

Dual inhibition of post-radiogenic angio-vasculogenesis in glioblastoma

Results of the phase 1/2 GLORIA trial

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DECLARATION OF INTERESTS

Frank A. Giordano

AstraZeneca PLC: Advisory Boards, Honoraria, Travel Expenses

Biotex, Inc.: Consulting, Honoraria, Travel Expenses

Carl Zeiss Meditec AG: Consulting, Research Grants, Honoraria, Travel Expenses, Speaker's Bureau

Cureteq AG: Advisory Boards, Honoraria

ELEKTA Instrument AB: Research Grants, Reference Site Contracts, Travel Expenses

Oncare GmbH: non-financial support (software)

Opasca AG: non-financial support (software)

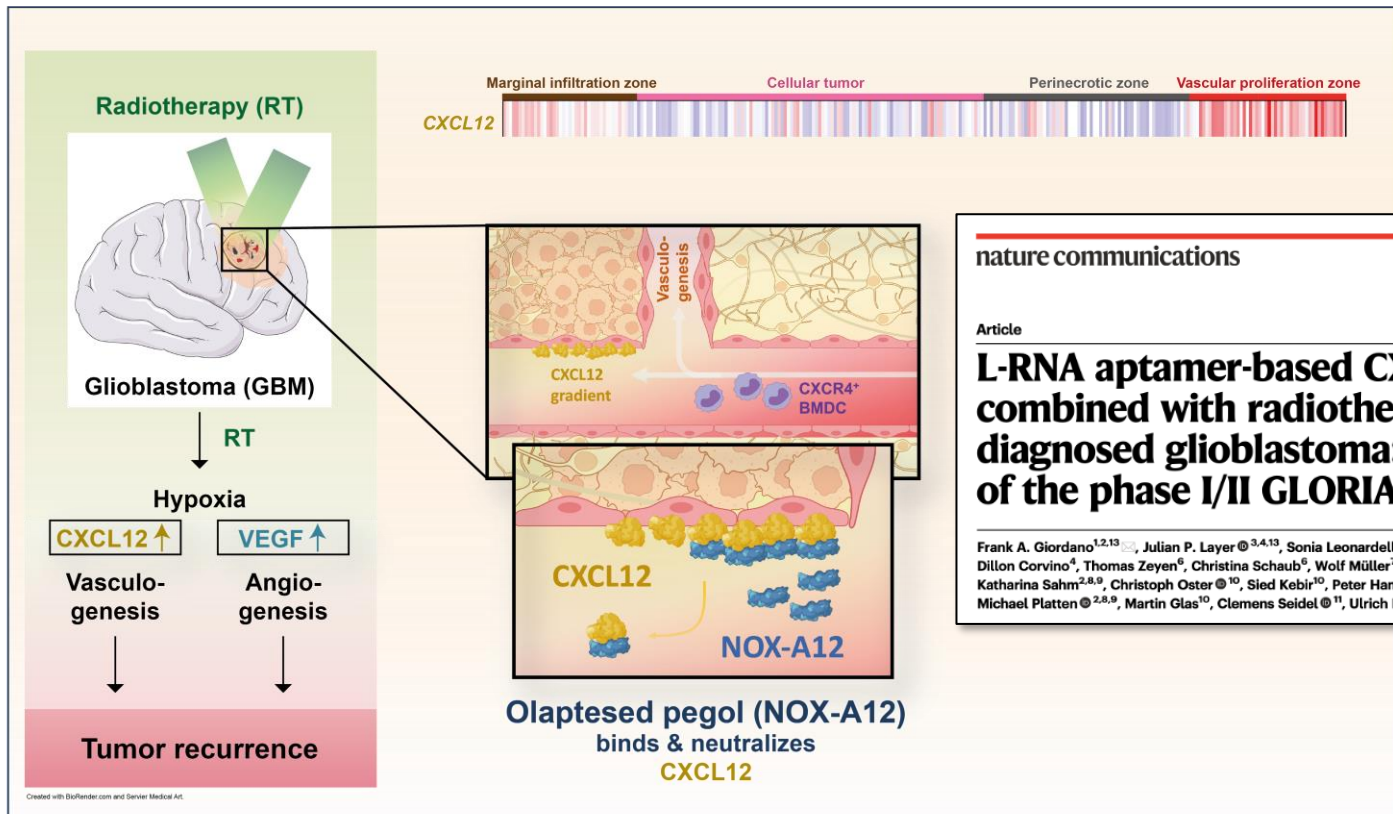
Siemens Healthineers AG: Honoraria, Travel Expenses

TME Pharma AG: Consulting, Research Grants, Honoraria, Travel Expenses

Varian, Inc.: Research Grants, Travel Expenses

VisionRT Ltd.: Research Grants, Reference Site Contracts, Travel Expenses

Background



nature communications



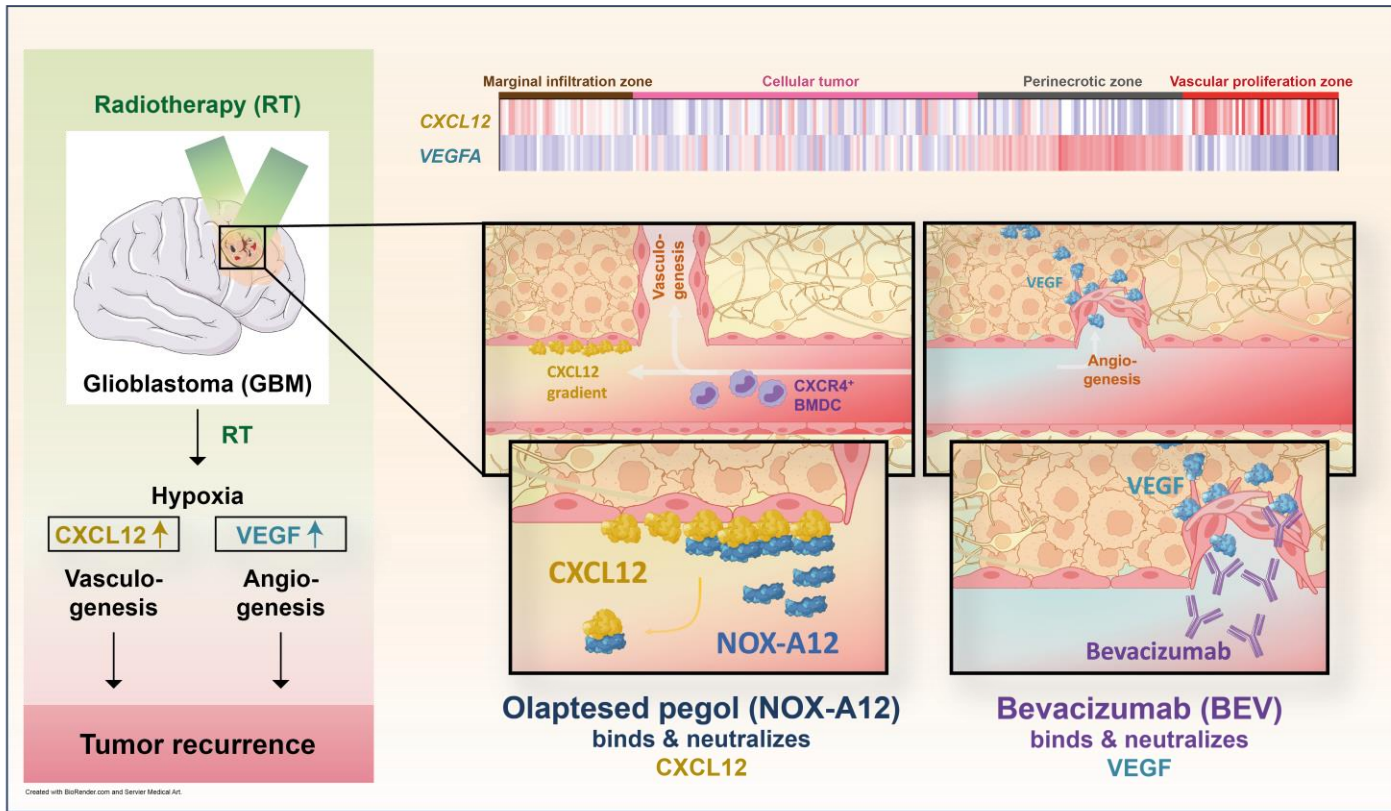
Article

<https://doi.org/10.1038/s41467-024-48416-9>

L-RNA aptamer-based CXCL12 inhibition combined with radiotherapy in newly-diagnosed glioblastoma: dose escalation of the phase I/II GLORIA trial

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Background

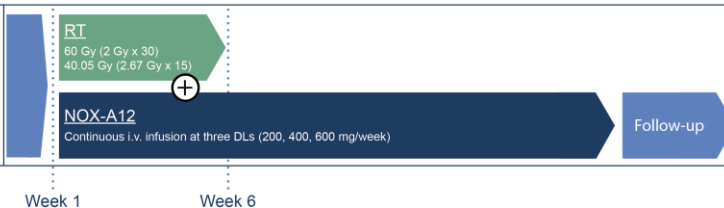


GLORIA study design

Dose escalation arm

Key inclusion criteria

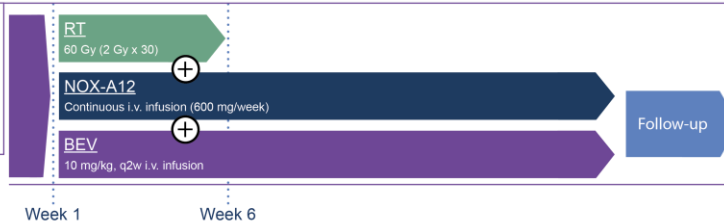
- Newly-diagnosed supratentorial GBM (WHO CNS grade 4)
- MGMT promoter unmethylated
- Incomplete resection/biopsy only
- ECOG ≤ 2



Expansion arm

Key inclusion criteria

- Newly-diagnosed supratentorial GBM (WHO CNS grade 4)
- MGMT promoter unmethylated
- Incomplete resection
- ECOG ≤ 2



Safety monitoring
Clinical assessments
Advanced MRI (incl. perfusion)

Key endpoints

Primary:
Safety

Secondary:
Radiographic response
Progression-free survival
Overall survival



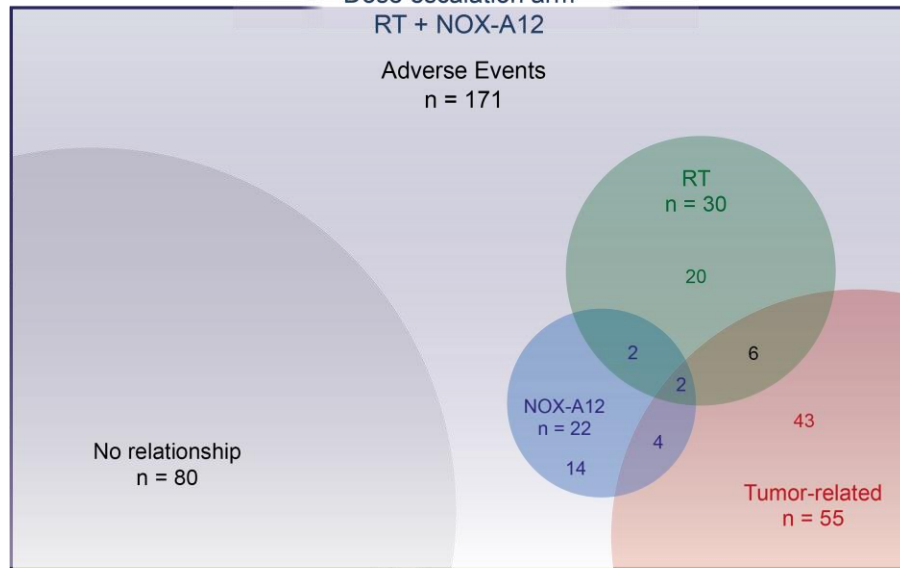
Safety

Dose escalation arm

RT + NOX-A12

Adverse Events

n = 171

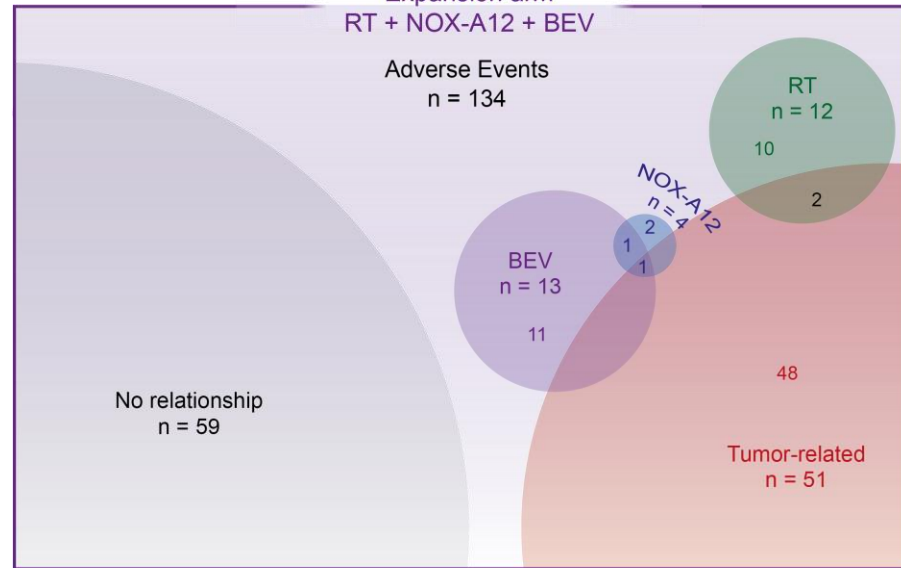


Expansion arm

RT + NOX-A12 + BEV

Adverse Events

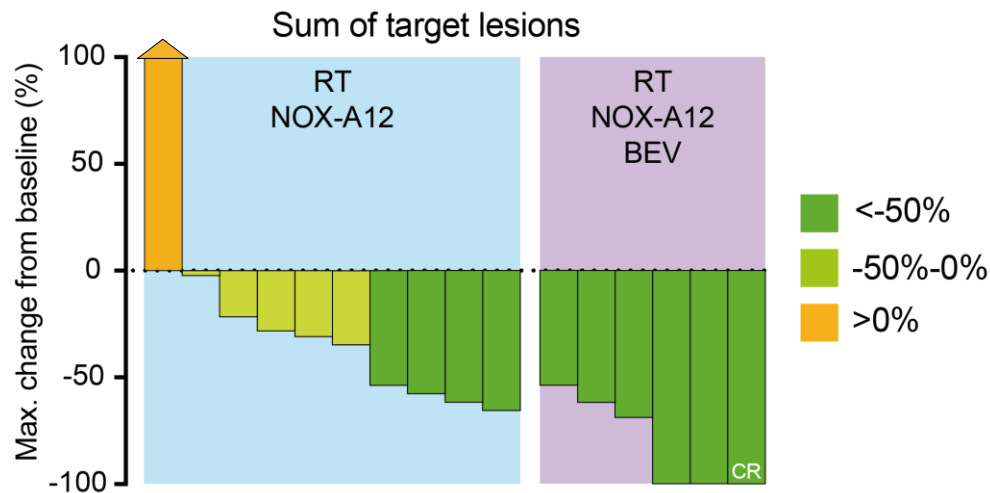
n = 134



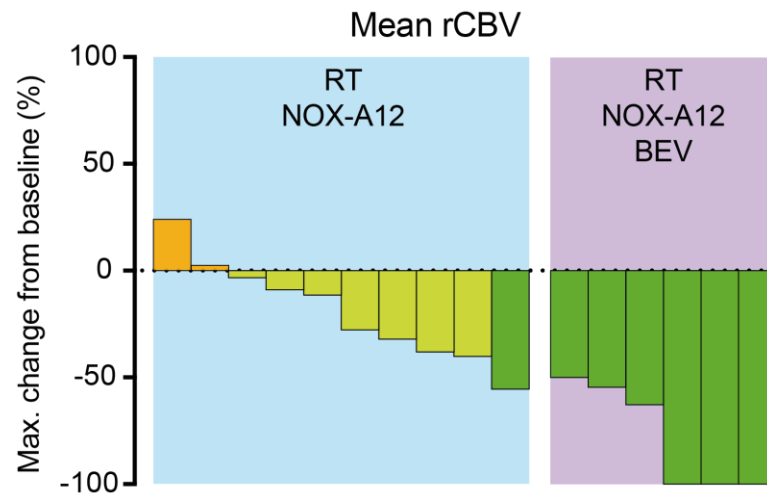
Comparable safety profile of RT + NOX-A12 + BEV

Therapy response

Tumor size



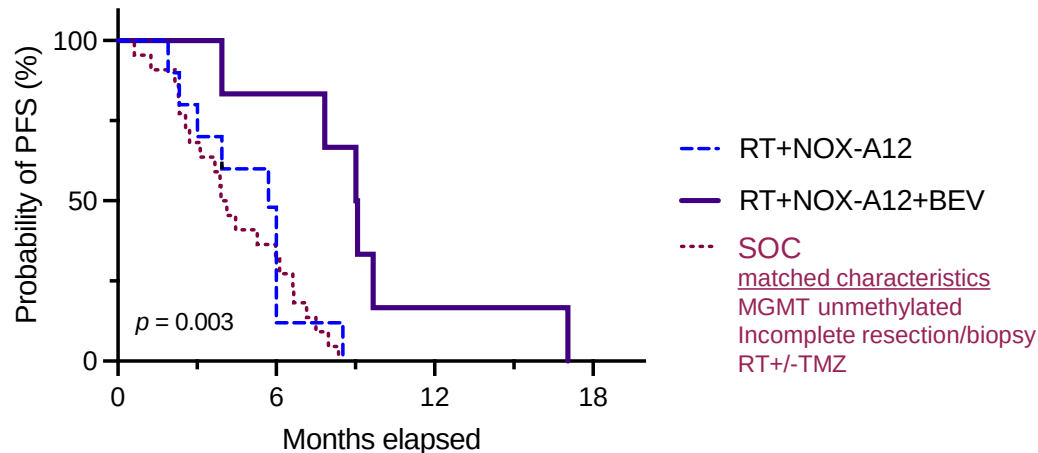
Tumor perfusion



Deeper responses with RT + NOX-A12 + BEV

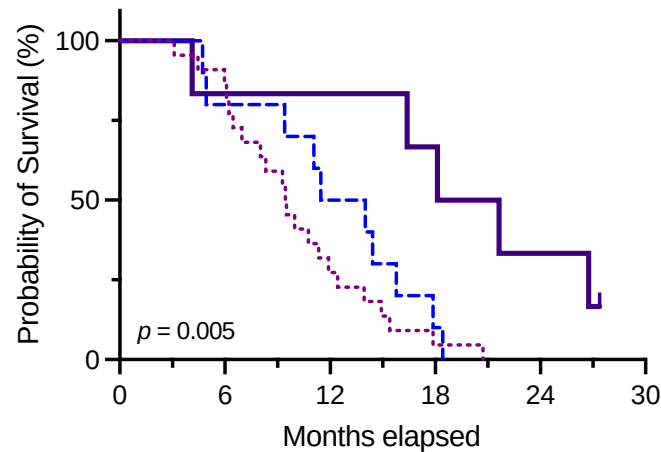
Clinical outcome

Progression-free survival



# at risk	6	6	5	4	1	1
	10	8	4	0	0	0
	22	15	7	0	0	0

Overall survival



# at risk	6	5	5	4	2
	10	8	5	1	0
	22	19	6	1	0

Significantly improved PFS/OS with RT + NOX-12 + BEV
One patient still alive

Conclusion

Spatially distinct expression patterns of CXCL12 and VEGF in GBM suggest two paths of GBM vasculature restoration after RT

Hypothesis of GLORIA trial: combined inhibition of angiogenesis (BEV) and vasculogenesis (NOX-A12) prevents/delays tumor recurrence after radiotherapy (RT)

Patients with newly-diagnosed, incompletely resected, MGMT unmethylated GBM (CNS WHO °4) included

Combination therapy with NOX-A12 and BEV is safe and tolerable

Markedly decreased tumor perfusion confirms suggested mode of action

Combination of NOX-A12 and BEV resulted in deeper responses

NOX-A12+BEV significantly improved mPFS (9.1 mo, $p=0.003$) and mOS (19.9 mo, $p=0.005$) compared to NOX-A12 alone (mPFS: 5.7 mo; mOS: 12.7 mo) and a matched SOC cohort (mPFS: 4.0 mo; mOS 9.5 mo)

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congress

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