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Cost Benefit Analysis of Laboratory Directed Chemotherapy for Advanced Pancreatic Cancer in the US and Brazilian patients.

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Abstract:
Background: Precision medicine offers improved response rates (RR) & cost containment. Pancreatic cancer (PC) with Stage IV 5-yr survival of 1-2% is ideal for strategies that pre-select responsive patients (pts) yet actionable molecular targets are few. Phenotypic assays, with the capacity to examine cytotoxic & targeted agents, the subject of prior meta-analysis (Apfel, Proc. ASCO, 2013), provided a 2.04 fold improvement in (RR) ($p<0.001$) & 1.44 fold improvement in 1-yr survival ($p=0.02$) in 2581 pts. **Methods:** We applied Ex Vivo Analysis of Programmed Cell Death (EVA-PCD) (Nagourney, Anticancer Res, 2012) in 23 US & Brazilian pt. tumors to identify the most active drugs, then used literature (RR) of standard PC regimens & hospital pharmacy charges/2 cycles ($ or $R/mg) @ 1.7 m2 (BSA) for predictions. **Results:** Drug selection frequency (N/%), RR (post-test) & cost/2-cycles reveal: CDDP + Gemcitabine 4/23 (17.9%); RR = 40.8%; $534/R$5748; FOLFIRINOX 8/23 (37.7%) RR = 63.4%, $2988/R$27,592; GTX 2/23 (8.6%) RR = 40.8%; $6538/R$31,776; nab-Paclitaxel + Gemcitabine 3(13%) RR =46.9%, $13,480/$R239,548; CDDP + Gemcitabine + Capecitabine 4/23 (17.9%) RR = 40.8% $2838/R$31,948; 5-FU 2(8.6%) RR = 20% $306/R$10,448. Costs include EVA-PCD @ $4000/pt ($92,000/23) but no growth factors, anti-emetics, infusion pumps or hospital stays. As nab-Paclitaxel use in Brazil is off label, skewing costs, the cost/response analyses use only US $ in final comparisons. Weighted RR for EVA-PCD selected drugs = 47.6% at aggregate 2-cycle costs for all 23 (+EVA-PCD) = $184,096 ($16,736/response, compared with FOLFIRINOX, RR = 31% aggregate 2-cycle cost ($68,724 ($9817/response) and nab-Paclitaxel + Gemcitabine, RR = 23%, aggregate 2-cycle cost $310,040 ($62,008/response). **Conclusions:** Clinically validated drug selection methods can provide superior RR in PC at comparable or lower costs/response. As a non-recurring cost, EVA-PCD savings improve over successive cycles. Including growth factors & toxicity of intensive regimens enhances EVA-PCD savings. Finally phenotypic platforms like EVA-PCD have the potential to improve pt. selection, contain costs, reduce futile care & streamline drug discovery.