Phase 1 study of escalating-dose OncoGel® (ReGel®/paclitaxel) depot injection, a controlled-release formulation of paclitaxel, for local management of superficial solid tumor lesions

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OncoGel is a novel depot formulation of paclitaxel designed for intralesional injection with a sustained paclitaxel delivery over approximately 6 weeks from a single administration. This phase 1 study was designed to characterize the toxicity, pharmacokinetics and preliminary antitumor activity associated with OncoGel administered directly into solid tumors. OncoGel was injected into 18 superficially accessible advanced solid cancerous lesions among 16 adult patients for whom no curative therapy was available. Four dose cohorts were evaluated, ranging from 0.06 to 2.0 mg paclitaxel/cm^3 tumor volume. OncoGel injections were generally well tolerated. There was one report of grade 3 injection site pain for a patient in the 0.25 mg paclitaxel/cm^3 tumor volume dose cohort. Other adverse events considered related to the study drug included mild to moderate local responses to the injection itself. Systemic levels of paclitaxel were detectable only in 3.3% of the samples analyzed (range: 0.53–0.71 ng/ml). For the 14 patients evaluable for disease progression, stable disease was noted among six patients and progressive disease among eight patients. Although the maximum tolerated dose was not identified, the planned maximum dose was administered in the study. OncoGel delivered intralesionally at doses up to 2.0 mg paclitaxel/cm^3 tumor volume was well tolerated and paclitaxel remained localized at the injection site, confirming design principles to minimize systemic exposure. Therefore, localized paclitaxel administration using OncoGel merits continued clinical development. *Anti-Cancer Drugs* **18:283–289 © 2007 Lippincott Williams & Wilkins.**

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Introduction

Paclitaxel is one of the most widely used anticancer agents [1]. Paclitaxel's mechanism of action includes interference with mitotic spindle formation [1–4]. In addition, it potentiates the effect of radiation on cancer cells by arresting the cell cycle in the G_2/M phase of cell division, a stage at which cells are particularly sensitive to radiation [5].

Paclitaxel's lipophilicity and low water solubility necessitates the use of solubilizers for intravenous administration [6]. Cremophor-EL, an excipient commonly used to solubilize paclitaxel, is known to produce serious and potentially fatal hypersensitivity reactions [1,6–8]. The US Food and Drug Administration recently approved a Cremophor-free, albumin-stabilized, formulation of intravenously administered paclitaxel (Abraxane) for the treatment of metastatic breast cancer, which avoids most hypersensitivity reactions, although systemic toxicities owing to paclitaxel were still reported [9].

The cytotoxic potency of paclitaxel depends on its intracellular concentration [10]. Paclitaxel is, however, highly protein bound (95–98%), which limits penetration into solid tumors because of its high tumor cell density [11]. It has been suggested that the duration of exposure, rather than the systemic concentration alone, may be more predictive of tumor response [12]. Optimal dosing of paclitaxel may be compromised owing to accompanying systemic toxicities; therefore, the need for better delivery is well recognized and different formulations for localized delivery have been described in the literature [13–18].

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Direct intralesional delivery with controlled drug release is attractive, because it could result in the maintenance of cytotoxic drug levels within the tumor over a sustained period of time, as well as attenuate systemic toxicity.

Paclitaxel in ReGel® (OncoGel®; MacroMed, West Valley City, Utah, USA) is a unique controlled-release formulation designed for use as an intralesional depot injection. ReGel, a triblock copolymer consisting of poly(lactide-*co*-glycolide) and polyethylene glycol (PEG), biodegrades into lactic acid, glycolic acid and PEG. Copolymers of poly(lactide-*co*-glycolide and PEG have been studied extensively as potential biomaterials, and their biodegradation behavior is desirable because it eliminates the need to retrieve the depot once the drug is released [16,19,20]. The ReGel polymer is unique in that it transforms from a water-soluble polymer at administration temperature to a water-insoluble, biodegradable gel depot at body temperature.

Preclinical toxicology studies demonstrated that OncoGel injection has an acceptable safety profile, with local skin injection site reactions as the only dose-limiting toxicity (DLT) [21–24]. Animal studies using breast tumor xenografts demonstrated that intralesional administration of OncoGel has primary activity equal to or greater than the maximum tolerated systemic doses of intravenous or intraperitoneal paclitaxel, with controlled release of active drug within the tumor over a half-life of approximately 3 weeks [16]. In addition, an in-vivo biodistribution study in nude mice demonstrated that the OncoGel depot was highly localized, remaining at the injection site for a prolonged period with minimal paclitaxel levels detected in any other tissue or blood [25]. OncoGel injections into the porcine pancreata also demonstrated that the OncoGel depot was localized both grossly and histologically 7 and 14 days after injection [26]. Paclitaxel concentrations in surrounding pancreatic tissue were inversely related to the distance from the depot with high concentrations in the section containing the OncoGel depot and lower concentrations at distances up to 50 mm from the injection site. Higher injection volumes of OncoGel showed higher tissue concentrations of paclitaxel in the corresponding sections of the specimens.

The objectives of this phase 1 study were to characterize the toxicities and pharmacokinetics, and to indicate evidence of activity, associated with OncoGel administered intralesionally to superficially accessible solid tumor lesions.

Methods

Eligibility criteria

Patients with one or more discrete biopsy-confirmed, tumor masses accessible by percutaneous injection, and for whom no known curative therapy was available, were candidates for this study. Patients were required to be at least 18 years of age, have an Eastern Cooperative Oncology Group performance status of 2 or less and a life expectancy of at least 3 months. Any prior chemotherapy, major surgery or radiotherapy to nonstudy lesions must have been completed at least 4 weeks before the study enrollment. Local therapy to the study lesion area must have been completed at least 16 weeks before enrollment. Patients must have had adequate hematopoietic, hepatic and renal functions. Exclusion criteria included clinically apparent central nervous system metastases or carcinomatous meningitis, active or uncontrolled infections, or a primary diagnosis of leukemia.

Pretreatment and follow-up evaluations

Local ethics committee approval of the study was required and all patients provided informed consent before the enrollment. Medical histories, physical examinations, identification of all tumor masses by body location, and assessment of hematopoietic, hepatic and renal functions were performed before the treatment began and weekly thereafter. Pretreatment examinations also included evaluation of the local skin condition, lesion biopsy if not performed within the previous 6 months, and three-dimensional imaging of the study lesion (computed tomography, magnetic resonance imaging or three-dimensional ultrasound).

Baseline medical conditions and treatment-emergent adverse events were graded according to the National Cancer Institute Common Toxicity Criteria version 2. Adverse event data were collected for all treatment-emergent adverse events, regardless of potential attribution to the study drug. Serum blood chemistries and complete blood count (CBC) differential and platelets were conducted every other week from weeks 1 to 9.

Tumors were evaluated for response according to a modified World Health Organization criteria by comparing the change from baseline of the tumor volume, with the two evaluations separated by a minimum of 4 weeks. The same three-dimensional imaging technique was used for each patient throughout the study. Tumor responses included: partial response (at least a 45% decrease in volume) progressive disease (PD: at least a 40% increase in the tumor volume) and stable disease (SD: neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for PD).

Dose and drug administration

OncoGel was supplied by MacroMed in single-use, ready-to-use syringes containing 0.5 ml of study drug. Each syringe contained 0.65 mg paclitaxel/g ReGel (0.68 mg paclitaxel/ml used for the two lowest dose levels) or 6.0 mg paclitaxel/g ReGel (6.3 mg paclitaxel/ml

used for the two highest dose levels). Syringes were stored at −10°C or below and thawed at 2–8°C for 12–72 h before injection. In order to evenly disperse the paclitaxel solution throughout the tumor, separate intralesional injections were made using a 23-gauge needle. A new needle was used for each entry through the skin and no more than five separate injections were made for each tumor. Patients with multiple eligible lesions had one or more treated, with one tumor selected by the investigator for purposes of assessing tumor response.

Dose escalation and dose-limiting toxicity definition

The original study protocol included six dose levels (Table 1). For each dose level, the volume of OncoGel injected varied such that the same concentration of paclitaxel in the tumor tissue (mg paciltaxel/cm^3 tumor volume) was obtained. Dose level 0 was the approximate local site maximum tolerated dose (MTD) determined following subcutaneous injection into normal tissue of dogs [24]. Dose level 3 was prospectively identified as the maximum dose for this study, resulting in a total intralesional dose of approximately one-third of the tumor volume using the highest concentration of paclitaxel available in the current formulation (6.3 mg paclitaxel/ml OncoGel). In light of safety data acquired during enrollment, two dose levels (0.13 and 1.0 mg paclitaxel/cm^3 tumor volume) were skipped. Consequently, patients were enrolled in this study at four dose levels: 0.06, 0.25, 0.63 and 2.0 mg paclitaxel/cm^3 tumor volume.

Toxicities were assessed using a modified National Cancer Institute Common Toxicity Criteria in that injection site pain was graded independently of other injection site reactions. Local and systemic DLTs are defined in Table 2. The planned dose escalation scheme was to enroll three patients in each cohort. If no DLTs were observed for 9 weeks after dosing, the next dose cohort was enrolled. At any dose level, if one patient experienced a DLT an additional three patients would be enrolled at that dose level. If two or more patients experienced a DLT, the MTD had been exceeded and additional patients would be enrolled at the dose level below that at which the DLTs were observed. A maximum of six patients would be enrolled at any dose level. The MTD was defined as the highest dose level at which no more than one of six patients experienced a DLT.

In order to assess the toxicity of OncoGel without a background of other anticancer treatments, patients were not allowed to receive any other chemotherapy or hormone therapy. If a patient elected to receive either of these agents owing to malignant disease progression, they were discontinued from the study.

Plasma sampling and assay

Plasma samples were collected for pharmacokinetic analysis before intralesional injection; at 3, 6, 24 and 72 h after injection; and at weekly intervals from weeks 1 to 9. Paclitaxel concentrations were determined using a validated high-performance liquid chromatography tandem mass spectrometer assay [27].

Results

Patient characteristics

A total of 16 patients participated in the study between June 2001 and July 2003. Patient characteristics are presented in Table 3.

Doses administered

A total of 18 tumors among 16 patients were injected with OncoGel (Table 4). An average of 21% of tumor volume was injected.

Patient disposition

Eleven patients completed all 9 weeks of the study. Three patients in the 0.63 mg/cm^3 cohort discontinued early from the study owing to malignant disease progression at week 4 ($n = 2$) and week 5 ($n = 1$). Two patients in the 2.0 mg/cm^3 cohort discontinued early from the study owing to malignant disease progression at week 2 ($n = 1$) and week 4 ($n = 1$).

Table 2 Local and systemic dose-limiting toxicity definitions

Local dose-limiting toxicities
≥ grade 3 injection site pain
≥ grade 3 injection site reaction such as ulceration or necrosis that is severe or prolonged
Systemic dose-limiting toxicities
grade 4 neutropenia lasting 5 days
≥ grade 3 febrile neutropenia regardless of duration
grade 4 thrombocytopenia
≥ grade 3 nonhematological toxicity
≥ grade 3 diarrhea or vomiting persisting after treatment with optimal antidiarrheals or antiemetics

Table 1 Dose escalation scheme

Dose level	Dose escalation[a]	OncoGel concentration (mg/ml)	Paclitaxel concentration in the lesion (mg/cm^3)	Percent of total tumor volume injected	Number of patients per cohort
0	original starting dose	0.68	0.06	10	3
1	revised starting dose	0.68	0.25	33	3–6
2	2 × dose level 1	6.3	0.63	10	3–6
3	4 × dose level 2	6.3	2.0	33	3–6

[a]On the basis of a review of safety data during enrollment, two dose levels (0.13 and 1.0 mg paclitaxel/cm^3) were skipped.

Toxicity

All 16 patients were evaluable for toxicity. Local and systemic toxicities are presented in Table 5. One patient (0.25 mg/cm^3) reported grade 3 injection site pain. The injected tumor was located on the left side of the neck, and this event resolved rapidly following a local injection of meperidine. No other patients reported a DLT of injection site pain during the course of the study or received analgesics before injections.

Table 3 Patient characteristics at baseline

	No. of patients
Total no. of patients	16
Sex, Men/women	9/7
Age (years)	
mean	65
range	41–89
ECOG performance status	
0	5
1	4
2	7
Primary tumor histology	
breast (n=4)	–
adenocarcinoma	1
ductal	2
unknown	1
non-Hodgkin's lymphoma (n=3)	–
marginal zone B cell	1
follicular cell	1
mantle cell	1
lung (n=2)	–
squamous cell	1
small cell undifferentiated	1
malignant melanoma	2
laryngeal–squamous cell	1
thyroid–medullary	1
skin–squamous cell	1
floor of mouth–squamous cell	1
unknown primary	1

ECOG, Eastern Cooperative Oncology Group.

Two patients in the 0.63 mg/cm^3 dose group with abnormal laboratory values met the protocol-defined criteria for systemic DLTs; however, owing to underlying conditions these events were not considered as DLTs by either the investigator or the sponsor. One patient developed grade 3 elevation of total bilirubin (3.2 mg/dl) and grade 2 elevation of alkaline phosphatase (536 IU/l) 9 weeks after administration of OncoGel. The patient was originally diagnosed with infiltrating ductal breast cancer approximately 3 years before study entry. From baseline to week 7, her total bilirubin and alkaline phosphatase levels were grade 1 (within the normal range). All serum paclitaxel levels for this patient from study day 1 to study week 9 were below the quantifiable limit. A computed tomography scan of the abdomen and pelvis was performed, which revealed biliary obstruction because of tumor. Therefore, elevated bilirubin levels were related to disease progression and not due to OncoGel administration as per investigator's assessment.

A second patient entered the study with grade 3 neutropenia and leukopenia owing to long-term treatment (3.5 years) for lymphoma. From week 1 to week 5, the patient's white blood cells and neutrophils returned to grade 1. At study week 7, the patient developed grade 4 neutropenia (absolute neutrophil count of 0.3×10^3 cells/μl) and grade 4 leukopenia (white blood cells of 0.5×10^3 cells/μl), and was discontinued from the study. All serum paclitaxel levels for this patient from study day 1 through study week 7 were below the quantifiable limit. Owing to persisting leukopenia and neutropenia subsequent to the study, a bone marrow biopsy was performed. Findings were considered consistent with

Table 4 Doses administered

	Dose level (mg paclitaxel/cm^3 tumor volume)				Overall
	0.06	0.25	0.63	2.0	
Total number of patients	3	3	6	4	16
Total number of tumors injected	3	3	8	4	18
Size of tumors injected (cm^3)					
mean	7.3	5.5	5.9	5.7	6.0
range	1.1–16.7	2.5–9.8	0.6–19.0	0.7–15.0	0.6–19.0
Total number of injections per tumor					
1	0	0	5 (62.5%)	1 (25.0%)	6 (33.3%)
2	2 (66.7%)	0	0	0	2 (11.1%)
3	0	2 (66.7%)	2 (25.0%)	0	4 (22.2%)
4	0	1 (33.3%)	1 (12.5%)	2 (50.0%)	4 (22.2%)
5	0	0	0	0	0
6	0	0	0	1 (25.0%)	1 (5.5%)
7	1 (33.3%)	0	0	0	1 (5.5%)
Number of injections per tumor					
mean	3.7	3.3	1.9	3.8	2.8
median	2	3	1	4	3
Total volume injected per tumor (ml)					
mean	0.73	1.97	0.63	2.03	1.18
range	0.1–1.6	0.7–3.7	0.1–1.9	0.3–4.8	0.1–4.8
Percent of tumor volume injected (%)					
mean	10.4	33.8	11.6	39.6	21.3
range	9.1–12.5	28.0–37.8	9.1–16.7	32.0–43.5	9.1–43.5
Actual amount of paclitaxel administered per patient (mg)					
mean	0.50	1.3	5.3	13	5.5
range	0.07–1.1	0.48–2.5	0.63–12	1.9–30	0.07–30

Table 5 Local and systemic toxicities by dose level (National Cancer Institute Common Toxicity Criteria)

	Dose level (mg paclitaxel/cm^3 tumor volume)							
	0.06 (n=3)		0.25 (n=3)		0.63 (n=6)		2.0 (n=4)	
	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3	Grade 4
Injection site pain	0	0	1	0	0	0	0	0
Injection site reaction	0	0	0	0	0	0	0	0
Neutropenia	0	0	0	0	0	1	0	0
Thrombocytopenia	0	0	0	0	0	0	0	0
Leukopenia	0	0	0	0	0	1	0	0
Total bilirubin	0	0	0	0	1	0	0	0
Diarrhea, persistent	0	0	0	0	0	0	0	0
Vomiting, persistent	0	0	0	0	0	0	0	0

Patients were counted once for each parameter at the highest reported toxicity grade that occurred after treatment.

Table 6 Adverse events related to study drug or injection procedure

Adverse event	Number of events	Number of patients	Maximum grade per patient
Related to study drug			
injection site pain	5	1	1
		2	2
		1	3
injection site or tumor site erythema	4	4	1
injection site bruising	1	1	1
post-procedural discharge	1	1	2
muscle spasm	1	1	1
Related to injection procedure but not related to study drug			
oozing at injection site	2	1	1
injection site hemorrhage	2	1	1
injection site burning	1	1	1

myelodysplastic syndrome, thought to be related to patient's prolonged prior cytotoxic chemotherapy. No other patients in the 0.63 or 2.0 mg/cm^3 cohorts exhibited any systemic DLTs.

Twelve adverse events reported during the study were considered to be related to study drug and all were reflective of local responses to OncoGel administration. In addition, five adverse events that were reported among two patients were considered to be related to the injection procedure itself but not related to study drug. These adverse events are presented in Table 6.

Immediately following injection, partial displacement of OncoGel was noted on the skin at the injection site for five of the 18 tumors injected. An apparent tendency for displacement with higher percent tumor volume injected was observed: four of the five leakages reported were for tumors injected with greater than 30% of the tumor volume. OncoGel displacement to the skin surface would not be expected to cause local toxicity. This was supported by reports of localized adverse events such as pain and erythema occurring with similar frequency among patients with and without injection site displacement.

Tumor response

Of the 14 patients evaluable by the modified World Health Organization criteria, six patients had SD and eight patients had PD at their final assessment. Two tumors were not evaluable owing to the patient's early study termination, which resulted in final assessments occurring less than 4 weeks after study drug injection. Changes in tumor volumes from the smallest reported tumor volume to the final assessment ranged from 56.3% reduction to 232.5% increase in volume.

Pharmacokinetic analyses

Data were obtained from 153 plasma samples collected from the 0.25 mg/cm^3 and higher dose groups. No detectable paclitaxel levels were observed at any time point for nine patients. Four patients had minimal but detectable levels (range: 0.53–0.71 ng/ml) in five plasma samples. The small number of samples with quantifiable paclitaxel levels did not permit pharmacokinetic analyses. A dependence of plasma paclitaxel concentrations versus absolute paclitaxel dose was not evident.

Discussion

The delivery of chemotherapeutic agents to tumor cells is limited by the disorganized, torturous hypervascularized tumor periphery and necrotic hypovascularized tumor centers [28]. In addition, the increased pressure within the tumor minimizes the movement of chemotherapeutic agents across the blood vessel walls to the tumor interstitium. In-vitro studies of systemically administered paclitaxel have shown that the majority of paclitaxel remains at the tumor periphery and that suboptimal concentrations are found in cells in the middle of the tumor [29–32].

Intralesional exposure of paclitaxel is also important for maximum pharmacological effect. In-vitro studies have also indicated that duration of exposure is more important than concentration for apoptosis, with prolonged infusion resulting in more cells being exposed to paclitaxel during sensitive cell cycle phases [30]. Therefore, direct

sustained delivery of paclitaxel into the tumor core may result in an increased pharmacological effect.

A new depot formulation of paclitaxel (OncoGel) has been developed that allows direct delivery into the tumor, with sustained delivery of paclitaxel over approximately 6 weeks from a single administration using a biodegradable polymer that does not require retrieval. This study was designed to characterize the toxicities associated with OncoGel delivery directly into solid tumors and to define the MTD. Single doses of OncoGel ranging from 0.06 to 2.0 mg paclitaxel/cm^3 tumor volume were evaluated. On the basis of evenly distributed injections of OncoGel within the tumor and paclitaxel's diffusion distance, injections of approximately one-third of the tumor volume would be expected to result in diffusion to 100% of a tumor's total volume based on mathematical modeling of paclitaxel diffusion from polymer-based delivery systems [33,34].

The 2.0 mg paclitaxel/cm^3 tumor volume dose represented the maximum dose for this study, although additional dosing regimens may be used in future studies. Results from this study indicate that injection of OncoGel directly into the tumor was well tolerated at doses up to 2.0 mg paclitaxel/cm^3 tumor volume and injection volumes up to 44% of the tumor volume. One local DLT of grade 3 injection site pain was reported in the 0.25 mg paclitaxel/cm^3 cohort. There was one report in one patient of a grade 3 elevated bilirubin, and one report each in one patient of grade 4 neutropenia and grade 4 leukopenia in the 0.63 mg paclitaxel/cm^3 cohort, which met the protocol-defined criteria for systemic DLTs. Owing to the patients' diagnoses of biliary obstruction because of a tumor and myelodysplastic syndrome because of previous chemotherapy treatment (respectively), and that both patients had serum paclitaxel levels below quantified limits throughout the study, these events were not considered related to the OncoGel injection and therefore were not considered to be DLTs. No local or systemic DLTs were reported in the highest dose cohort, 2.0 mg paclitaxel/cm^3 cohort; therefore, an MTD was not identified.

The highest dose delivered in this study (2.0 mg paclitaxel/cm^3 tumor volume) is comparable to a systemic paclitaxel dose of 20 mg/m^2 released over approximately 6 weeks or 0.48 mg/m^2/day for an average patient (20 cm^3 tumor, 2 m^2 patient). This was far lower than the 17 mg/m^2/day of paclitaxel administered as a low-dose, continuous infusion without DLTs, as reported by Dowell *et al.* [35]. Therefore, systemic toxicity was not expected to be dose limiting in this study. Although three systemic DLTs were reported (grade 3 elevated bilirubin, grade 4 neutropenia, grade 4 leukopenia) among two patients, the MTD was not reached at the maximum delivered dose of 2.0 mg paclitaxel/cm^3 injected at approximately 40% of the tumor volume. In addition, no patterns of toxicities related to OncoGel were observed except for mild to moderate local injection site reactions.

Following a single dose of OncoGel ranging from 0.25 to 2.0 mg paclitaxel/cm^3 tumor volume for a total dose of 0.07–30 mg paclitaxel, only 3.3% of the samples analyzed had quantifiable plasma levels that ranged from 0.53 to 0.71 ng/ml, indicating that paclitaxel remained in the tumor with limited systemic exposure. Ideally, biopsies in areas contiguous to the injected lesions would have been obtained to establish the diffusion distance from the tumor. Biopsies were not, however, taken in this study. Determination of paclitaxel tissue concentrations and diffusion distance from the OncoGel depot in normal pancreatic tissue has been reported in a porcine model [26]. Both preclinical data [25,26] and the lack of hematologic toxicities observed during the study support that paclitaxel remained in or near the tumor. Of note, these plasma levels were lower than those reported in a prolonged, continuous intravenous administration of 6.5 mg/m^2/day dose that ranged from 4 to 6 ng/ml in a phase 1 study, [36] and were considerably below those reported following 3- and 24-h infusions of paclitaxel at dose levels of 135 and 175 mg/m^2. The latter were determined in a phase 3 randomized study in ovarian cancer patients in whom C_{max} plasma levels ranged from 195 to 3650 ng/ml [1].

Limited indication of antitumor response was observed during this study, with SD noted among six patients and PD noted among eight patients. The significance of this observation is uncertain, owing to the small sample size and varying tumor types injected with OncoGel. These responses may reflect extensive prior patient treatment as previous paclitaxel or other chemotherapy regimens were allowed.

Most tumors are treated with combination therapies, such as chemotherapy, radiation and surgery [29]. It is expected that OncoGel would be used in combination with other regimens such as radiation therapy, thereby increasing their effectiveness without contributing to the associated systemic toxicities. Preclinical data demonstrated that 18- to 24-h incubation with paclitaxel was needed before tumor cells were sensitized to radiation [12,37] and that this radiosensitization declined rapidly after exposure to paclitaxel was removed [38]. Therefore, direct intralesional injection of OncoGel with its slow release of paclitaxel over a 6-week period, as supported by preclinical studies [25,26], may result in increased radiosensitization of tumor cells with minimal systemic toxicities.

This phase 1 study found that OncoGel administered intralesionally was well tolerated, remained localized at the injection site and did not reach the systemic circulation in clinically significant concentrations. An MTD was not reached at the maximum delivered dose of 2.0 mg paclitaxel/cm^3 tumor volume. Further evaluation of OncoGel in solid tumors is warranted.

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