NOXXON SUMMARIZES ESSENTIAL POINTS FROM KEY OPINION LEADER EVENT ON NOX-A12 & RADIOTHERAPY COMBINATION IN BRAIN CANCER HELD ON NOVEMBER 23, 2021 WITH DR FRANK A. GIORDANO

Berlin, Germany, December 02, 2021, 08:00 a.m. CET - NOXXON Pharma N.V. (Euronext Growth Paris: ALNOX), a biotechnology company focused on improving cancer treatments by targeting the tumor microenvironment (TME), hosted a Key Opinion Leader (KOL) event with Frank A. Giordano, M.D. on November 23, 2021, to discuss the combination of NOX-A12 and radiotherapy in brain cancer (glioblastoma, GBM). Dr. Giordano is Director and Chair of the Department of Radiation Oncology, University Hospital Bonn, Germany, and lead investigator of the ongoing NOX-A12 Phase 1/2 study GLORIA in glioblastoma.

"*I have been involved in research and treatment of glioblastoma for many years, and we've not seen major changes in the management of this terrible disease for almost two decades. Although the development of an effective treatment for glioblastoma has proved extremely challenging, the data from the GLORIA study are very promising and, if confirmed in a pivotal clinical study, could be transformational for patients affected by this devastating disease,*" **commented Dr. Frank Giordano**.

"*Dr. Giordano is a research pioneer and expert in precision radiation therapy and intraoperative irradiation of malignant tumors. He has brought together an exceptional team around the GLORIA study which was evident from the data presentation at SNO. His leadership of the trial will ensure that all the insights we can derive will be put to use in future trials of NOX-A12,*" **commented Aram Mangasarian, CEO of NOXXON.**

Glioblastoma is a devastating disease affecting 23,000 new patient each year in the US and Europe. The median overall survival for this patient population is only 14 months, and even lower in the MGMT unmethylated (chemotherapy refractory) patient subpopulation. The KOL webinar highlighted data from the Phase 1/2 GLORIA study presented at the Society for Neuro-Oncology (SNO) Annual Meeting, where tumor shrinkage for patients in the study was significantly stronger compared to those of a historic matched cohort that received standard of care. Eight of 9 MGMT unmethylated glioblastoma patients (89%) receiving NOX-A12 demonstrated tumor size reductions, while only 1 of 13 patients from a matched cohort (8%) showed any tumor shrinkage.

During the KOL event, Dr. Giordano emphasized several other important points, summarized in the Annex to this press release.

The webinar recording is available here, and the webinar slides can be accessed here.

For more information, please contact:

NOXXON Pharma N.V.
Aram Mangasarian, Ph.D.
Chief Executive Officer
Tel. +49 (0) 30 726247 0
amangasarian@noxxon.com

Investor and Media Relations:

LifeSci Advisors
Guillaume van Renterghem
Tel. +41 (0) 76 735 01 31
gvanrenterghem@lifesciadvisors.com

NewCap
Arthur Rouillé
Tel. +33 (0) 1 44 71 00 15
arouille@newcap.fr

About NOXXON

NOXXON's oncology-focused pipeline acts on the tumor microenvironment (TME) and the cancer immunity cycle by breaking the tumor protection barrier and blocking tumor repair. By neutralizing chemokines in the TME, NOXXON's approach works in combination with other forms of treatment to weaken tumor defenses against the immune system and enable greater therapeutic impact. NOXXON's lead program NOX-A12 has delivered final top-line data from a Keytruda® combination trial in metastatic colorectal and pancreatic cancer patients published at the ESMO conference in September 2020 and in July 2021 the company announced its Phase 2 study, OPTIMUS, to further evaluate safety and efficacy of NOX-A12 in combination with Merck's Keytruda® and two different chemotherapy regimens as second-line therapy in patients with metastatic pancreatic cancer. NOXXON is also studying NOX-A12 in brain cancer in combination with radiotherapy which has been granted orphan drug status in the US and EU for the treatment of certain brain cancers. GLORIA, a trial of NOX-A12 in combination with radiotherapy in newly diagnosed brain cancer patients who will not benefit clinically from standard chemotherapy has delivered interim data from the first two cohorts showing consistent tumor reductions and objective tumor responses. The company's second clinical-stage asset NOX-E36 is a Phase 2 TME asset targeting the innate immune system. NOXXON plans to test NOX-E36 in patients with solid tumors. Further information can be found at: www.noxxon.com.

Keytruda® is a registered trademark of Merck Sharp & Dohme Corp.

Visit NOXXON on LinkedIn and Twitter.

About the GLORIA Study

GLORIA (NCT04121455) is NOXXON's dose-escalation, phase 1/2 study of NOX-A12 in combination with irradiation in first-line glioblastoma (brain cancer) patients with unmethylated MGMT promoter (resistant to standard chemotherapy).

About the OPTIMUS Study

OPTIMUS (NCT04901741) is NOXXON's open-label two-arm phase 2 study of NOX-A12 combined with pembrolizumab and nanoliposomal irinotecan/5-FU/leucovorin or gemcitabine/nab-paclitaxel in microsatellite-stable metastatic pancreatic cancer patients.

Disclaimer

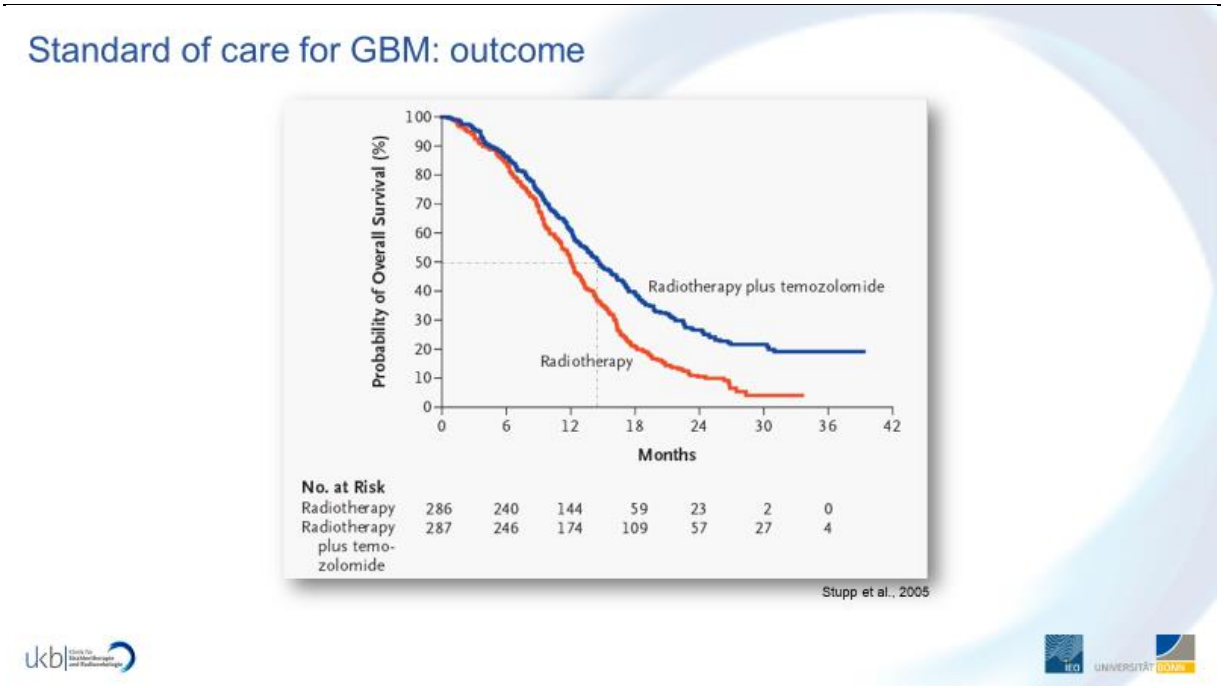
Certain statements in this communication contain formulations or terms referring to the future or future developments, as well as negations of such formulations or terms, or similar terminology. These are described as forward-looking statements. In addition, all information in this communication regarding planned or future results of business segments, financial indicators, developments of the financial situation or other financial or statistical data contains such forward-looking statements. The company cautions prospective investors not to rely on such forward-looking statements as certain prognoses of actual future events and developments. The company is neither responsible nor liable for updating such information, which only represents the state of affairs on the day of publication.

Annex

Key messages from the KOL event on NOX-A12 and radiotherapy combination in brain cancer held on November 23, 2021 with Dr. Frank. Giordano.

As highlighted by Dr. Giordano, prognosis of glioblastoma (GBM) patients is very poor with the current standard of care (surgical tumor resection to the maximum extent possible, followed by radiochemotherapy with temozolomide), reaching a median overall survival (mOS) of approximately 14 months (see Figure 1). Temozolomide was approved in 2005 for the treatment of adult patients with newly diagnosed glioblastoma concurrently with radiotherapy and has remained since then the standard of care, underpinning the need for a new wave of innovation for the treatment of glioblastoma.

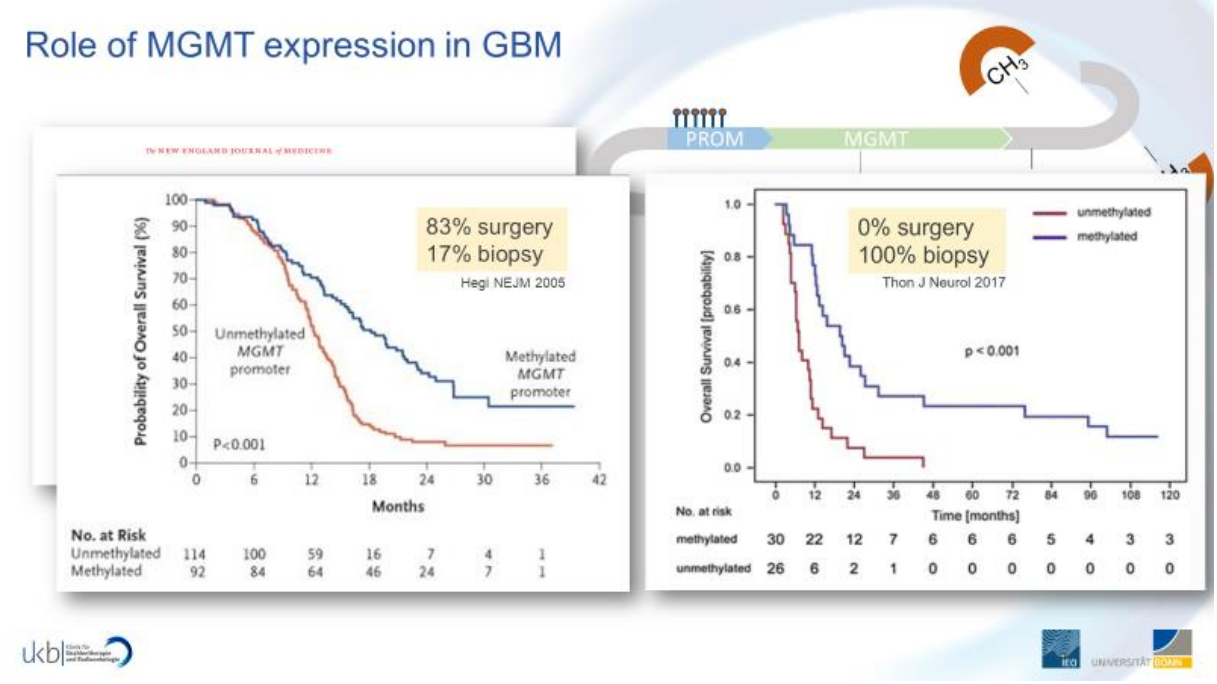
Figure 1: The limited benefit of current standard of care in glioblastoma



Source: Dr Frank Giordano, 2021

Outcomes are even poorer in MGMT unmethylated patients with mOS well below 12 months (see Figure 2) since they do not respond to the standard of care chemotherapy agent, temozolomide. This population represents approximately 55% of newly diagnosed patients and as such is a population of particular importance.

Figure 2: Significantly worse prognosis in GBM patients with unmethylated MGMT promoter

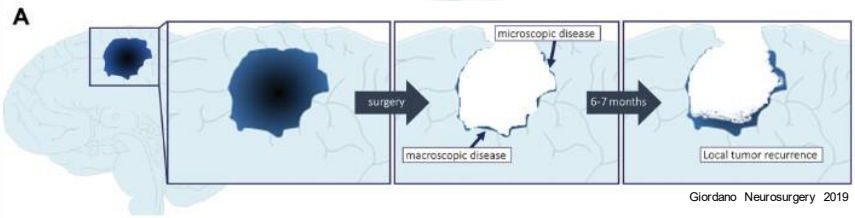


Source: Dr Frank Giordano, 2021

While surgery to the maximum extent possible remains important to debulk the tumor, at least microscopic disease will remain around the resection cavity. The standard of care radiochemotherapy that follows the resection aims at reducing the recurrence of the tumor from the remaining disease, but as these cells show a high degree of radio- and chemoresistance, there is generally rapid local recurrence within months after radiochemotherapy (see Figure 3).

Figure 3: Reasons for Rapid Local Recurrence of Glioblastoma

Reasons for rapid local recurrence



Giordano Neurosurgery 2019

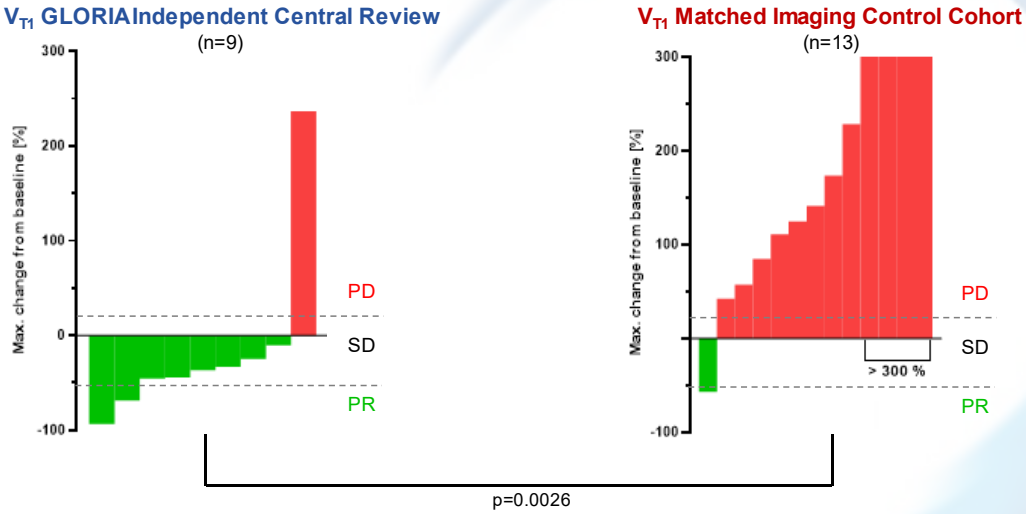
- residual tumor cells remain even after "perfect" (or supramaximal) surgery
- GB stem cells show a high degree of radio- and chemoresistance
- highly effective revascularization after radiotherapy

Source: Dr Frank Giordano, 2021

NOX-A12 (OLA, olaptesed pegol), an inhibitor of CXCL12 is being tested in 9 patients affected with MGMT unmethylated glioblastoma. Out of the 9 patients treated with NOX-A12, 2 patients had a partial response (PR, >50% reduction in tumor size) and 6 patients achieved stable disease (SD, <50% reduction in tumor size), while only one patient progressed as a best response. This compared favourably with the matched imaging control cohort for which 12 out of 13 patients had progressive disease and only 1 out of 13 patients achieved any tumor size reduction vs. baseline (see Figure 4), underpinning the extremely poor prognosis of this patient population.

Figure 4: Best imaging response under Online Longitudinal Assessment (OLA)

Best response under OLA (volume of T1 enhancing lesions)

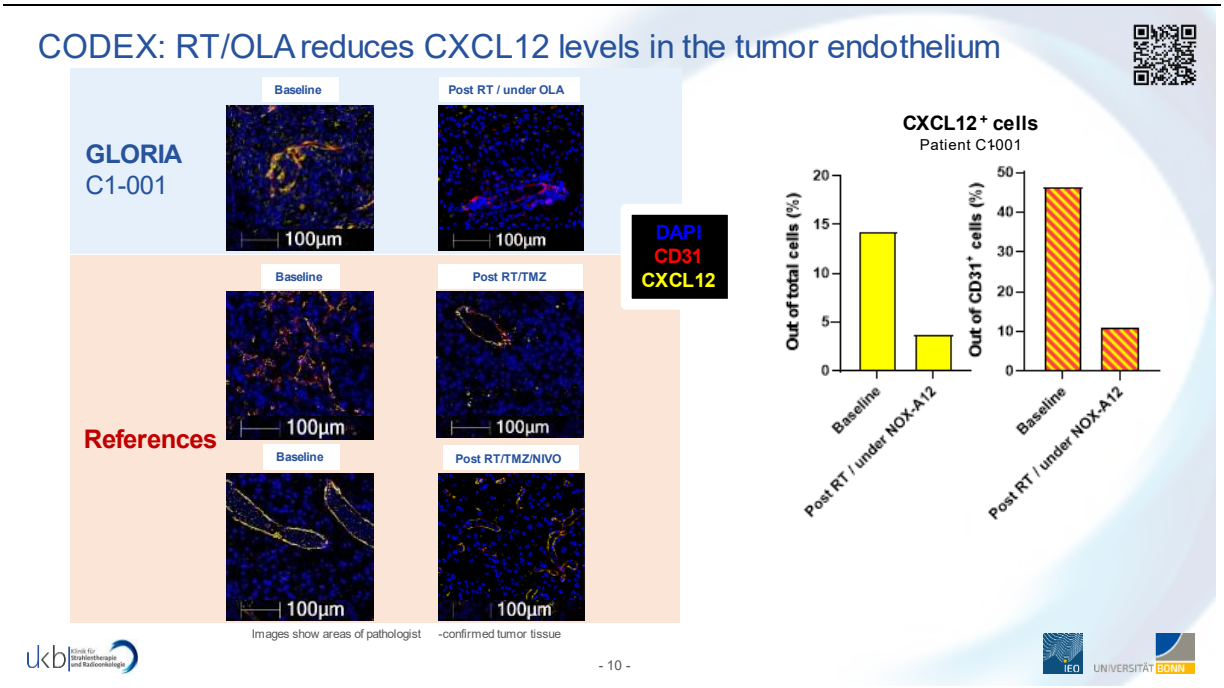


Source: Dr Frank Giordano, 2021

Also, NOX-A12 demonstrated a significant reduction of CXCL12 levels in the blood vessels of the tumor (see Figure 5) and a significant increase in cytotoxic T-cell infiltration (see Figure 6) both suggesting an ability to NOX-A12 to reshape the tumor microenvironment and to allow immune cells to enter the tumor and destroy it.

In the images on *Figure 5* below, DAPI stains the nuclei of all cells, CD31 is a marker of endothelial cells (blood vessel cells), and CXCL12 is the chemokine that is targeted by NOX-A12. At baseline (left column of images), CXCL12 appears in the same location as CD31, suggesting that CXCL12 is present on the blood vessel walls where it can attract cells to repair blood vessels and also prevent entry of cytotoxic T-cells. Under therapy with NOX-A12, the CXCL12 signal is no longer present on endothelium (top right image), while reference patients treated with other therapies show continued presence of CXCL12 on blood vessel walls. The percentage of cells expressing CXCL12 is strongly reduced both overall in the tumor tissue and when considering only endothelial cells (see bar graphs).

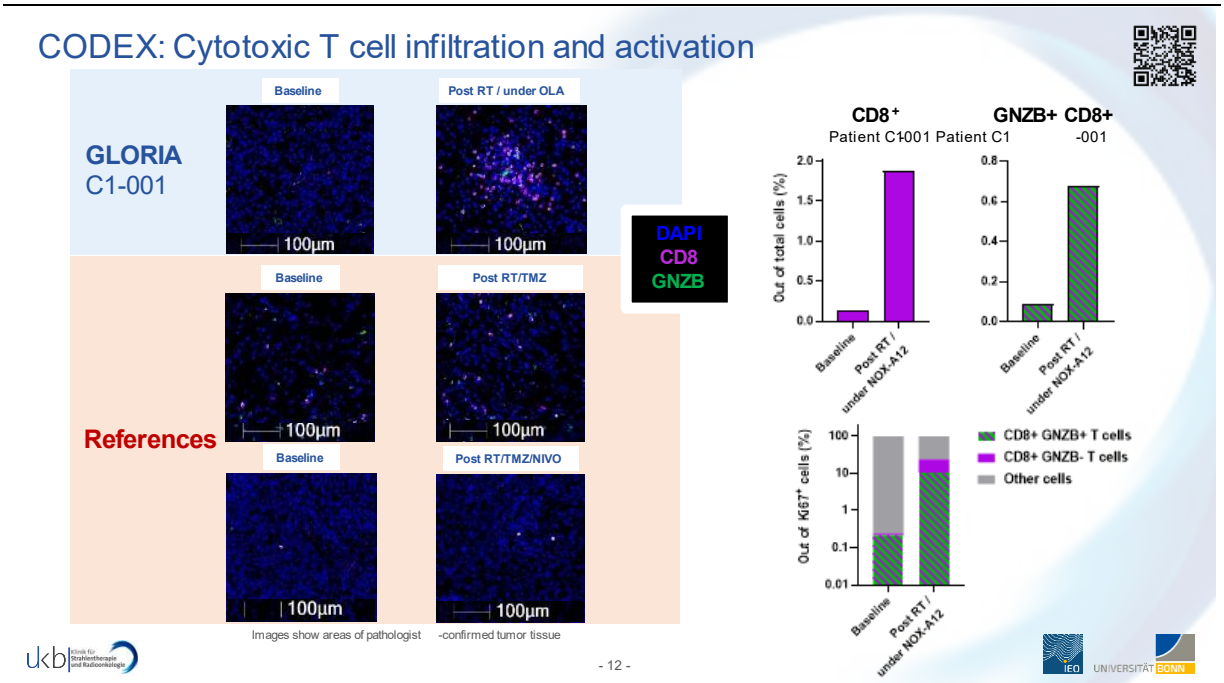
Figure 5: NOX-A12 leads to a significant reduction in CXCL12 levels in tumor endothelium



Source: Dr Frank Giordano, 2021

In the images on *Figure* 6 below, DAPI stains the nuclei of all cells, CD8 is a marker of cytotoxic T-cells, and granzyme B (GNZB) is a marker of activated cytotoxic T-cells. At baseline (left column of images), there are almost no cytotoxic T-cells present in tumor tissue, which is typical for glioblastoma. Under therapy with NOX-A12, there is a 15-fold increase in numbers of CD8+ cytotoxic T cells into the tumor tissue, the vast majority of which are also activated as shown by co-staining with GNZB. In addition, these T-cells cluster in a manner similar to that seen in repeat biopsies of pancreas cancer patients after monotherapy with NOX-A12 for 2 weeks – a phenomenon that is typically associated with enhanced antigen presentation and T cell activation (Suarez-Carmona, 2021). The combination of enhanced infiltration, activation and clustering was not seen in the reference patients, including those treated with checkpoint inhibitors.

Figure 6: NOX-A12 leads to a significant increase in cytotoxic T-cell infiltration

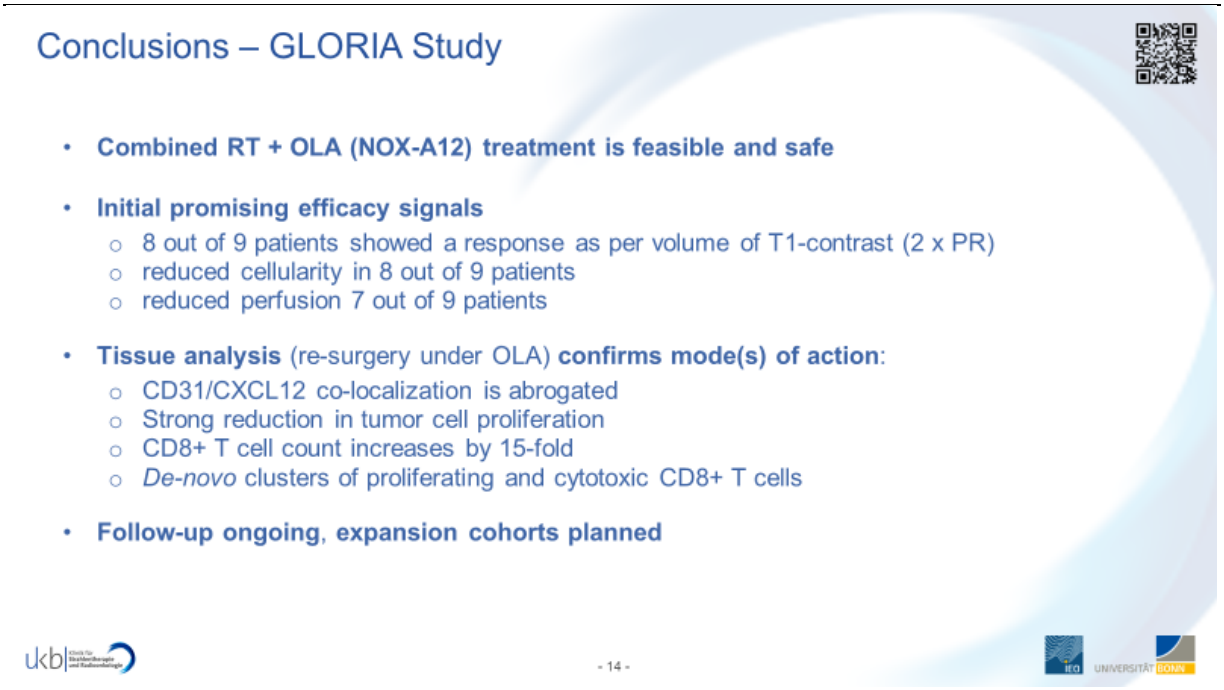


Source: Dr Frank Giordano, 2021

Taken together, these results confirm the unique mechanism of action of NOX-A12 on CXCL12 and provide initial promising efficacy signals of the NOX-A12-radiotherapy treatment combination (see Figure 7). The GLORIA clinical trial is currently underway with read-out of the high-dose cohort expected in Q1 2022. Follow-up of patients is ongoing. In addition, expansion arms are being initiated looking at combination of NOX-A12 with PD-1 and anti-VEGF. Citing examples of rapid progression following cessation of NOX-A12 therapy, Dr. Giordano noted that, in his view, NOX-A12 therapy should be carried out longer than the 6 months originally planned in this trial in order to see its full effects.

More information about the GLORIA study can be found at ClinicalTrials.gov number NCT04121455.

Figure 7: Efficacy signals in the GLORIA study and Conclusions



Source: Dr Frank Giordano, 2021