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Safety Evaluation of Dose-escalated Carbon-ion Radiotherapy Using SIB and LET optimization in Pancreatic Cancer: A Phase I Study

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Objectives

Currently, carbon-ion radiotherapy (C-ion RT) for pancreatic cancer is delivered at a relative biological effectiveness (RBE)-weighted dose of 55.2 Gy in 12 fractions; however, achieving satisfactory local control remains a challenging. To address this, we have conducted a phase I study of intensity-modulated ion therapy with the simultaneous integrated boost (SIB) technique in combination with linear energy transfer (LET) optimization to evaluate the safety of dose escalation using these advanced techniques.

Methods

Eligible patients had pathologically confirmed pancreatic cancer without distant metastasis. Dose-limiting toxicity (DLT) was defined as Grade ≥3 non-hematological or Grade ≥4 hematological toxicity occurring within 90 days of initiating C-ion RT. Clinical target volume (CTV) 2 encompassed the gross tumor volume and high-risk regions for recurrence, while CTV1 included CTV2 plus prophylactic lymph node areas. C-ion RT consists of 12 fractions over three weeks, with 43.2 Gy delivered to CTV1. The dose to CTV2 was escalated in four steps, ranging from 55.2 Gy to 67.2 Gy. LET within CTV2 was optimized to a minimum of 44 keV/μm or higher. The primary endpoint was acute toxicity. This single-center, phase I trial employed a standard 3 + 3 dose-escalation design.

Results

Twelve patients were enrolled, with three patients assigned to each dose level. The median age was 67 years (range, 37-80). Tumor locations included the pancreatic head (n=4) and body/tail (n=8). 11 had stage III and 1 had stage IB disease; all cases were considered unresectable. All patients completed treatment as scheduled, and C-ion RT was tolerated. No DLTs were observed. The one-year local control rate and overall survival rates were both 92%.

Conclusions

Dose-escalated C-ion RT for unresectable pancreatic cancer using the SIB method and LET optimization, up to 67.2 Gy in 12 fractions, was feasible and well tolerated. A multicenter phase II trial is planned to further evaluate this regimen, with 67.2 Gy in 12 fractions as the recommended dose.