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Use of Percuteneous Transhepatic Biliary Drainage (PTBD) to reduce the jaundice in biliary obstruction in advanced pancreato-biliary cancers – an experience from a developing country

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Background: Adenocarcinoma of gall bladder accounts for approximately 4% of all malignant neoplasm. Majority of the patients present in late stage with liver metastasis and biliary obstruction. The only treatment option at this stage is to reduce the jaundice by either bypass surgery, ERCP stenting or Percutaneous transhepatic biliary drainage. In some of the cases palliative chemotherapy is possible after reduction of jaundice. The aim of our study was to see affectivity and cost effectiveness of percuteneous transhepatic biliary drainage to reduce jaundice in advanced gall bladder carcinoma.
Material & Methods: During period from January 2005 – December 2008 we selected 300 consecutive cases of advanced gall bladder and pancreatic cancer in the Medical Oncology department of Netaji Subhash Chandra Bose Cancer Research Institute, a tertiary cancer center of Eastern India. The inclusion criteria were performance status more than 50% (Kornofsky) normal renal function (creatinine <2) and absence of ascitis. All patients were tried for PTBD with plastic stents. Mean pre-stenting serum bilirubin was 15.3 mg% (Range 7.2−28 mg%).
Result: Percuteneous transhepatic biliary drainage was possible to introduce in 240 patients (80%). They tolerated the procedure well. In 210 patients (70%) the serum bilirubin came down to less than 2 mg% in average of 14 days (Range 9−22 days). Palliative chemotherapy with Gemcitabine & Cisplatin was possible in those cases. In rest 30% cases jaundice did not come down and those were managed with other palliative care. The cost of average PTBD was 40 Euro (approx) where as metallic stent costs 800 Euro (approx).
Conclusion: We concluded that percuteneous transhepatic biliary drainage was cost effective method of reducing obstructive jaundice in advance gall bladder and pancreatic cancer. It was very much cost effective and well tolerated by the patients.

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Multicenter phase II trial of trastuzumab and capecitabine in patients with HER2 expressing metastasized pancreatic cancer

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Background: Patients (pts) with metastatic pancreatic cancer (PaCa) have a dismal prognosis with systemic chemotherapy being of little benefit. New therapeutic options are therefore urgently needed. In PaCa overexpression of the epidermal growth factor receptor 2 (HER2) has been reported in up to 82% of cases, suggesting its use as a therapeutic target. Therefore, this phase II study was conducted to determine the efficacy and toxicity of capecitabine (CAP) and trastuzumab (TRAS) in pts with metastatic PaCa.
Material and Methods: Eligible patients had histologically confirmed metastatic pancreatic adenocarcinoma. The primary endpoint was progression free survival (PFS) after a treatment period of 12 weeks. Pts with PaCa immunohistochemically (IHC) overexpressing HER2 grade 3 or grade 2 with gene amplification (FISH) received TRAS 4 mg/kg at first infusion followed by weekly 2 mg/kg combined with CAP 1250 mg/m^2 bid day 1−14, q21. The study was prematurely closed due to unexpected low HER2 expression.
Results: Between May 1994 and February 1998 a total of 212 pts, 97 women (46%), 115 men (54%); median age 64 years (38−86) were screened for HER2 expression at 9 german institutions. In 207 pts the tumor specimens could be assessed for HER2 expression and gene amplification. In IHC 83 (40%) were grade 0, 71 (34%) grade 1, 31 (15%) grade 2, and 22 (11%) grade 3, respectively. One IHC grade 2 and all grade 3 specimens showed gene amplification. From the 23 pts with HER2 gene amplification 17 could be assessed for response to treatment and toxicity in an intention-to treat analysis. Reported grade 3/4 toxicities in 88 cycles of chemotherapy were: leucopenia 6%, anemia 0%, thrombocytopenia 0%, diarrhea 6%, nausea 6%, hand-foot syndrome 6%. There had been no TRAS-attributable cardiac toxicity. The PFS after 12 weeks had been 24% and the median overall survival 211 days.
Conclusion: In conctrast to previous findings, this multi-center study demonstrates HER2 overexpression and gene amplification in only 11% of patients with metastatic PaCa. This discrepancy can be explained by the use of standardized test methods and the examination of a large unselected cohort in this study. Due to the low incidence of HER2 overexpression only 17 pts could be treated with CAP and trastuzumab. Although the therapy was well tolerated, PFS and OS did not perform favourably compared to standard gemcitabine chemotherapy. Due to the low HER-2 overexpression found in this study we do not recommend further evaluation of anti-HER2 treatment in pts with metastatic PaCa.

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Erlotinib (E) combined with fixed dose-rate gemcitabine (FDR-Gem) as first-line treatment for advanced adenocarcinoma of the pancreas (PDAC): preliminary results from a multicenter phase II study

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Background: E combined with weekly Gem infused over 30 min provides a small, but statistically significant, survival advantage in advanced PDAC. Building on our previous experience with FDR-Gem, we have assessed activity and tolerability of E combined with FDR-Gem as first-line treatment for advanced PDAC.
Material and Methods: FDR-Gem was given weekly at 1000 mg/m^2, infused over 100 min; E was given orally at 100 mg/d, w/o scheduled interruptions. Primary endpoint was 6-month PFS rate. Secondary endpoints were ORR (RECIST criteria), toxicity, OS and QoL.
Results: From May 2007, 44 pts were enrolled (eligible: 43 pts); 38 pts with measurable disease are currently evaluable (M/F: 20/18; median age: 64 yrs, range: 35−81; median baseline CA19.9: 852 U/mL, range: 1–49483; locally advanced/metastatic: 4/34). PR was obtained in 3/38 pts (8%); 50% of pts achieved SD and 42% had PD. Overall disease control rate (DCR) was 58%. Clinical benefit was achieved in 13/32 pts (41%). Treatment was very well tolerated with only 3 pts (8%) experiencing G4 toxicity (elevated transaminases, 1 pt; neutropenia, 2 pts); the most common grade 3 toxicities were neutropenia (16%), anemia, thrombocytopenia, and elevated transaminases (8% each). Median PFS was 14 wks (95% CI: 8−21) and median OS 22 wks (95% CI: 4−39). Cutaneous toxicity (any grade) significantly correlated with DCR ($p = 0.01$). Cutaneous toxicity and a decline >25% in CA19.9 levels were the only independent predictors of longer OS ($p = 0.05$ and $p = 0.042$, respectively) at multivariate analysis. Cutaneous toxicity was also the strongest predictor of longer PFS ($p = 0.002$), together with female sex ($p = 0.042$), DCR ($p = 0.021$), and CA19.9 reduction ($p = 0.067$). Pts experiencing cutaneous toxicity had significantly longer PFS (median 30 wks, 95% CI 3−57, vs. 10 wks, 95% CI 9−11, for patients with and w/o cutaneous toxicity, respectively, Log-rank $p = 0.001$) and OS (median 50 wks, 95% CI 37−63 vs. 14 wks, 95% CI 8−20, respectively, Log-rank $p = 0.01$).
Conclusions: E combined with FDR-Gem is feasible and well-tolerated. While overall results do not appear dramatically different from those obtained with Gem monotherapy, there is a clear, highly significant (from both a statistical and a clinical standpoint) advantage for pts developing E-related cutaneous toxicity. Further investigation of pharmacodynamically-based strategies (e.g. dose-to-rash) aimed at optimizing E treatment is warranted.