

SWOG S0727: A Phase I and Randomized Phase II Trial of Gemcitabine + Erlotinib (NSC-718781) + IMC-A12 (NSC-742460) vs. Gemcitabine + Erlotinib as First-Line Treatment in Patients with Metastatic Pancreatic Cancer

Fast Facts

IMC-A12 and erlotinib provided

ELIGIBILITY CRITERIA

1. Patients must have histologically or cytologically confirmed diagnosis of pancreatic adenocarcinoma. Patients with endocrine or neuroendocrine tumors, lymphoma of the pancreas, or ampullary cancer are not eligible. If the histologic diagnosis is based on a metastatic site, the histology must be compatible with pancreatic cancer.
2. Patients must have Stage IV disease that is not surgically resectable. Patients with macroscopic residual disease post-resection as the only site of disease are not eligible. Patients must not have clinically significant ascites.
3. Patients must not have received any prior chemotherapy, hormonal therapy, immunotherapy or chemoradiotherapy for advanced or locally advanced pancreatic cancer, including drugs that target either EGFR or IGFR. Patients must not have received prior gemcitabine for any reason. Prior surgery is allowed provided at least 14 days elapse between surgery and registration. Prior adjuvant chemotherapy is allowed provided that the last day of therapy was at least 6 months prior to registration. Prior radiation for palliation to metastatic sites is allowed provided that at least 28 days have elapsed since last treatment and that patient has other untreated metastatic sites that would disqualify them for this protocol.
4. Patients must have measurable and/or non-measurable disease. X-rays, scans or physical examinations for assessment of measurable disease must have been completed within 28 days prior to registration. X-rays, scans or other tests for assessment of non-measurable disease must have been completed within 42 days prior to registration. All disease must be assessed and documented on the Baseline Tumor Assessment Form
5. Sites must seek additional patient consent for the submission of specimens as described in Section 15.0.
6. Patients must have a Zubrod performance status 0-1 (see Section 10.4).
7. Patients must have adequate marrow function as evidenced by

a. ANC \geq 1,500/mcL,	c. hemoglobin \geq 9 g/dL and
b. platelets \geq 100,000/mcL,	d. leukocytes \geq 3,000/mcL

 These results must be obtained within 14 days prior to registration.
8. Patient must have total bilirubin \leq institutional upper limit of normal (IULN) and SGOT or SGPT \leq 2.5 x IULN. These results must be obtained within 14 days prior to registration.
9. Patient must have serum Creatinine \leq 1.5 x IULN or measured or estimated Creatinine clearance \geq 60 ml/min for patients with creatinine levels above IULN. Measured creatinine clearance or creatinine level (mg/dl) must be obtained within 14 days prior to registration.
10. Patients must have fasting serum glucose $<$ 120 mg/dL or below the IULN within 14 days prior to registration. Patients with diabetes mellitus who meet this criterion must be on a stable dietary or therapeutic regimen for this condition.
11. Patients must have adequate coagulation function as defined by international normalized ratio (INR) \leq 1.5 and partial thromboplastin time (PTT) no more than 5 seconds above IULN. These results must be obtained within 14 days prior to registration. Patients receiving prophylactic low dose coumadin or low molecular weight heparin are eligible as long as they meet these coagulation criteria. Patients requiring full dose (therapeutic) anticoagulation are eligible provided that they have been on a stable dose of anticoagulation and the coagulation parameters are stable within the therapeutic range (e.g., INR 2-3 for patients on therapeutic warfarin).
12. Patients must not have a history of allergic reaction attributed to compounds of similar chemical or biologic composition to IMC-A12. Patients must not have received prior chimerized or murine monoclonal antibody therapy.
13. Patient must not be receiving concurrent treatment with drugs that are known inducers or inhibitors of CYP3A4, because these may interact with erlotinib. Known inducers include but are not limited to: rifampicin, rifabutin, rifapentine, phenytoin, carbamazepine, phenobarbital, and St. John's Wort.

Known inhibitors include but are not limited to: atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin, and voriconazole.

14. Patients must have no plans to receive concurrent chemotherapy, hormonal therapy, radiotherapy, immunotherapy or any other type of therapy for treatment of cancer while on this protocol treatment.
15. Patients must not have active acute or chronic infections requiring antibiotics.
16. Patients must not have significant ongoing cardiac problems, myocardial infarction within the last six months, uncontrolled hypertension, unstable angina, uncontrolled arrhythmia or congestive heart failure.
17. Patients with known brain metastases are not eligible. However, brain imaging studies are not required for eligibility if the patient has no neurologic signs or symptoms. If brain imaging studies are performed, they must be negative for disease.
18. Due to the undetermined effect of this treatment regimen in patients with HIV-1 infection and the potential for serious interaction with anti-HIV medications, patients known to be infected with HIV are not eligible for this study.
19. Due to the possibility of harm to a fetus or nursing infant from this treatment regimen, patients must not be pregnant or nursing. Women and men of reproductive potential must have agreed to use an effective contraceptive method.
20. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for five years.
21. All patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
22. At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered into the data base.

Pre-Study Parameters.

1. History and physical including weight, height, performance status, baseline AE assessment
2. Labs including CBC with differential and platelets, serum creatinine, bilirubin, SGOT/SGPT, glucose, alk phos, albumin, lipid profile, INR and PTT
3. X-rays for disease assessment, ECG

Treatment

See section 7.5 for complete treatment plan.

Required pre-meds for IMC-A12 patients (section 7.3).

Arm 1 : erlotinib + gemcitabine + IMC-A12

Cycle = 28 days

Agent	Dose	Route	Schedule
Erlotinib*	100 mg	PO	daily
Gemcitabine	1000 mg/m ²	IV over 30 min	Days 1, 8, 15
IMC-A12*	6 mg/kg	IV over 60 min	Days 1, 8, 15, 22

Arm 2: erlotinib + gemcitabine

Cycle = 28 days

Agent	Dose	Route	Schedule
Erlotinib*	100 mg	PO	daily
Gemcitabine	1000 mg/m ²	IV over 30 min	Days 1, 8, 15

*provided drug