STATISTICAL ANALYSIS PLAN (SAOP)

FOR

CLINICAL STUDY PROTOCOL

An Open Label Phase 2 Trial to Evaluate Safety, Tolerability, and Efficacy of G-FLIP (Low Doses of Gemcitabine, Fluorouracil [5FU], Leucovorin, Irinotecan, and Oxaliplatin), Followed by G-FLIP-DM (G-FLIP + Low Doses of Docetaxel and Mitomycin C), When Used in Combination with Vitamin C, in Patients with Advanced Pancreatic Cancer

Protocol Number: G-FLIP-VitC-Ph2

NCT Number: NCT01905150

Study Drugs: G-FLIP, G-FLIP-DM, and Vitamin C (Ascorbic Acid)

Current Version: January 6, 2015

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This is a Phase II single-arm. Therefore, results are not compared to any concurrent control group. The primary endpoint is 12-month survival rate, and the secondary endpoints include QOL, RR, PFS, CA 19-9, and safety.

Efficacy: Distributions of the time-to-event endpoints (i.e., OS and PFS) will be estimated using Kaplan-Meier methodology. The medians of these time-to-event endpoints, as well as the number of treatment cycles of G-FLIP and G-FLIP-DM, will be presented with the appropriate 95% CIs. Results derived from this trial will be cross-referenced with the recent Phase 3 trial of FOLFIRINOX in patients with metastatic pancreatic cancer (Thierry C, et al. FOLFIRINOX versus Gemzar® for Metastatic Pancreatic Cancer. NEJM 2011, **364**:1817-1823.) for comparison purposes.

QOL and CA 19-9 will be assessed at baseline, as well as at multiple time points during G-FLIP and G-FLIP-DM treatments. QOL and CA 19-9 results at baseline, during G-FLIP vs. G-FLIP-DM treatments will be compared using Within-Subject Analysis of Variance (ANOVA).

RR during G-FLIP treatment will be cross-referenced to the Phase 3 trial of FOLFIRINOX in patients with metastatic pancreatic cancer (Thierry C, et al. 2011), for comparison purposes. RR associated with G-FLIP vs. G-FLIP-DM treatments will be compared using Within-Subject ANOVA. RR associated with G-FLIP-DM treatment is not expected to be as high as RR associated with G-FLIP treatment, since G-FLIP-DM is to be given to study subjects who exhibit DP with G-FLIP treatment. However, a significant RR associated with G-FLIP-DM would suggest that G-FLIP-DM may be a viable "salvage" or "rescue" regimen for patients with advanced pancreatic cancer who have failed G-FLIP regimen.

Safety: Safety data (vital signs, laboratory parameters, and ADRs, etc.) will be tabulated for all subjects. ADRs will be evaluated according to the latest version of National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

Treatment of ascorbic acid will begin on the same week as G-FLIP in 50% of the study subjects, and in the other 50% of the study subjects, ascorbic acid treatment will be delayed by 2 cycles. The safety results collected during this 4-week period between the 2 groups of study subjects will be compared using between-subject ANOVA to assess the acute safety of ascorbic acid, when used in combination with G-FLIP.