

Clinical response to the PDGFRA/KIT inhibitor avapritinib in pediatric and young adult high-grade glioma patients with H3K27M or *PDGFRA* genomic alterations

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Cancer Institute



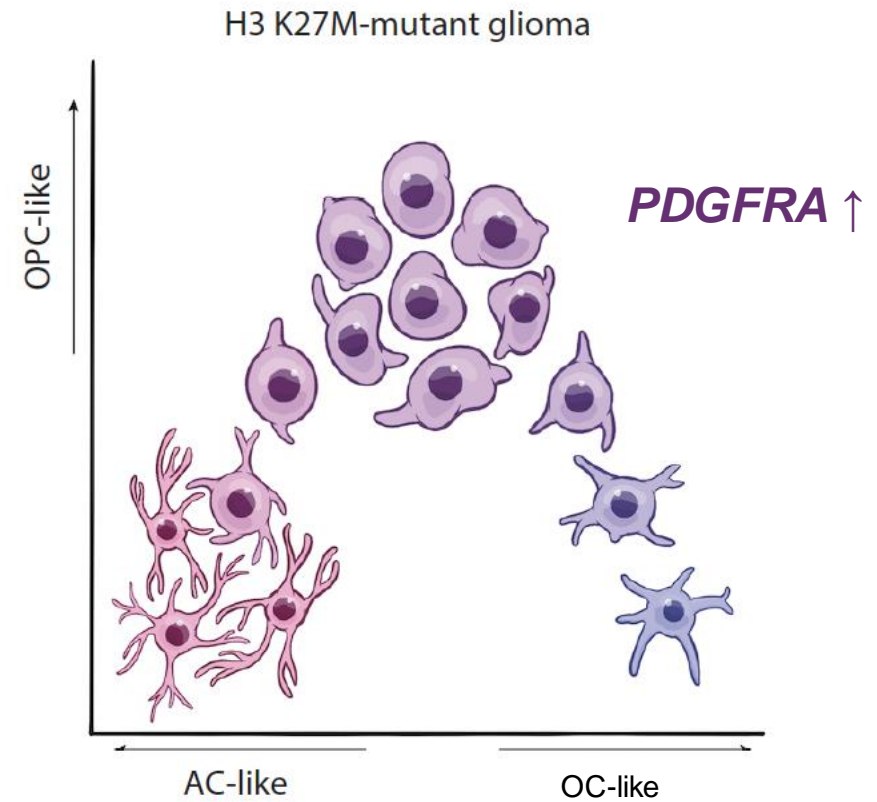
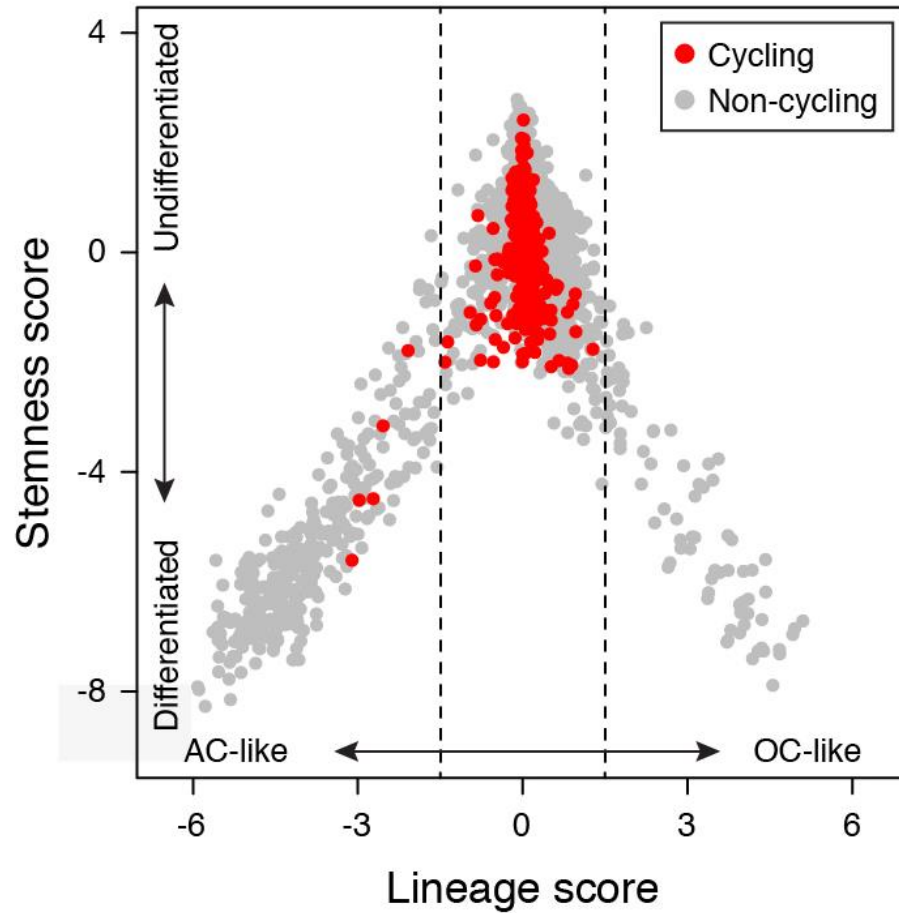
Boston
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Dana-Farber/Boston Children's Cancer and Blood Disorders Center

Disclosures

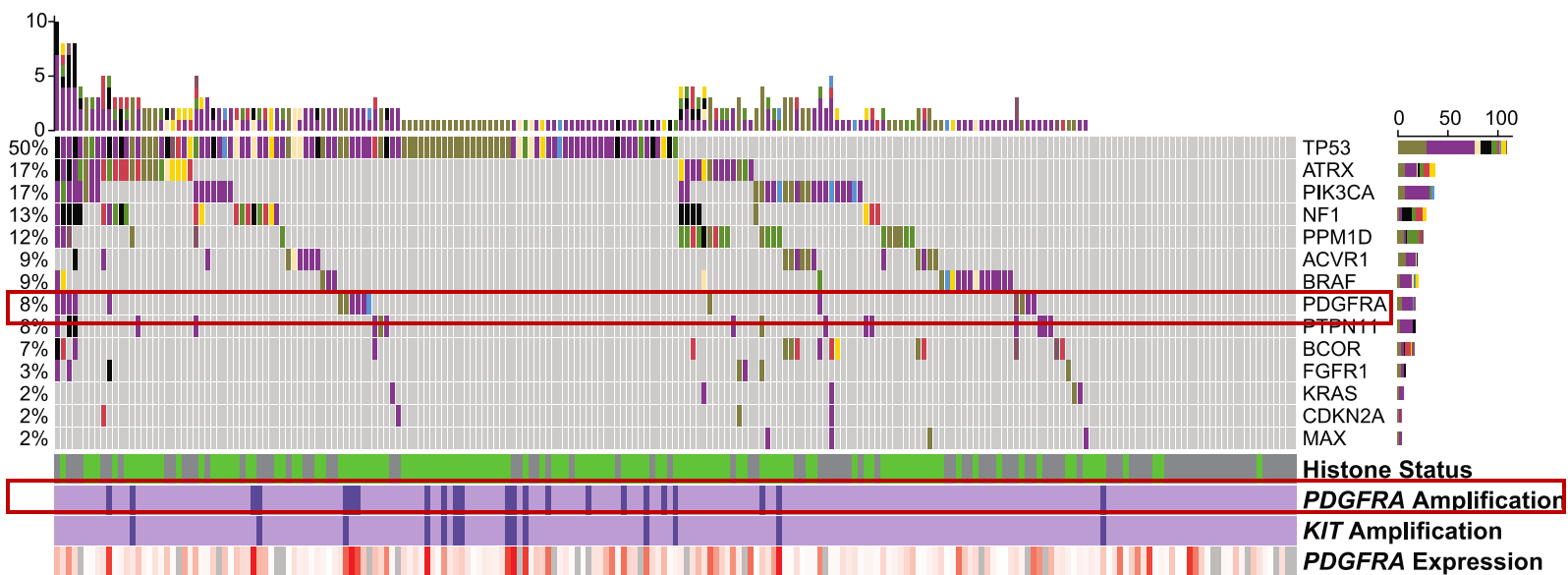
I have nothing to disclose.

H3K27M diffuse midline glioma are primarily composed of stem-like cells with high *PDGFRA* expression

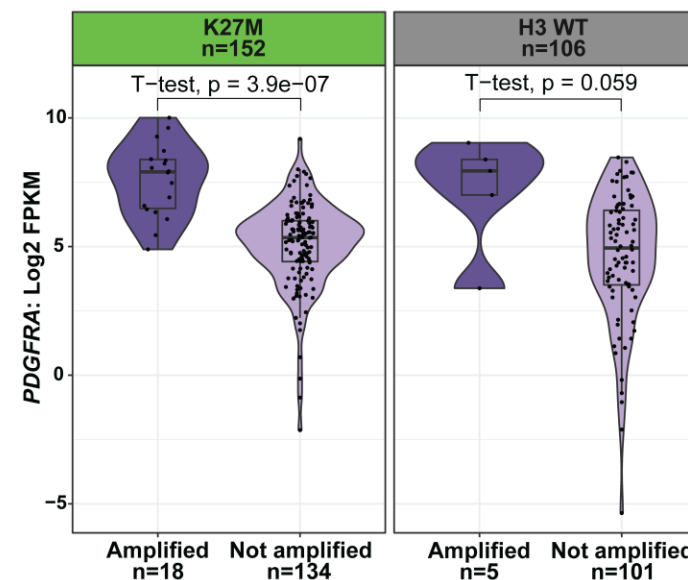
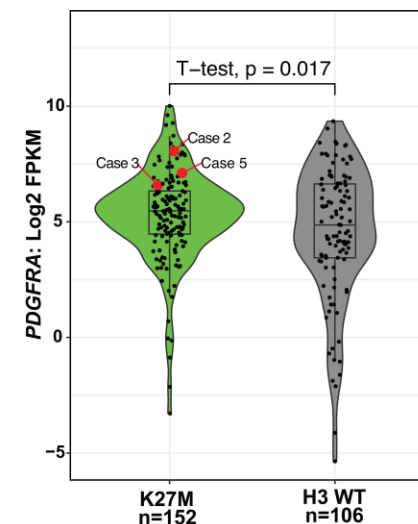


Filbin M, et al 2018

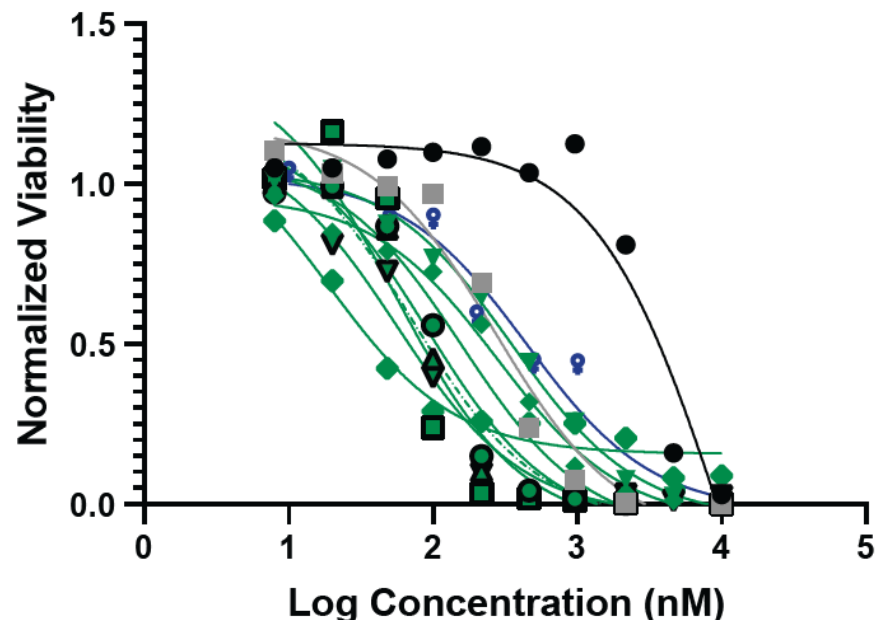
PDGFRA is altered in 15% of all pHGG cases



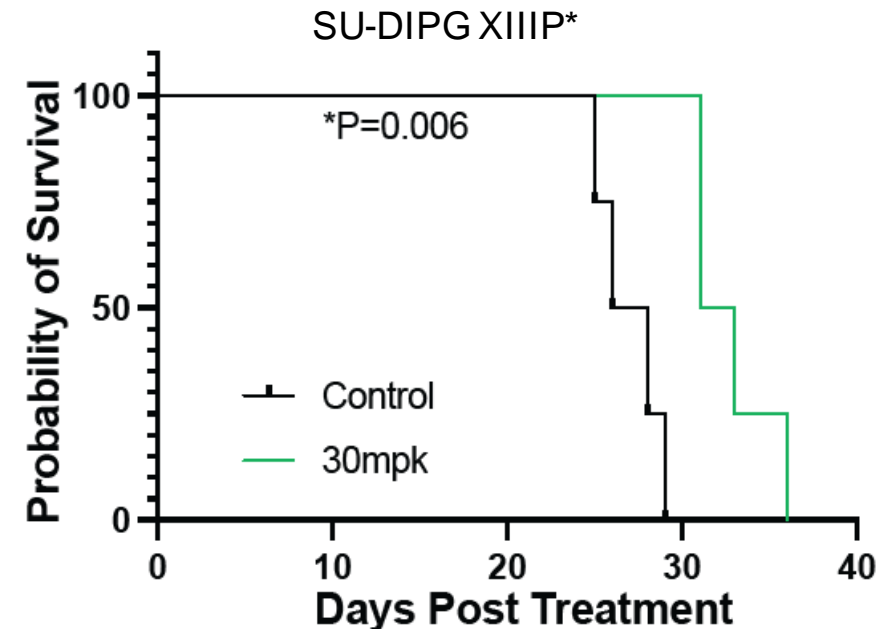
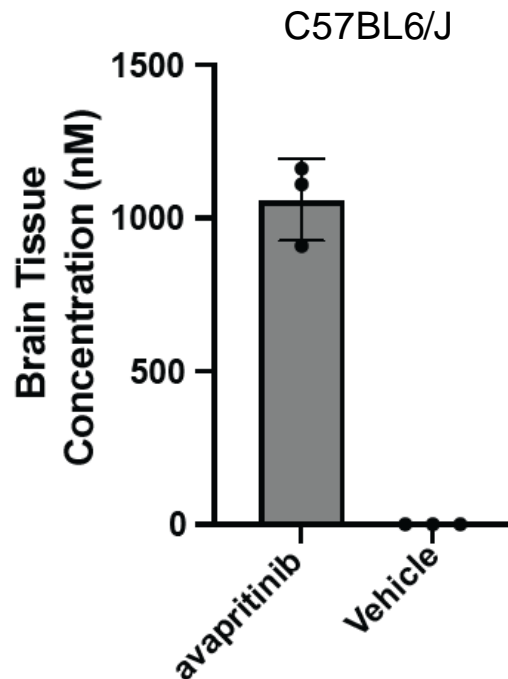
PDGFRA mutations in ~8%
 PDGFRA amplifications in ~10% → ~ 15% PDGFRA alterations



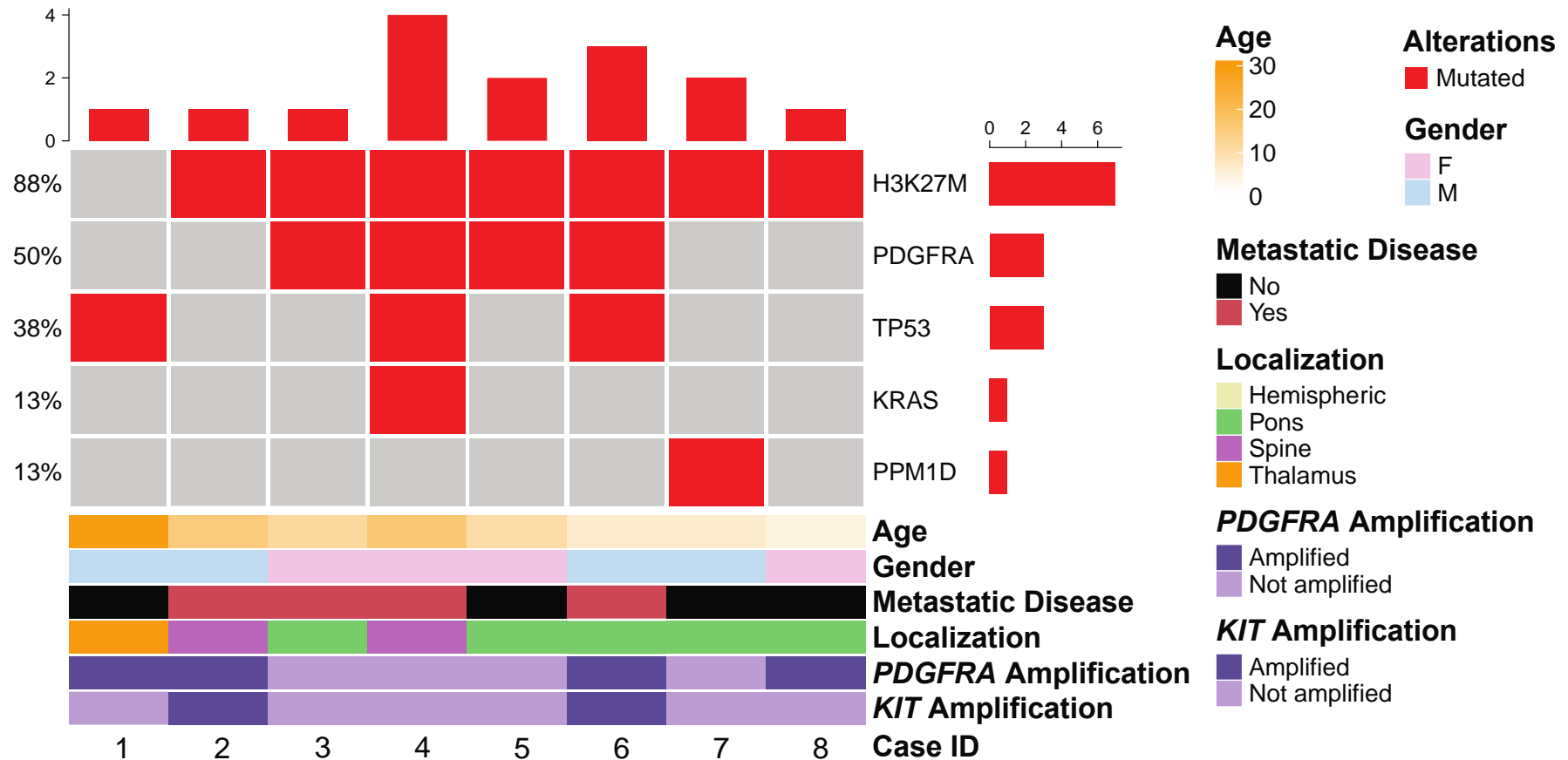
Avapritinib is active in patient-derived glioma lines *in vitro* and *in vivo*



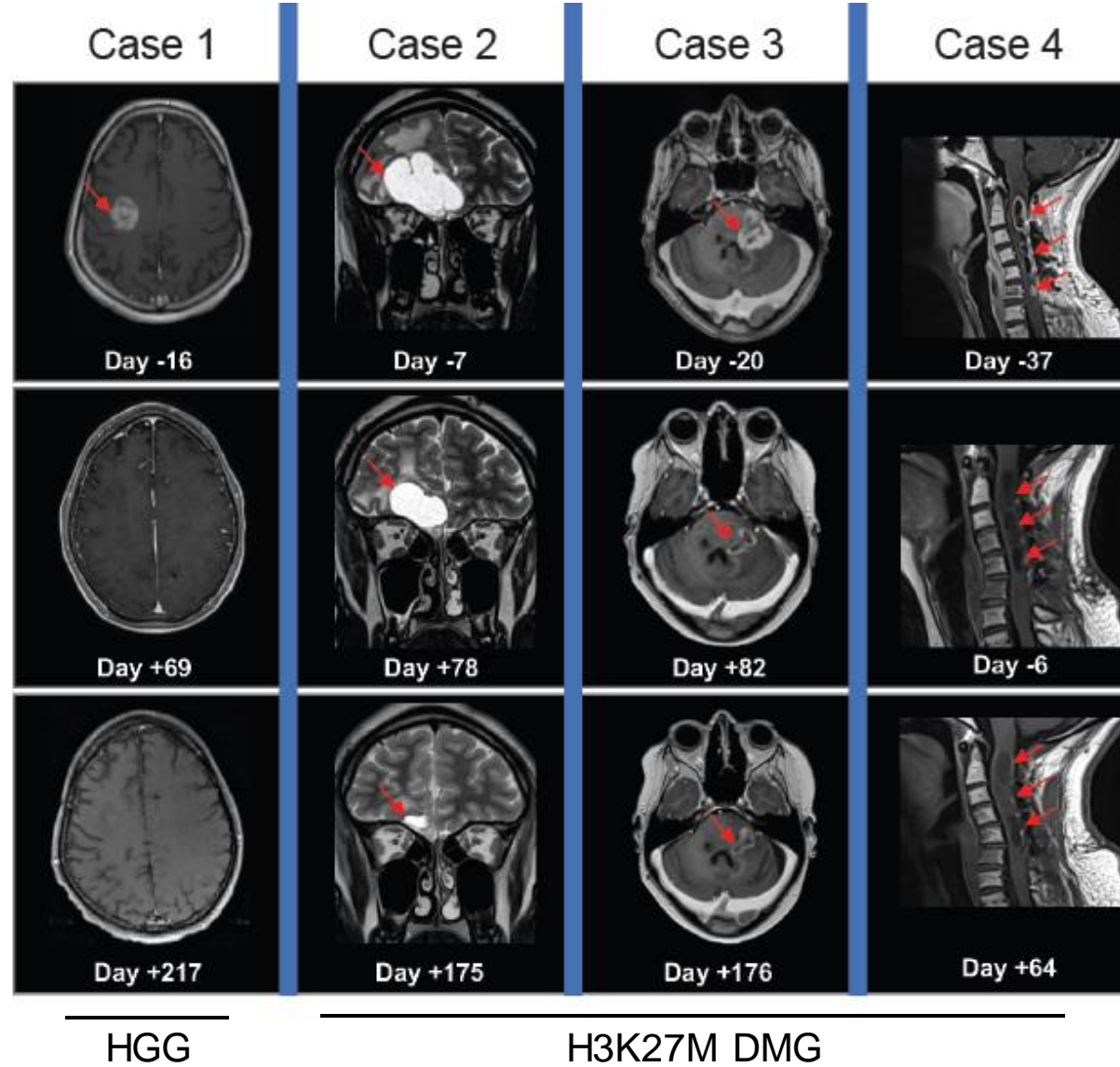
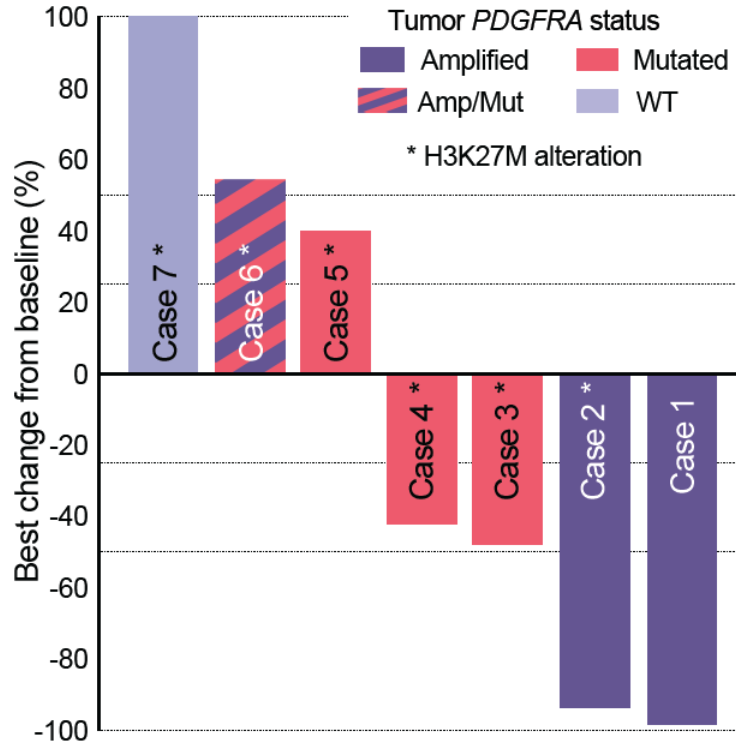
- | | |
|------------------------------|-------------------------------|
| H3K27M pHGG PDGFRA WT | H3K27M pHGG PDGFRA AMP |
| ▼ BT869 (IC50=356nM) | ▲ BT245 (AMP) (IC50=70nM) |
| ◆ SU-DIPG XXV (IC50=280nM) | |
| ● SU-DIPG IV (IC50=90nM) | H3 WT pHGG PDGFRA WT |
| ■ DIPG 007 (IC50=55nM) | ■ DIPG48 (IC50=270nM) |
| ▼ SU-DIPG XIII (IC50=56nM) | Adult HGG PDGFRA MUT |
| ◆ SU-DIPG XIIP* (IC50=20nM) | ◆ 154C (IC50=440nM) |
| | Non-malignant control |
| | ● NHA-hTERT (IC50=10080nM) |



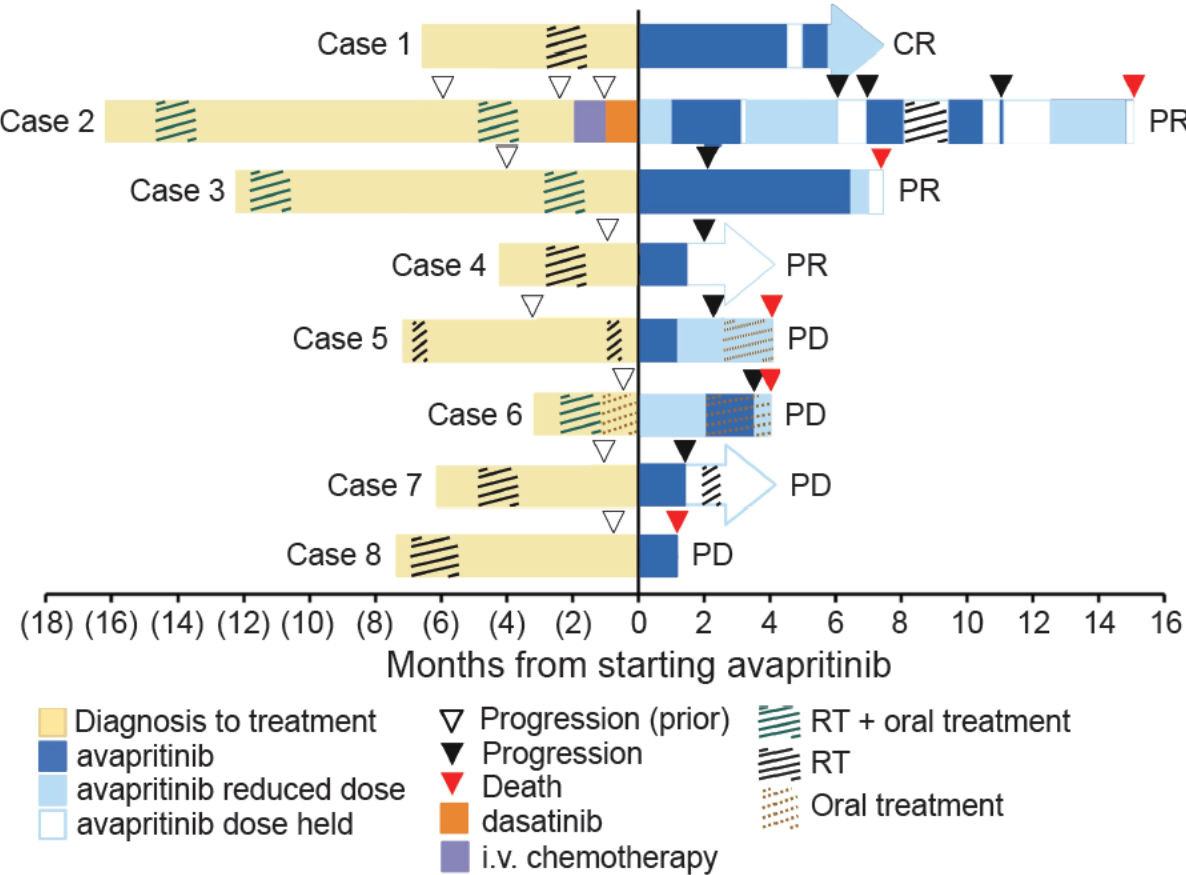
Clinical series of 8 pHGG patients treated with avapritinib



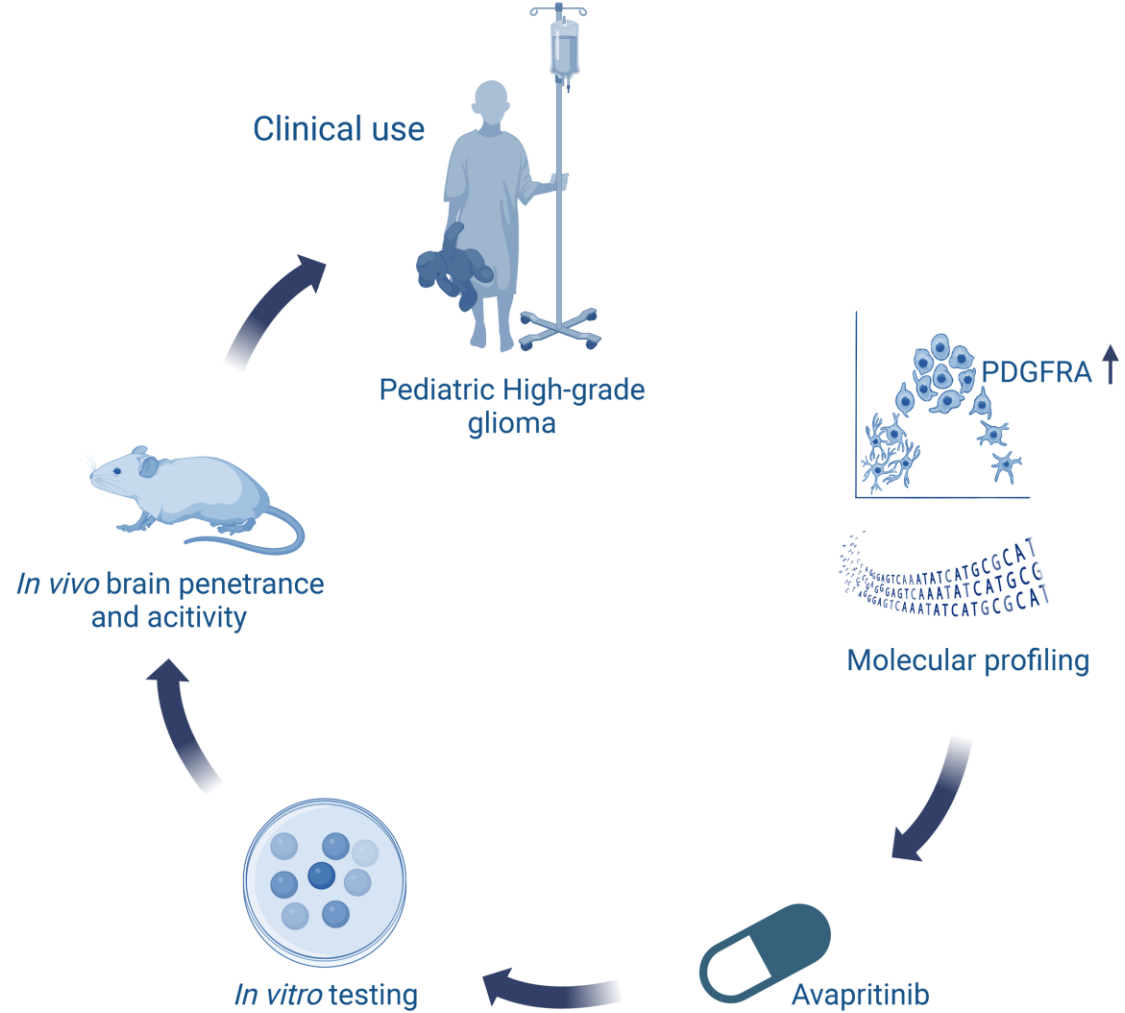
Avapritinib results in clinical response in a subset of pHGG patients



Avapritinib results in clinical response in a subset of pHGG patients



Conclusions



Thank you!

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David Jones

Natalie Jäger

Mary Skrypek



All patients & families!



Provided Avapritinib for clinical cases under CUP agreement

