Toxicity and efficacy of stereotactic body radiation therapy vs. intensity-modulated radiation therapy for the treatment of locally advanced pancreatic cancer in a phase 3 trial

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BACKGROUND

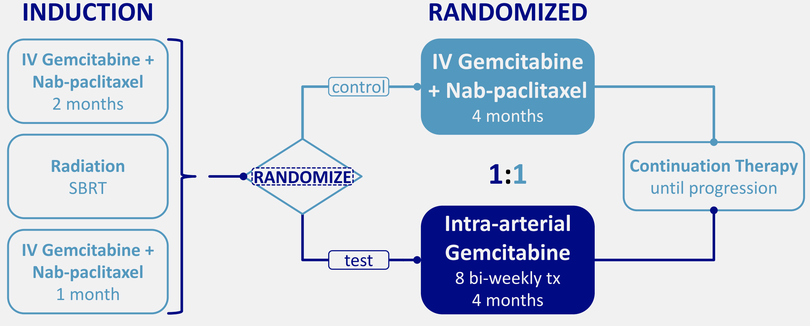
Locally advanced pancreatic cancer (**LAPC**) is one of the deadliest cancers. Radiotherapy (RT) is part of standard management[1], but the optimal RT technique has not been determined. The most common approaches are:

- Stereotactic body radiation therapy (**SBRT**) or
- Chemoradiation using Intensity-modulated radiation therapy (**IMRT**)

TIGeR-PaC[i] is a phase III clinical trial investigating the efficacy of intra-arterial chemotherapy treatment utilizing a novel dual-balloon catheter compared to the standard of care. Prior to randomization, patients undergo radiation therapy during the **induction phase**. Herein, we use clinical data to compare **toxicity** and **efficacy** between SBRT and IMRT.

METHODS

LAPC patients with a 0-1 ECOG and diagnosis within 6 weeks begin induction with chemo (**IV gemcitabine/nab-paclitaxel**) and radiation therapy (SBRT or IMRT) per the study schema:



We analyzed data from **134** patients:

- 75 IMRT patients (50 Gy in 25 fractions; concurrent PO capecitabine BID Mon-Fri) or
- 59 SBRT patients (33 Gy in 5 fractions)

The decision for SBRT vs. IMRT was site-driven and not pre-specified by TIGeR-PaC protocol

Analyzed:

- Adverse event (**AE**) — Incidence[ii] during, and 2 weeks post radiation
- Tumor size — Mean percent change[iii]
- CA 19-9 — Mean percent change[iii]

Of the 134 patients, **104** had interpretable imaging data to analyze tumor size and only **31** with analyzable CA 19-9 data.

CONCLUSION

While this study was not designed as a head-to-head comparison of SBRT versus IMRT, these data suggest that SBRT is better tolerated than IMRT without any compromise in efficacy in patients with LAPC.

- With SBRT, there was less investigator-led withdrawal of patients due to SAE than IMRT
- No statistically significant difference in local tumor response between SBRT and IMRT

[1]National Comprehensive Cancer Network. Pancreatic Adenocarcinoma (Version 2.2022). https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed December 13, 2022.

[i]ClinicalTrials.gov

RESULTS

The 134 patients across 22 sites (63 male; 68.5 yr median age) showed no significant difference in baseline demographics between patients treated with SBRT or IMRT.

However, AEs were significantly different between the two:

AE

Category	IMRT (N=75)	SBRT (N=59)	p-value[ii]
Any AE	49 (65.3)	26 (44.1)	*0.015
Gastrointestinal AE	33 (44.0)	10 (16.9)	**0.001
Grade ≥3 AE	20 (26.7)	6 (10.2)	*0.026
Serious AE	10 (13.3)	2 (3.4)	0.066
On-Study Death	1 (1.3)	0 (0.0)	1.000
Withdrawal	9 (12.0)	1 (1.7)	*0.042

[ii]Calculated using Fisher's exact test; *p-value ≤ 0.05; **p-value ≤ 0.01

Additionally, there was no significant difference between mean CA 19-9 change and mean tumor size change and at baseline between patients treated with SBRT or IMRT.

CA 19-9

Measurement	IMRT (N=17)	SBRT (N=14)	p-value[iii]
Mean CA 19-9 Change (%)	-40.7 ±40	+9.8 ±111	0.262

TUMOR SIZE

Measurement	IMRT (N=54)	SBRT (N=50)	p-value[iii]
Mean Baseline Long Axis (cm)	4.30	4.04	0.336
Mean Tumor Size Change (%)	-11.7	-12.6	0.792

[iii]Calculated using independent samples t-test

FUTURE

Further prospective studies addressing this question are needed to determine the optimal RT modality for patients with LAPC. SBRT appears to be the best RT backbone for adding novel therapies such as intra-arterial chemotherapy.