MADRID 2023 ESMO congress

Spatial remodeling of the immune tumor microenvironment after radiotherapy and CXCL12 inhibition in glioblastoma in the phase 1/2 GLORIA trial

Abstract #6407

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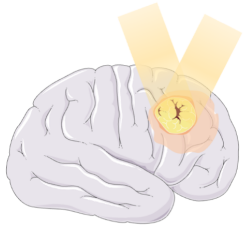
October 21, 2023

DECLARATION OF INTERESTS

Julian P. Layer

Stocks: TME Pharma AG, Siemens Healthineers AG, Bayer AG, BioNTech AG
Travel expenses: TME Pharma AG, Carl Zeiss Meditec AG
Honoraria: Siemens Healthineers AG

Phase I/II GLORIA trial



Radiotherapy

↓

Hypoxia

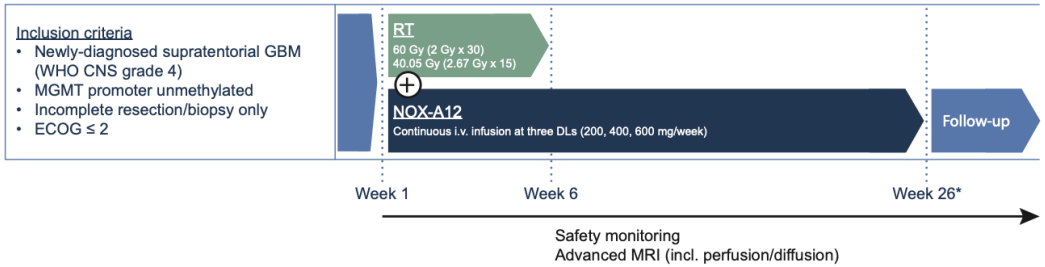
CXCL12 ↑

↙ ↘

Vasculo-genesis **Immunosup-pressive TME**

↓

Tumor recurrence



2/10 patients undergoing re-surgery
C1-001: Pseudo-PD (week 13)
C3-001: PD (week 31)

↓

Exploratory endpoint: mIF

Multiplex IF panel

IMMUNE MARKERS	FUNCTIONAL MARKERS	AUXILIARY MARKERS
Myeloids / Monocytes CD14 ***Granulocytes*** CD15 CD11b CD66b ***TAMs*** CD68 CD163/CD206 ***NK cells*** CD56 ***DCs*** CD11c ***T cells*** CD3 CD4 CD8 FOXP3 CXCR3 ***B cells*** CD20	***Multifunctional*** HLA-ABC ***Activation / Proliferation*** GranzymeB Ki67 NKG7 ***Inhibition / Checkpoint*** PD-1PD-L1 LAG-3 TIM-3 ***Cytokine signaling*** CXCL12 CXCR7	***Membrane*** ***Cytoplasm*** CD45 Vimentin ***Nucleus*** DAPI ***Smooth muscle*** a-SMA ***Epithelia*** Pan-CK ***Blood vessels / Lymphatics*** CD31 Podoplanin VEGFB PTN

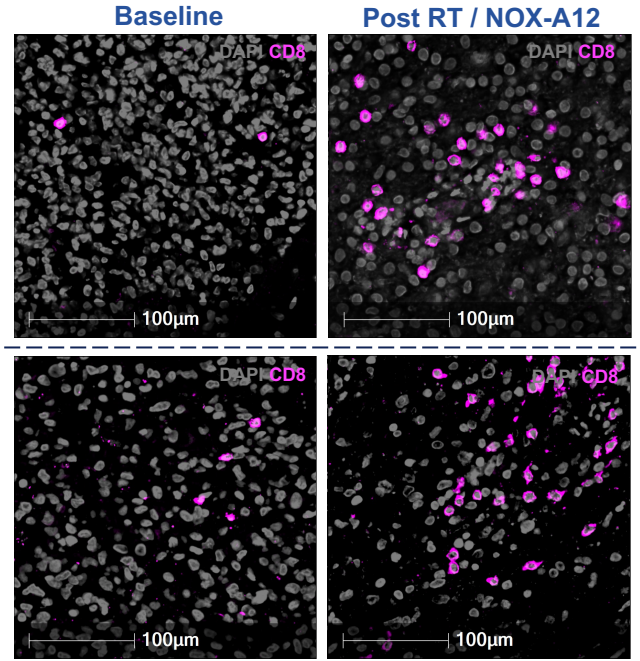
GBM MARKERS

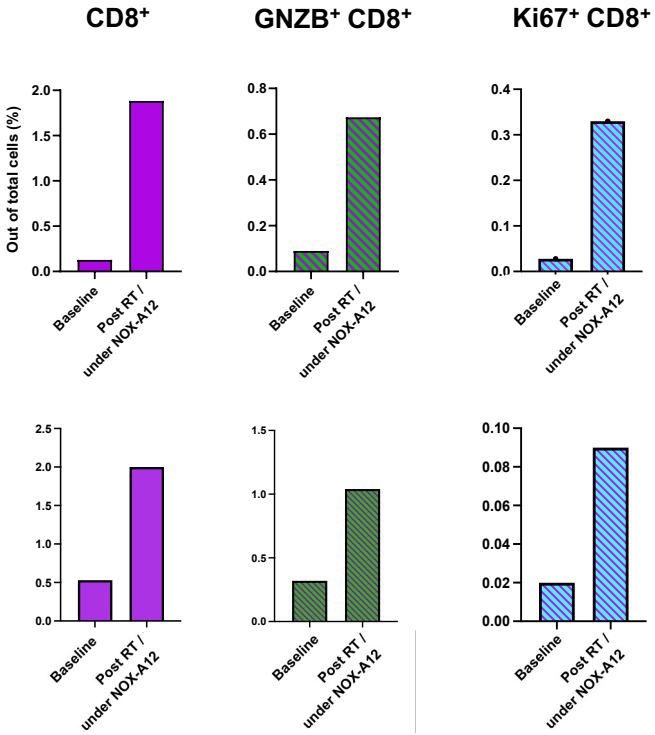
Tumor marker
Olig2 CD44 EGFR SOX2 CD56 p53 MAP2

T cell infiltration following RT+NOX-A12

GLORIA
C1-001
Pseudo-PD

GLORIA
C3-001
PD



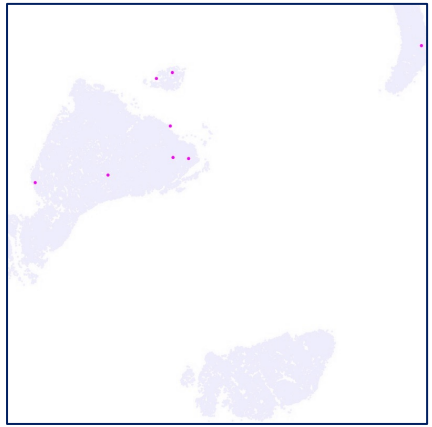


Julian P. Layer, MD

De novo CD8⁺ T cell clustering

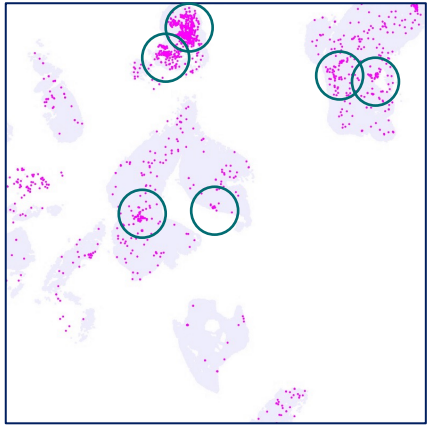
C1-001 (Pseudo-PD)

Baseline



Proliferating or activated CD8⁺ T cells
Tumor cells

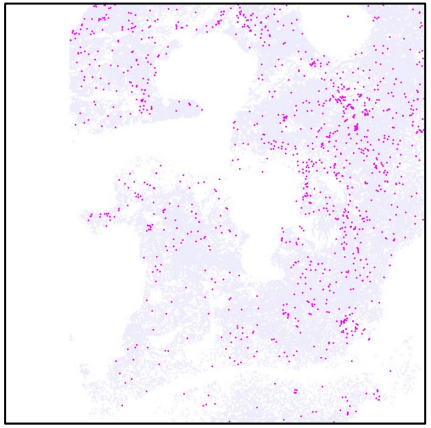
Post RT / Under NOX-A12



Proliferating or activated CD8⁺ T cells
Tumor cells

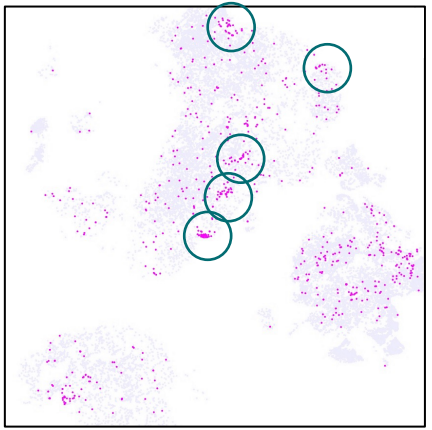
C3-001 (PD)

Baseline



Proliferating or activated CD8⁺ T cells
Tumor cells

Post RT / NOX-A12



Proliferating or activated CD8⁺ T cells
Tumor cells

Intralesional clustering of proliferating/activated CD8⁺ T cells following RT+NOX-A12 in both re-resection samples

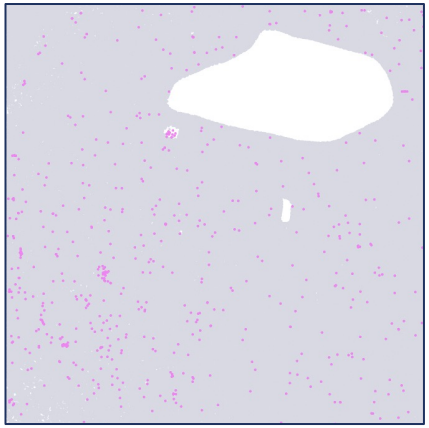
No CD8+ T cell clustering under SOC

SOC #21

Baseline

Proliferating or activated CD8+ T cells
Tumor cells

Post RT / Under SOC



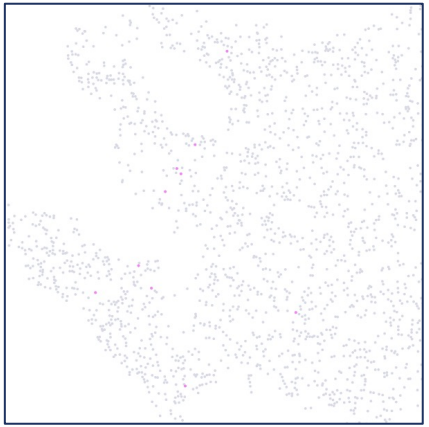
Proliferating or activated CD8+ T cells
Tumor cells

SOC #34

Baseline

Proliferating or activated CD8+ T cells
Tumor cells

Post RT / Under SOC

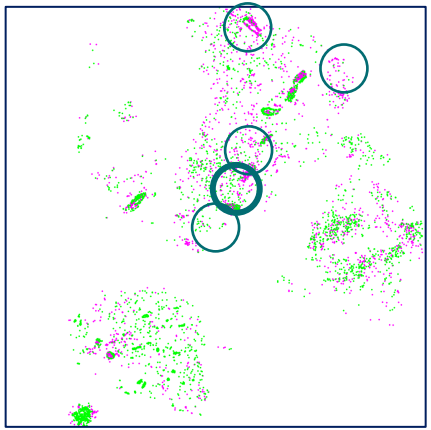


Proliferating or activated CD8+ T cells
Tumor cells

Rearrangement of TAMs

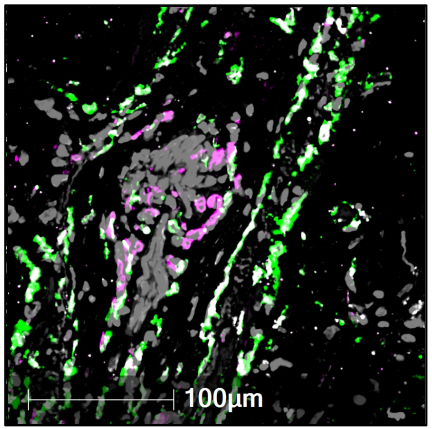
C3-001 (PD)

Post RT / NOX-A12



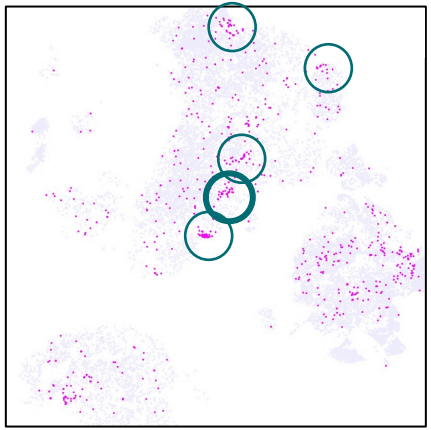
Proliferating or activated CD8⁺ T cells
Pro-tumor TAMs

Post RT / NOX-A12



Proliferating or activated CD8⁺ T cells
Pro-tumor TAMs
DAPI

Post RT / NOX-A12



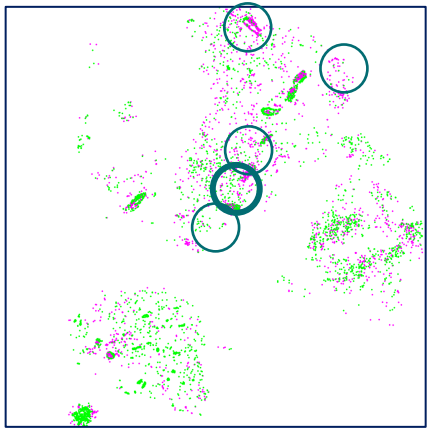
Proliferating or activated CD8⁺ T cells
Tumor cells

Encapsulation of perivascular CD8⁺ T cell clusters by M2-like TAMs following RT+NOX-A12 in PD sample

Rearrangement of TAMs

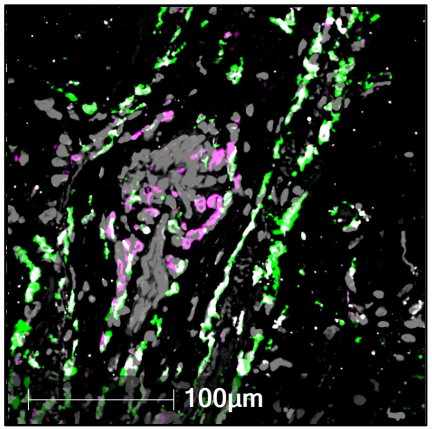
C3-001 (PD)

Post RT / NOX-A12



Proliferating or activated CD8⁺ T cells
Pro-tumor TAMs

Post RT / NOX-A12



Proliferating or activated CD8⁺ T cells
Pro-tumor TAMs
DAPI

Encapsulation of perivascular CD8⁺ T cell clusters by M2-like TAMs following RT+NOX-A12 in PD sample

Conclusions

- T cell infiltration following RT + CXCL12 inhibition
- *De novo* T cell clustering
- Spatial rearrangement of TME as possible counter mechanism

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Thank you very much for your attention.

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