Committed to Advancing the Understanding of Immunotherapy-Resistant Cancers and Providing Effective Treatment Solutions to Improve Patient Outcomes

About NEX-I and their Immuno-Oncology

NEX-I is a pioneering biotech headquartered in South Korea, specializing in next-generation cancer therapies with a focus on **immunotherapy-resistant cancers**. Leveraging its proprietary platform, NEX-I has developed robust models for immunotherapy-refractory cancers to comprehensively analyze their characteristics and **identify novel therapeutic targets**. This unique and dedicated research has led to the discovery of **a soluble target, ONCOKINE-1 (OK-1)**, which highly expresses and plays a critical role in refractory cellular mechanisms, through ONCOKINE® screening platform. Employing this insight, NEX-I developed NXI-101, a treatment designed to inhibit the biological functions of OK-1, offering a promising new avenue for cancer treatment.

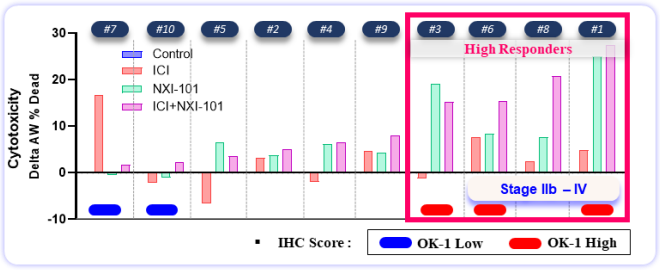
Many companies confirmed their promising anticancer efficacy across various types of traditional animal models, but they often fail to accurately predict human response to cancer drugs as we face significant percentage of oncology drugs failing clinical trials today.

NEX-I employed a unique and innovative method by **Xsphera Biosciences** to predict human response most accurately by creating spheroids from fresh human tissue. This system **effectively preserves the unique tumor microenvironment including autologous tumor, immune, and stromal cells** of each patient. Please move on to the next paragraph to deepen your understanding of the topic.

NXI-101 Exhibits Potent Anticancer Effects in the Lung Cancer Patient-Derived Model

Freshly isolated cancer tissues from patients with Non-Small Cell Lung Cancer (NSCLC) were placed in a microfluidic device to establish ex vivo tumor spheroids. These were then **treated with NXI-101, either alone or in combination with an immune checkpoint inhibitor (ICI)**, for three days. The anticancer effects were quantified by assessing cellular death within the tumor spheroids. The ratio of dead cell area (identified via Propidium Iodide staining) to total spheroid area (identified via Hoechst staining) was calculated for individual spheroids, and the mean percentage of cell death across all spheroids was determined. This value was subsequently normalized to the spheroid's area to yield the area-weighted percentage of cell death. Notably, in 4 out of 10 NSCLC patient (**"High-Responders"**) samples (#1, #3, #6, #8), significant increases in cytotoxicity were observed with NXI-101 monotherapy or combination therapy with ICI (**Fig. 1**), and it was **interesting to note that 3 out of the high-responders were late-stage NSCLC patients**.

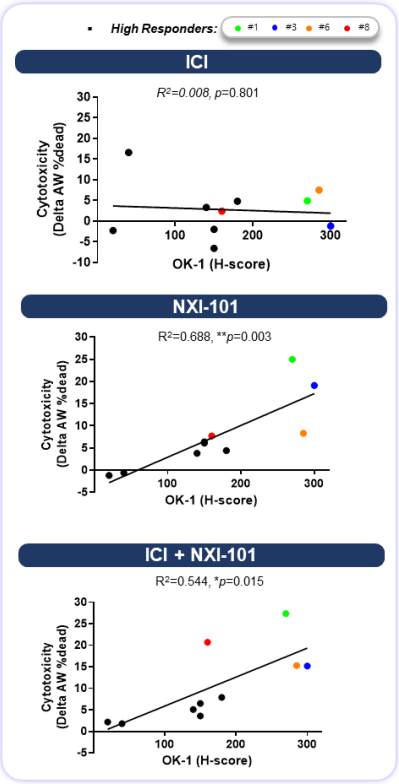
Figure 1. Anti-tumor efficacy of NXI-101 in NSCLC PDOTS system (**N=10**)



High Levels of OK-1 Correlated to the High Responders after NXI-101 Treatment

To explore the potential of **OK-1 levels in tumors as a predictive biomarker** for NXI-101 efficacy, we performed a correlation analysis between OK-1 expression and anticancer effects. The data revealed a **positive correlation between OK-1 levels in tumor tissues and the anticancer effects of NXI-101** (**Fig. 2**).

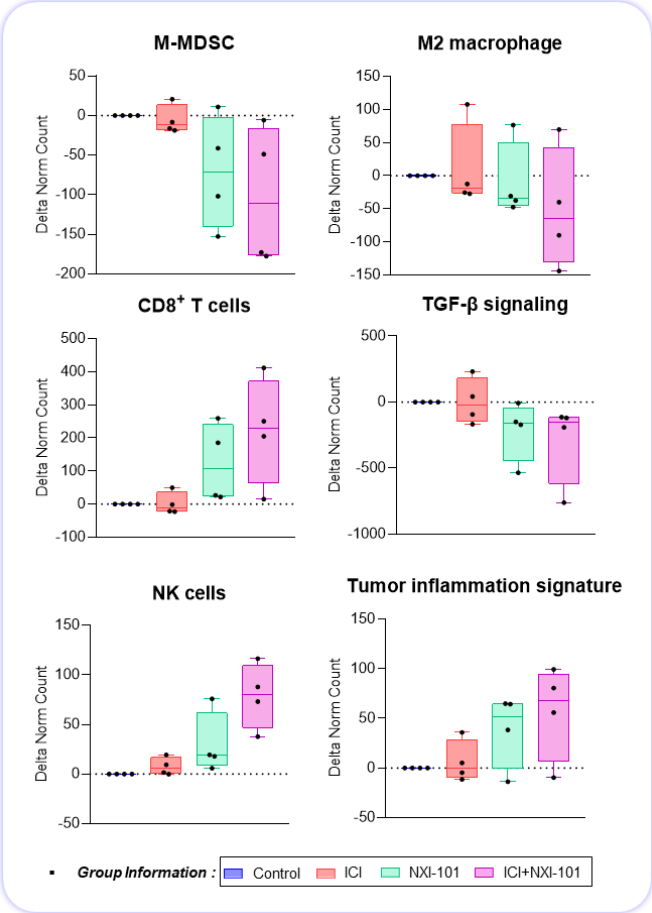
Figure 2. Correlation of anticancer efficacy of NXI-101 with OK-1 level in NSCLC Patients (**N=10**)



Immune Signature Changes after NXI-101 Treatment ("High-Responders")

To investigate the molecular mechanisms underlying NXI-101's anticancer effects, we conducted transcriptomic analyses of treated tumor spheroid samples using the NanoString nCounter system. In the high-responder samples (#1, #3, #6, #8), we observed a **decrease in the expression of immune-suppressive myeloid cell signatures (M-MDSC and M2 macrophages)** and TGF-β signaling. Concurrently, we detected an **increase in the signatures of cytotoxic effector cells (CD8⁺ T cells, NK cells)** and tumor inflammation (**Fig. 3**). These findings lend support to the hypothesis that the anticancer activity of NXI-101 in NSCLC is mediated by an **enhanced antitumoral immune response via inhibition of immune-suppressive mechanisms** within the tumor microenvironment.

Figure 3. Immune signatures after NXI-101 treatment in **"High-Responders"** to NXI-101



Conclusion

From "Immune-COLD" to "Immune-HOT"

In summary, NXI-101 exhibited potent anticancer effects in the NSCLC PDOTS model. Particularly noteworthy is **the enhanced efficacy observed in NSCLC samples that expressed elevated levels of OK-1**. This suggests that OK-1 expression could serve as a predictive biomarker for the effectiveness of NXI-101 in cancer therapy. Additionally, NXI-101 altered the tumor microenvironment from an **"Immune-COLD"** to an **"Immune-HOT"** state, as **evidenced by a decrease in immune-suppressive myeloid cell signatures and an increase in immune-activating signatures**. These results underscore the potential utility of NXI-101 as a novel immuno-oncology therapeutic agent and present it as a promising candidate for future cancer treatment regimens.

First-in-class NXI-101 Summary

Fully human anti-ONCOKINE-1-IgG4S228P mAb

- ✓ ONCOKINE-1 is a novel soluble protein, causing tumor microenvironment to become resistant against various I-O therapies
- ✓ Validated predictive and prognostic biomarkers for treatment response by tissue & blood measurement of ONCOKINE-1
- ✓ Confirmed Efficacy, Safety, and Pharmacokinetics in pre-clinical study and Ready for an IND submission by 1H 2024

NEX-I Company Information

Established	Apr 12th, 2021
Employees	31 (2023)
Researchers	25 including 12 PhDs (2023)
Investment	Series A (Oct. 2022)

Contact Us

For more information, please contact JayJay Jang (Director, Global Business Development) at jayjay@nex-i.co.kr

Office (+82)-2-6951-0412
Web www.nex-i.co.kr
Address A-923 9F, Tera tower 2, 201 Songpa-daero, Songpa-gu, Seoul, 05854, Republic of Korea