Phase I Study of DNX-2401 (Delta-24-RGD) Oncolytic Adenovirus: Replication and Immunotherapeutic Effects in Recurrent Malignant Glioma


ABSTRACT

Purpose
DNX-2401 (Delta-24-RGD; tasadenoturev) is a tumor-selective, replication-competent oncolytic adenovirus. Preclinical studies demonstrated antiglioma efficacy, but the effects and mechanisms of action have not been evaluated in patients.

Methods
A phase I, dose-escalation, biologic-end-point clinical trial of DNX-2401 was conducted in 37 patients with recurrent malignant glioma. Patients received a single intratumoral injection of DNX-2401 into biopsy-confirmed recurrent tumor to evaluate safety and response across eight dose levels (group A). To investigate the mechanism of action, a second group of patients (group B) underwent intratumoral injection through a permanently implanted catheter, followed 14 days later by en bloc resection to acquire post-treatment specimens.

Results
In group A (n = 25), 20% of patients survived >3 years from treatment, and three patients had a ≥95% reduction in the enhancing tumor (12%), with all three of these dramatic responses resulting in >3 years of progression-free survival from the time of treatment. Analyses of post-treatment surgical specimens (group B, n = 12) showed that DNX-2401 replicates and spreads within the tumor, documenting direct virus-induced oncolysis in patients. In addition to radiographic signs of inflammation, histopathologic examination of immune markers in post-treatment specimens showed tumor infiltration by CD8+ and T-bet+ cells, and transmembrane immunoglobulin mucin-3 downregulation after treatment. Analyses of patient-derived cell lines for damage-associated molecular patterns revealed induction of immunogenic cell death in tumor cells after DNX-2401 administration.

Conclusion
Treatment with DNX-2401 resulted in dramatic responses with long-term survival in recurrent high-grade gliomas that are probably due to direct oncolytic effects of the virus followed by elicitation of an immune-mediated antiglioma response.

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INTRODUCTION

Newly diagnosed glioblastoma (GBM) is treated with surgery, radiochemotherapy, and adjuvant chemotherapy, with a median survival time of approximately 15 months.1-3 Despite maximal initial therapy, tumors invariably recur, after which the median survival time is typically only 6 months, even with reirradiation, repeat surgery, or chemotherapy.4 Oncolytic adenoviruses are attractive therapeutic agents because they can kill tumor stem cells5 and induce cell death by several mechanisms, including direct lysis, expression of toxic proteins, induction of cytokines, and T-cell–mediated immunity.5,6

DNX-2401 (Delta-24-RGD; tasadenoturev) is an oncolytic adenovirus designed to be tumor selective, infectivity enhanced, and replication competent.7 Tumor selectivity is achieved by a 24-base pair deletion in the E1A gene, which renders the virus unable to replicate in normal cells that maintain a functional Rb pathway but fully
replication competent in tumor cells. To enhance potency, an RGD-motif was engineered into the fiber H-loop, enabling the virus to use αvβ3 or αvβ5 integrins to enter cells. These integrins are typically enriched on tumor cells, including glioma stem cells. In preclinical models, DNX-2401 kills glioma cells by direct oncolysis and by inducing immune responses against tumor antigens, leading to sustained antitumor immunity and tumor regression.

To determine safety, evaluate efficacy, and define the biologic effect of escalating doses of DNX-2401, we performed a phase I clinical trial with biologic end points in patients with recurrent malignant glioma. Remarkably, 20% of patients (five of 25) survived more than 3 years after a single DNX-2401 administration, and three of these five patients had >95% reduction in tumor volumes that evolved over several months after treatment and that extended survival for >3 years from the time of treatment. Biologic evaluations of post-treatment tumor specimens demonstrate that tumor regression induced by DNX-2401 seems to be due to the direct oncolytic effects of virus infection as well as activation of an immune-mediated anticancer response.

**Study Design**

A dose-escalation trial in patients with recurrent malignant glioma was conducted. Patients were enrolled in one of two groups (Fig 1A). Group A (treatment-only group) underwent stereotactic biopsy to document recurrence, followed by a single intratumoral injection of DNX-2401 at the assigned dose through the biopsy needle into the contrast-enhancing tumor mass. Group B (treat-resect-treat group) underwent stereotactic biopsy and intratumoral injection of DNX-2401 through an implanted catheter (to mark the injection site), followed 14 days later by craniotomy with en bloc tumor resection, including the catheter, and injection of a second dose of DNX-2401 into multiple sites in the wall of the resection cavity. This approach provided a post-treatment specimen in which the injection site was marked by the catheter. Dose escalation in group A used a 3 + 3 design, starting at 1 x 10^7 viral particles (vp; Data Supplement). Enrollment in group B lagged behind group A, opening only after safety of the dose level was established for intratumoral injection. The study was approved by the MD Anderson Institutional Review Board.

**Patients and Study Treatment**

Eligible patients were enrolled between 2009 and 2012, were older than 18 years of age with a Karnofsky performance scale score ≥ 70, and had histologically confirmed recurrent malignant glioma. Failure of standard or additional therapy was demonstrated by tumor progression as visualized on magnetic resonance imaging (MRI), and all patients underwent stereotactic biopsy before DNX-2401 administration (Data Supplement). DNX-2401 was manufactured at the Biopharmaceutical Development Program at SAIC-Frederick (Frederick, Maryland; Data Supplement).

**Study Evaluations**

Medical history, MRI, blood counts, and chemistry values were documented at screening and follow-ups (Data Supplement). Adverse events (AEs) were graded using Common Terminology Criteria for Adverse Events (version 3), and the relationship to DNX-2401 was assessed. Dose-limiting toxicity was defined as any DNX-2401-related, non-hematologic AE ≥ grade 3. Tumor response was based on Macdonald criteria, with the modification that (1) increases in tumor size (contrast-enhancing volume) were allowed within the first 3 to 4 months to account for potential immune-mediated inflammatory responses as long as the patient was clinically stable, and (2) responses were judged as a complete response (CR) if there was ≥ 95% reduction in size of the enhancing tumor, a partial response if there was >50% reduction, progressive disease if there was >25% increase, and stable disease in all other situations.

**Biologic Assessments**

Pretreatment biopsy specimens obtained before injection were stained with hematoxylin and eosin and evaluated by a certified neuropathologist to document recurrent tumor. Post-treatment surgical specimens were immunostained for adenosvirus proteins (hexon [AB1056; Millipore, Burlington, MA] and E1A [sc-430; Santa Cruz Biotech, Dallas, TX]) and for immune cell infiltrates (CD3 [LN10; Vector Laboratories, Burlingame, CA], CD4 and CD8 [both VP-C320; Vector Laboratories], and T-bet [H-210; Santa Cruz Biotech]). Independent studies were also performed to quantify immune cell density (CD3, CD4, CD8) and checkpoint proteins from pretreatment and post-treatment specimens (programmed death ligand-1 [PD-L1], programmed death-1 [PD-1], transmembrane immunoglobulin mucin-3 [TIM-3], indoleamine 2,3-dioxygenase [IDO-1]). Quantification was performed as previously described (Data Supplement).

Damage-associated molecular patterns were evaluated by enzyme-linked immunosorbent assay in glioma sphere-forming cell (GSC) lines, GSC327 and GSC308, which were generated from fresh surgical tumor specimens from patients in group B (Data Supplement).

Serum, sputum, and urine were analyzed for the presence of adenovirus genomes using the polymerase chain reaction technique, as previously described (Data Supplement). Serum was tested for antiadenovirus (type 5; anti-Ad5) by an indirect immunofluorescence assay before and at multiple times after treatment.

**Statistics**

Statistical justification is shown in the Data Supplement.

**RESULTS**

**Demographics and Safety**

Thirty-seven patients were enrolled in groups A (n = 25; Table 1) or B (n = 12) and received DNX-2401 according to the assigned regimen (Fig 1A). Histology across both groups included GBM (89%), gliosarcoma (5%), or anaplastic astrocytoma (5%; Table 1). Median tumor diameter was 30 mm for group A and 41 mm for group B. Patients were enrolled at first (62%), second (32%), or third recurrence (5%) and had received a median of two prior treatment regimens. Three patients in group A (12%) were refractory to prior anti–vascular endothelial growth factor therapy.

In group A, eight dose-escalation cohorts were administered a single intratumoral dose of DNX-2401 into the contrast-enhancing portion of the tumor (1 x 10^7 – 3 x 10^10 vp in 1 mL; Data Supplement). In group B, 11 patients underwent initial injection of DNX-2401 across four cohorts (1 x 10^7 – 3 x 10^8 vp) via an implanted catheter, and 14 days later underwent en bloc tumor resection and second injections into the wall of the resection cavity. One patient underwent surgical resection and injection of DNX-2401 into the residual tumor. Enrollment in group B was stopped at cohort 4 after assessment of post-treatment specimens indicated that the predefined biologic end point of viral replication had been achieved (see Viral Replication).

No dose-limiting toxicities were observed in the study; therefore, a maximum tolerated dose was not identified (Data
Clinical and Biological Effects of DNX-2401 in Recurrent Glioma

Fig 1. In situ replication and clinical activity of DNX-2401 in recurrent malignant glioma. (A) Schema outlining treatment strategies for group A (single injection of DNX-2401 into recurrent tumor without other therapeutic interventions to evaluate safety and efficacy), and group B (two-stage surgical design to provide post-treatment specimens for analysis). (B) Photomicrograph of en bloc resected post-treatment surgical specimen (left) obtained at open craniotomy from a patient in group B who underwent intratumoral injection of DNX-2401 14 days before this specimen was obtained. The arrows indicate the location of the proximal end (continued on next page).
Viral Replication

The ability of DNX-2401 to replicate within human glioma was evaluated by assessing surgical specimens from patients in group B (n = 11). Tumor samples were cut perpendicular to the catheter, which marked the injection site (Fig 1B). Immunostaining revealed viral E1A or hexon protein in six of 11 tumors (55%), thus demonstrating virus replication in these tumors 14 days after treatment (Fig 1C; Data Supplement). Expression of E1A or hexon coexisted with prominent inclusion bodies, characteristic of adenovirus replication (Fig 1C, left and right). The pattern of staining resembled the three zones of viral spread observed in animal models (zone 1: virus-induced necrosis; zone 2: active virus replication; zone 3: peripheral uninfected cells). These data demonstrate the ability of DNX-2401 to lyse glioma cells and provide evidence for active oncolytic adenovirus replication in human gliomas.

Efficacy

Tumor reductions were observed in 72% of patients (18 of 25) enrolled in group A (Fig 1D), with a median overall survival time of 9.5 months regardless of dose. Most remarkably, five patients (20%) in group A survived for more than 3 years, three of whom had ≥ 95% reduction in a cross-sectional area of the enhancing tumor (designated as CRs; see Methods), and two patients had sustained stable disease after an initial tumor regression, all occurring at or above the 1 × 10^8 vp dose level (cohort 3; Fig 1E). Importantly, all three of these dramatic (≥ 95%) responses resulted in progression-free periods of ≥ 3 years from the time of treatment, attesting to the durability of the treatment effects of DNX-2401 (Fig 1E; Data Supplement). Because of tumor resection on day 14, patients in group B were assessed only for survival; two patients (17%) survived for 2 years (Data Supplement), and the overall median survival time was 13.0 months across all cohorts.

Complete Responder No. 1 (Patient No. 12). A 53-year-old woman (Fig 2A) with a left parietal GBM underwent subtotal resection followed by radiation therapy and concurrent temozolomide plus dasatinib. One and one-half months after completing radiation therapy, MRI revealed progressive contrast enhancement at the site of the residual tumor that was present after the initial resection. Advanced brain imaging (including dynamic contrast enhancement MRI, dynamic susceptibility MRI, and magnetic resonance spectroscopy) was consistent with recurrent disease. The patient underwent stereotactic biopsy of the enhancing mass, documenting recurrent GBM (IDH1 wild type) and was treated with intratumoral injection of DNX-2401 (1 × 10^8 vp; cohort 3). MRI scans after virotherapy showed an initial decrease in contrast-enhancing tumor, followed by increased enhancement that peaked

(Continued) of the injection catheter whose distal end extends into the center of the tumor and marks the site of DNX-2401 administration. After fixation, the en bloc specimen was blocked perpendicular to the catheter, and these blocks (right) were then sectioned and analyzed for viral replication; the arrows indicate the location of the catheter in each block, which allowed for precise identification of the site of DNX-2401 injection. (C) Photomicrographs of sections from en bloc resection specimens taken in serum and bone marrow; repeat testing was negative 4 months later (Data Supplement). Overall, adenoviral DNA was detected in < 3% of post-treatment serum, sputum, or urine samples and was not associated with AEs.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics of Patients</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<tr>
<td>----------------</td>
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<tr>
<td>Median age, years (range)</td>
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<tr>
<td>Sex</td>
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<td></td>
</tr>
<tr>
<td>Karnofsky performance score</td>
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<tr>
<td></td>
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<tr>
<td>Histology</td>
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<tr>
<td></td>
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<tr>
<td>Median tumor size, longest diameter</td>
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<tr>
<td>mm (range)</td>
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<tr>
<td>Median time since initial diagnosis, months (range)</td>
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<tr>
<td>Recurrences</td>
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<td></td>
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<tr>
<td>Resections</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Median No. of prior regimens (range)</td>
</tr>
<tr>
<td>Radiotherapy</td>
</tr>
<tr>
<td>Temozolomide</td>
</tr>
<tr>
<td>Anti-VEGF</td>
</tr>
<tr>
<td>Alkylating agent (BCNU, CCNU, CPT-11)</td>
</tr>
</tbody>
</table>

NOTE. Data presented as No. (%) unless otherwise indicated. Abbreviations: BCNU, carmustine; CCNU, lomustine; CPT-11, irinotecan; VEGF, vascular endothelial growth factor.
after 4 months and then progressively decreased, to achieve dramatic regression (95% reduction) 17.6 months after treatment. From this point, serial MRI scans remained stable for 24.9 months, for a total progression-free period of 42.5 months (3.5 years) from initial treatment (Fig 2A). At this time, an area of new enhancement appeared and progressed, requiring surgical resection that showed gliosarcoma. The patient died 14 months after the second recurrence (4.8 years after DNX-2401 treatment).

Complete responder No. 2 (Patient No. 33). A 38-year-old woman, diagnosed with a GBM of her left superior temporal gyrus, underwent resection, followed by concurrent radiation therapy, temozolomide, and adjuvant isotretinoin (Fig 2B). Three months after the completion of radiation therapy, progressive enhancement was identified, and advanced brain tumor imaging was consistent with recurrent tumor. The patient underwent stereotactic biopsy documenting recurrent GBM with atypical cells and microvascular proliferation (IDH1 wild type), followed by intratumoral injection of DNX-2401 (3 × 10^10 vp; cohort 8). The patient resumed temozolomide treatment per his oncologist’s preference. MRI initially showed an increase in tumor size that was followed by tumor regression until a complete response (100% reduction) was achieved after 12 months (Fig 2C). Seventeen months after achieving a complete response, a new enhancing lesion was detected distant from the treated recurrence (Fig 2C), and surgical resection of this lesion revealed only necrosis and no tumor cells. The patient remained stable for another 12 months until he experienced recurrence (ie, 29 months from the time of complete response and 41 months [3.4 years] from the treatment with DNX-2401). Resection of this recurrent mass revealed gliosarcoma. Despite repeated radiation therapy and chemotherapy, the recurrent tumor progressed, and 9 months after the second surgery, the patient was retreated with DNX-2401. He is currently alive 4.5 years after initial treatment with DNX-2401.

### Immune Effects

In preclinical studies, DNX-2401 induces a T_{H1}-skewed CD8+ cytotoxic T-cell response. Consistent with an immune-mediated response, contrast enhancement on MRI increased in all three complete responders from group A within 4 months after injection of DNX-2401, followed by a reduction in the size of the enhancing lesion over the next 12 to 18 months (Fig 2). One patient with recurrent GBM of the left temporal lobe (Patient No. 20) underwent surgical resection 1.5 months after injection of DNX-2401 (3 × 10^10 vp) because of progressive symptoms. At this time, MRI showed necrosis at the injection site but increased contrast enhancement throughout the tumor (Fig 3A). Analyses of the resected tumor revealed that 80% of the mass was necrotic, and the remaining specimen was largely acute with chronic inflammatory cell infiltration (macrophages and CD8+ T cells; Fig 3B), without evidence of adenovirus-infected cells. Equally important, 2.5 years after treatment with DNX-2401, complete responder No. 3 (Patient No. 37) underwent resection for a new enhancing nodule distant from the initial lesion as described previously (Fig 2C, bottom right). Pathologic examination revealed necrosis and inflammation, but no evidence of tumor, potentially indicative of an adaptive memory antitumor response.

Group B tumor specimens resected 14 days after DNX-2401 treatment (n = 9) were analyzed by immunohistochemistry for the presence of CD3, CD4, CD8, and T-bet (Fig 3C; Data Supplement). CD3+ T cells were detected in all specimens either throughout the tumor or around the vessels (perivascular cuffing). The majority

### Table 2. Adverse Events in 37 Patients

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Any Grade</th>
<th>≥ Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients (%)</td>
<td></td>
</tr>
<tr>
<td>Study-drug-related adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Confusional state</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>All adverse events</td>
<td>25 (68)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Headache</td>
<td>15 (41)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Speech disorder</td>
<td>15 (41)</td>
<td>7 (19)</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>12 (32)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>12 (32)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Confusional state</td>
<td>11 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Edema, peripheral</td>
<td>11 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Convulsion</td>
<td>9 (24)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9 (24)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Memory impairment</td>
<td>9 (24)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vision, blurred</td>
<td>9 (24)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Cushingoid</td>
<td>8 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Depression</td>
<td>8 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>8 (22)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (22)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Constipation</td>
<td>7 (19)</td>
<td>0 (0)</td>
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<tr>
<td>Decreased appetite</td>
<td>7 (19)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6 (16)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6 (16)</td>
<td>0 (0)</td>
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<tr>
<td>Increased appetite</td>
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<tr>
<td>Pain in extremity</td>
<td>6 (16)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>6 (16)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Visual field defect</td>
<td>6 (16)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

NOTE. Adverse events that were reported in at least 15% of the patients. Patients reporting a particular adverse event more than once are counted only once. Related events include those classified as possibly, probably, or definitely related to study drug. Laboratory abnormalities are not included; no study-drug-related events reported.
were CD8+, with lower representations of CD4+ cells. Lymphocytes were positive for T-bet, suggestive of a TH1 response (Fig 3C), as in preclinical experiments. To quantify these results, we conducted an independent automated image analysis of immunohistochemically stained tumors and determined cell density. For post-treatment specimens (n = 10), the mean density of CD3+, CD4+, and CD8+ cells was 119 ± 21, 336 ± 350, and 104 ± 177 cells/mm², respectively. Compared with five pretreatment specimens (three of five matched to post-treatment specimens), an increase in CD4 and CD8 cell density after treatment with DNX-2401 was observed, although...
Fig 3. Immune-mediated response to DNX-2401. (A and B) Magnetic resonance imaging (MRI) scans and pathologic specimens of left temporal glioblastoma from Patient No. 20. (A) Baseline MRI (far left) and the exact site of DNX-2401 injection into recurrent glioblastoma of the left temporal lobe (second from left shows enlarged image with yellow line and red dot showing trajectory of injection needle and site of injection of DNX-2401, respectively). MRI 1.5 months after treatment (third and fourth from left) shows necrosis near injection site (star) and worsening of enhancement. This entire tumor was resected, and postoperative MRI (continued on next page).
Anti-Ad5 Titers

Anti-Ad5 antibodies were detected in low titers (1:8) before treatment in five of 25 patients (20%) in group A and none of 12 patients (0%) in group B (Data Supplement). Increases in anti-Ad5 titers were observed in 12 patients in group A and four patients in group B after treatment with DNX-2401. Two of the three patients with CR had an increase in anti-Ad5 titer.

**DISCUSSION**

In this dose-escalation study, we show that DNX-2401, a novel tumor-selective adenovirus, is safe and capable of robust viral replication and killing of recurrent high-grade glioma cells. Secondary antiangioma immune-mediated responses were observed. Importantly, these biologic mechanisms translated into clinical benefit, including three dramatic responses (≥95% reduction in tumor size) with long progression-free intervals and long-term survival after treatment with DNX-2401. To our knowledge, this is the first clinical study to show direct oncolysis and replication of a therapeutic adenovirus in human brain tumors and to provide correlative evidence for a viral-induced antiangioma immune response.

By marking the injection with a catheter, we were able to localize the site of virus injection and assess viral replication. DNX-2401 in vitro, and assayed for immunogenic cell death. A significant increase in damage-associated molecular patterns was detected in GSCs after treatment, indicating that DNX-2401 induces immunogenic cell death (Fig 3F).

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By marking the injection with a catheter, we were able to localize the site of virus injection and assess viral replication. DNX-2401 infection, replication, and killing followed the three-concentric-zone pattern that we described in preclinical animal models (Fig 1C).4,7 In these biologic mechanisms translated into clinical benefit, including three dramatic responses (≥95% reduction in tumor size) with long progression-free intervals and long-term survival after treatment with DNX-2401. To our knowledge, this is the first clinical study to show direct oncolysis and replication of a therapeutic adenovirus in human brain tumors and to provide correlative evidence for a viral-induced antiangioma immune response.

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In all, these results provide the first clinical correlates that DNX-2401 can induce a direct oncolytic effect followed by an antitumor immune response. Insofar as DNX-2401 is highly efficient because of expanded infection conferred by the RGD motif, and insofar as it is capable of enhancing antigen presentation,1 we speculate that these effects lead to immune cell infiltration and antitumor activity.
DNX-2401 warrants further study as a single agent and in combination with other immune-modulatory therapeutics.

**Authors’ Disclosures of Potential Conflicts of Interest**

Disclosures provided by the authors are available with this article at jco.org.

**Author Contributions**

Conception and design: Frederick F. Lang, Charles Conrad, Candelaria Gomez-Manzano, W.K. Alfred Yung, Gregory N. Fuller, Clemens M.F. Dirven, Frank Tufaro, Juan Fueyo

**References**


**Affiliations**


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**Administrative support:** Frederick F. Lang, Joanna J. Peterkin, Frank Tufaro

**Provision of study materials or patients:** Frederick F. Lang, Charles Conrad, W.K. Alfred Yung, Raymond Sawaya, Jeffrey S. Weinberg, Sujit S. Prabhu, Ganesh Rao, Gregory N. Fuller, Kenneth D. Aldape

**Collection and assembly of data:** Frederick F. Lang, Charles Conrad, Candelaria Gomez-Manzano, Jeffrey S. Weinberg, Sujit S. Prabhu, Ganesh Rao, Kenneth D. Aldape, Joy Gumim, Brett Ewald, Joanna J. Peterkin, Juan Fueyo

**Data analysis and interpretation:** Frederick F. Lang, Candelaria Gomez-Manzano, Raymond Sawaya, Joy Gumim, Luis M. Vence, Ignacio Wistuba, Jaime Rodriguez-Canales, Pamela A. Villalobos, Sonia Tejada, Ricardo D. Valle, Marta M. Alonso, Brett Ewald, Juan Fueyo

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Phase I Study of DNX-2401 (Delta-24-RGD) Oncolytic Adenovirus: Replication and Immunotherapeutic Effects in Recurrent Malignant Glioma

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Frederick F. Lang
Patents, Royalties, Other Intellectual Property: Patent holder on DNX-2401
Travel, Accommodations, Expenses: Merck Sharp & Dohme

Charles Conrad
Stock or Other Ownership: DNATrix (I)
Patents, Royalties, Other Intellectual Property: Patent holder on DNATrix (I)

Candelaria Gomez-Manzano
Stock or Other Ownership: DNATrix, DNATrix (I)
Consulting or Advisory Role: DNATrix, DNATrix (I)
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Patents, Royalties, Other Intellectual Property: Delta-24-RGD intellectual property, Delta-24-RGD intellectual property (I)
Travel, Accommodations, Expenses: DNATrix (I)

W.K. Alfred Yung
Stock or Other Ownership: DNATrix
Honoraria: DNATrix
Consulting or Advisory Role: DNATrix
Patents, Royalties, Other Intellectual Property: DNATrix

Raymond Sawaya
No relationship to disclose

Jeffrey S. Weinberg
No relationship to disclose

Sujit S. Prabhu
No relationship to disclose

Ganesh Rao
Honoraria: Monteris Medical

Gregory N. Fuller
No relationship to disclose

Kenneth D. Aldape
Consulting or Advisory Role: Celldex
Speakers' Bureau: Merck
Travel, Accommodations, Expenses: Merck

Joy Gumin
No relationship to disclose

Luis M. Vence
No relationship to disclose

Ignacio Wistuba
Consulting or Advisory Role: Genentech/Roche, Eli Lilly, Bristol-Myers Squibb, Ariad, HTG Molecular Diagnostics, Asuragen, Pfizer, AstraZeneca/MedImmune
Speakers' Bureau: Pfizer, Boehringer Ingelheim, MSD Oncology, Bristol-Myers Squibb
Research Funding: Genentech, Merck, OncoPlex Diagnostics, Myriad Genetics, HTG Molecular Diagnostics, Silicon Biosystems, Adaptimmune, EMD Serono, Pfizer, MedImmune

Jaime Rodriguez-Canales
Employment: MedImmune

Pamela A. Villalobos
No relationship to disclose

Clemens M.F. Dirven
Consulting or Advisory Role: DNATrix (Inst)

Sonia Tejada
No relationship to disclose

Ricardo D. Valle
No relationship to disclose

Marta M. Alonso
Patents, Royalties, Other Intellectual Property: MD Anderson and DNATrix

Brett Ewald
Employment: DNATrix
Stock or Other Ownership: DNATrix

Joanna J. Peterkin
Employment: DNATrix
Leadership: DNATrix
Stock or Other Ownership: DNATrix
Consulting or Advisory Role: DNATrix
Patents, Royalties, Other Intellectual Property: DNATrix
Travel, Accommodations, Expenses: DNATrix
Other Relationship: DNATrix (I)

Frank Tufaro
Employment: DNATrix
Leadership: DNATrix
Stock or Other Ownership: DNATrix
Consulting or Advisory Role: DNATrix
Patents, Royalties, Other Intellectual Property: DNATrix
Travel, Accommodations, Expenses: DNATrix

Juan Fueyo
Stock or Other Ownership: DNATrix, DNATrix (I)
Consulting or Advisory Role: DNATrix, DNATrix (I)
Research Funding: DNATrix, DNATrix (I)
Patents, Royalties, Other Intellectual Property: Delta-24-RGD intellectual property, Delta-24-RGD intellectual property (I)
Travel, Accommodations, Expenses: DNATrix
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