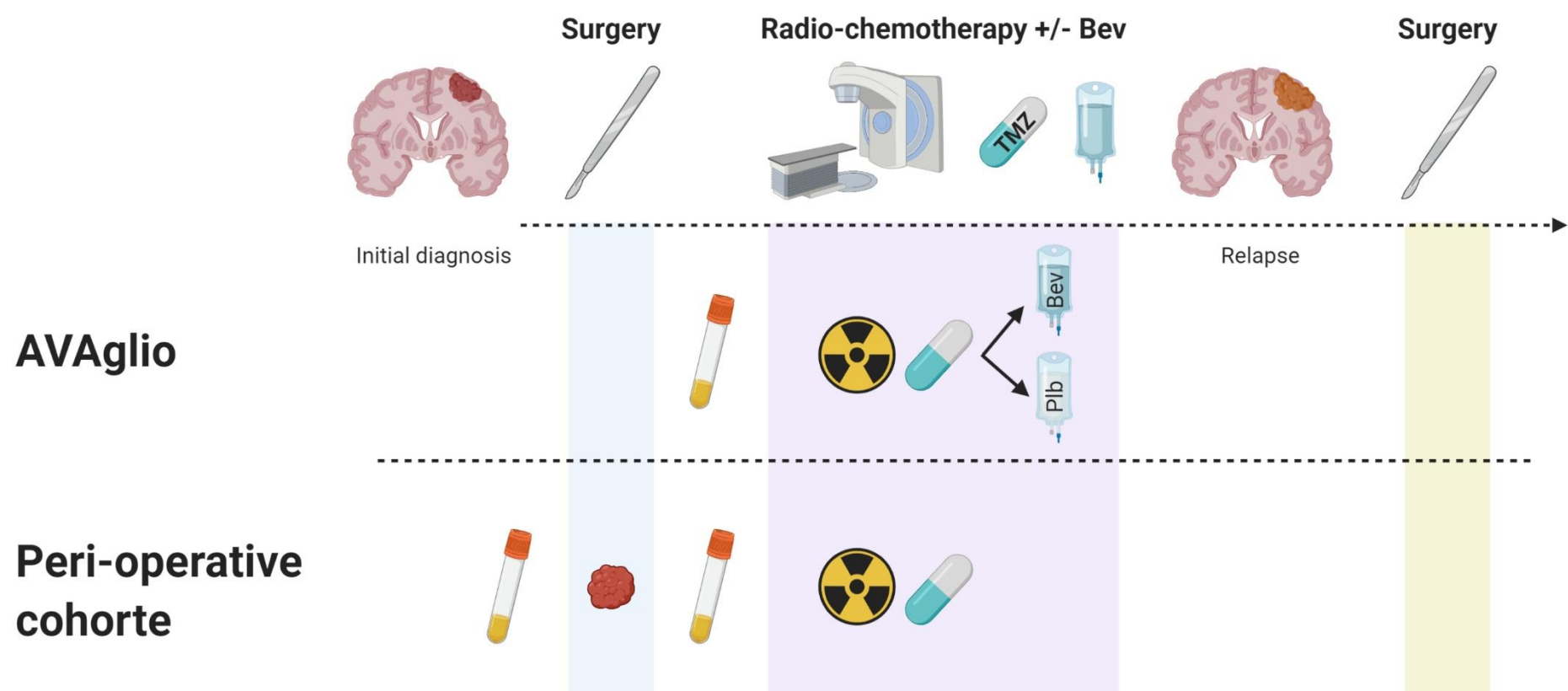
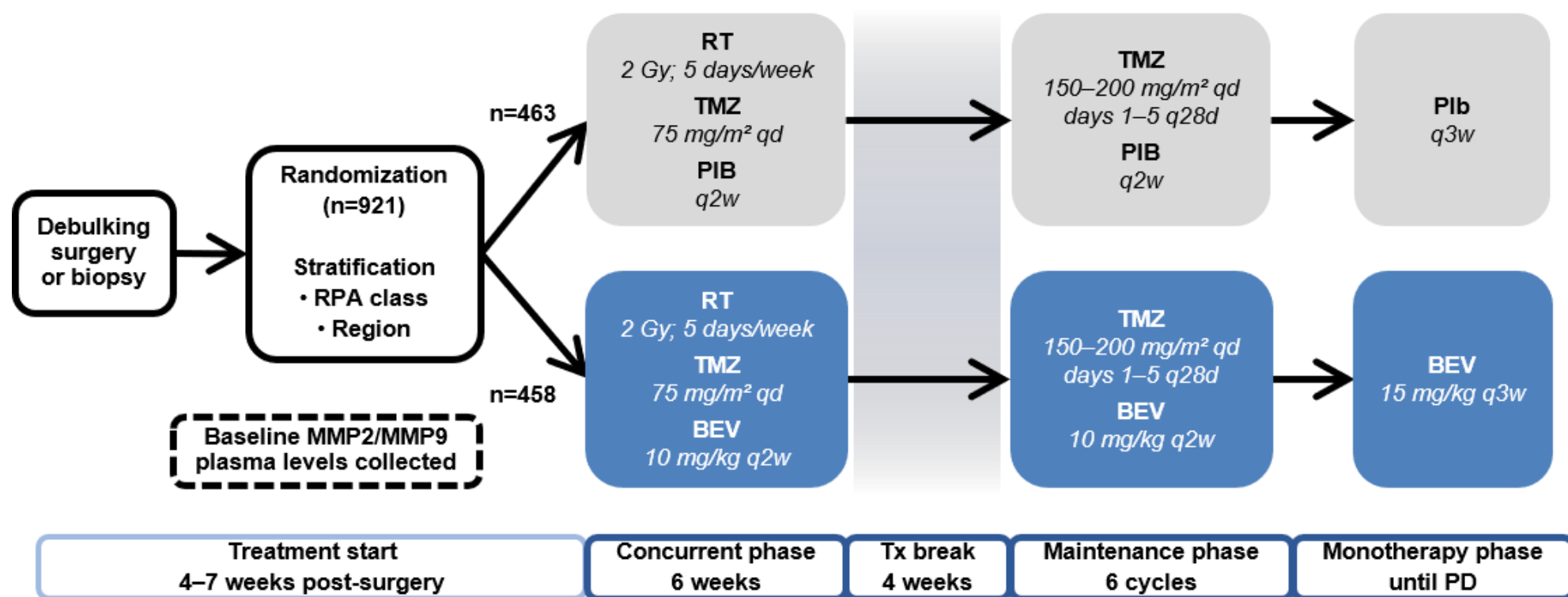


Supplementary Figure 1: Cohort and sample collection design.

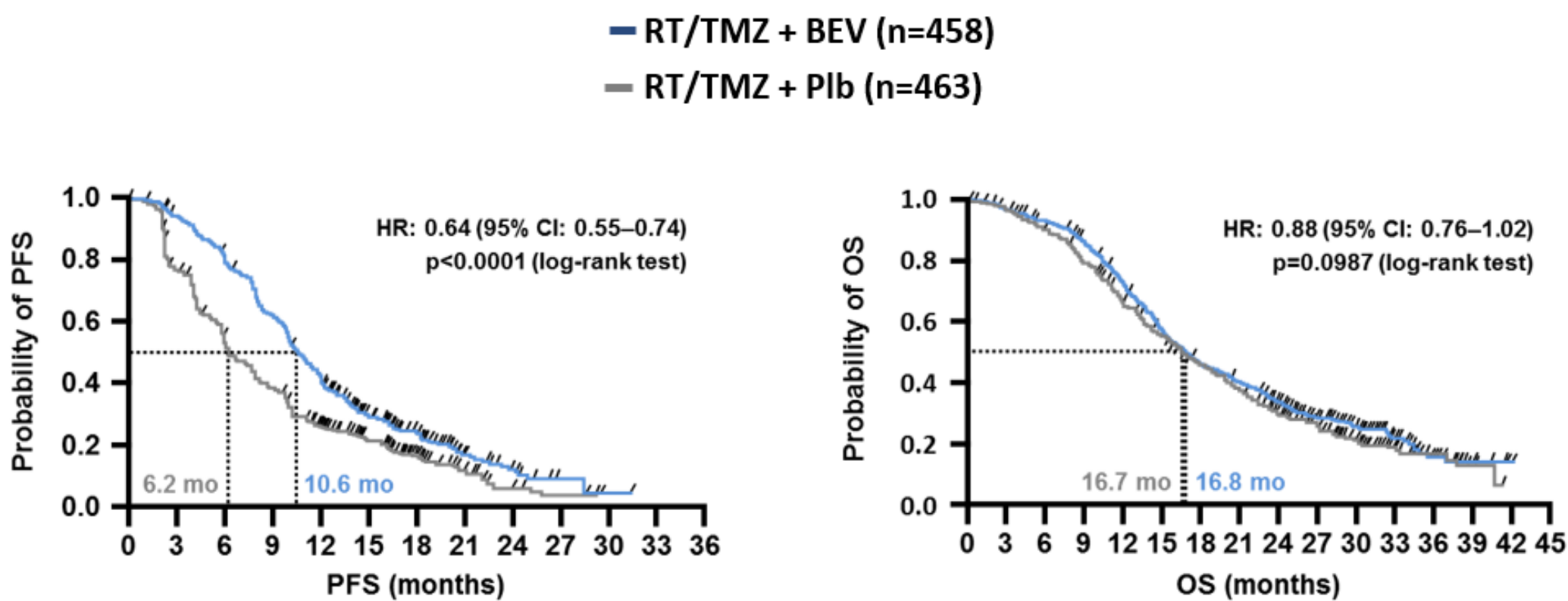
Bev: bevacizumab; TMZ: temozolomide; Plb: placebo



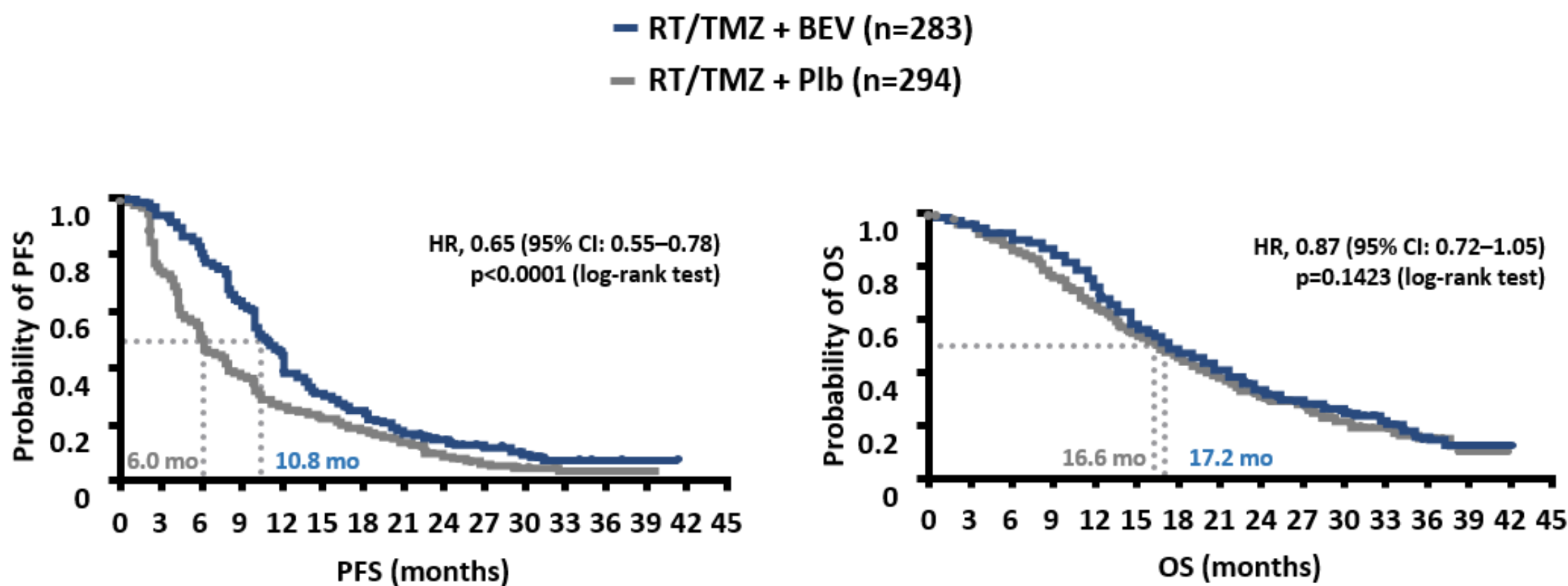
A



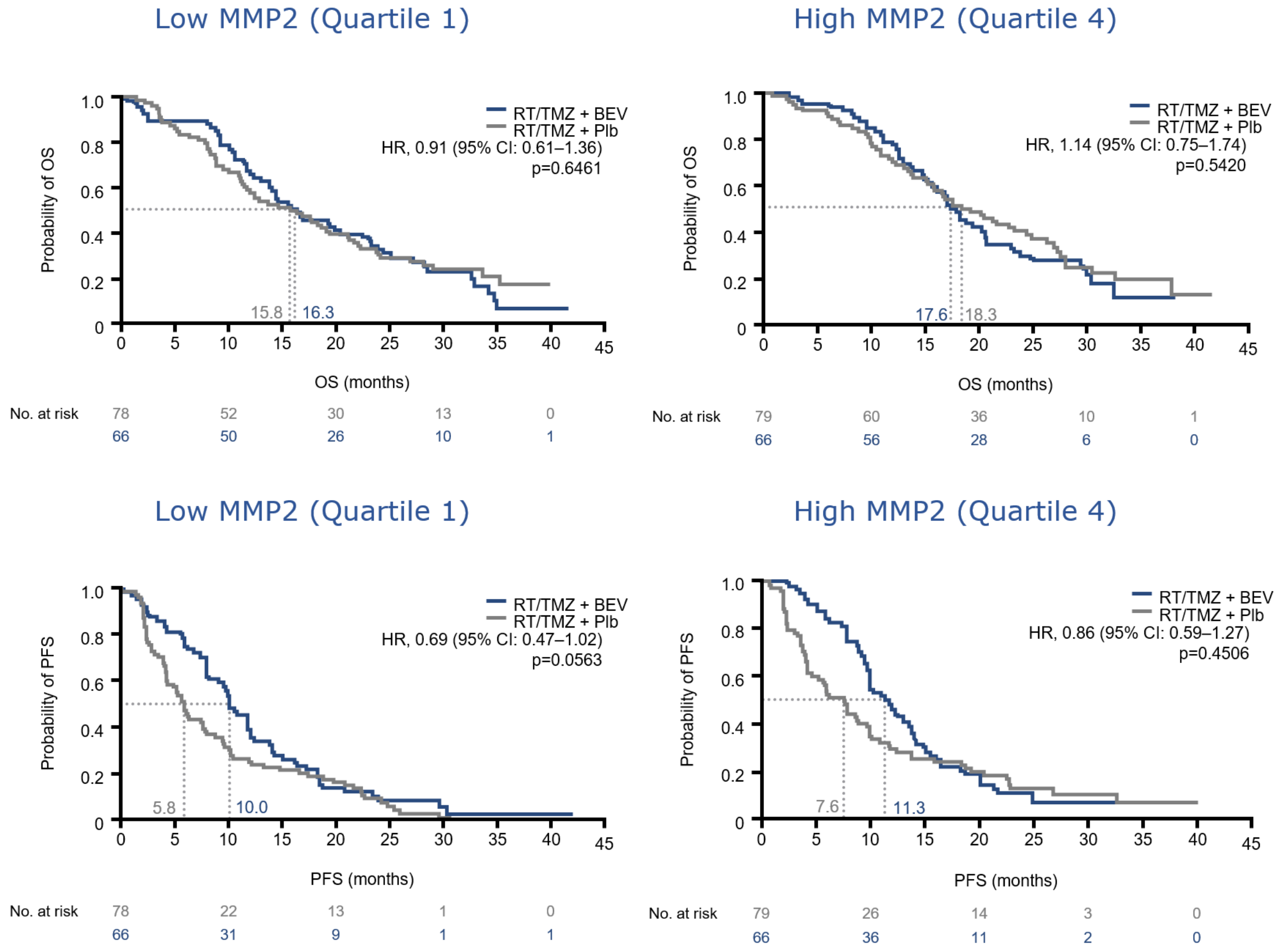
B



C

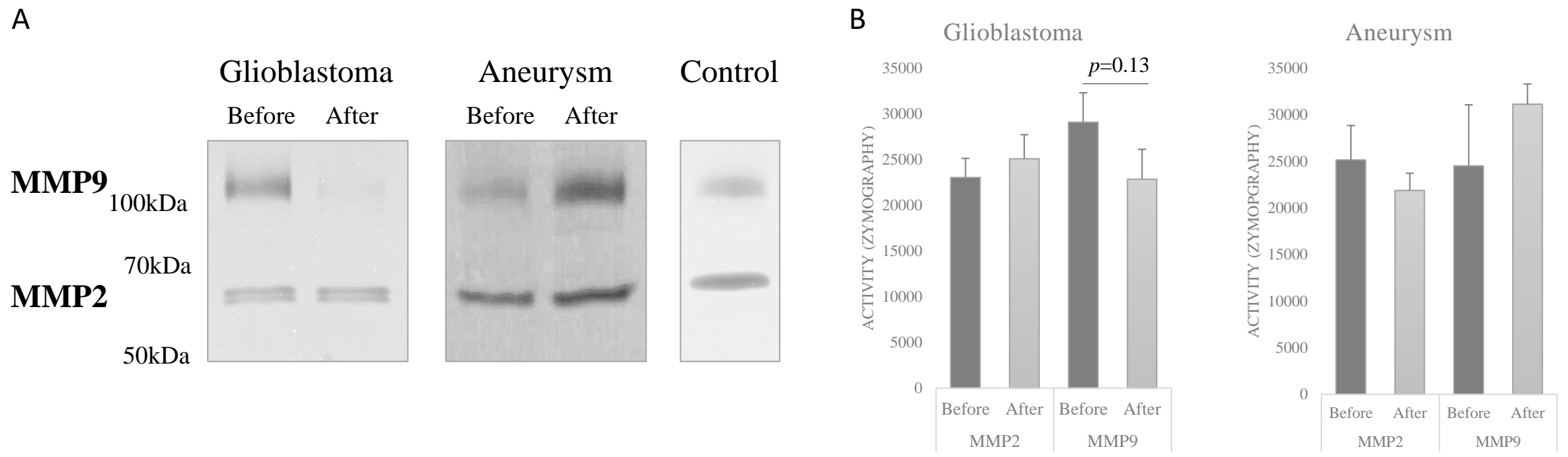


Supplementary Figure 2: AVAGLIO phase III clinical trial. A-AVAGLIO clinical trial design. B-Progression Free Survival and Overall Survival according to treatment arms in the whole trial cohort (921 patients). C- Progression Free Survival and Overall Survival according to treatment arms in the subgroups analyzed in the ancillary study (577 patients). No difference was observed between these two patient groups (original and ancillary). RT: radiotherapy; TMZ: temozolomide; Bev: bevacizumab; Plb: placebo



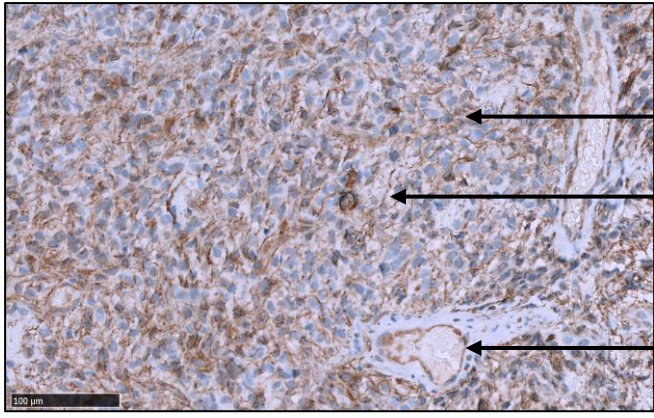
Supplementary Figure 3: Overall Survival (OS, top) and Progression-Free Survival (PFS, bottom) and according to MMP2 plasma level at baseline. RT: radiotherapy; TMZ: temozolomide; Bev: bevacizumab; Plb: placebo

Supplementary Figure 4 –Plasmatic MMP2 and MMP9 activity. Zymogram (A) and quantification (B) of MMP2 and MMP9 activity in plasma before and after surgery in patients with newly-diagnosed glioblastoma, cerebral aneurysm or healthy controls



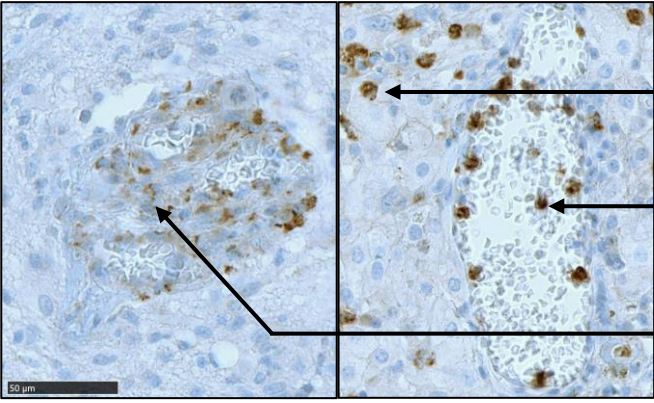
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MMP2



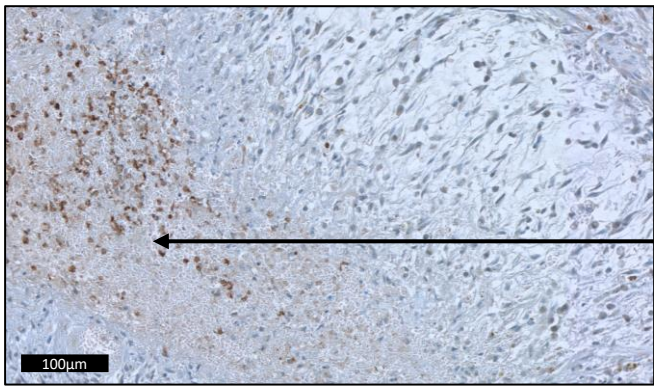
Tumor cells
Extracellular matrix
Endothelial cells

MMP9



Infiltrative cells
Intravascular cells
Microvascular Proliferation

MMP9

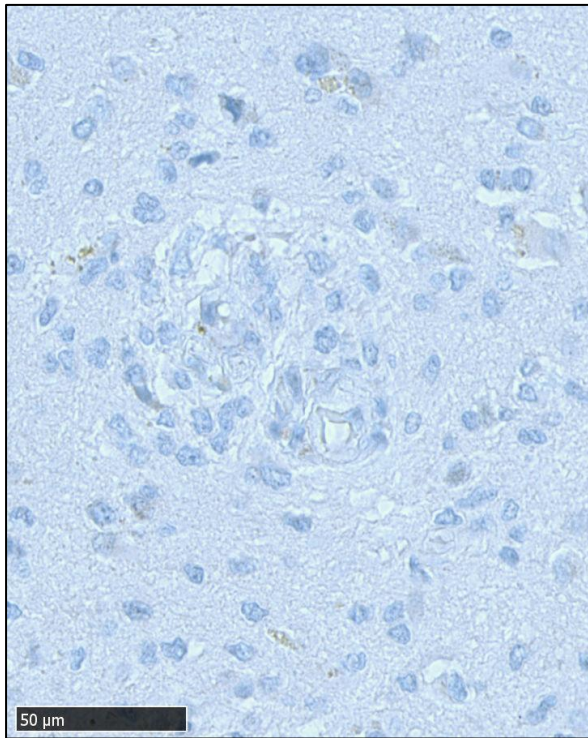


Necrosis

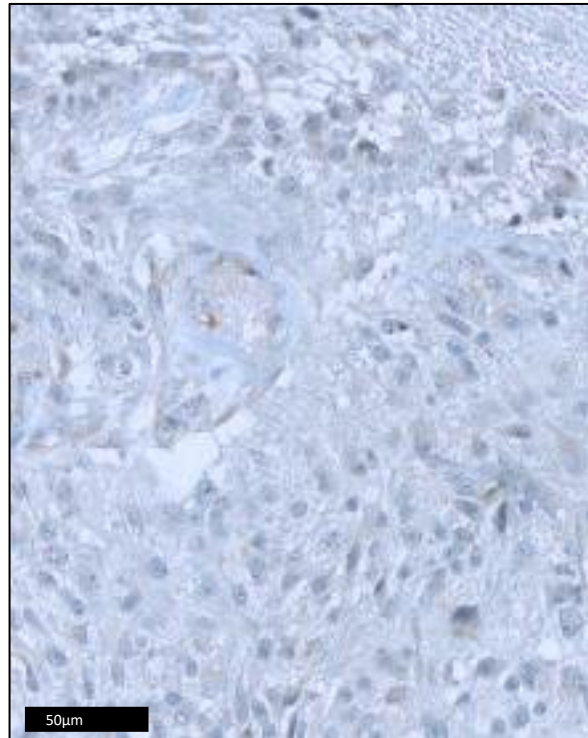
Supplementary figure 5 – Immunostaining illustration. A – Representative examples of regions of interest. B – Representative examples of immunostaining scores on microvascular proliferation.

B

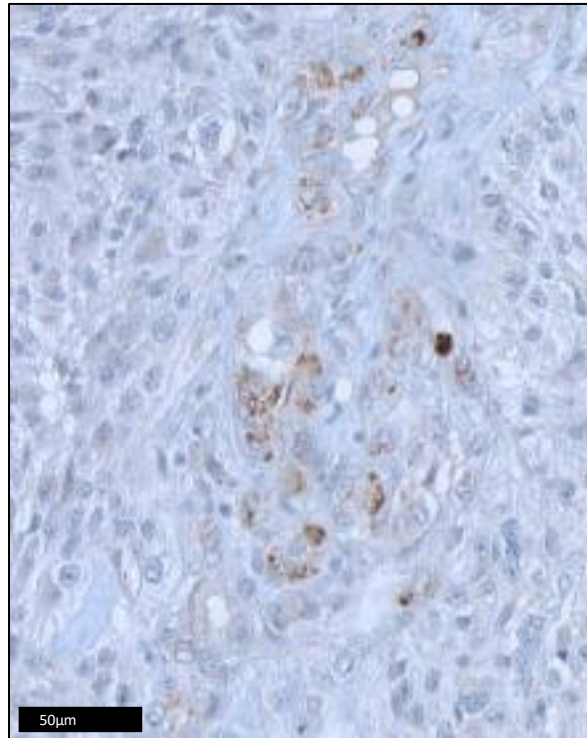
MMP9



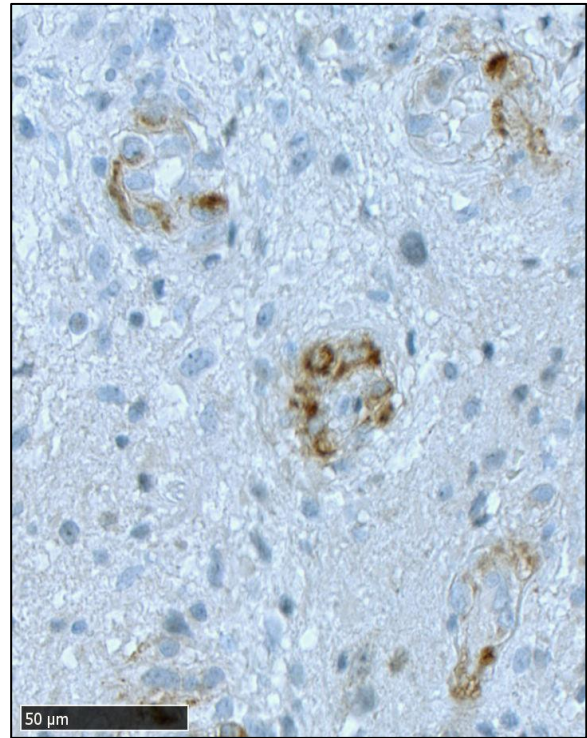
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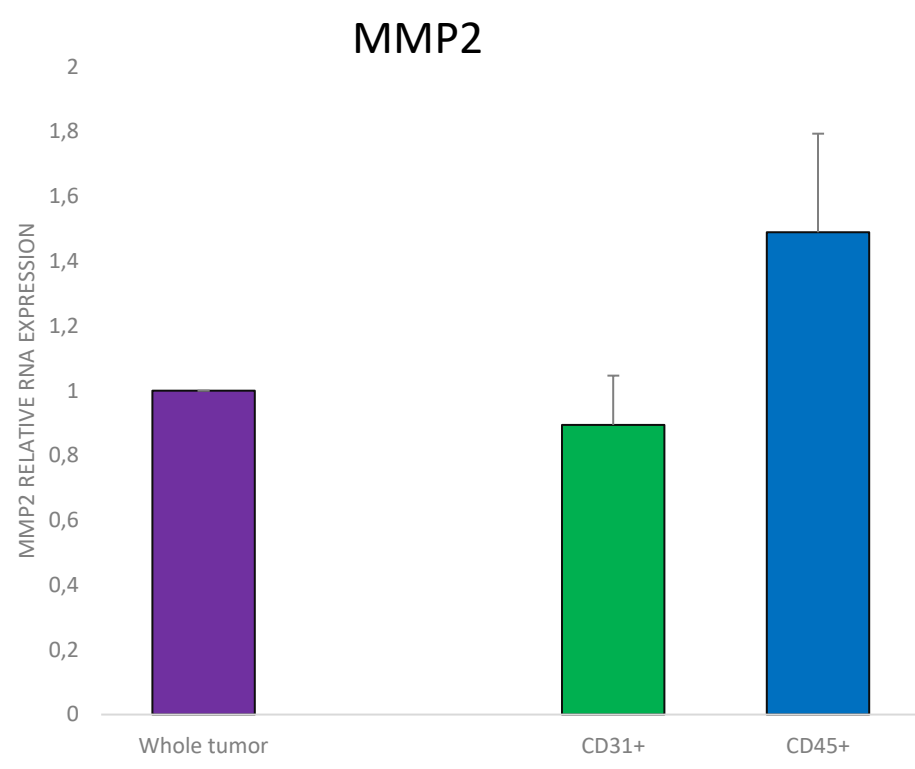
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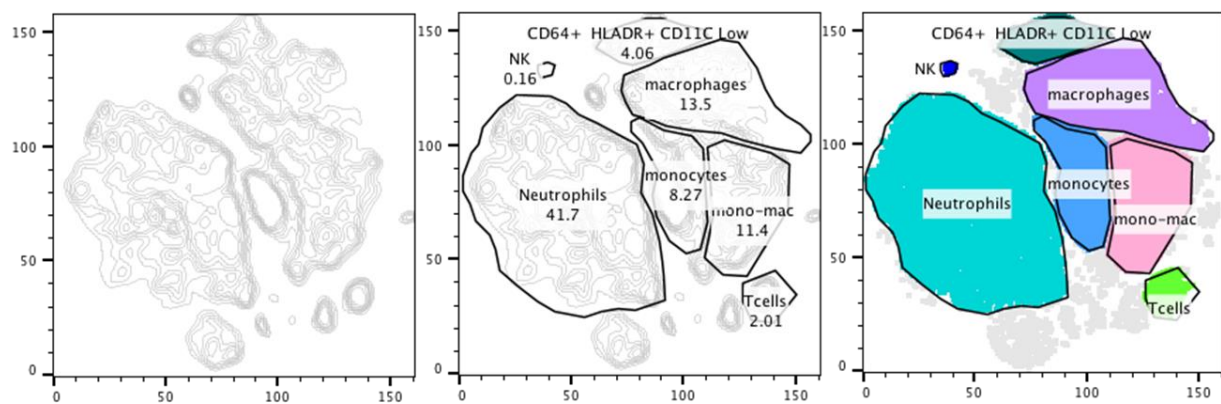


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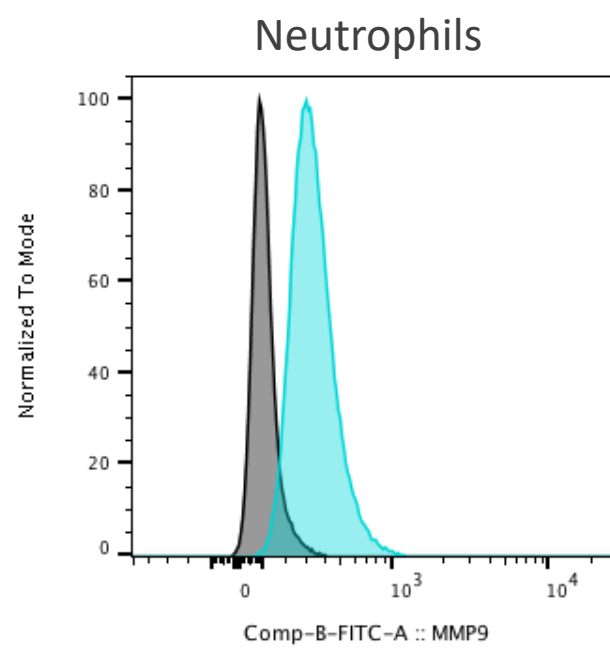


Supplementary Figure 6: MMP2 mRNA expression in CD31+ and CD45+ fraction cells. No difference was observed.

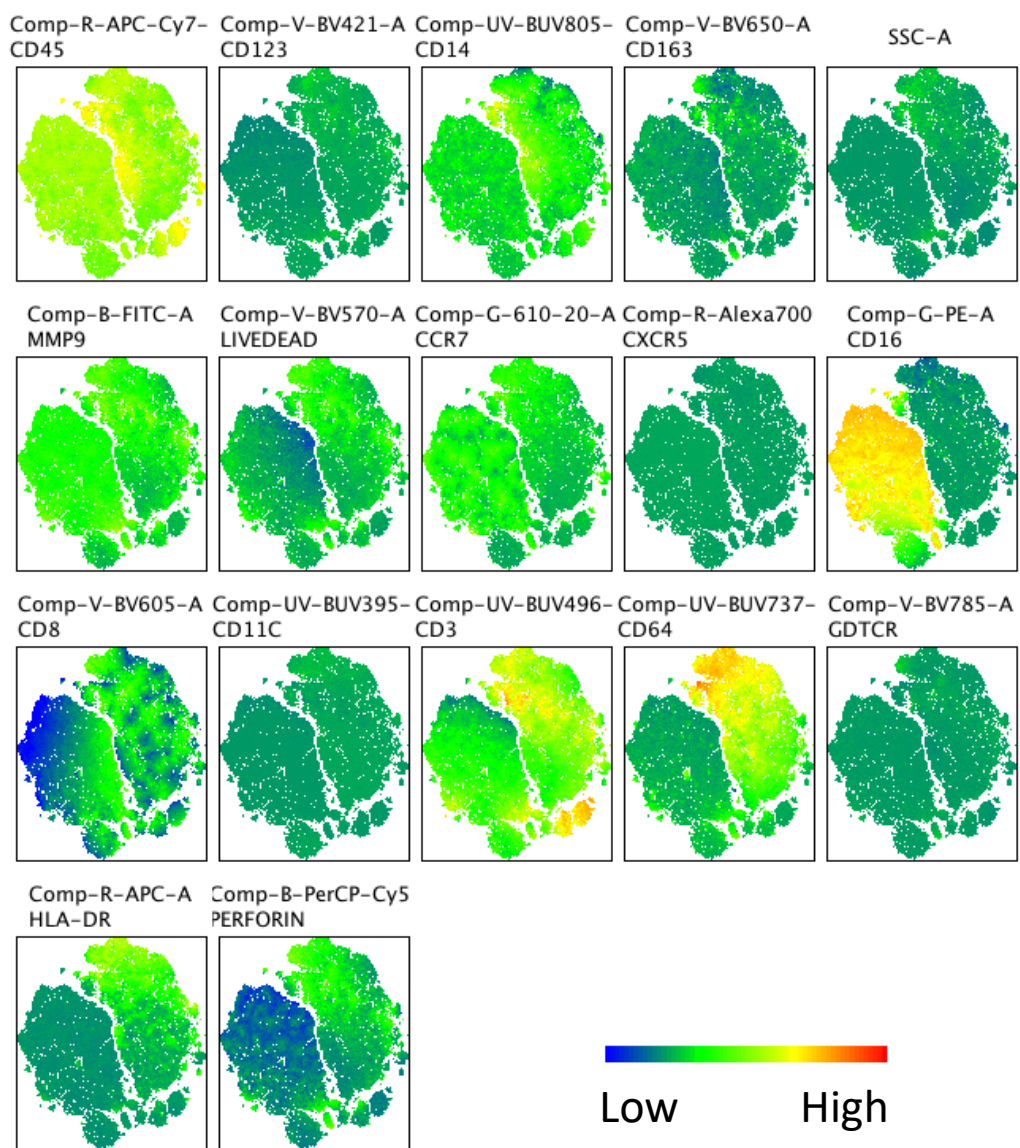
A



B



C



Supplementary Figure 7 – MMP9 is expressed by tumor-infiltrating CD16+ neutrophils: a second *IDHwt* GBM illustration (GBM2). A- T-Sne representation of immune subset. B - MMP9 mean fluorescence intensity (MFI) shift between stained and unstained neutrophils. C - T-Sne representation of each marker including MMP9.