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Basic Original Report

Patient-reported outcomes of a multicenter phase 2 study investigating gemcitabine and stereotactic body radiation therapy in locally advanced pancreatic cancer

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Abstract

Purpose: We previously reported clinical outcomes and physician-reported toxicity of gemcitabine and hypofractionated stereotactic body radiation therapy (SBRT) in locally advanced pancreatic cancer (LAPC). Here we prospectively investigate the impact of gemcitabine and SBRT on patient-reported quality of life (QoL).

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Methods and materials: Forty-nine LAPC patients received 33 Gy SBRT (6.6 Gy daily fractions) upfront or after ≤3 doses of gemcitabine (1000 mg/m^2) followed by gemcitabine until progression. European Organization for Research and Treatment of Cancer QoL core cancer (QLQ-C30) and pancreatic cancer-specific (European Organization for Research and Treatment of Cancer QLQ-PAN26) questionnaires were administered to patients pre-SBRT and at 4 to 6 weeks (first follow-up [1FUP]) and 4 months (2FUP) post-SBRT. Changes in QoL scores were deemed clinically relevant if median changes were at least 5 points in magnitude.

Results: Forty-three (88%) patients completed pre-SBRT questionnaires. Of these, 88% and 51% completed questionnaires at 1FUP and 2FUP, respectively. There was no change in global QoL from pre-SBRT to 1FUP ($P = .17$) or 2FUP ($P > .99$). Statistical and clinical improvements in pancreatic pain ($P = .001$) and body image ($P = .007$) were observed from pre-SBRT to 1FUP. Patients with 1FUP and 2FUP questionnaires reported statistically and clinically improved body image ($P = .016$) by 4 months. Although pancreatic pain initially demonstrated statistical and clinical improvement ($P = .020$), scores returned to enrollment levels by 2FUP ($P = .486$). A statistical and clinical decline in role functioning ($P = .002$) was observed in patients at 2FUP.

Conclusions: Global QoL scores are not reduced with gemcitabine and SBRT. In this exploratory analysis, patients experience clinically relevant short-term improvements in pancreatic cancer-specific symptoms. Previously demonstrated acceptable clinical outcomes combined with these favorable QoL data indicate that SBRT can be easily integrated with other systemic therapies and may be a potential standard of care option in patients with LAPC.

Introduction

In 2015, approximately 48,960 patients received a new diagnosis of pancreatic cancer in the United States.[1] Of these, nearly 40% presented with unresectable, locally advanced pancreatic cancer (LAPC).[2] LAPC is defined as a pancreatic tumor with no evidence of distant metastasis and >180° superior mesenteric and/or celiac artery involvement or unreconstructable portal vein or superior mesenteric vein involvement.[3] Standard of care for LAPC includes systemic chemotherapy with or without chemo-radiation (CRT; gemcitabine- or 5-florouracil-based chemotherapy concurrent with 45-54 Gy radiation therapy in 1.8- to 2.5-Gy fractions)[2-10]; however, even with CRT, local failure occurs in approximately 25% to 35% of patients[2,4] and survival rates remain poor with few surviving beyond 2 years.

Given the poor life expectancy of patients with LAPC, a major factor guiding patient and physician management decisions is treatment-related toxicity and impact on overall quality of life (QoL). Single-fraction stereotactic body radiation therapy (SBRT) for LAPC has demonstrated improved local control (80% to 100%)[11-14] compared with historical reports of standard CRT; however, late gastrointestinal toxicity rates up to 47% were observed.[14] Our recent multicenter phase 2 clinical trial implemented 5-fraction SBRT (33 Gy total, 6.6 Gy daily fractions) to determine if this fractionated regimen results in similar rates of local control with reduced late toxicities compared with those previously reported for single-fraction therapy. Median overall survival (OS) was 13.9 months with 78% freedom from local progression at 1 year and acceptable rates of acute and late grade ≥2 gastritis, fistula, enteritis, or ulcer toxicities of 2% and 11%, respectively.[15] Although these results are promising, patient-reported measures are crucial to fully evaluate the appropriateness of SBRT, given tendencies of physician assessments to inadequately reflect treatment-related morbidity.[16]

Several validated metrics to assess patient-reported outcomes have emerged. Based on literature review using PubMed, the most widely accepted cancer-specific QoL questionnaire is the European Organization for Research and Treatment in Cancer QoL core cancer questionnaire (EORTC QLQ-C30).[17,18] This questionnaire can be paired with an additional pancreatic cancer-specific module (EORTC QLQ-PAN26).[19] These metrics have been previously used to investigate the impact of various CRT regimens for borderline resectable and LAPC patients,[20-23] including 1 small study with 10 patients treated with gemcitabine and SBRT,[24] and thus were selected to evaluate QoL of patients in our study.

Herein, we report the QoL outcomes of patients treated with gemcitabine and fractionated SBRT in our phase 2 trial to evaluate the patient experience of this regimen.

Methods and materials

Study participants and treatment plan

The details of the treatment regimen and patient population are reported elsewhere.[15] In brief, 49 patients with histologically confirmed LAPC were treated at 3 academic institutions in the United States. Linear accelerator (Linac)-based SBRT was administered in 6.6 Gy daily fractions, 33 Gy total, upfront or after ≤3 weekly doses of gemcitabine (1000 mg/m^2) within 6 weeks before