Targeted Intra-arterial Gemcitabine vs. Continuation of IV Gemcitabine plus Nab-Paclitaxel following Induction with sequential IV Gemcitabine plus Nab-Paclitaxel and Radiotherapy for Unresectable Locally Advanced Pancreatic Cancer (TIGeR-PaC) – Phase 3 Trial Interim Analysis

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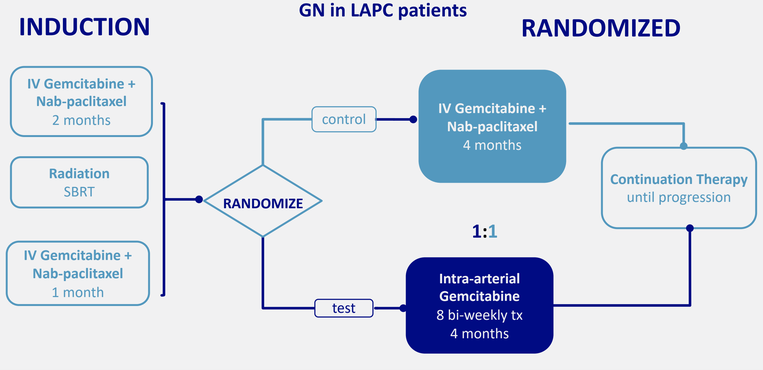
BACKGROUND

Treatment of locally advanced pancreatic cancer (LAPC) remains a clinical challenge with a median survival of 16-18 months[1,2]. Control of local disease, beyond systemic therapy, is part of the treatment paradigm being investigated in this patient population. Double balloon-mediated local delivery of intra-arterial gemcitabine (IAG) into the tumor has been demonstrated to be safe in this patient population[3]. TIGeR-PaC is an ongoing Phase-3 clinical trial comparing the efficacy of this approach compared to standard of care IV gemcitabine/ nab-paclitaxel (GN) for patients with LAPC.

DESIGN

The trial is designed with an induction phase of upfront systemic chemotherapy prior to IAG. Patients with LAPC diagnosed within 6 weeks and ECOG 0-1, receive 3 cycles of GN and 1 cycle of radiation – SBRT (33 Gy in 5 fractions). Following induction, patients with non-progressive disease are randomized to receive IAG (8 treatments every two weeks for 16 weeks) or continuing therapy with 4 cycles of GN. After the 16 weeks of randomized therapy, the patients with non-progressive disease go on to continue systemic therapy (GN or capecitabine, per investigator's preference) until disease progression and then followed for survival only. The primary endpoint is overall survival (OS) from time of randomization, and the study has an 80% power to detect a hazard ratio of 0.6 between the two arms. It is assumed that the hazard functions are proportional only during the randomized treatment period, after which the two hazard functions become approximately identical during the continuing treatment period.

The Phase III clinical trial, TIGeR-PaC[I], is investigating the benefits of IAG compared to SoC GN in LAPC patients

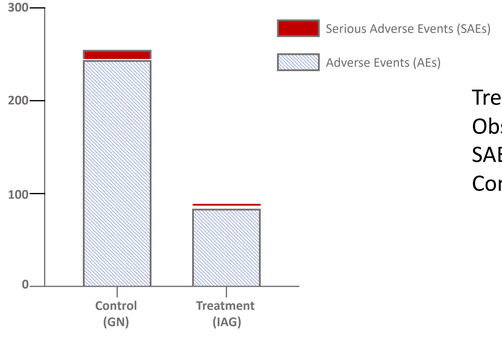


RESULTS

RR3 TIGeR-PaC Phase III Data Update (1st Interim Analysis):

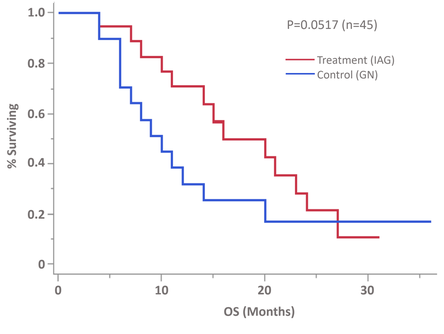
Treatment (IAG) Vs. Control (GN)

TOTAL SAEs and AEs



Treatment (IAG) arm Observes **>65% Fewer** SAEs and AEs compared to the Control (GN) arm

OVERALL SURVIVAL



Control (GN) arm exhibited a 10 months vs. 16 months of survival in the Treatment (IAG) arm after 4-5 months of Induction therapy = **6-month survival benefit**

ENDPOINT ANALYSIS

The primary endpoint of OS for the two arms was compared using 2-sided Wilcoxon test. An interim analysis of the primary endpoint of OS was conducted for the ITT population when 30% of the events (or 26 of 86 deaths) were observed. The 26th event occurred on 21st Dec 2022. Up until that time, 45 patients were randomized into the study. All surviving patients were censored for survival analysis.

- Twenty-three patients were randomized to intra-arterial gemcitabine (RenovoGem investigational treatment) arm and 22 to continuation of IV gemcitabine and nab-paclitaxel (standard of care control) arm
- The median overall survival in the IV gemcitabine and nab-paclitaxel control arm was 10 months (CI: 6-14), versus 16 months (CI: 10-24) in the intra-arterial RenovoGem arm from the time of randomization. (NOTE: Both arms' median overall survival calculations do not include 4 to 5-months of life from diagnosis to randomization during the induction chemotherapy and radiation phase of the trial)
- Observed a positive trend in median overall survival by 24-weeks (6 months); in this interim analysis, the statistical significance was not reached to stop the study early (p=0.051)
- Observed a 65% reduction in adverse events from the control arm to the treatment arm

CONCLUSION

With the first interim analysis of the TIGeR-PaC study comparing Treatment (IAG) to Control (GN):

- IAG treatment is associated with 65% reduced SAEs and AEs
- IAG treatment trends towards the survival benefit over IGN after 4 months of induction therapy
- The trial continues to enroll, with the next interim analysis expected in late 2024

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