Abstract: 4377

High affinity receptor bio-selected novel oncolytic RNA virus, IVX055, demonstrates potent anti-tumor activity in human NSCLC, hepatocellular carcinoma and bladder cancer with potential for immunotherapeutic combinations

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BACKGROUND

Oncolytic viruses are emerging as promising therapeutic agents that selectively infect and lyse cancer cells while enhancing responses to immunotherapies, including immune checkpoint inhibitors (CPIs). IVX055 is a novel, non-enveloped, single-stranded RNA oncolytic virus developed using a proprietary receptor-focused bioselection platform to optimize tumor targeting and entry. IVX055 engages distinct cell surface receptors to mediate efficient tumor cell binding and internalization, resulting in potent lytic replication. Mechanistically, MAPK pathway activation in cancer cells may potentiate viral replication, virion assembly, and lytic release, as a result of further attenuation of type I interferon anti-viral response ***(Figure 1)***. This convergence of MAPK-driven pro-viral signaling and impaired IFN-I responses may enhance replication and spread of IVX055 within tumors micro-environment. Infection with IVX055 induces cell lysis and potential pro-inflammatory signaling, including PD-L1 upregulation, which may increase immune cell infiltration and sensitize tumors to immune checkpoint inhibitors (ICIs). These immunostimulatory effects position IVX055 as a strong candidate for combination with ICIs, T-cell engagers, antibody-drug conjugates (ADCs), and bispecific antibodies to amplify anti-tumors responses.

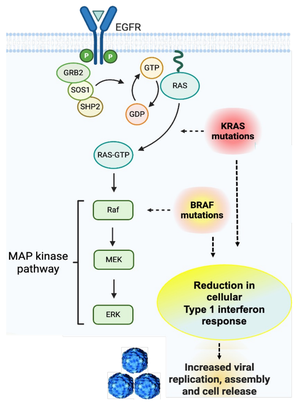

Figure 1. *Schematic of the MAP kinase pathway highlighting the potential impact of RAS and RAF mutations in elevating the anti-tumor activity of IVX055.*

METHODS

***In vitro* cytotoxicity and viral replication assays**
Human cancer cell lines were cultured as adherent monolayers under standard conditions. Cells were infected with IVX055 at a range of input multiplicities of infection (MOIs) to assess dose-dependent viral activity. Following infection, cell viability was quantified at defined time points using an XTT-based metabolic assay according to the manufacturer's instructions. Absorbance values were normalized to mock-infected controls to determine relative viability.
In parallel, viral-induced cytopathic effects (CPE) were monitored by phase-contrast microscopy to evaluate morphological changes associated with lytic infection, including cell rounding, detachment, and cytopathic effect. Representative images were captured to document infection kinetics and extent of oncolysis.

***In vivo* xenograft studies**
All animal studies were conducted in accordance with institutional guidelines for animal care and use. Immunocompromised mice (athymic nu/nu) were subcutaneously implanted in the flank with human tumor cell lines. Tumors were allowed to establish until they reached a palpable size (~50–150 mm³), at which point animals were randomized into treatment groups.
IVX055 was administered via intratumoral (IT) injection at defined doses and schedules. Control animals received vehicle alone. Tumor growth was monitored longitudinally using digital caliper measurements, and tumor volumes were calculated. Body weight and general health were assessed throughout the study.

RESULTS

- IVX055 demonstrated potent oncolytic *in vitro* activity and multicycle replication in human bladder cancer cell cultures (***Figure 2***).
- IVX055 demonstrated potent oncolytic *in vitro* activity and multi-cycle replication in human hepatocellular cancer (HCC) cell cultures across a wide range of viral input multiplicities (***Figure 3***).
- IVX055 induced rapid cell lysis in non-small cell lung *in vitro* cell preparations (***Figure 4***).
- Intratumoral administration of IVX055 in human tumor xenograft models using immunocompromised mice was well tolerated and highlighted potent anti-tumor activity against NSCLC cancer xenografts (NCI-H1299-NRAS mutated) (***Figure 5***).

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RESULTS – continued

In vitro Oncolytic activity of IVX055 in Bladder cancer

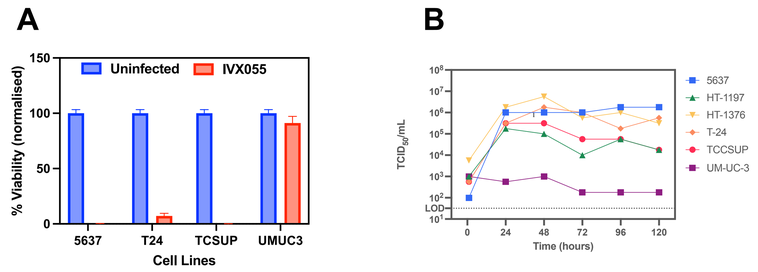


Figure 2. *IVX055-mediated destruction in a panel of bladder cancer cell lines.* ***(A)*** *IVX055-mediated oncolysis in a panel of human bladder cancer cells. Cells were infected with IVX055 at a MOI of 100 $TCID_{50}$/cell and viability was measured seven days later via the XTT viability assay. Results were expressed as mean percentages of viability, normalised to mock-infected ± SD.* ***(B)*** *Viral growth curve of IVX055 in various bladder cancer cell lines over 5 days post-infection. Cells were infected with IVX055 at MOI = 1 and viral titres were determined at 0, 24, 48, 72, 96, 120h post-infection. LOD denotes below the level of detection.*

In vitro Oncolytic activity of IVX055 in HCC

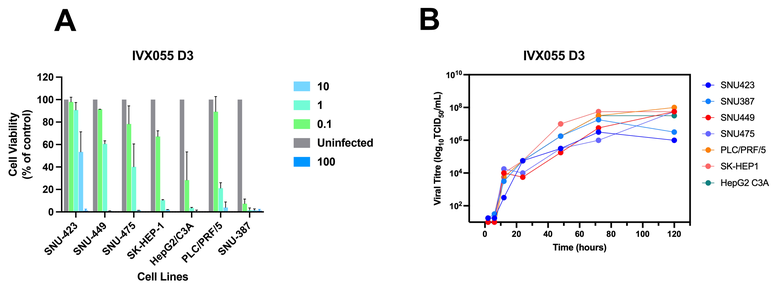


Figure 3. *IVX055-mediated destruction in a panel of liver cancer cell lines within three days.* ***(A)*** *IVX055-mediated oncolysis in a panel of liver cancer cells. Cells were infected with IVX055 at a MOI of 100 $TCID_{50}$/cell and viability was measured three days later via the XTT viability assay. Results were expressed as mean percentages of viability, normalised to mock-infected ± SD.* ***(B)*** *Viral growth curve of IVX055 in various liver cancer cell lines over 3 days post-infection. Cells were infected with IVX055 at a MOI = 1 and viral titres were determined at 72h post-infection.*

In vitro Oncolytic activity of IVX055 in NSCLC

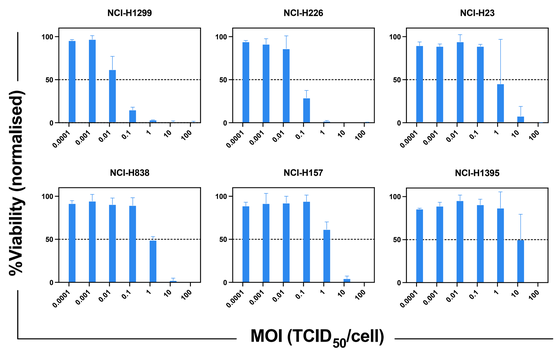


Figure 4. *IVX055 induces oncolysis across all NSCLC cell lines. Various non-small cell lung cancer cell lines were infected with IVX055 at MOI = 0.0001, 0.001, 0.01, 0.1, 1, 10, and 100 in reduced-serum media. Cell viability of the six cell lines was determined at 72h post-infection via the XTT viability assay (n=2). Results were expressed as mean percentages of viability, normalised to mock-infected ± SD.*

In vivo Oncolytic activity of IVX055 in NSCLC

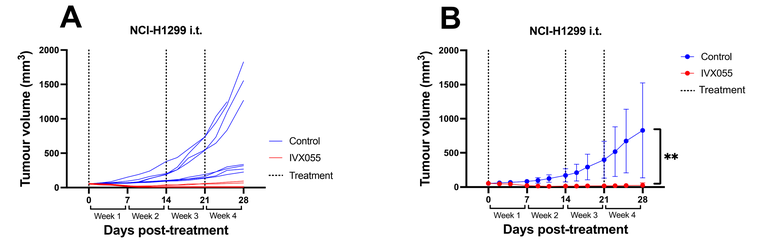


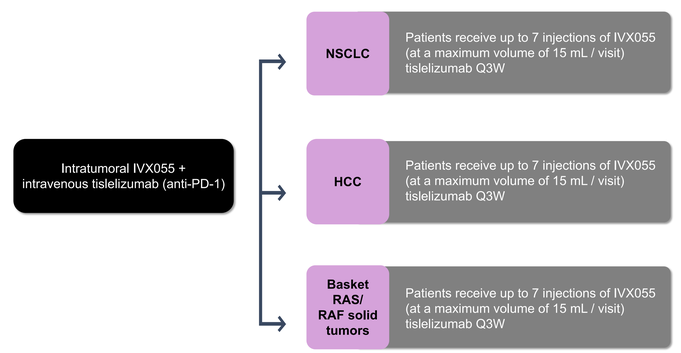
Figure 5. *IVX055 mediates robust oncolytic activity in a human non–small cell lung cancer (NSCLC) xenograft model. Intratumoral (IT) administration of IVX055 (1 × 10⁸ $TCID_{50}$; three doses) to NCI-H1299 (NRAS-mutated) xenografts resulted in significant tumor growth inhibition, consistent with productive viral infection and replication. Tumor volumes are shown as* ***(A)*** *individual tumor growth curves and* ***(B)*** *group mean ± SD (mm³). Statistical significance was determined relative to control (**p = 0.0017).*

CONCLUSIONS

- **IVX055 exhibits potent, broad-spectrum oncolytic activity** across diverse tumor types, including NSCLC, HCC, and bladder cancer—many of which harbor RAS and RAF alterations within the MAPK pathway.
- **IVX055 viral replication maybe enhanced in MAPK–activated and IFN-I–deficient cells**, supporting a mechanistically defined therapeutic window, as previously observed with the related IVX037 oncolytic virus.
- **Clinical translation is underway:** Phase 1b study of IVX037 + sintilimab (anti–PD-1) in advanced MSS-CRC, gastroesophageal, ovarian and HCC (AACR 2026: Poster CT183).
- **Next steps for IVX055:** Expansion into phase 1 clinical evaluation in metastatic NSCLC, HCC, basket RAS/RAF solid tumors and immunotherapy-refractory settings to further evaluate combination strategies.

FUTURE DIRECTIONS

Phase 1 (combination of IVX055 + tislelizumab)



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