Local treatment of inoperable esophageal cancer with OncoGel® (ReGel®/Paclitaxel) and radiation therapy

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conclusions

• OncoGel combined with radiation therapy for inoperable esophageal cancer was well-tolerated with no dose-limiting toxicities and negligible systemic exposure
• Tumor volume reduction, dysphagia improvement, and negative biopsies for carcinoma suggest this may be an effective therapy
• Data support investigation of OncoGel in combination with chemoradiotherapy in a phase 2b study

1 BACKGROUND

• Most esophageal cancer patients present with inaccessible disease and dysphagia
• Clinical management of inoperable disease includes dysphagia palliation, often using local interventions to avoid systemic toxicities
• OncoGel, a unique therapy of paclitaxel formulated in a thermosensitive biodegradable triblock copolymer of poly(lactide-co-glycolide) and poly(ethylene glycol) (ReGel), provides controlled release of paclitaxel for 4 to 6 weeks at the injection site
• This phase 2a dose-escalation study evaluated the safety, tolerability and pharmacokinetics of intralesional OncoGel administration combined with radiation therapy in patients with inoperable esophageal cancer
• OncoGel was well-tolerated when evaluated in a phase 1 study of superficially accessible tumors

2 METHODS

Inclusion: Adults with squamous cell or adenocarcinoma of the esophagus who were not surgical candidates but were eligible for radiation therapy for palliation of dysphagia grades 3 and 4

Dosing: OncoGel was injected into the primary tumor and adjacent accessible lymph nodes using endoscopic ultrasound (EUS) guidance
• Three dose cohorts: 0.66, 1.33 and 2.67 mg per cm3 tumor volume
• Injection volume: 30% of the tumor volume in 0.25 mL to 1.0 mL aliquots

Pre-defined systemic and local dose-limiting toxicities (grade 4) included: neutropenia; febrile neutropenia; anemia; and life-threatening tumor volume

Efficacy evaluations included change from baseline in tumor volume and patient-reported dysphagia
• Dysphagia grades: 1 = asymptomatic; 2 = difficulty swallowing some solids but able to swallow semisolids; 3 = difficulty swallowing solids but able to swallow liquids; 4 = difficulty swallowing liquids; 5 = inability to swallow anything, including saliva

3 RESULTS

Eleven patients completed the study (N = 3, 4 and 4 per cohort). Baseline esophageal tumor volumes ranged from 6 cm3 to 112 cm3. Involved lymph node volumes ranged from 0.5 cm3 to 6.1 cm3.

Dosing and PK
• Injection volumes ranged from 3 mL to 36 mL administered 4 to 53 injections
• Endoscopists reported no technical difficulties injecting OncoGel using EUS guidance
• Total paclitaxel delivered ranged from 16 mg to 188 mg
• Peak plasma concentrations (Cmax) ranged from 0.53 ng/mL to 2.37 ng/mL, 1% of total paclitaxel administered for all patients, which are 70 to 7000 times lower than Cmax reported after systemic injections [2]

Endoscopists reported no technical difficulties injecting OncoGel using EUS guidance
• Plasma paclitaxel levels were detectable for 24 hours in all 11 patients, 72 hours in 10 patients, and 3 weeks in 7 patients, supporting controlled release of paclitaxel from OncoGel

Safety
• No local or systemic dose-limiting toxicities were observed
• No OncoGel-related serious or hematologic adverse events were reported

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• Adverse events considered related to both OncoGel and radiation were often indistinguishable from events commonly associated with radiation therapy

Efficacy: Tumor volumes decreased for 8 of 10 patients at Week 11, despite radiation-induced inflammation/erythema being indistinguishable from residual tumor
• Dysphagia improved in 8 patients and remained unchanged for 2 patients

No OncoGel-related serious or hematologic adverse events were reported
• Biopsies were negative for carcinoma in 4 patients
• An additional patient underwent a successful esophagectomy with negative margins after completing the study

REFERENCES:


2. AGA Disclosure (Abstract No. 315756). Authors listed below DO NOT have any financial or other relationship(s) to disclose:

• NL Elstad, employee of Protherics Salt Lake City, Inc
• KD Fowers, employee of Protherics Salt Lake City, Inc

3. Local treatment of inoperable esophageal cancer with OncoGel® (ReGel®/Paclitaxel) and radiation therapy (grade 4) included: neutropenia; fever, neutropenic fever, anemia, and life-threatening dysphagia palliation, often using local interventions to avoid systemic toxicities. OncoGel, a unique therapy of paclitaxel formulated in a thermosensitive biodegradable triblock copolymer of poly(lactide-co-glycolide) and poly(ethylene glycol) (ReGel), provides controlled release of paclitaxel for 4 to 6 weeks at the injection site. This phase 2a dose-escalation study evaluated the safety, tolerability and pharmacokinetics of intralesional OncoGel administration combined with radiation therapy in patients with inoperable esophageal cancer. OncoGel was well-tolerated when evaluated in a phase 1 study of superficially accessible tumors.