KOL WEBINAR WITH DR. FRANK GIORDANO

GLORIA Top-Line Results of NOX-A12 & Radiotherapy Combination in First-Line Glioblastoma Presented at ASCO 2022

June 10, 2022 | 8:00 AM EDT / 2:00 PM CEST

WEBINAR PRESENTERS

MODERATOR

Guillaume van Renterghem
Managing Director
LifeSci Advisors

PRESENTERS

Dr. Frank Giordano
Chair & Director
Radiation Oncology Dept.
University Hospital Bonn

Lead Investigator of NOX-A12
GLORIA Phase 1/2 Study

Aram Mangasarian
CEO
NOXXON Pharma

Glioblastoma is a Devastating Orphan Brain Cancer where the TME Plays a Significant Role

LACK OF EFFECTIVE THERAPIES & LOW OVERALL SURVIVAL

Orphan Status
29,000 New Cases per year[1]

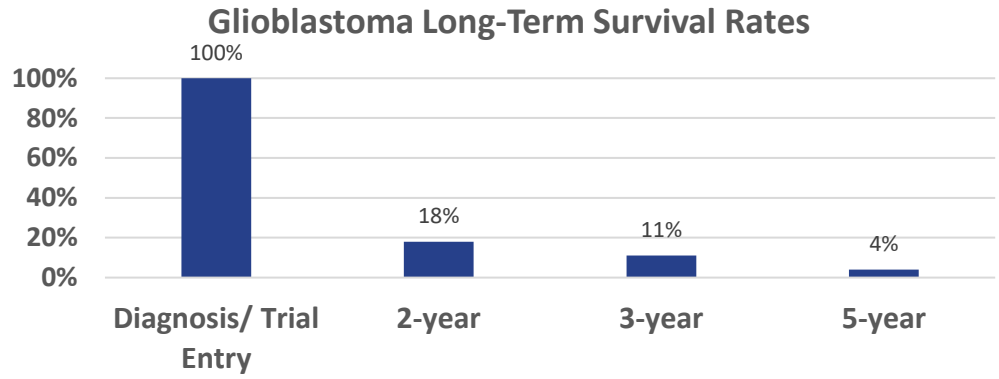
4%
5Y

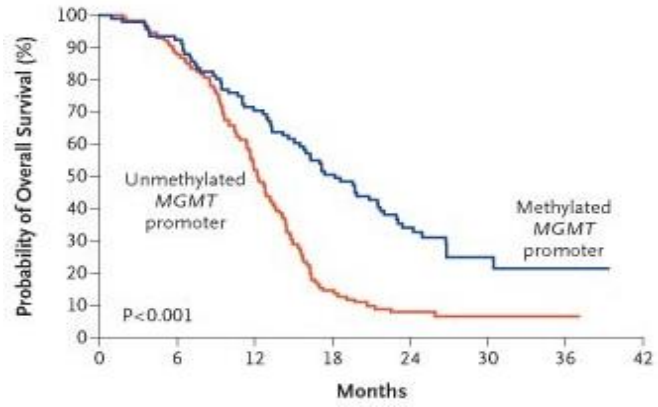
mOS
12-15 months

~ 160 active clinical trials

HIGH UNMET NEED PATIENT SEGMENTS

- MGMT unmethylated promoter – chemotherapy ineffective
- NOX-A12 to focus on MGMT unmethylated patients
- Incomplete resection – poor prognosis & therapeutic responses





1. In the US, UK, FR, ES, DE & IT, Global Data April 2022

Sources: Poon MTC, et al., Scientific Reports 2020 Vol. 10 Issue 1; Hegi ME et al. N Engl J Med 2005;352:997-1003; Global Data, ClinicalTrials.gov & NOXXON Pharma analysis, April 2022

Frank A. Giordano, MD

Professor of Radiation Oncology
Director and Chair, Department of Radiation Oncology
University Hospital Bonn

Lead Investigator of NOX-A12 GLORIA Phase 1/2 Study

ukb Klinik für Strahlentherapie und Radioonkologie

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Study Arms

Dose Escalation Cohorts
Recruitment Completed

Key inclusion criteria:
- Newly-diagnosed supratentorial glioblastoma WHO IV
- MGMT promoter unmethylated
- Incomplete resection/biopsy only
- ECOG ≤ 2

RT
60 Gy (2 Gy x 30)
40.05 Gy (2.67 Gy x 15)

OLA
continuous i.v. infusion at three doses (200, 400, 600 mg/week)

FU

1 6

OLA-BEV Cohort
Recruiting

Key inclusion criteria:
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allowing completely resected GBM with v7.0

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60 Gy (2 Gy x 30)

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continuous i.v., 600 mg/week

BEV
10 mg/kg, q2w i.v.

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OLA-PEM Cohort
Recruiting

Key inclusion criteria:
- Newly-diagnosed supratentorial glioblastoma WHO IV
- MGMT promoter unmethylated
- Incomplete resection < 5cm
- ECOG ≤ 2
- no immunosuppression

allowing completely resected GBM with v7.0

RT
60 Gy (2 Gy x 30)

OLA
continuous i.v., 600 mg/week

PEM
200 mg, q3w i.v.

FU

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2022 ASCO ANNUAL MEETING

ukb Klinik für Strahlentherapie und Radioonkologie

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2022 ASCO®
ANNUAL MEETING

Radiotherapy and olaptesed pegol (NOX-A12) in partially resected or biopsy-only MGMT-unmethylated glioblastoma: Interim data from the German multicenter phase 1/2 GLORIA trial

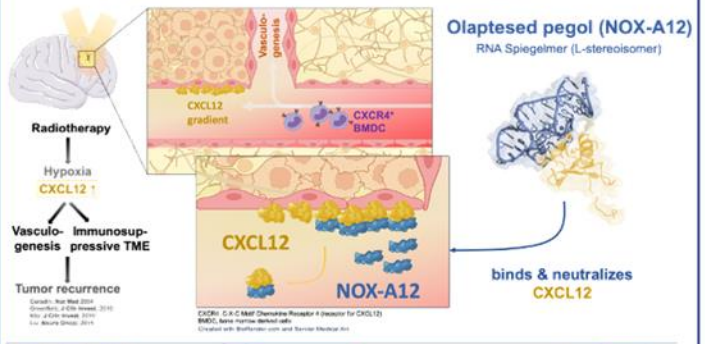
Frank A. Giordano[1], Julian P. Layer[1,2], Sonia Leonardelli[2], Lea L. Friker[3], Clemens Seidel[4], Christina Schaub[5], Roberta Turiello[2], Elena Sperk[6], Franziska Grau[7], Daniel Paech[7], Barbara Link[1], Wolf Mueller[8], Ghazaleh Tabatabai[9], Katharina Sahm[10], Sied Kebir[11], Torsten Pietsch[3], Martin Glas[11], Sotirios Bisdas[12], Ulrich Herrlinger[5], Michael Hölzel[2]

[1] Department of Radiation Oncology, University Hospital Bonn; [2] Institute of Experimental Oncology, University Hospital Bonn; [3] Department of Neuropathology, University Hospital Bonn; [4] Department of Radiotherapy, University Hospital Leipzig; [5] Department of Neurology, University Hospital Bonn; [6] Department of Radiation Oncology, University Hospital Mannheim, University of Heidelberg; [7] Department of Neuroradiology, University Hospital Bonn; [8] Institute of Neuropathology, University Hospital Leipzig; [9] Department of Neurology, University Hospital Tübingen; [10] Department of Neurology, University Hospital Mannheim, University of Heidelberg; [11] Department of Neurology, University Hospital Essen; [12] Department of Neuroradiology, National Hospital for Neurology London

2022 ASCO ANNUAL MEETING
Abstract #2050

1 BACKGROUND & STUDY DESIGN

- Inhibition of the CXCL12/CXCR4/CXCR7 axis
  - abrogates recruitment of pro-vasculogenic bone marrow-derived cells after radiotherapy (RT) of glioblastoma (GBM)
  - prevents T cell exclusion from the tumor microenvironment (TME)

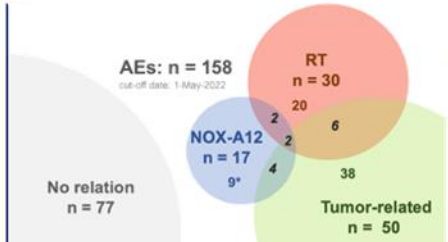


Primary Endpoint: Safety as per # of patients with treatment-related CTCAE

Secondary Endpoints: NOX-A12 plasma levels, tumor vascularization/perfusion as per advanced MRI, PFS-6, mPFS, OS, QoL, NANO

Exploratory Endpoint: Translational characterization of TME response by CODEX®

2 SAFETY

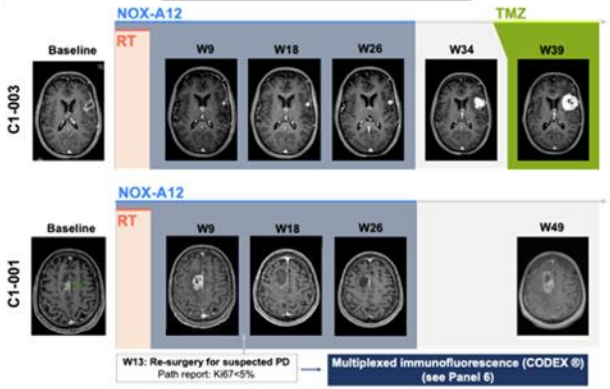


- Combination of RT and NOX-A12 well-tolerated and safe
- Of all G≥2 AEs (n = 77), 3 (4%) solely NOX-A12-related
- No dose limiting toxicities (DLT) and no treatment-related deaths

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

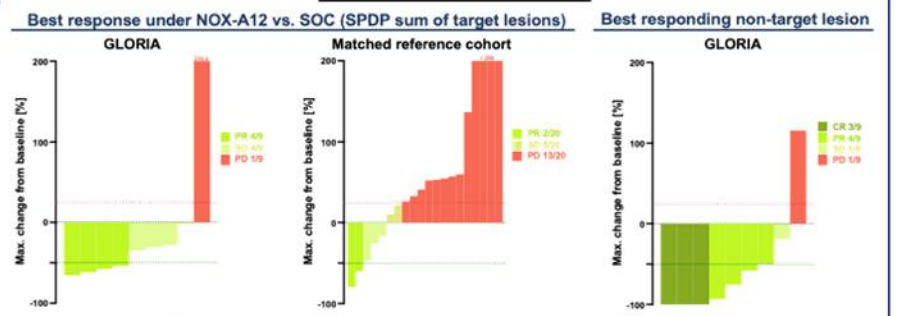
GGT increased	G3
2 x ALT increased	G2
Dyspnea	G1
3 x Leukocytosis	G1
Paresthesia	G1
Pyrexia	G1

3 EXEMPLARY COURSE



Pathology-confirmed early pseudoprogression (PsP) at W9 for C1-001 (lower panel)

4 LESION RESPONSE



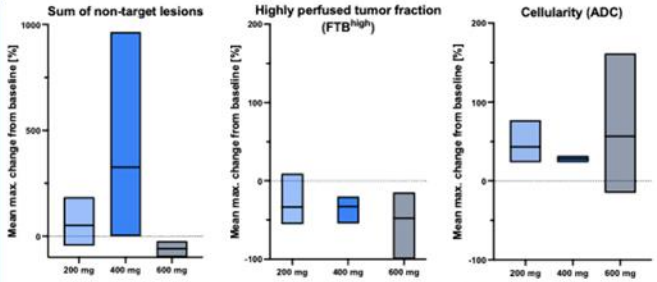
- Trial results were compared to a matched imaging reference cohort treated with standard of care (SOC)
- Of 10 patients, one had only target lesions (TLs) and another one had only non target lesions (NTLs)
- 9/10 patients showed response to NOX-A12 either in TL or NTL
- 8/9 patients with detectable TLs responded to NOX-A12, 4/9 reaching partial remission (PR; n = 2 at DL1 and n = 2 at DL3)
- 3/3 patients of DL1 and 4/4 of DL3 reached PR or CR of one or more NTLs
- In 3/9 cases (n = 2 at DL1; n = 1 at DL3), at least one NTL completely disappeared

Radiotherapy + NOX-A12 in chemotherapy refractory GBM

Safe | No DLT | Promising clinical efficacy | T cell recruitment + clustering

Expansion arms with Bevacizumab or Pembrolizumab initiated

5 ADVANCED IMAGING



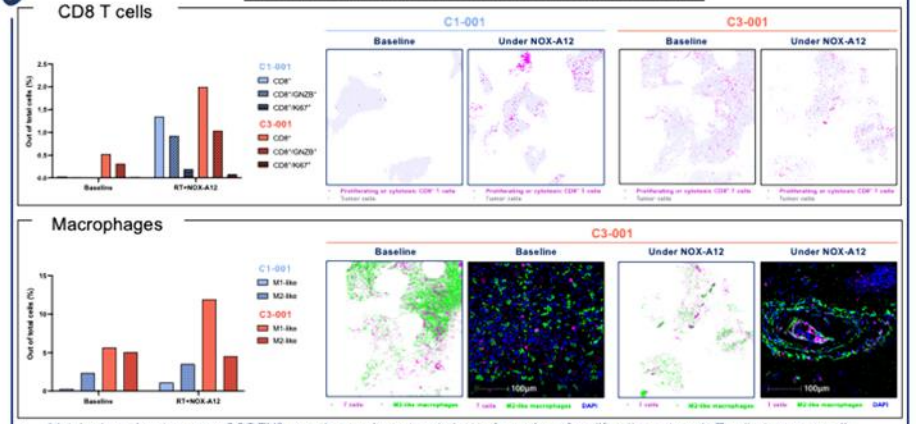
Under NOX-A12 radiographic responses of NTL were best at the highest DL, as was the increase in diffusion and the decrease in FTBhigh

REGISTRATION & CONTACT

Registered with clinicaltrials.gov, ID: NCT04121455

Frank.Giordano@ukbonn.de

6 TUMOR MICROENVIRONMENT



- Matched pre-/post-surgery CODEX® reveals recruitment and cluster formation of proliferating cytotoxic T cells (upper panel)
- Matched pre-/post-surgery CODEX® of non-responding patient show T-cell encapsulation by M2-like macrophages (lower panel)

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- Inhibition of the CXCL12/CXCR4/CXCR7 axis
  - ➢ abrogates recruitment of pro-vasculogenic bone marrow-derived cells after radiotherapy (RT) of glioblastoma (GBM)
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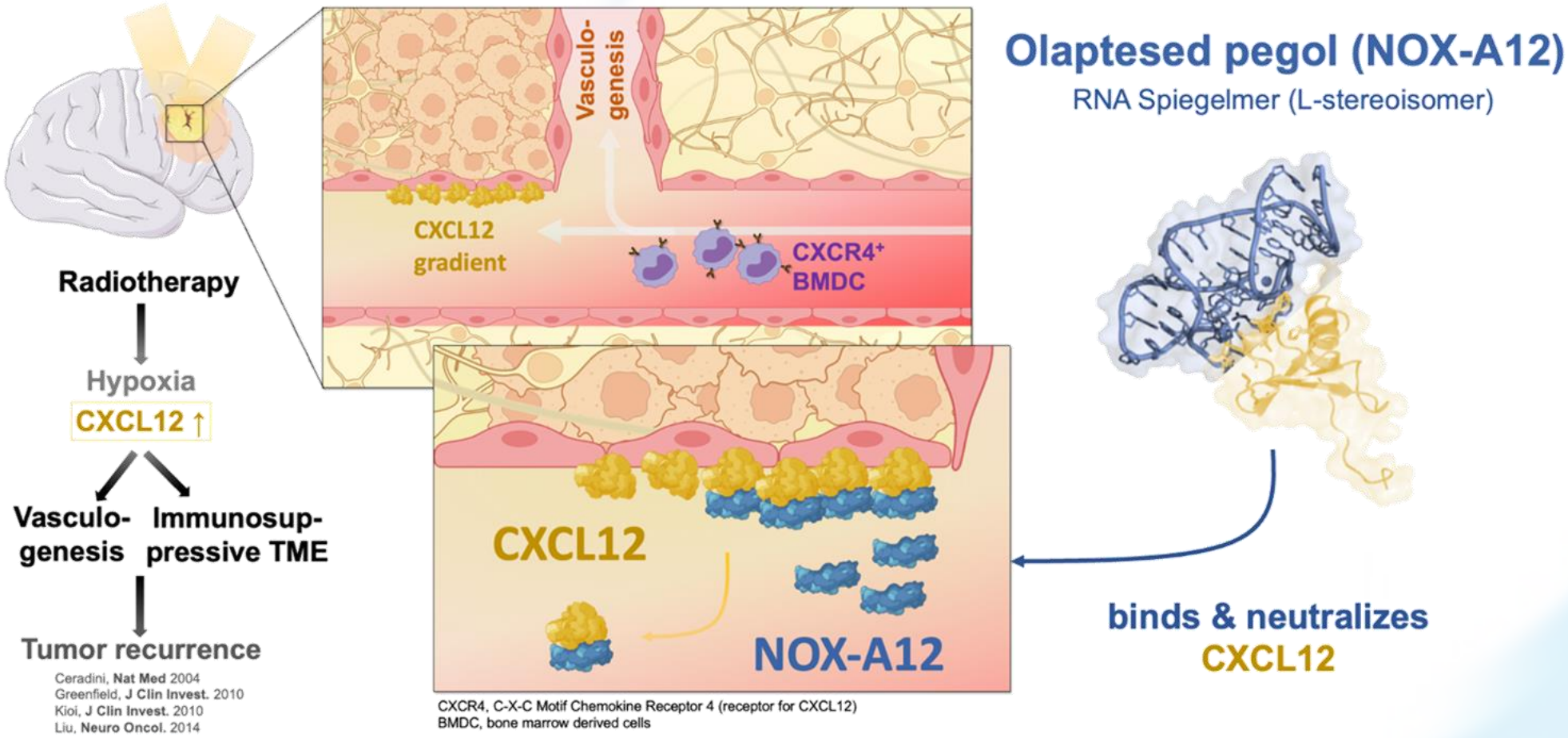
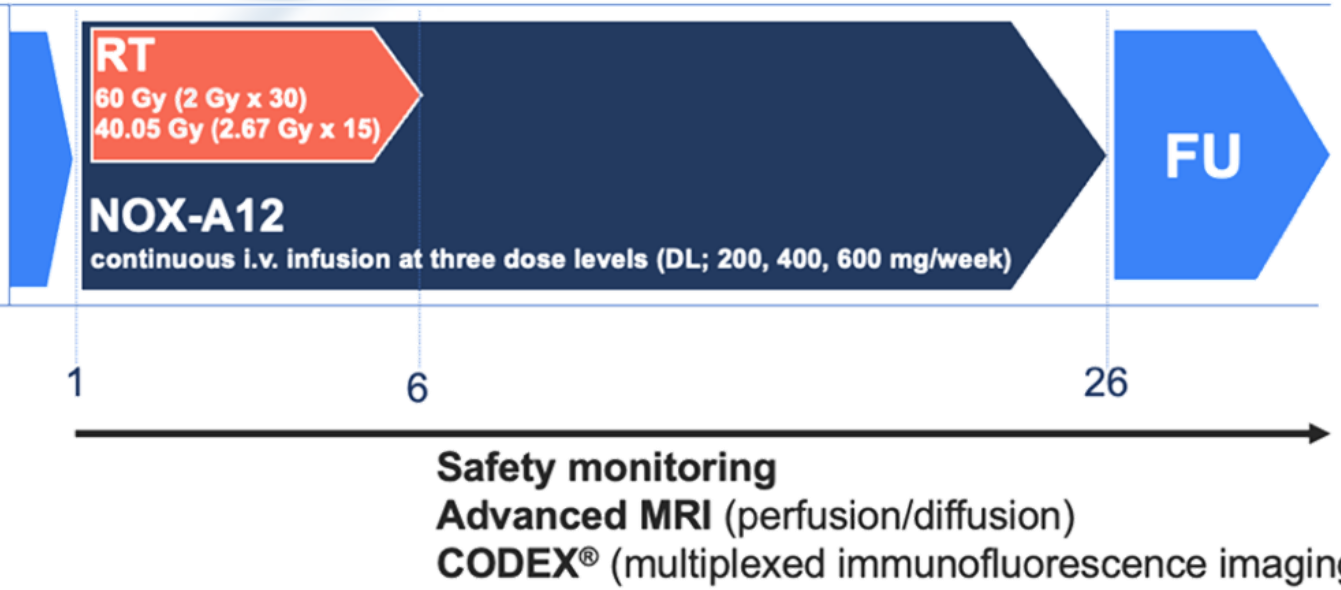


1 BACKGROUND & STUDY DESIGN

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



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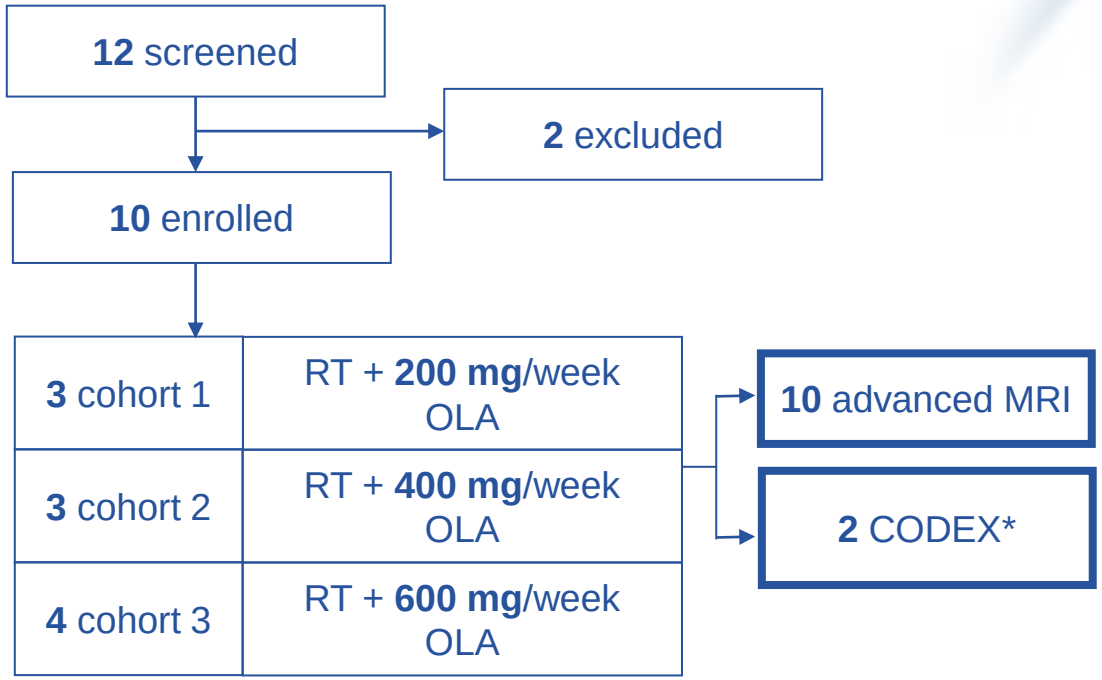
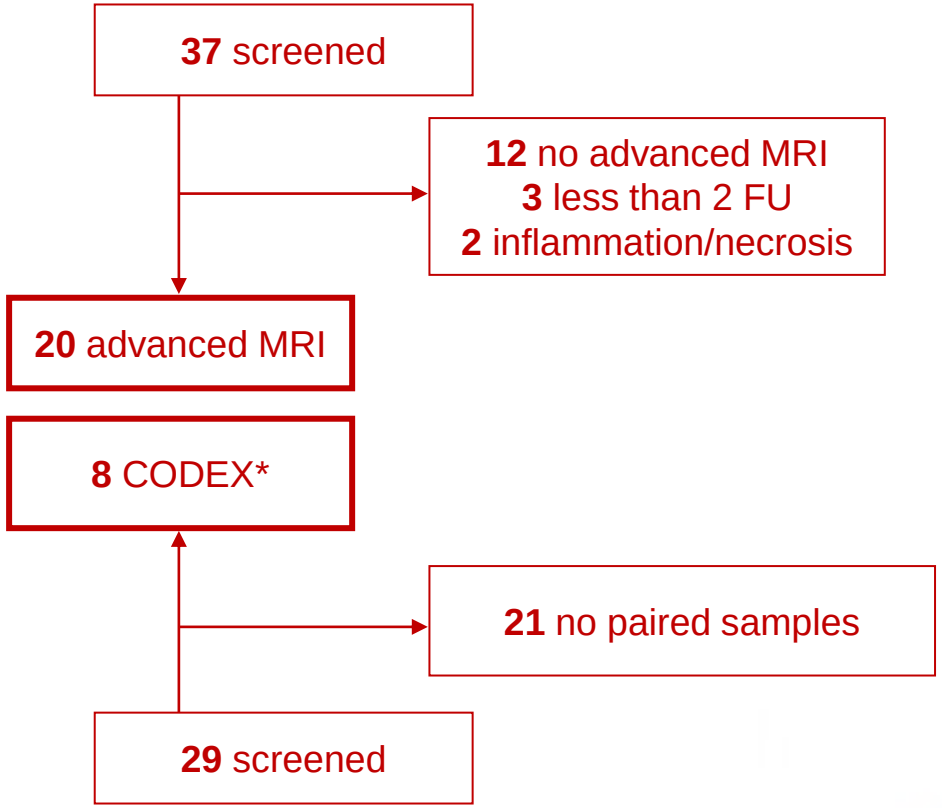
FOCUS: CONSORT of GLORIA and controls

GLORIA



Matched Imaging Control Cohort**

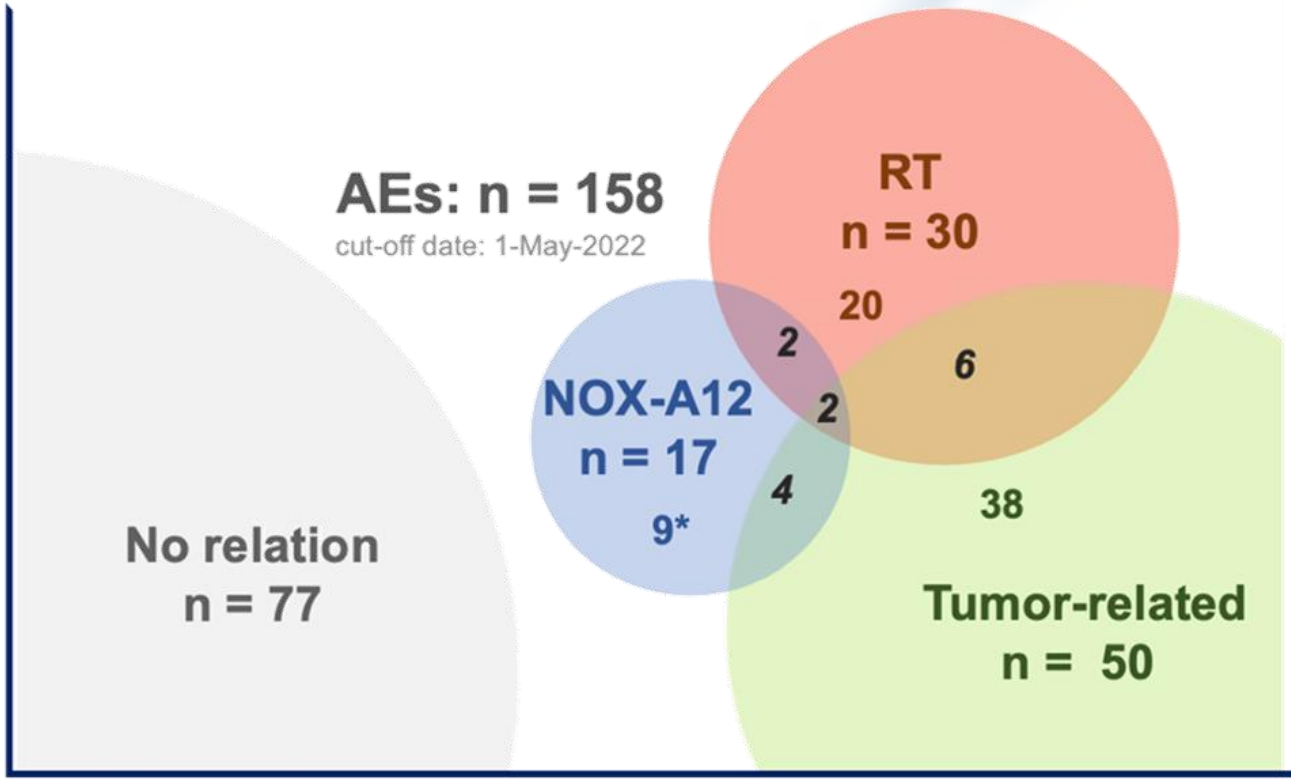


CODEX Control Cohort

* Only performed for paired samples from 1st and 2nd surgery.

** Matched per MGMT promoter methylation status and extent of resection. Patients in the control cohort needed to have at least 3 consecutive scans.

SAFETY



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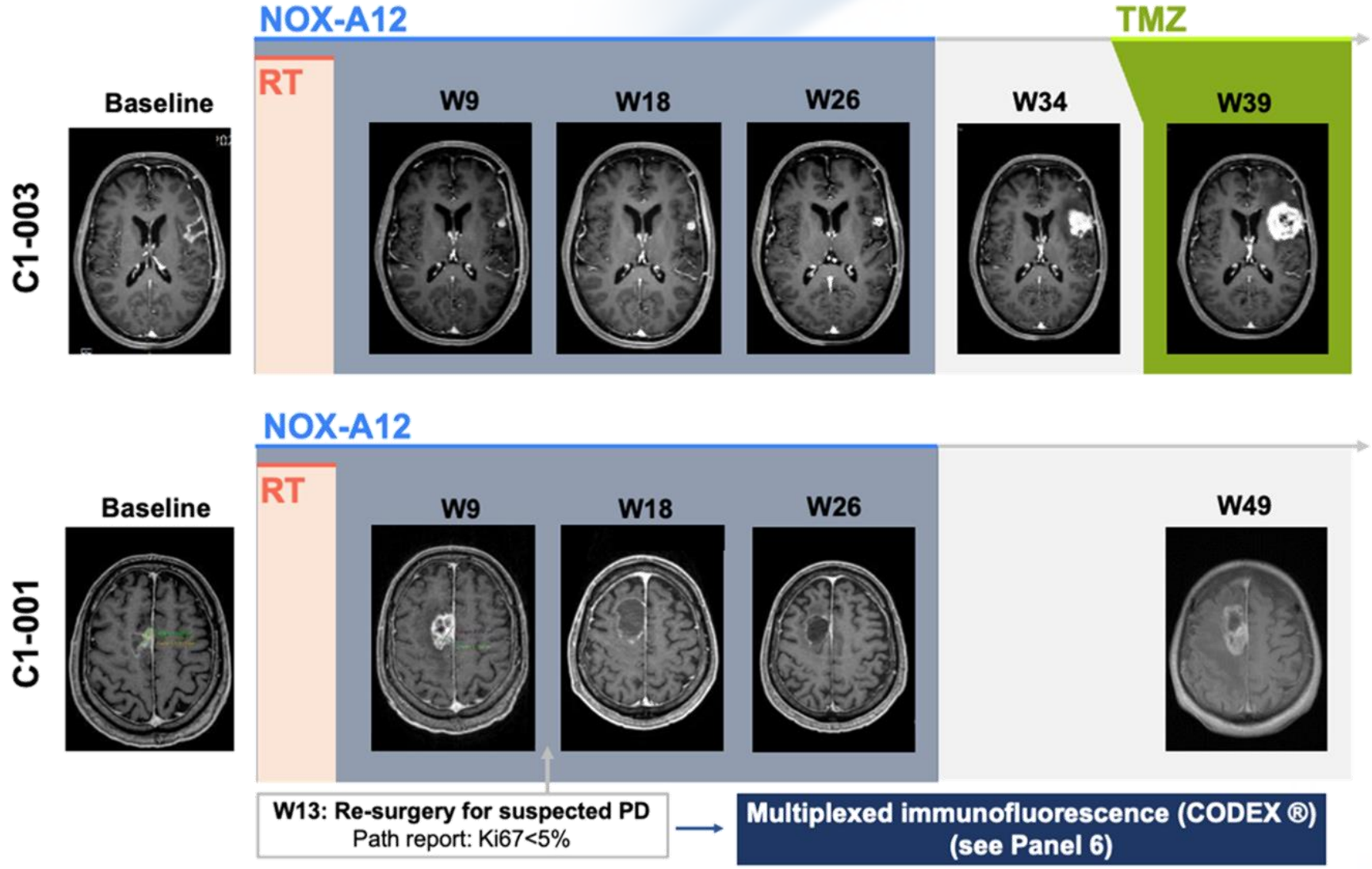

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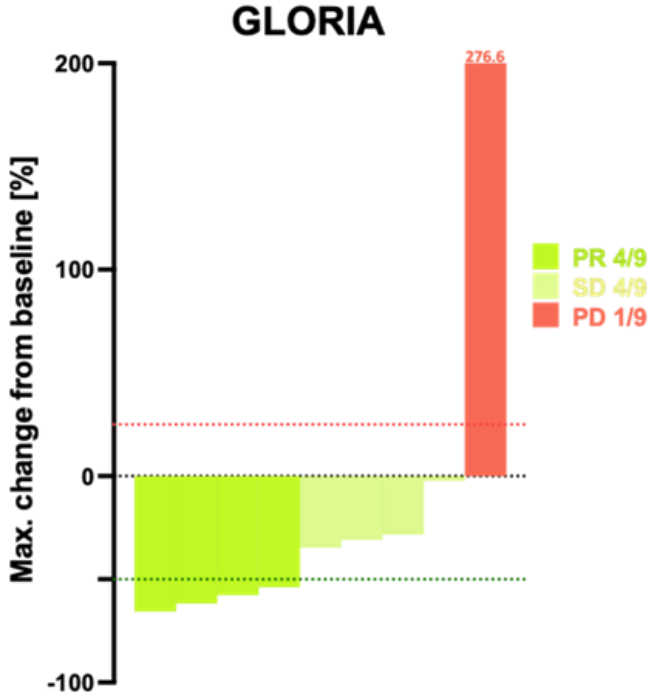
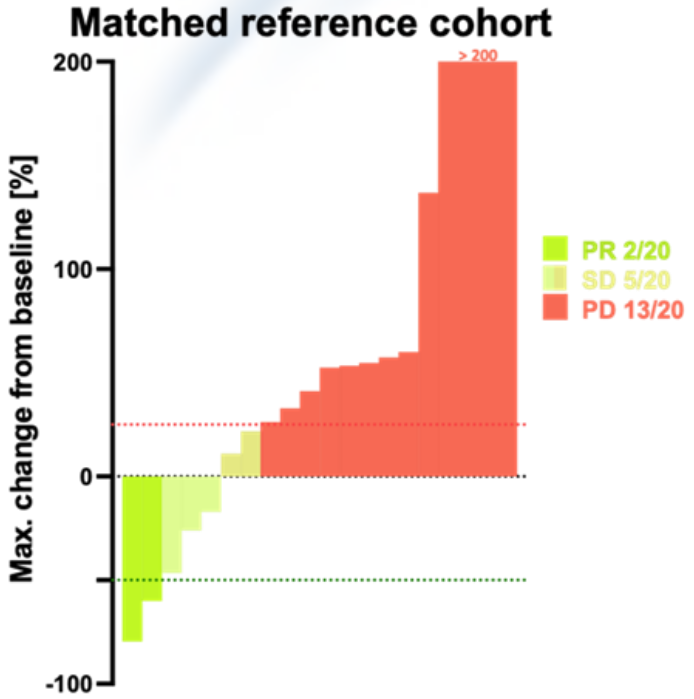
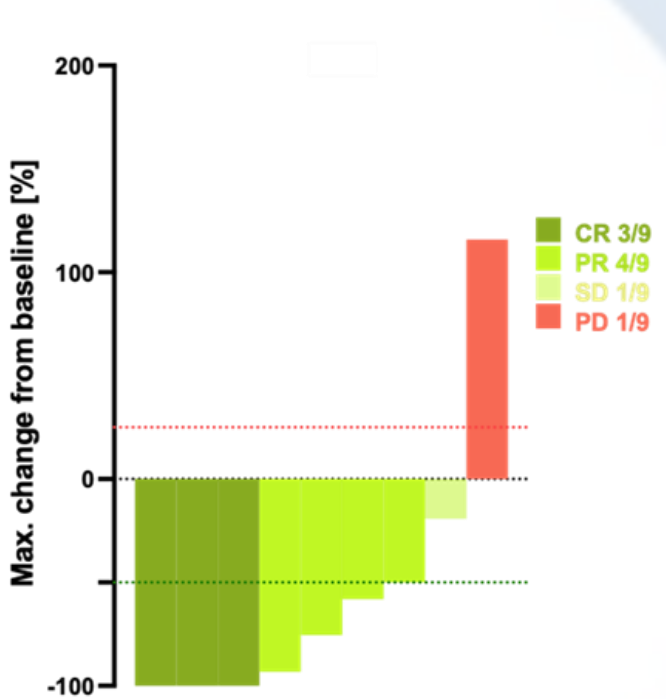
LESION RESPONSE

Best response under NOX-A12 vs. SOC (SPD sum of target lesions)





Best responding non-target lesion



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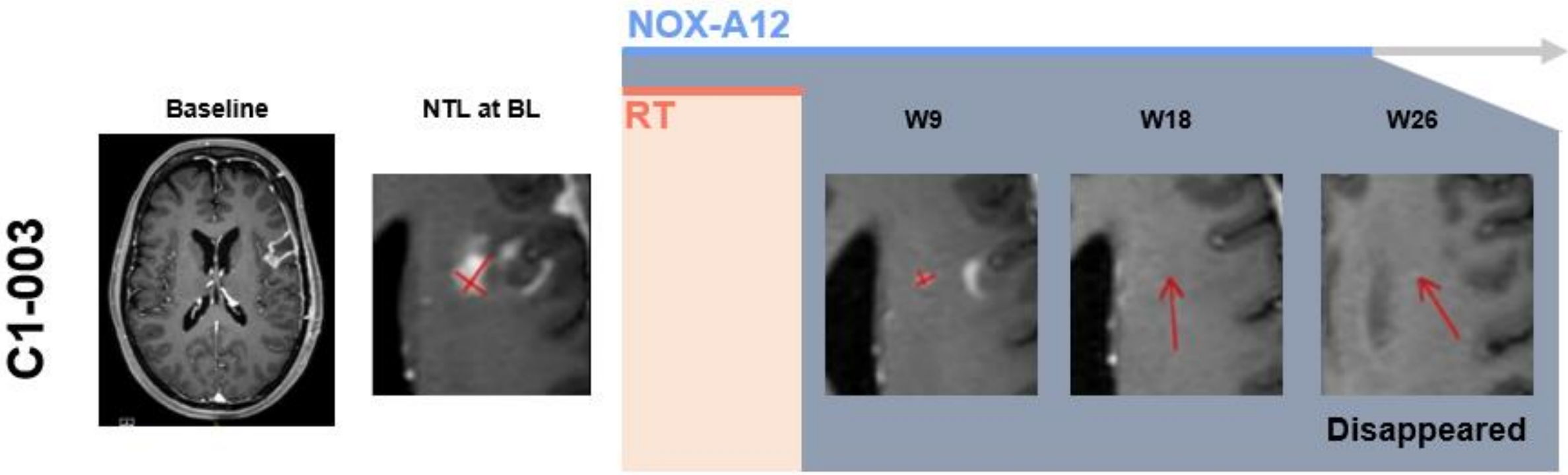

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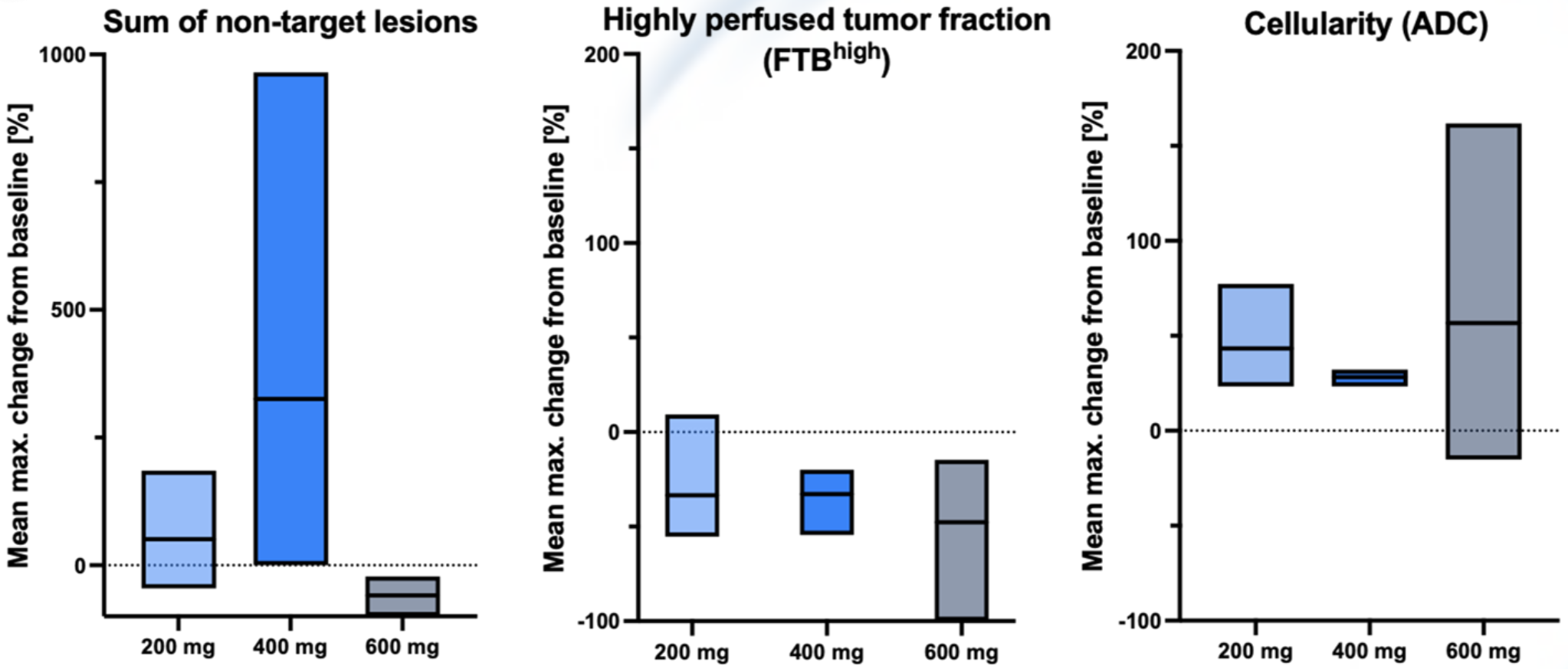

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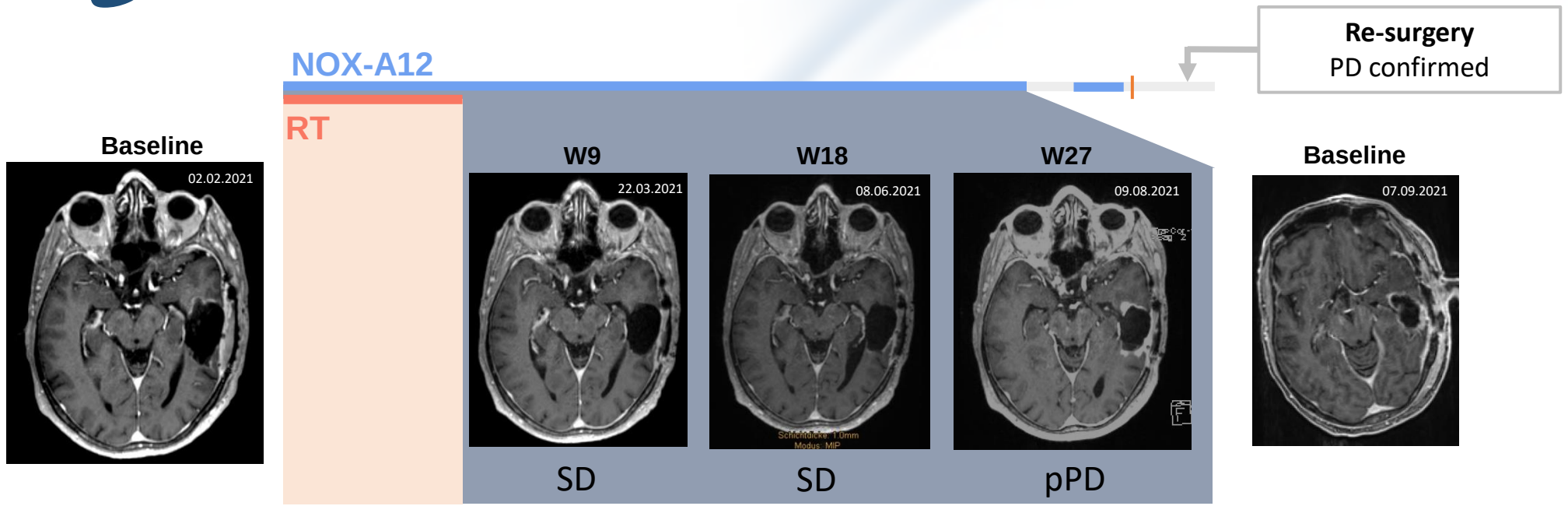
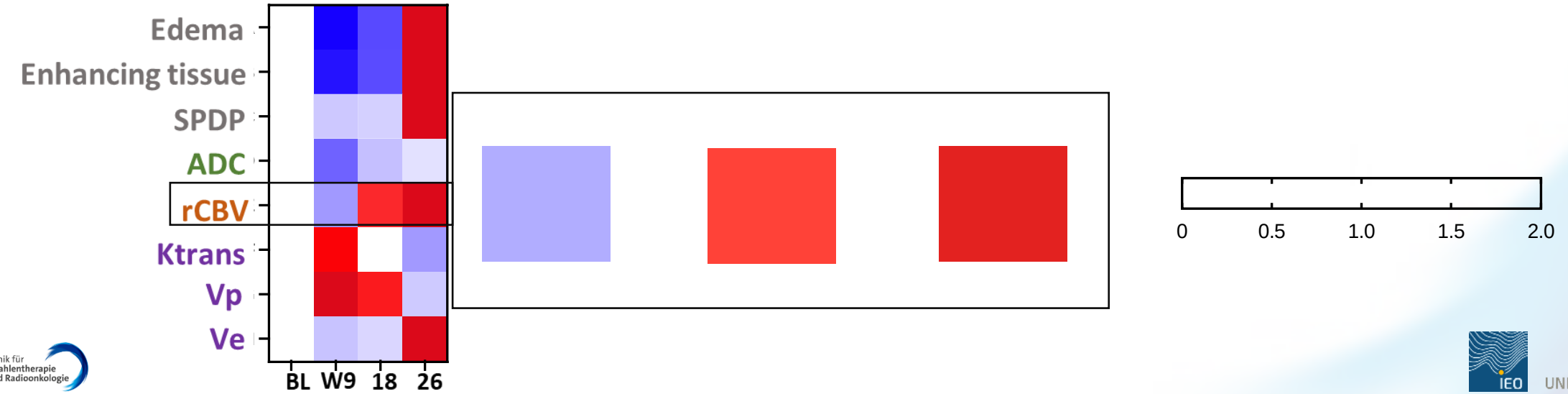
FOCUS: Value of rCBV under NOX-A12

C3-001





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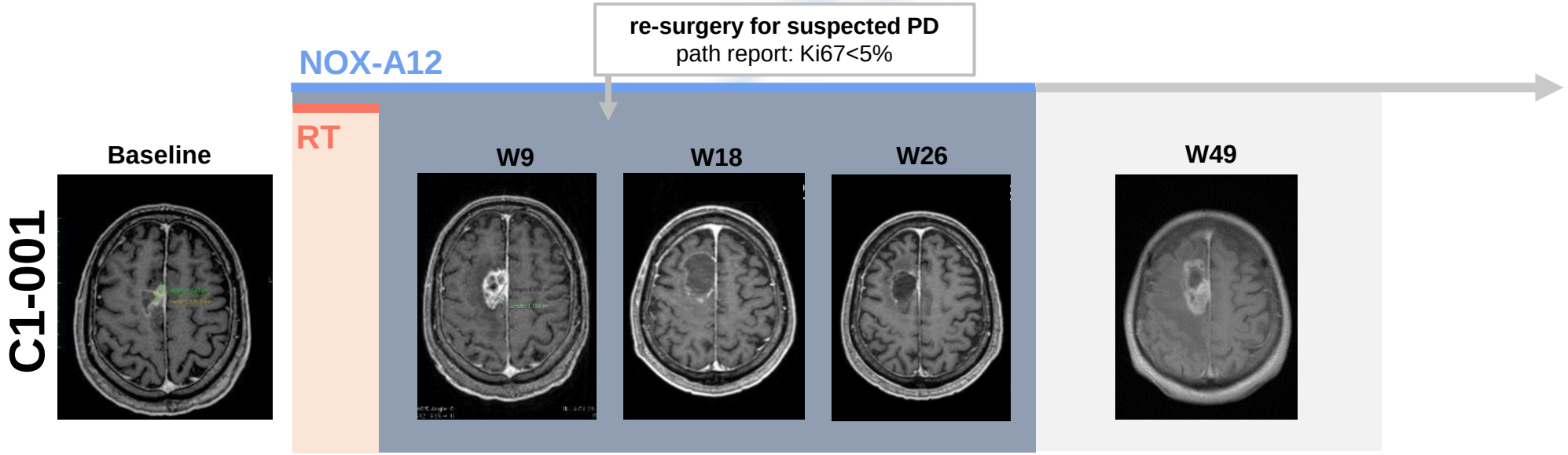
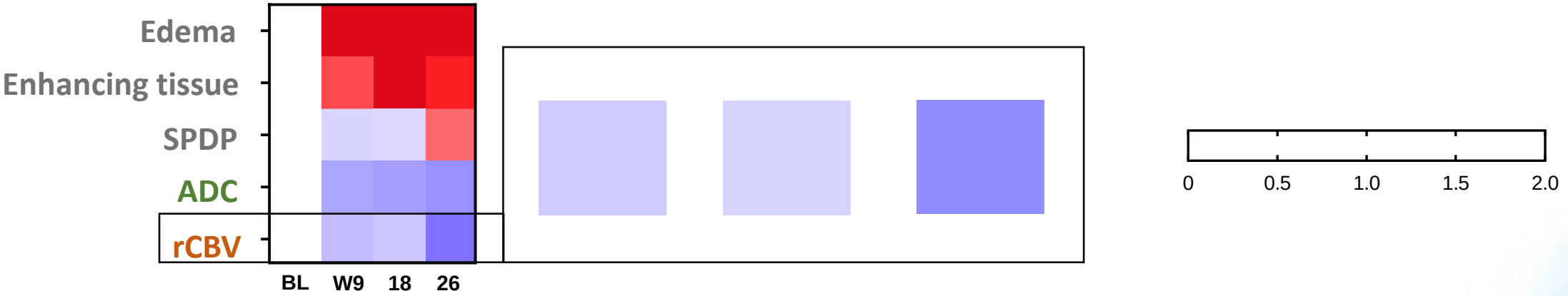
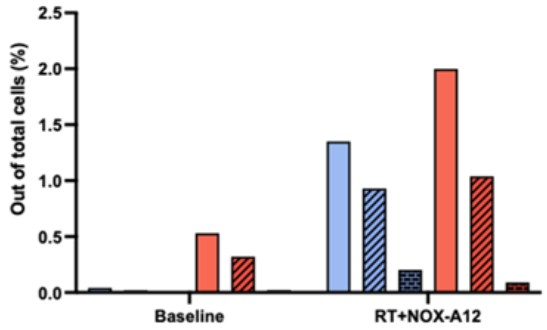




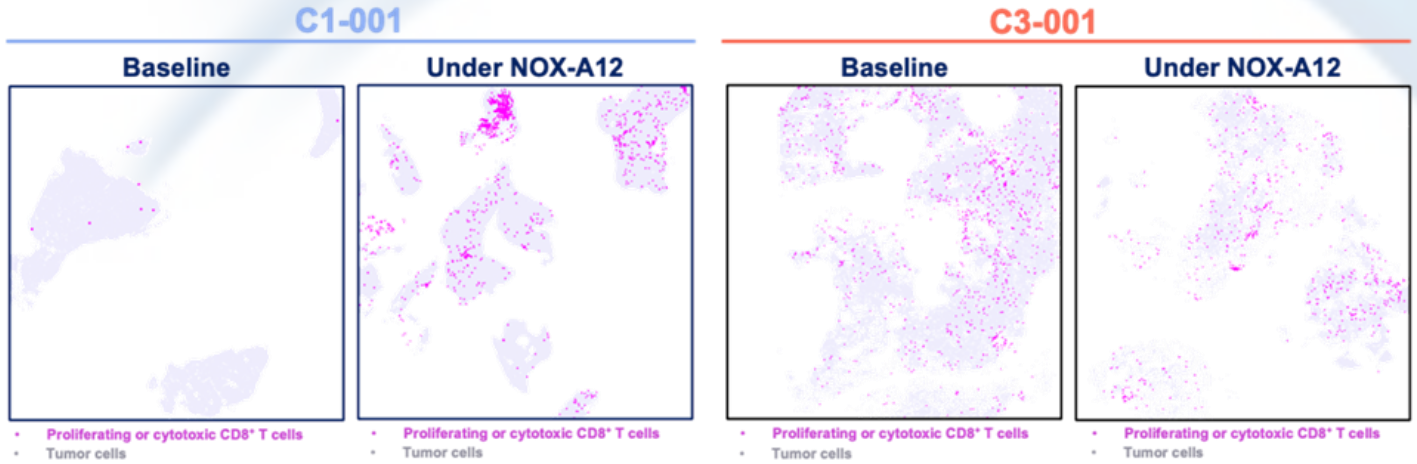
6 TUMOR MICROENVIRONMENT

CD8 T cells

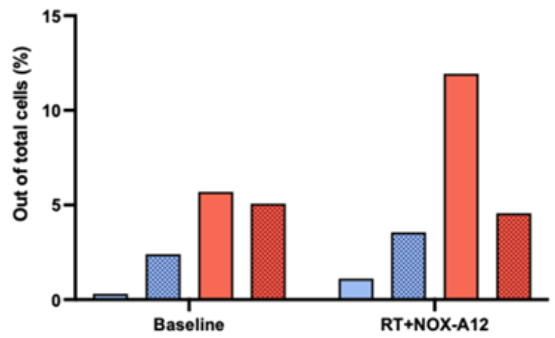


C1-001
- CD8⁺
- CD8⁺/GNZB⁺
- CD8⁺/Ki67⁺

C3-001
- CD8⁺
- CD8⁺/GNZB⁺
- CD8⁺/Ki67⁺

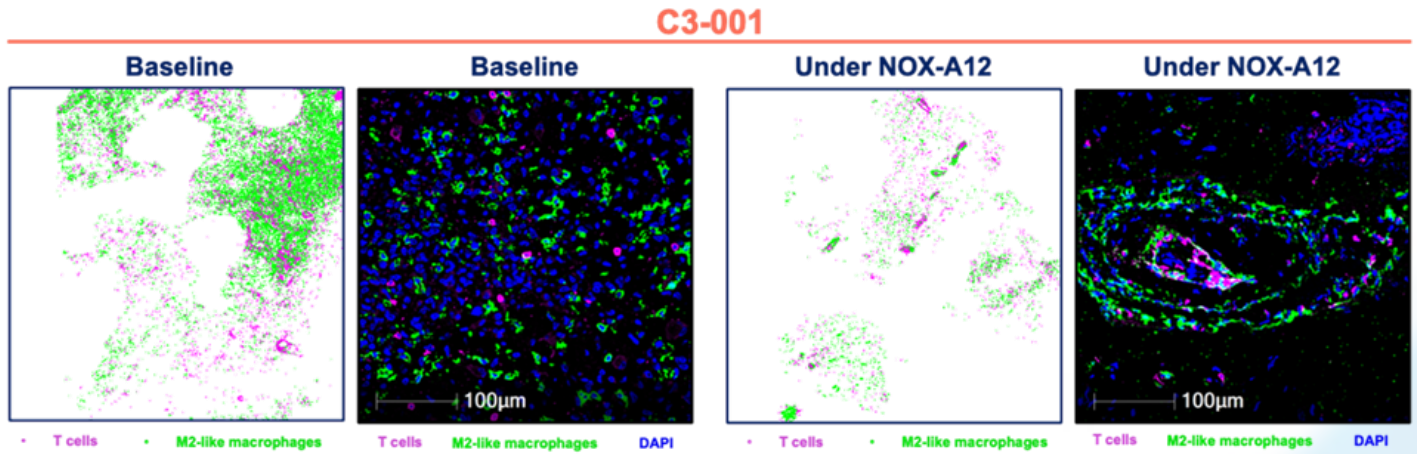


Macrophages



C1-001
- M1-like
- M2-like

C3-001
- M1-like
- M2-like



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- Matched pre-/post-surgery CODEX® of non-responding patient show T-cell encapsulation by M2-like macrophages (lower panel)

Conclusions:

- **Radiotherapy** + **NOX-A12** in chemotherapy-refractory GBM is safe
- No DLT
- Promising clinical efficacy
- T cell recruitment + clustering
- Expansion arms with bevacizumab or pembrolizumab initiated

Q&A Session

Dr. Frank Giordano
Chair & Director
Radiation Oncology Dept.
University Hospital Bonn

Lead Investigator of NOX-A12
GLORIA Phase 1/2 Study

Aram Mangasarian
CEO
NOXXON Pharma

Thank you!

Contact Us:

noxxon@noxxon.com

NOXXON PHARMA