Supplemental Figure 1

Phase IIA Trial Testing Erlotinib As An Intervention Against Intraductal Pancreatic Mucinous Neoplasms

Study Population
Brief: 30 patients with a diagnosis of resectable pancreatic Intraductal Papillary Mucinous Neoplasm.

Inclusion (selected)
1. IPMN histological diagnosis with planned pancreatic surgical resection.

Exclusion (selected)
1. Intake of other EGF Receptor antagonists.
2. Previous history of sensitivity to EGF

Baseline Data Collection
History and physical examination, PT, PTT, CBC, SGOT/SGPT, alkaline phosphatase and total and free bilirubin, <4 weeks from visit. Consent for study enrollment obtained. Quantitative immunohistochemistry (IHC) levels of MUCIN 5AC (MUC5AC).

Erlotinib 100mg po qD for 21-42 Days

Endpoints
(Comparison of pre and post treatment levels )
in EUS-FNA and pancreatectomy tissue

Primary
Quantitative IHC level change of MUC5AC

Secondary
Safety
Supplemental Figure 2. CT scan of pre-Erlotinib IPMN in participant with Complete Clinical Response. The IPMN is indicated by a red arrow as a reduced density lesion in the head and body of the pancreas. Multiple images from the same CT scan are shown.
Supplemental Table 1

Inclusion and Exclusion Criteria

Inclusion Criteria

1.1 Confirmed IPMN histological diagnosis, EUS-FNA Core Biopsy Tissue specimen with plan for pancreatic surgical resection. Histological diagnosis should be within 6 months of entry into protocol.

1.2 Patients must have adequate bone marrow function at study entry.

   4.1.2.1 WBC > 3000
   4.1.2.2 Platelets>100,000/mm3,
   4.1.2.3 Hemoglobin > 10g/dl.

1.3 Patients must have satisfactory renal and hepatic function, defined as

   4.1.3.1 Plasma creatinine of <1.6mg/dl
   4.1.3.2 Total bilirubin < 1.5
   4.1.3.3 Serum AST/ALT < 1.5 x the upper limit of normal..

1.4 Patients with evidence of obstructive lung disease (FEV1 < 80% predicted and FEV1/FVC ratio < 90% of predicted value) as the etiology of a low diffusing capacity will still be eligible as long as the chest radiograph or CT does not demonstrate interstitial changes.

1.5 ECOG performance status 0-1

1.6 The effects of Erlotinib on the developing human fetus at the recommended therapeutic dose are unknown. For this reason and because Erlotinib could be teratogenic, women of child-bearing potential and men taking study drug must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation.

1.7 Ability to understand, as well as sign the written informed consent document.

1.8 Age ≥ 18 years

1.9 If a woman of child-bearing potential, must have a negative pregnancy test prior to study entry. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her study physician immediately.

Exclusion Criteria

2.1 Intake of EGF Receptor antagonist, Erbitux.

2.2 Previous history of sensitivity to Tarceva, Iressa, or Erbitux, such as a rash that is uncontrollable by topical steroids and/or antibiotics.

2.3 Uncontrollable diarrhea of any cause.

2.4 Active keratoconjunctivitis, or corneal surgery in the past three weeks.

2.5 Participants taking a known CYP 3A4 inducer (eg, phenytoin, carbamazepine, St. John’s wort, and rifampin) and medications known to be inhibitors or metabolized by CYP3A4. These inhibitors include erythromycin, clarithromycin and ketoconazole, and patients taking them will be excluded since these drugs may be expected to result in altered exposure of Erlotinib.

2.6 Hospitalization within the past 5 years for mania or for bipolar disease.

2.7 Participants may not be receiving any other investigational pharmaceutical agents.

2.8 Women who are breast-feeding should not receive Erlotinib, as there are no defined studies to indicate the effect on the infant and because no dosing or adverse event data are currently available on the use of Erlotinib in patients <18 years of age.

2.9 Any medical or psychosocial condition that, in the opinion of the investigator, could jeopardize the subject’s participation in and compliance to the study.
### OSI-774

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### OSI-420

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Supplemental Table 2. Plasma and pancreatic tissue concentration levels of Erlotinib (OSI-774) and its major active metabolite (OSI-420).