Antitumor activity of the oncolytic virus JX-594 in patient-derived xenograft models of triple-negative breast cancer

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Introduction

Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). This profile limits treatment options primarily to chemotherapy, which is often associated with drug resistance, poor clinical outcomes, and is further challenged by the intrinsic heterogeneity and immunosuppressive tumor microenvironment of TNBC. JX-594 (pexastimogene devacirepvec; Pexa-Vec®), an oncolytic vaccinia virus derived from the Wyeth vaccine strain, has demonstrated multiple antitumor mechanisms, including direct oncolysis, immune activation, and disruption of tumor vasculature. In this study, we investigated the antitumor efficacy of intratumoral JX-594 administration in TNBC PDX models and assessed its effects on tumor cell proliferation, angiogenesis, and viral replication.

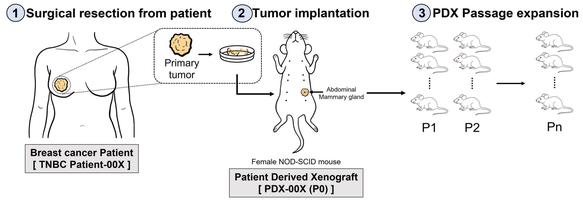


Figure 1. Patient-Derived Xenograft (PDX) Models of TNBC.

Fresh tumor tissues were obtained from TNBC patients after surgical resection. (1) The tumor fragments were implanted into immunodeficient mice to establish PDX models. (2) Engrafted tumors were serially passaged in mice for model expansion and drug efficacy studies. (3)

Methods and Materials

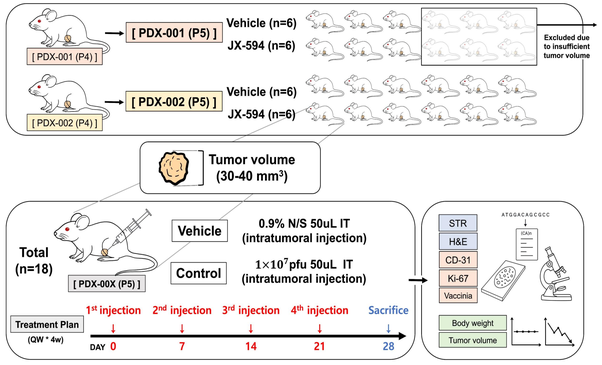


Figure 2. PDX models were established in NOD/SCID mice and treated with JX-594.

Patient-derived xenograft (PDX) models were established by implanting fresh tumor tissues from two TNBC patients (ages 54 and 55) into the mammary fat pads of female NOD/SCID mice. Tumors were serially passaged and confirmed to retain human origin via Short Tandem Repeat (STR) profiling. Once tumors reached approximately 30 mm^3 in volume, mice were randomized into two groups (n=6 per group per model): vehicle or JX-594 treatment. JX-594 (1×10^7 PFU in 50 µL saline) was administered intratumorally once weekly for four weeks.

Table 1. Human Short Tandem Repeat (STR) 10 marker panel.

Sample ID	TH01	D21S11	D5818	D13S317	D7S820	D16S539	CSF1PO	AMEL	vWA	TPOX
TNBC patient-001	7,9	31	11,12	8,13	11	10,11	11,13	X	16,18	8
PDX-001 (P5)	7,9	31	12	8	11	10,11	11,13	X	16,18	8
TNBC patient-002	6,9,3	31	11	8,10	11,14	10,12	10,12	X	14,17	8
PDX-002 (P5)	6	31	11	8,10	14	12	10	X	17	8

STR analysis verification demonstrates that each PDX model faithfully retains the genetic identity of the original tumor, ensuring the reliability and authenticity of these preclinical models.

Results

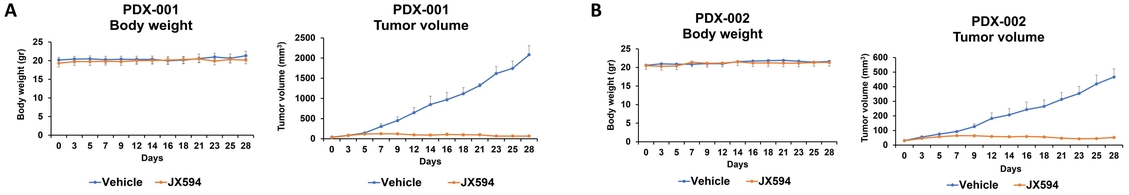


Figure 3. Treatment with JX-594 significantly reduces tumor growth in both PDX-001 and PDX-002 PDX.

Treatment with JX-594 significantly reduced tumor growth in PDX-001 (A) and PDX-002 (B) compared with the vehicle (*$p < 0.05$), demonstrating potent antitumor activity in patient-derived xenografts of triple-negative breast cancer.

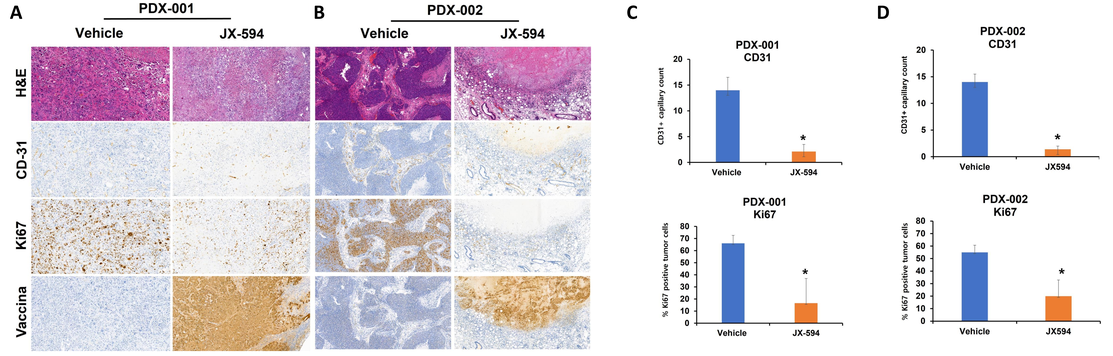


Figure 4. Histological and IHC analysis of TNBC PDX models after JX-594 treatment . Histological analysis of PDX-001 and PDX-002 tumors (panels A and B) showed that JX-594 treatment induced extensive tumor necrosis, decreased Ki-67 staining (proliferation), and reduced CD31 expression (vessel). Graphical quantification is shown in panels C and D (*$p < 0.05$), indicating significant effects of JX-594.

Discussion

This study demonstrates that intratumoral administration of the oncolytic vaccinia virus JX-594 effectively suppresses tumor growth in PDX models of TNBC. JX-594 induces tumor cell death, inhibits proliferation, and disrupts tumor vasculature, collectively contributing to its potential antitumor activity. These findings support the potential of JX-594 as a promising therapeutic strategy for treatment of TNBC.

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Reference

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