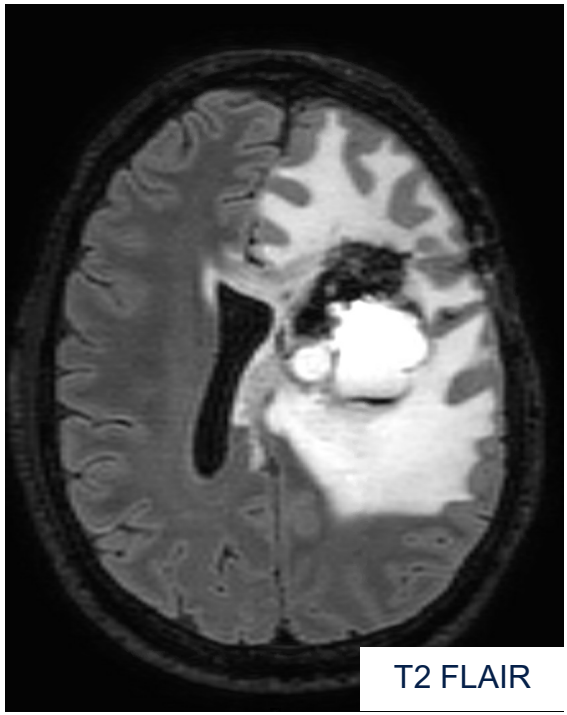




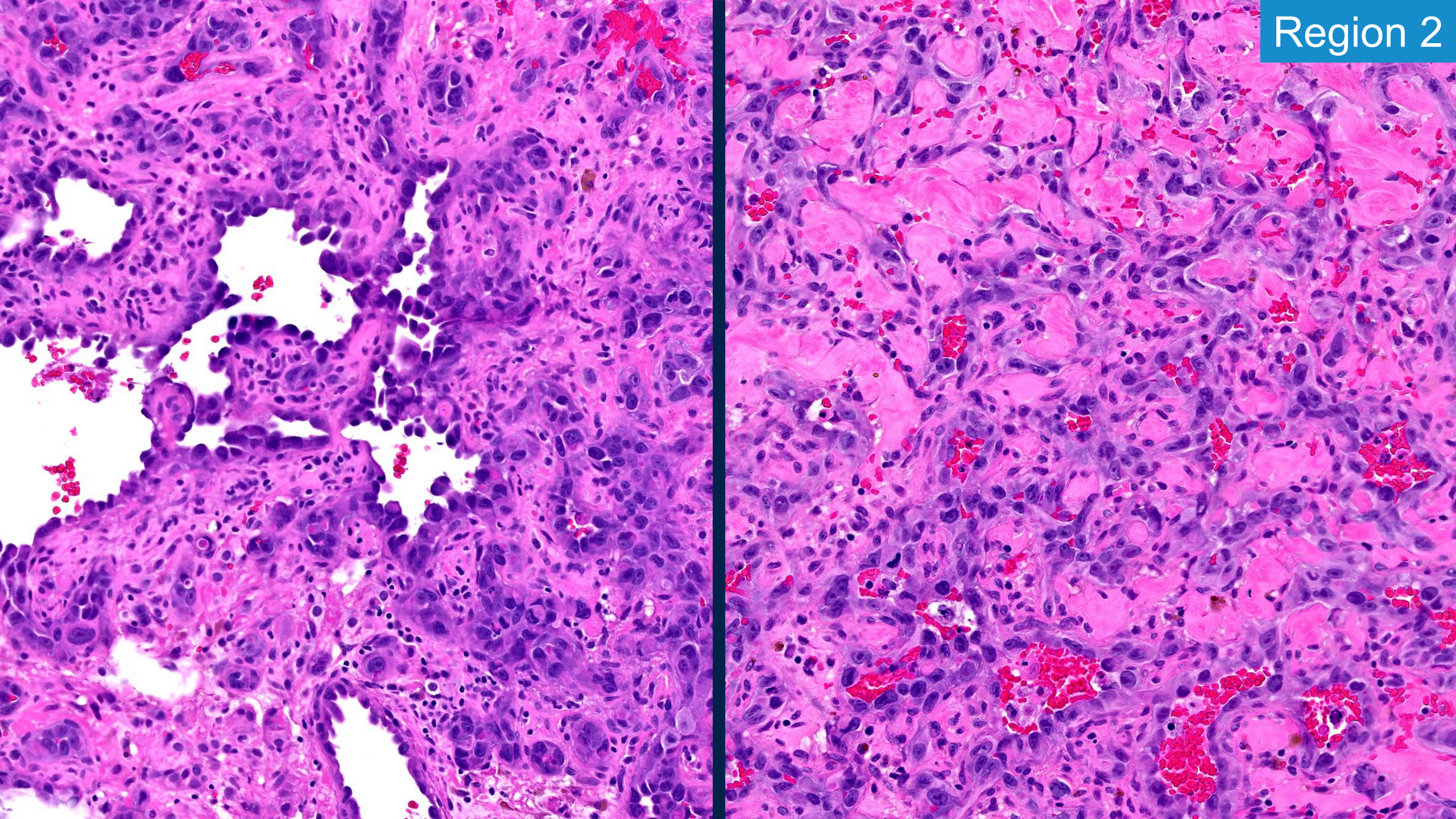


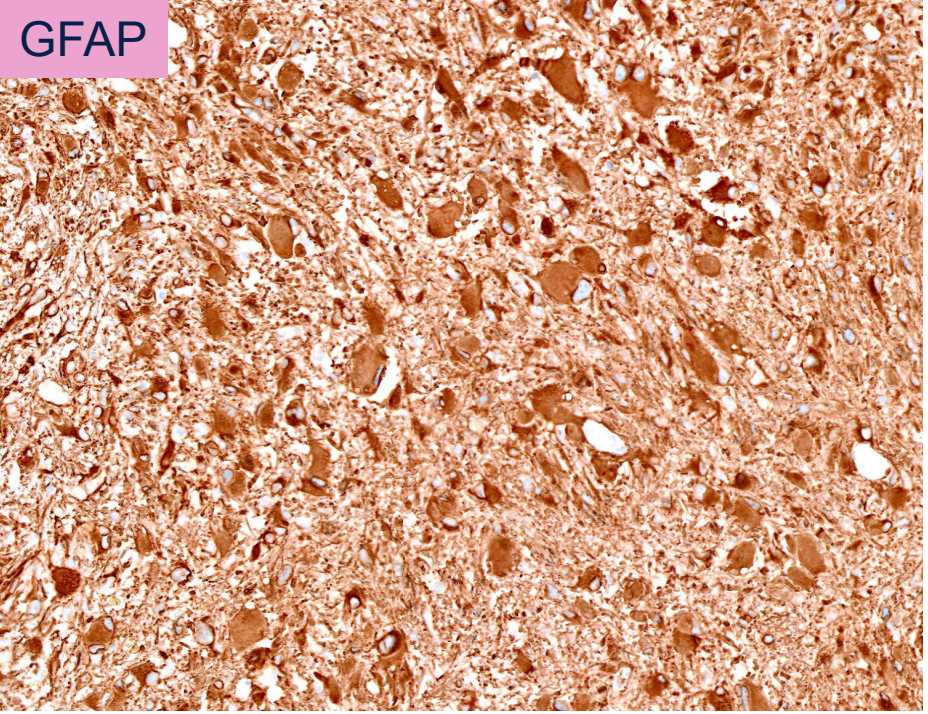


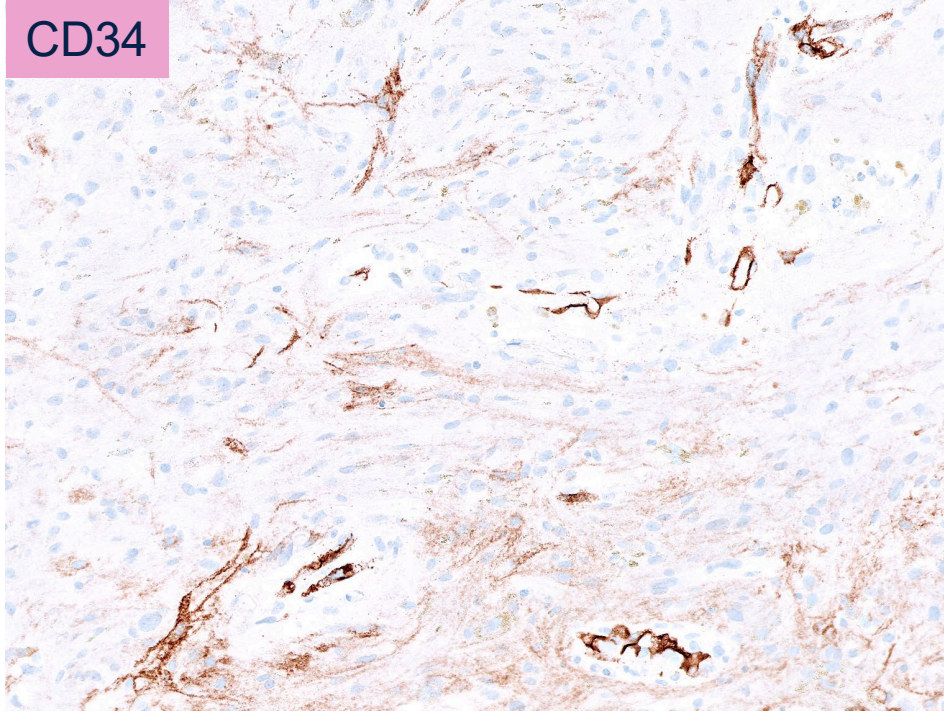
T1 with contrast

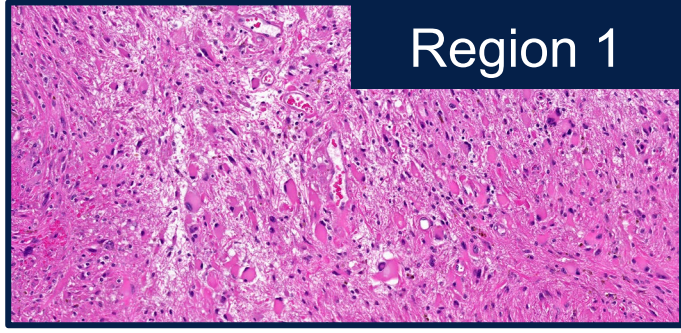


T2 FLAIR

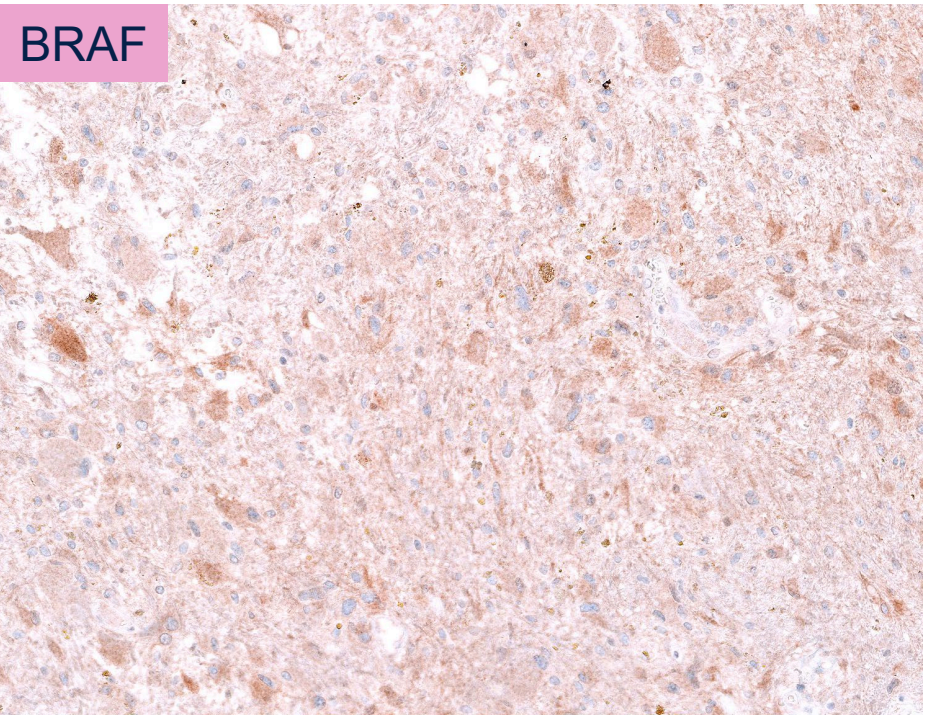

Region 2

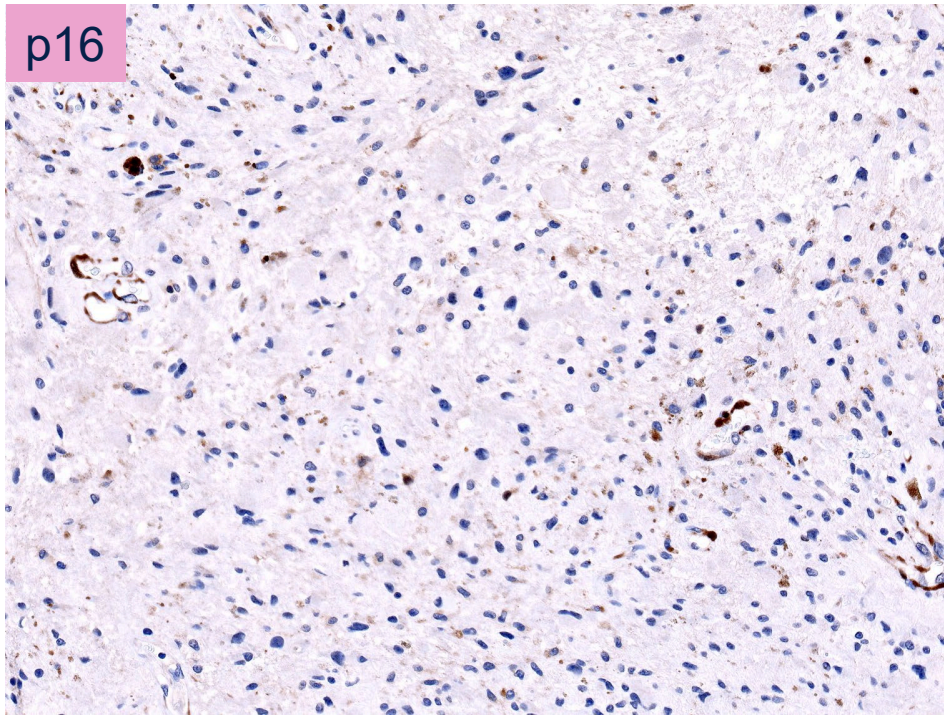


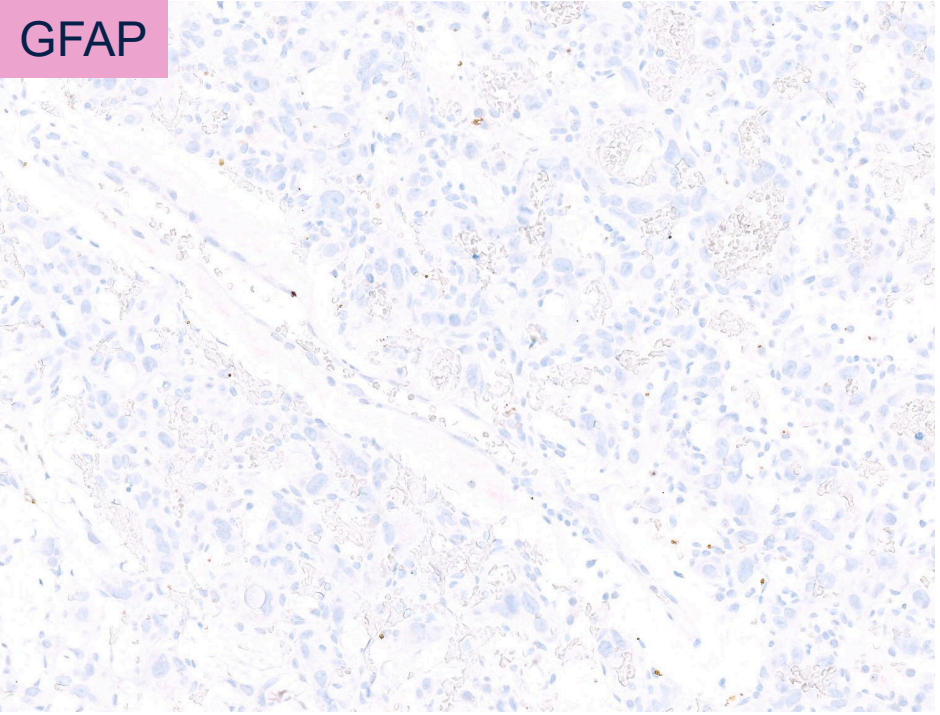


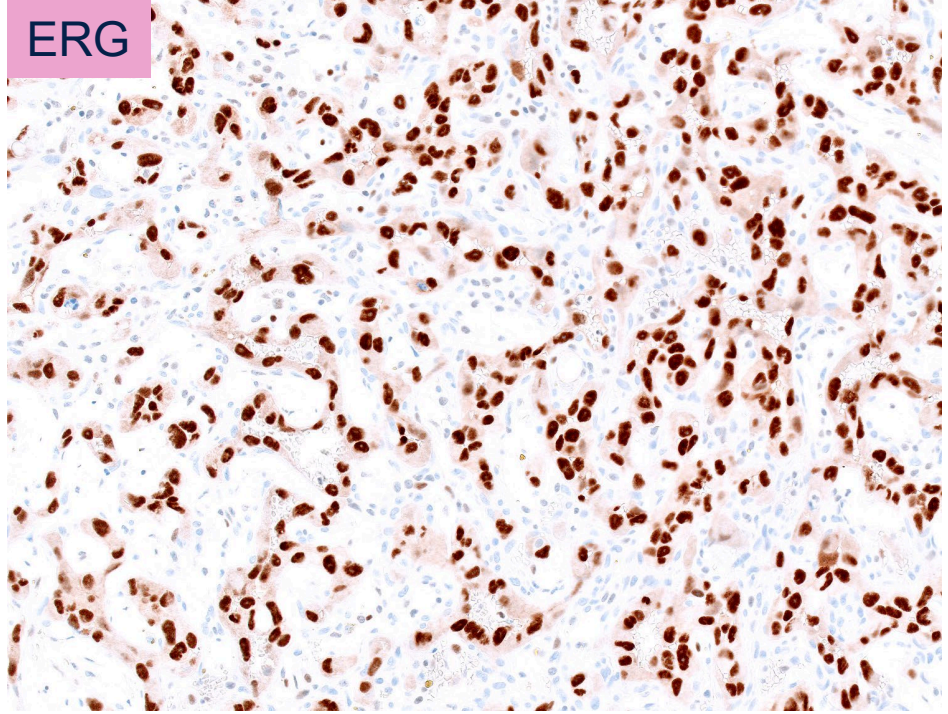


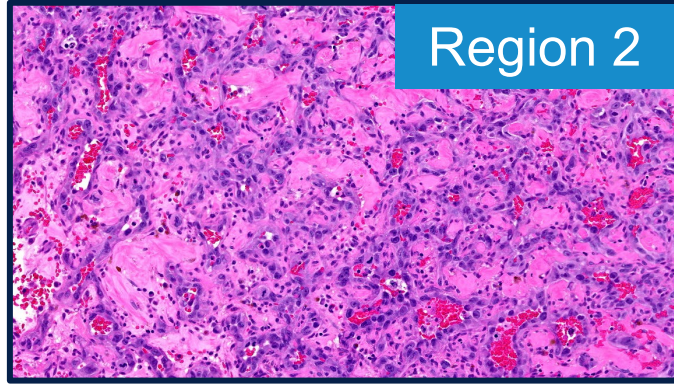
Recurrent tumor



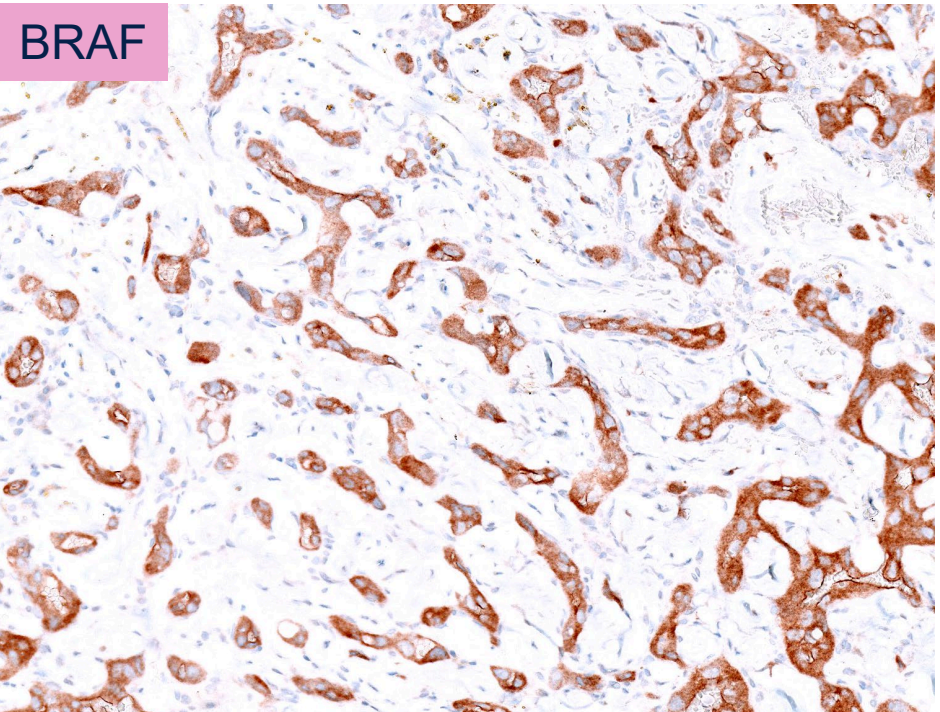


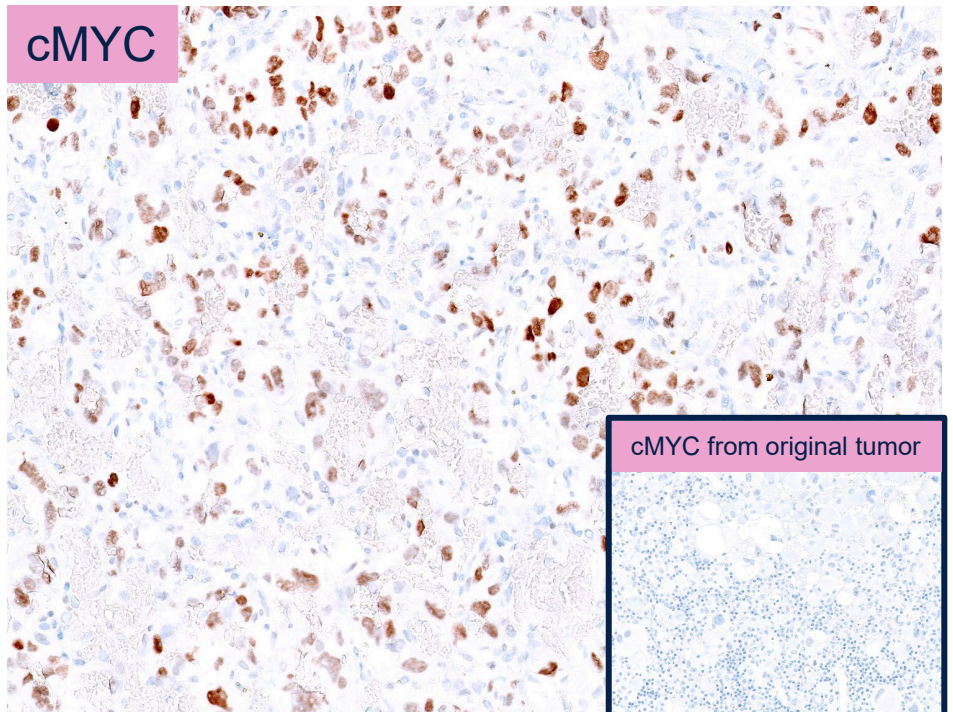






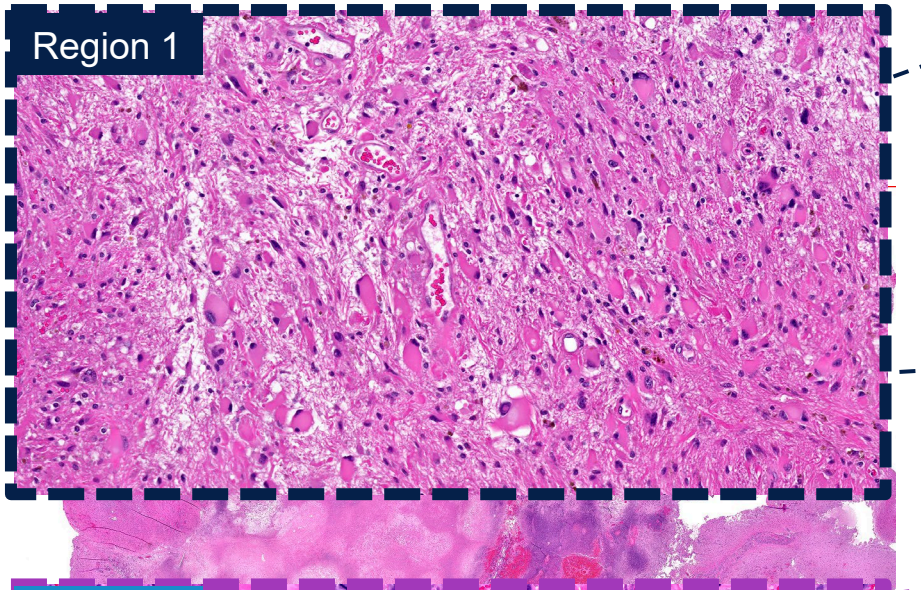
Recurrent tumor





Final diagnosis:
Pleomorphic xanthoastrocytoma, CNS WHO grade 3 with transformation to an epithelioid angiosarcoma

Region 1

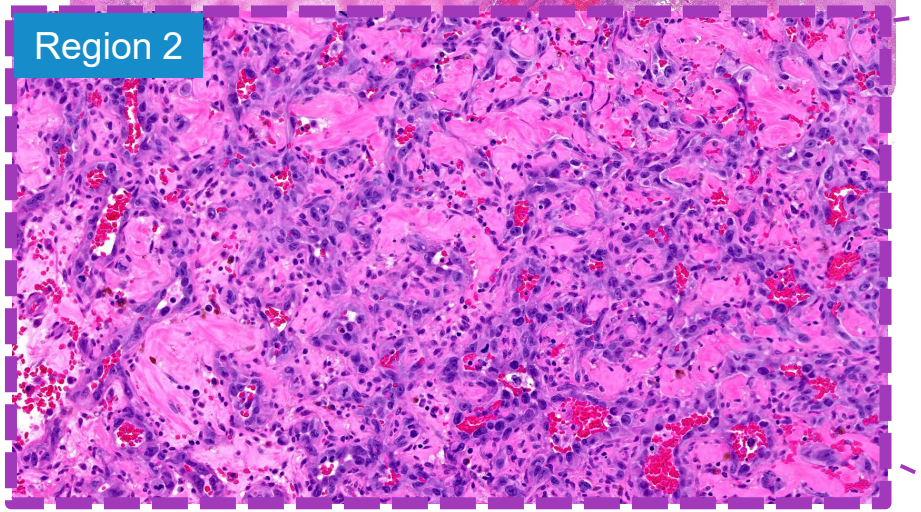


GENOMIC VARIANTS — TEMPUS | xT 648 gene panel

Potentially Actionable			Variant Allele Fraction
BRAF	p.V600E	Missense variant - GOF	5.4%

Pathogenic / Likely Pathogenic

Region 2



GENOMIC VARIANTS — TEMPUS | xT 648 gene panel

Potentially Actionable			Variant Allele Fraction
BRAF	p.V600E	Missense variant - GOF	17.7%

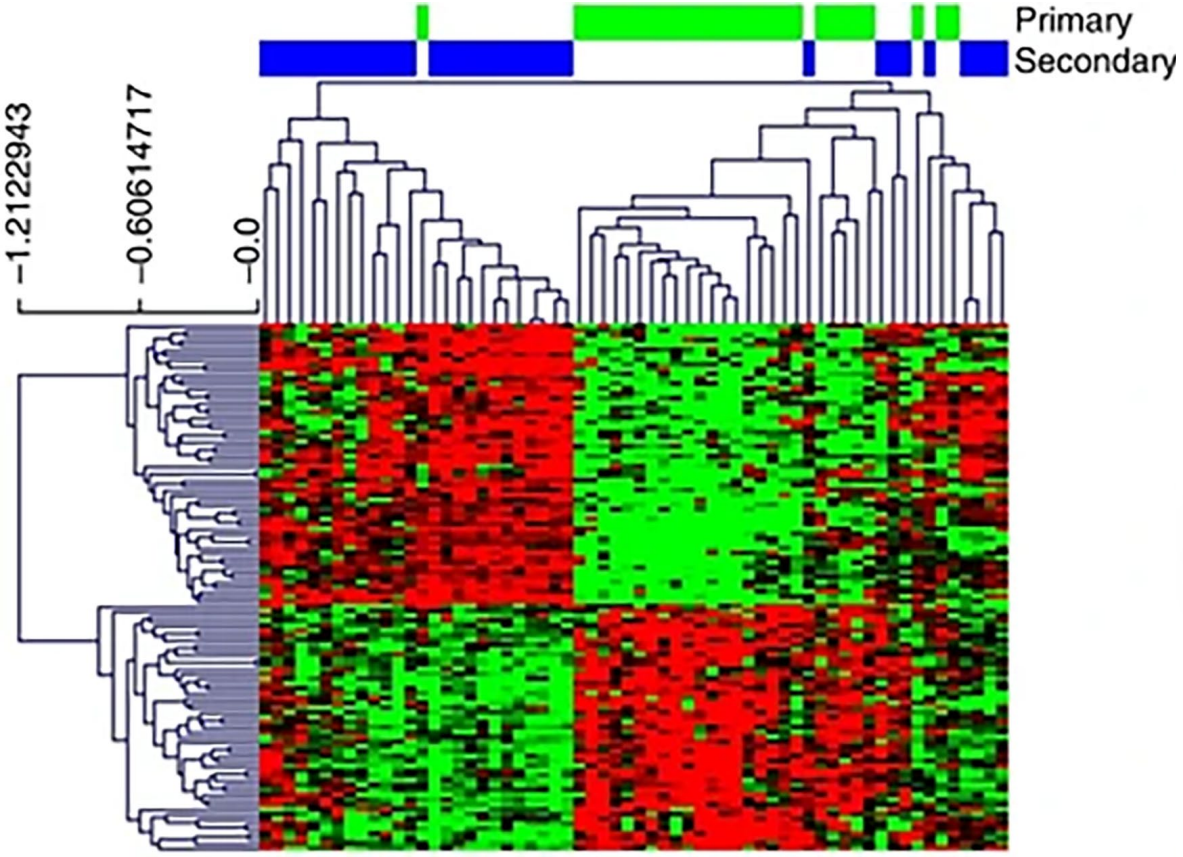
Biologically Relevant			
SMARCB1	c.1118+2T>C	Splice region variant - LOF	8.4%

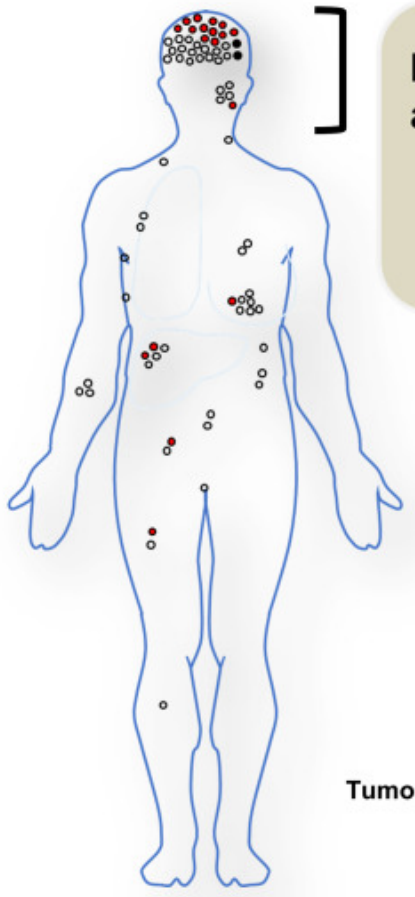
Pathogenic / Likely Pathogenic

Clinical course

- MRI 6 weeks post-operatively demonstrated an expanding mass, concerning for tumor recurrence.
- He subsequently presented with intracerebral hemorrhage, was placed on comfort care, and passed away (11 weeks after the second surgery).

Role of radiation and *cMYC* in angiosarcoma

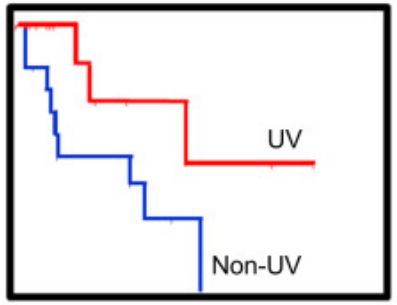




Head & neck angiosarcomas

~50% UV-related

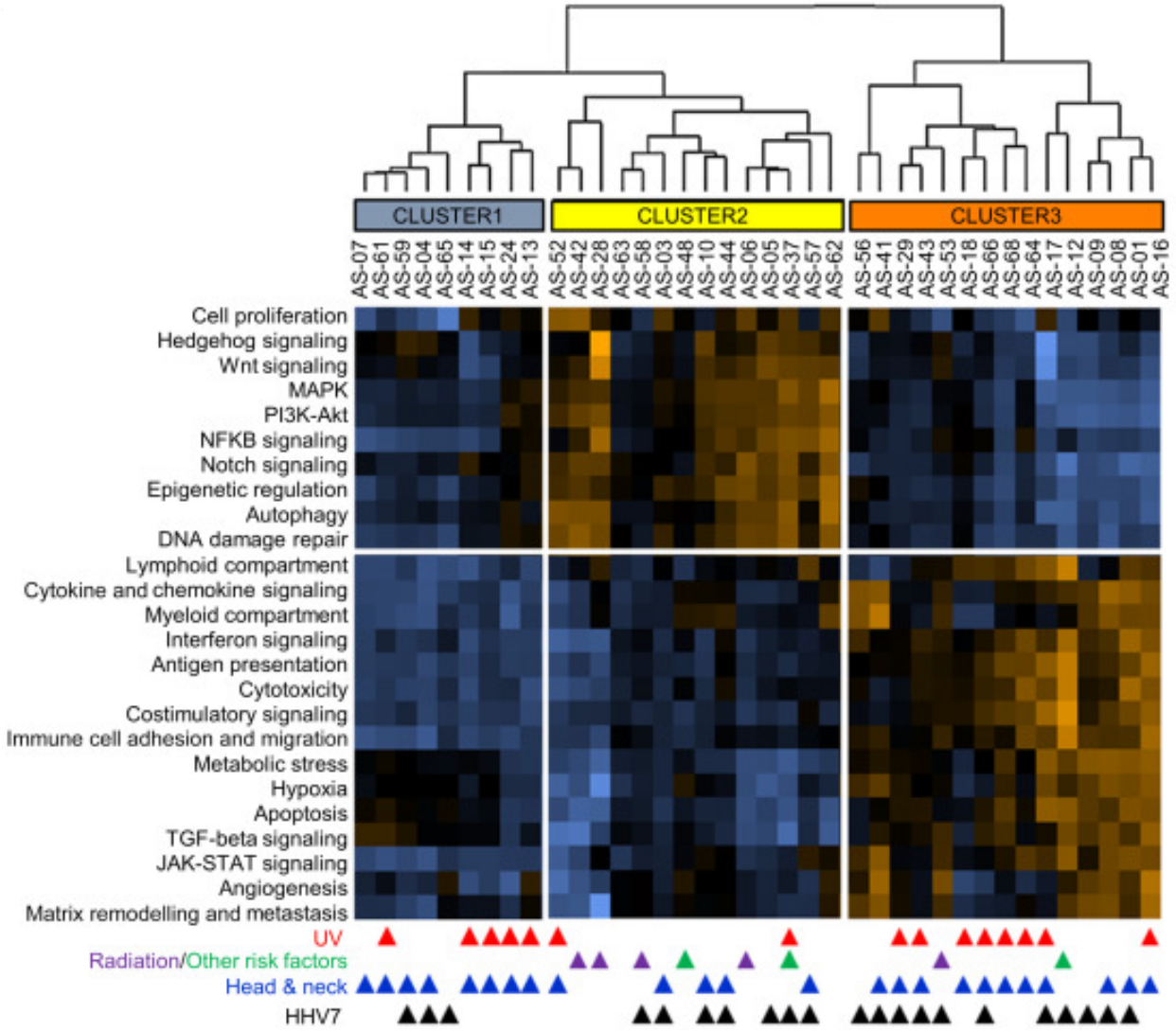
↑Tumor mutation burden

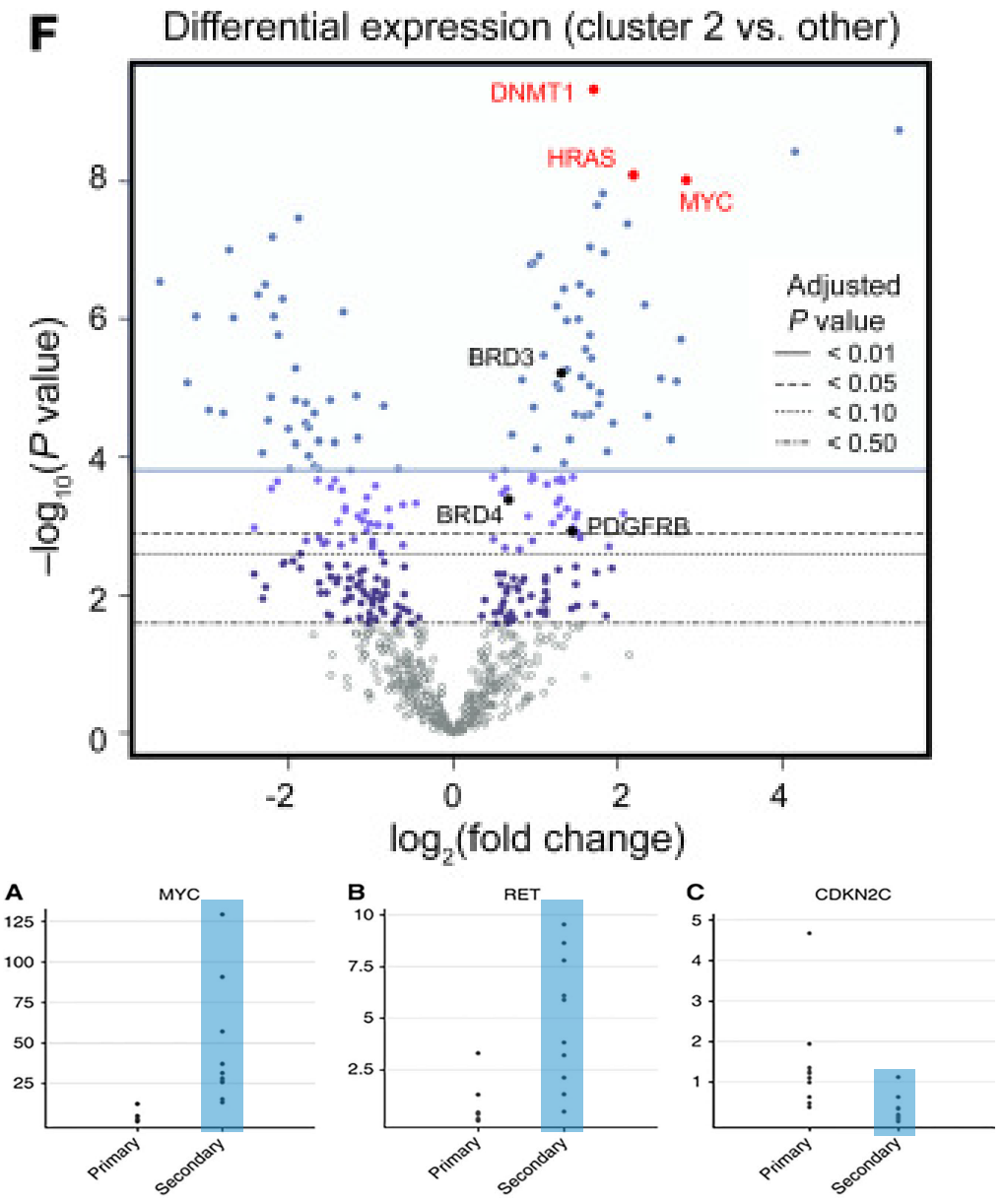


	CLUSTER 1	CLUSTER 2	CLUSTER 3
Etiology	Primary	Secondary	Primary
Anatomical origin	Head & neck		Head & neck
Risk factors	UV	RT & others	UV
Signaling pathways		Oncogenic & Epigenetic	Immune-related
Tumor inflammation signature	Low	Moderate	High

- Chan JY, Lim JQ, Yeong J, et al. Multiomic analysis and immunoprofiling reveal distinct subtypes of human angiosarcoma. *J Clin Invest*. 2020 Nov 2;130(11):5833-5846. doi: 10.1172/JCI139080. PMID: 33016928.
- Styring E, Seinen J, Dominguez-Valentin M, et al. Key roles for MYC, KIT and RET signaling in secondary angiosarcomas. *Br J Cancer*. 2014 Jul 15;111(2):407-12. doi: 10.1038/bjc.2014.359. Epub 2014 Jul 1. PMID: 24983371.

Role of radiation and *cMYC* in angiosarcoma





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Acknowledgements

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  - Dr. Arie Perry
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  - Dr. Calixto-Hope Lucas
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- **University of Nebraska**
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