DUAL INHIBITION OF POST-RADIOGENIC ANGIO- VASCULOGENESIS BY OLAPTESED PEGOL (NOX-A12) AND BEVACIZUMAB IN GLIOBLASTOMA – INTERIM DATA FROM THE FIRST EXPANSION ARM OF THE GERMAN PHASE 1/2 GLORIA TRIAL.

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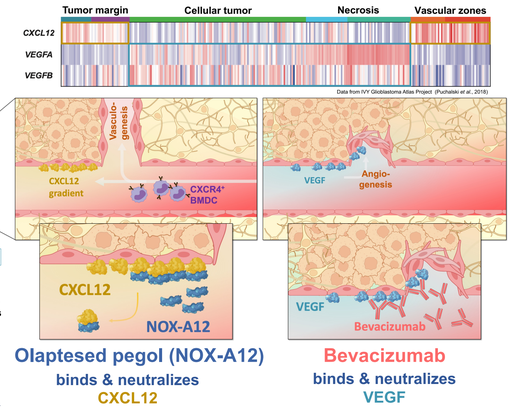
1 RATIONALE & STUDY DESIGN

Dual inhibition of the CXCL12- and VEGF-axes after radiotherapy (RT) of glioblastoma (GBM)

- abrogates CXCL12-dependent recruitment of pro-vasculogenic/tumorigenic bone marrow-derived cells (BMDC)
- prevents VEGF-driven angiogenesis within the tumor compartments



Ceradini, Nat Med 2004
Greenfield, J Clin Invest, 2010
Kioi, J Clin Invest, 2010
Liu, Neuro Oncol, 2014

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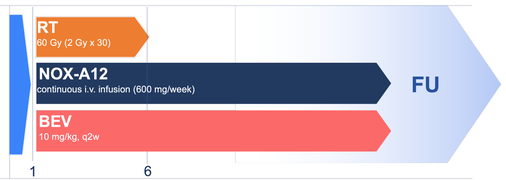
Key inclusion criteria:

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



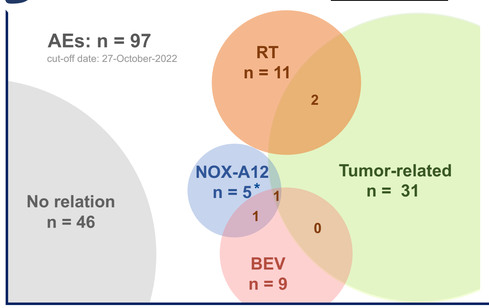
Primary Endpoint: Safety as per # of patients with treatment-related CTCAE

Secondary Endpoints: NOX-A12 plasma levels, tumor vascularization/perfusion as per advanced MRI, PFS-6, mPFS, OS, QoL (Quality of Life), NANO (Neurologic Assessment in Neuro-Oncology)

Exploratory Endpoint: Translational characterization of TME by CODEX®

2 SAFETY

AEs: n = 97
cut-off date: 27-October-2022

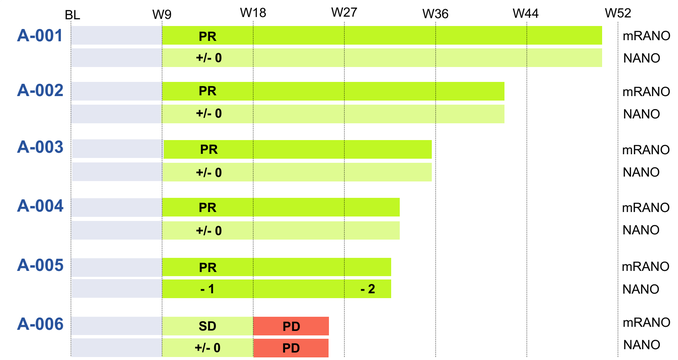


- Triple treatment well-tolerated and safe
- Of all G≥2 AEs (n = 66), 3 (4.5%) NOX-A12-related (all G2)
- No dose limiting toxicities (DLT) and no treatment-related deaths

***NOX-A12-only related AE**

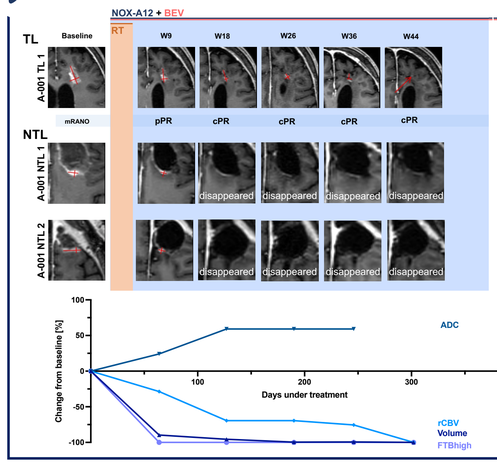
Extravasation	G2
Infusion site reaction	G2
Peripheral edema	G2

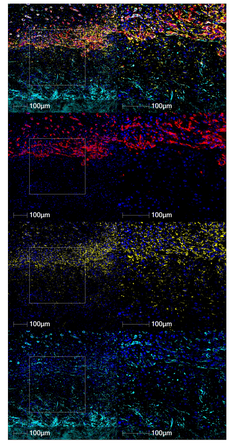
3 TREATMENT COURSE



- 5/6 patients achieved partial responses (PRs) as per mRANO in week 9
- All PRs remained durable at a median follow-up (FU) of 7.6 months
- Longitudinal NANO assessment revealed stable neurologic functioning in 5/6 patients
- PD in A-006 due to CSF metastases while target lesion control was maintained

4 EXEMPLARY PATIENT





Left panel:
Radiographic treatment course of patient A-001 with target lesion (TL), non target lesions (NTLs) and MRI volumetric, diffusion (ADC) and perfusion (rCBV, FTBhigh) parameters (treatment ongoing)

Right Panel:
Multiplexed immunofluorescence (CODEX®) analysis of pretherapeutic tumor tissue of the same patient confirms distinct spatial distribution of CXCL12 and VEGFB in tumor compartments

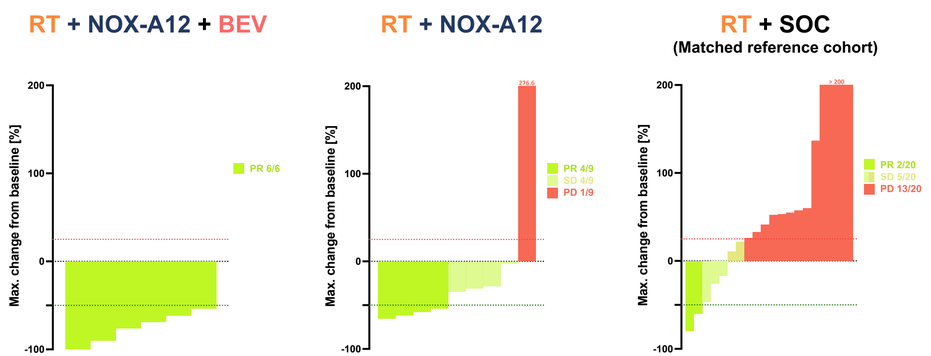
DAPI
CD31
CXCL12
VEGFB

Radiotherapy + NOX-A12 + Bevacizumab in chemotherapy refractory GBM

Safe | No DLT | Encouraging efficacy of dual inhibition of angio-vasculogenesis

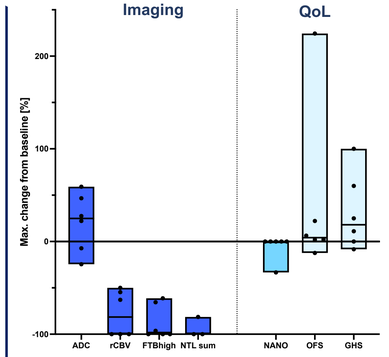
Treatment and follow up ongoing

5 TARGET LESION RESPONSE



- Trial results (left) were compared to the previously reported dose escalation cohorts (center) and a matched imaging reference cohort (right) treated with standard of care (SOC)
- The mean best sum of perpendicular diameters (SPD) response was -74.9% (-53.8% to -99.9%) for TL sums
- In 3/3 patients with NTL at least one lesion disappeared (not shown)

6 ADVANCED IMAGING & QoL



Mean best changes from baseline

Advanced imaging:

- Apparent Diffusion Coefficient (ADC) 20.6% (-24.5% to 59.1%)
- relative Cerebral Blood Volume (rCBV) -77.9% (-50 to -100%)
- Highly perfused-tumor fraction (FTB_{high}) -87.2% (-61.3% to -100%)
- SPD response of NTL sums -93.8% (-81.4% to -100%)

Clinician reported outcome:

- NANO response -5.6% (0% to -33.3%)

Patient reported outcome:

- Overall Function Score (OFS) 40.7% (-12.4% to 224.4%)
- Global Health Score (GHS) 31.3% (-8.3% to 100%)

REGISTRATION & CONTACT

Trial sponsored by TME Pharma AG
Registered with clinicaltrials.gov, ID: NCT04121455

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