Intra-Arterial Gemcitabine vs IV Gemcitabine PK Substudy in Patients with Locally Advanced Pancreatic Cancer

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BACKGROUND

Localized dual-balloon-mediated, intra-arterial delivery of gemcitabine (**IAG**) into tumors/tissue:

- May lead to decreased systemic drug concentration and associated side effects compared to intravenous delivery (**IVG**)
- Can lead to higher local drug potency[1]

This approach is currently being tested with locally advanced pancreatic cancer (**LAPC**) patients in TIGeR-PaC, a contemporary phase III clinical trial. Herein, we report the results of a 13-patient pharmacokinetic (**PK**) analysis substudy within TIGeR-PaC

METHODS

COHORT

The planned PK analysis of 15 patient substudy of TIGER-PAC study is near completion; this substudy is designed to collect blood samples for PK analysis including peak plasma level (Cmax) and Area Under the Curve/dose (AUC/d). Five sites are participating in this substudy.

IAG/IVG TREATMENT

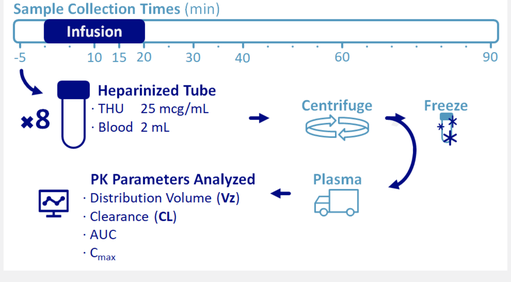
Gemcitabine delivered per following rate and duration:

IAG	IVG
1000 mg/m^2	1000 mg/m^2
20 minutes	30 minutes

The collection time includes baseline,10m, 15m, 20m, 30m, 40m, 60m, 90m for IAG and 10m,15m, 20m, 30m, 40m, 50m, 70m, 100m for IVG after start of infusion

SAMPLE PROCESSING & ANALYSIS

Samples collected, processed, and analyzed at the Core Lab (SKCCC at Johns Hopkins). The data were quality controlled for administration and collection of drug and analyzed using standard software.



CONCLUSION

Local and targeted intra-arterial delivery of gemcitabine in patients with LAPC demonstrates a PK profile that may affect both clinical efficacy and side effect profile of gemcitabine in this setting.

The Phase III Tiger-PAC study, currently enrolling, aims to determine the impact of this approach on Overall Survival in patients with LAPC.

[1]Farsad K, et al. 04:21 PM Abstract No. 392. *J Vasc Intervent Radiol*. 2019; 30(3):S172. doi:10./1016/j.jvir.2018.12.467

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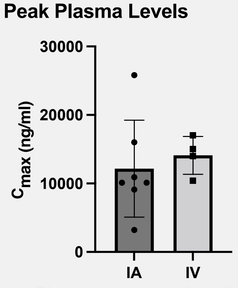
RESULTS

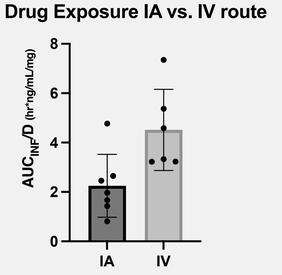
From the 15 patient substudy, results for 13 patients are available (7 IAG, 6 IVG) and presented here.

Two patients in IVG arm received a dose modified regimen at 80%; for these 2 patients the AUC/d analysis was performed but they were omitted for Cmax analysis.

The results for Cmax and AUC/d are as follows:



Peak Plasma Concentration of gemcetabine (20 minutes IA infusion vs. 30 minutes IV infusion)



Impact of route of administeratiob on Drug Exposure Area Under the Curve-Normalized for Total Dose (hr*ng/mL/mg, p<0.015)

Despite 33% increased concentration of infusion (due to increased infusion rate), the IAG Cmax was not higher than IVG.

In terms of systemic drug exposure, IAG was associated with greater than 50% reduction in AUC/d vs. IVG administration.

FUTURE

IAG may be better tolerated than IVG with less systemic drug exposure due to local metabolism prior to systemic exposure; this theory is being assessed formally as a secondary endpoint of the phase III TIGeR-PaC clinical trial by assessing quality of life and use of medications to overcome myelosuppression side effects associated with chemotherapy administration.