

Journal of Gastrointestinal Surgery
Proceedings of the 46th Annual Pancreas Club Meeting
 --Manuscript Draft--

Manuscript Number:	
Full Title:	Proceedings of the 46th Annual Pancreas Club Meeting
Article Type:	Original Article
Keywords:	Pancreas Club; Pancreatic Cancer; Laparoscopic Pancreaticoduodenectomy; Tumor Biology; Surgical Quality
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Proceedings of the 46th Annual Pancreas Club Meeting

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ABSTRACT:

The 46th Annual Pancreas Club meeting was held May 18th and 19th at the Hyatt Regency Mission Bay in San Diego, California. A brief summary of the meeting including an overview in Table form is presented below.

REPORT:

The 46th Annual meeting of the Pancreas Club consisted of 51 oral presentations and 98 posters culled from a record number of 218 abstracts; 100 institutions from 18 countries were represented. Two hundred seventy eight pancreatologists are active members of the Pancreas Club. An overview of the oral presentations is summarized in the table; abstracts for all oral presentations and posters are available at the pancreas club website, www.pancreasclub.com/final-program/. Highlights from each session are presented below.

SESSION #1: Cancer Clinical/Translational/Neuroendocrine Tumors/Emotional Impact of Pancreatic Cancer.

The highlight of this session was two papers drawing attention to the emotional impact of pancreatic cancer. Paper #8; THE EFFECT OF DEPRESSION ON DIAGNOSIS, TREATMENT, AND SURVIVAL IN PANCREATIC CANCER was presented by Boyd on behalf of her colleagues from the University of Texas Medical Branch, Galveston. These authors highlighted a high preexisting incidence of depression in pancreatic cancer patients. They noted that patients who are depressed are less likely to receive treatment and perhaps not surprisingly had a significantly decreased survival relative to those who are not depressed. Vigorous discussion pointed out the fact that these data paralleled similar outcomes observed in patients with dementia. A question was raised regarding changes seen over the 25 year time period of the study; the authors were not able to identify any changing trends in the incidence of depression over this time. The coexistence of pain with depression was pointed out, as was the

lack of difference in depression incidence by race (which was included in the author's regression analysis). Finally, a question highlighted the fact that depression (despite this startlingly high incidence) may actually be underreported. It is at least clear that depression in pancreatic cancer patients is overlooked, not prioritized, and represents a potential area for clinical intervention that may substantially improve patient care outcomes.

The subject of fear of cancer recurrence and quality of life among survivors of pancreatic and periamplary neoplasms from the MD Anderson Cancer Center in Houston was examined in Paper #9 entitled FEAR OF CANCER RECURRENCE AND QUALITY OF LIFE AMONG SURVIVORS OF PANCREATIC CANCER. The authors identified 30% of long term cancer survivors as having a pathologic fear of cancer recurrence. Subsequent discussion highlighted the fact that therapy consists of education as well as increased awareness for a surveillance strategy. A question regarding whether depression trumped KRAS gene mutation and tumor biology in terms of potential therapeutic intervention highlighted the point that screening for depression is inexpensive and treatment is relatively easy compared to traditional cytotoxic chemotherapeutics and biologic agents typically used to destroy tumors.

SESSION #2: Cancer, Basic and Translational

Paper #10; CLINICAL IMPLICATIONS OF THE SEQUENCING OF THE EXOMES OF ALL OF THE MOST COMMON TYPES OF PANCREATIC NEOPLASMS was presented by Dr. Christopher Wolfgang from Johns Hopkins Medical Institute. This outstanding review of recent genome level discoveries highlighted their impact on pancreatic cancer diagnosis and treatment. For example, the discovery of PALB2 as a familial pancreatic cancer gene has implications for genetic counselors in terms of breast, ovarian and pancreatic cancer screening. In addition, the small percentage of patients with PALB2 mutations develop tumors with increased sensitivity to mitomycin C. Sequencing of the pancreatic neuroendocrine neoplasm genome has led specifically to the discovery to mTOR mutations, which have been translated

already to clinical applicability with everolimus. Finally, discovery of GNAS mutations in IPMN has shown great promise in differentiating IPMN from serous cystadenomas. The review of these exciting findings nicely highlighted contemporary advances into the era of personalized medicine.

SESSION #3: Cancer Basic

This session featured two basic papers that were directed at determining genetic profiles associated with improved survival in pancreatic cancer. Paper #17; GENETIC VARIANTS IN THE NFkB PATHWAY PREDICTS SURVIVAL IN PATIENTS WITH SURGICALLY RESECTED, LOCALLY ADVANCED AND METASTATIC PANCREATIC CANCER was presented by Dr. Kay Reid-Lombardo on behalf of her colleagues at the Mayo Clinic. This work examined 102 candidate genes and identified two single nucleotide polymorphisms (SNPs – specifically MAPK81P1 and SOCS3) in the NFkB pathway that were associated with improved overall survival in patients with resected pancreatic cancer. Each SNP was associated individually with an improved overall survival at 6 and 18 months but having both alleles provided a median survival of 4 years. The authors suggested that polymorphisms in these genes might be used to determine who would be best treated with surgical resection in the future. Discussion identified the most significant potential difficulty in these types of studies: the problem of false positive associations (as the technique involves examining thousands of polymorphisms). The authors addressed this difficulty by using very strict statistical criteria (very low p-values) to determine statistical associations. Validation studies using additional pancreatic cancer samples from other centers would be necessary to more definitively demonstrate the potential prognostic utility of these SNPs.

Paper #18 GENE EXPRESSION MOLECULAR PROFILES ASSOCIATED WITH CLINICOPATHOLOGICAL CRITERIA AND SURVIVAL IN RESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA was presented by Nigel Jamieson from the West of Scotland

Pancreatic Unit in Glasgow. This group performed micorarrays on 48 banked samples of resected pancreatic cancers and 10 matched normal controls and used bioinformatic analysis to correlate with genetic profile with survival. They identified a 107 gene profile that was able to cluster the cohort into long surviving and short surviving subgroups. The use of this profile was then validated in an independent group of 27 additional samples of resected pancreatic ductal adenocarcinoma. Those identified in this validation cohort as short survivors using the 107 gene profile demonstrated a hazard ratio for shortened overall survival of 4.34. The authors identified their work as proof of principal that microarray gene profiling can be used to identified predictors of poor survival and thus to better counsel patients and guide research on therapeutic agents. Discussion highlighted the fact that the 107 gene profile was not evaluated for consistent replicability from tumor to tumor, critical validation in the context of the broad genetic heterogeneity in pancreatic ductal adenocarcinoma.

SESSION #4: Cancer Clinical\Techniques

The first three papers of this session sparked significant discussion from the audience. The first two presented evidence supporting the use of minimally invasive techniques in pancreatic head resection. Paper #26 MAJOR COMPLICATION AND OPEN APPROACH ARE PREDICTORS OF PROLONGED HOSPITAL STAY AFTER PANCREATICODUODENECTOMY was presented by Dr. Michael Ferrara on behalf of his colleagues at the Mayo Clinic. This was a retrospective review of their pancreaticoduodenectomy series over the years from 2007 through 2010 including 125 laparoscopic pancreaticoduodenectomies and 402 open pancreaticoduodenectomies. They included readmissions to 30 days post operatively and graded complications by the Clavien-Dindo method. The authors acknowledged their selection bias of more pancreatic cancers in the open resection group. There was also noted, however, a benefit to the laparoscopic approach of 3 hospital days stay including 30 day readmissions (8 days vs. 11 days). On multivariate modeling, Clavien grade > III complication and the open

approach were independent predictors of prolonged hospital length of stay. This paper was followed by a brisk discussion which identified the importance of this work given anticipated changes in reimbursement for readmissions but also brought out several potential limitations: the potential for selection bias, the need for a more detailed comparison of costs between the two approaches, the fact that 30 day readmission is potentially too short to correctly identify differences in overall length of stay (benefit to the minimally invasive approach may actually be greater when a 90 day readmission horizon is used).

Paper # 27 ROBOTIC PANCREATECTOMY: EXPERIENCE IN 80 CONSECUTIVE PATIENTS was presented by Ugo Boggi on behalf of the group from Pisa, Italy. This series consisted of 30 pancreaticoduodenectomies, 36 distal pancreatectomies, 6 total pancreatectomy, 5 enucleations and 3 central pancreatectomies done over 3 years between 2008 to 2011. The authors showed an impressive video of a portal vein resection done robotically and their results in terms of operative time and post operative morbidity (overall complication rate, fistula rate) were compared to published experiences. They identified that 12% of the operative time was spent in changing robotic instruments and placing needles but concluded that the approach was safe with morbidity rates comparable to those for procedures done open. Several questions from the audience addressed the learning curve that the authors experienced. Dr. Boggi described starting with open surgery and then doing simpler cases laparoscopically (donor hepatectomy) prior to moving into using the robot. Other questions were directed toward understanding selection criteria for robotic pancreaticoduodenectomy and for more detail regarding who is there to assist the robotic surgeon. The authors reported having two attendings in the room for each case with one at the console and one at the bedside. They described selecting patients for pancreaticoduodenectomy who had no central obesity.

Paper #28 DUCT-TO-MUCOSA PANCREATICOGASTROSTOMY REDUCES POSTOPERATIVE PANCREATIC STUMP LEAK RATES AFTER DISTAL PANCREATECTOMY was presented by Dr. Yasushi Hashimoto from Hiroshima. The authors described an interesting approach to mitigating risk of pancreatic duct stump leak following distal pancreatectomy. They present a series of 30 patients who underwent distal pancreatectomy and had their pancreatic tail stump managed with a two layer duct to mucosa pancreaticogastrostomy. They compared leak rates in this group to a historical cohort who had their pancreatic tails oversewn. The authors report an improvement in the rate of clinical significant (ISGPF grade B and C) pancreatic fistulas (3% vs. 20%). The authors did identify a longer operative time in the pancreaticogastrostomy group (237 minutes vs. 198 minutes). There were several questions from the audience following this presentation. Concern was raised for an increase in severe complications with adding pancreaticogastrostomy to distal pancreatectomy with the feeling that the leaks will be mixed containing gastric contents and pancreatic juice. The authors answered that this was not something observed in their study and they felt safe pursuing it given that gastric bacterial counts are relatively low. Another question related to improvement in the pancreatic function (any less pancreatic enzymatic insufficiency) with their approach. The authors reported no noted improvement.

How I Do It Session: Minimally Invasive pancreaticoduodenectomy: ready for prime time?

Drs. L. William Traverso, Michael Kendrick, and Horacio Asbun, provided insight into application of minimally invasive techniques to pancreatoduodenectomy. Dr. Mark Talamini provided “almost unbiased” commentary. The “How I Do It” session is available on the Pancreas Club website, www.pancreasclub.com.

SESSION #5: Pancreatitis/Clinical and Basic Science Studies

An exciting report from the group in Freiberg, Paper #36, MINIMALLY INVASIVE OPERATIONS FOR ACUTE NECROTIZING PANCREATITIS: COMPARISON OF MINIMALLY INVASIVE RETROPERITONEAL NECROSECTOMY TO ENDOSCOPIC TRANSGASTRIC NECROSECTOMY illustrated the heterogeneity of necrotizing pancreatitis and emphasized the fact that one type of operation does not fit every patient. Comments highlighted the role of ultrasonography (either transabdominal or endoscopic) in terms of distinguishing solid verses liquid necrosis. The authors confirmed that percutaneous radiologic directed drains were used for guidance in their retroperitoneal approach. Dr. Santhi Vege from the Mayo Clinic pointed out the fact that the consensus conference statement regarding necrotizing pancreatitis will be published shortly in the journal *Pancreas*. Questions from the floor asked whether advances in minimally invasive techniques had led to expanding indications for one operation or another (the answer was resoundingly, no). Finally, a representative of the Dutch pancreatitis study group pointed out a major finding of their PANTER trial (which is similar to the original percutaneous drain report of Freeney published in the *American Journal of Radiology* in 1998 and subsequently validated by Horvath and her colleagues in the *Archives of Surgery* 2010) that 30% of patients with necrotizing pancreatitis were adequately treated simply with drain placement alone. The challenge remains to determine which of these patients is which.

SESSION #6: Cancer Clinical/Quality/Margin Status/Down Staging/Adjuvant

The final session of the meeting was focused on new approaches to measuring the quality of our outcomes following pancreaticoduodenectomy. The first paper in the session presented results from a survey administered to the members of the pancreas club by the group at the BI Deaconess and Dr. William Nealon from Vanderbilt. Paper #42 QUALITY ASSESSMENT IN PANCREATIC SURGERY: WHAT MIGHT TOMORROW BRING was presented by Dr. Brian

Kalish. Survey responders identified Multidisciplinary Care and metrics tracking mortality, complication severity and readmission as the most important indicators of quality out come following pancreatic surgery. Patient satisfaction with care, costs of care and demographics were felt to be of limited relevance to quality.

Paper #43, DEFINING QUALITY FOR PANCREATICODUODENECTOMY:SEVERE ADVERSE POSTOPERATIVE OUTCOMES INDLUDING THOSE REQUIRING MULTIPLE READMISSIONS WITH 90-DAYS, PROLONGED OVERALL LENGTHS OF STAY OR MULTIPLE INVASIVE INTERVENTIONS ARE PREDICTABLE was presented by Dr. Karen Sherman on behalf of her colleagues at Northwestern University and The NorthShore University Health System, Chicago, IL. This studied identified limitations to the Clavien-Dino and Accordian grading systems in discriminating acceptable and poor outcomes among patients having grade II and IIIa complications: neither grading system accounts for prolonged readmissions and/or multiple procedures used to manage these complciations. The authors used a modified Clavien-Dindo system to grade outcomes adding readmission lengths of stay out to 90 days post procedure and accounting for multiple invasive interventions in scoring outcomes as good or bad. The redefined a poor outcome as one involving prolonged overall lengths of stay or multipl invasive interventions and they identified advanced age (>75 years), excessive blood loss (>1500 mLs) and prolonged OR time (>8 hours) as independent predictors in of a poor outcome using multivariable regression. A spirited discussion from the audience at the end of this talk raised questions about the validity of the overall length of stay as a metric of quality given that it is so often influenced by the social standing of the patient and the support they have at home. Several audience members asked for greater detail on what was considered a “procedure” used to manage patients with complications; were drain checks considered a procedure. The answer from the authors was no; only new drain placements or formal repositionings were considered

procedures. Several audience members also made a plea for uniformity of method in complication grading in hopes to make separate studies more easily comparable.

The day concluded with the annual banquet honoring Dr. Howard Reber of UCLA for his substantive accomplishments in pancreatology over the past 42 years.

Scientific Session I: Clinical/Translational/Neuroendocrine Tumors/Emotional Impact of Pancreatic Cancer		
1	THE PROGNOSTIC IMPLICATION OF KRAS MUTATION IN AMPULLARY ADENOCARCINOMA: ONLY THE KRASG12D GEONTYPE PREDICTS POOR SURVIVAL	MASSACHUSETTS GENERAL HOSPITAL
2	CORRELATION OF DPC4 STATUS WITH OUTCOMES IN PANCREATIC ADENOCARCINOMA PATIENTS RECEIVING ADJUVANT CHEMORADIATION	JOHNS HOPKINS
3	PROGNOSTIC SIGNIFICANCE OF HUMAN EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (HENT1) EXPRESSION IN PANCREATIC CANCER PATIENT TREATED WITH GEMCITABINE-BASED CHEMORADIOTHERAPY AND AVAILABILIGY OF ENDOSCOPIC ULTRASONOGRAPHY GUIDED FINE NEEDLE BIOPSY SAMPLES	MIE UNIVERSITY, JAPAN
4	ACTIVATION OF THE IL6-R/JAK/STAT PATHWAY IS ASSOCIATED WITH A POOR OUTCOME IN RESECTED PANCREATIC DUCTAL ADENOCARCINOMA	GLASGOW ROYAL INFIRMARY
5	PHASE II TRIAL OF FIXED-DOSE RATE GEMCITABINE, BEVACIZUMAB, AND CONCURRENT 30 GY RADIOTHERAPY AS PREOPERATIVE TREATMENT FOR POTENTIALLY RESECTABLE PANCREATIC ADENOCARCINOMA	UNIVERSITY OF PITTSBURGH
6	COMPARISON BETWEEN MDCT POST-CONTRASTOGRAPHIC PATTERN AND MICROVASCULAR DENSITY (MVD) IN PANCREATIC NEUROENDOCRINE TUMORS: CORRELATION WITH THE NEOPLASMS NATURE	UNIVERSITY OF PISA, ITALY
8	THE EFFECT OF DEPRESSION ON DIAGNOSIS, TREATMENT, AND SURVIVAL IN PANCREATIC CANCER	UNIVERSITY OF TEXAS MEDICAL BRANCH, GALVESTON
9	FEAR OF CANCER RECURRENCE AND QUALITY OF LIFE AMONG SURVIVIOBS OF PANCREATIC AND PERIAMPULLARY NEOPLASMS	MD ANDERSON CANCER CENTER
Scientific Session II: Cancer Basic and Translational		
10	CLINICAL IMPLICATIONS OF THE SEQUENCING OF THE EXOMES OF ALL OF THE MOST COMMON TYPES OF PANCREATIC NEOPLASMS	JOHNS HOPKINS
11	PANCREATIC DUCT GLANDS (PDG) ARE THE ORIGIN OF GASTRIC-TYPE IPMN	MASSACHUSETTS GENERAL HOSPITAL
12	INHIBITOR OF DIFFERTIATION-1 (ID1) EXPRESSION IN PANCREATIC ADENOCARCINOMA EXHIBITS SIGNIFICANT TRANSLATIONAL IMPLICATIONS	UNIVERSITY OF FLORIDA
13	GRANULOCYTE MACROPHASE COLONY STIMULATING FACTOR (GM-CSF)PANCREAS TUMOR VACCINE IN COMBINATION WITH BLOCKADE OF PD-1 IN A PRECLINICAL MODEL OF PANCREATIC CANCER	JOHNS HOPKINS
14	IDENTIFICATION OF NOVEL HIGHLY-SPECIFIC MARKERS OF PANCREATIC CANCER USING GENOME-WIDE SCREENING	JOHNS HOPKINS
15	WHICH IS MORE USEFUL AS A PREDICTIVE MARKER OF ADJUVANT GEMITABINE-BASED CHEMOTHERAPY FOR PANCREATIC CARCINOMA AFTER SURGICAL RESECTION, INTRATUMORAL HENT1 OR RRM1 EXPRESSION	HIROSHIMA UNIVERSITY, JAPAN
16	EPIDURAL USE DURING PANCREATICODUODENECTOMY	OCHSNER CLINIC
Scientific Session III: Cancer Basic		
17	GENETIC VARIANTS IN THE NFKB PATHWAY PREDICTS SURVIVAL IN PATIENTS WITH SURGICALLY RESECTED, LOCALLY ADVANCED AND METASTATIC PANCREATIC CANCER	MAYO CLINIC ROCHESTER
18	GENE EXPRESSION MOLECULAR PROFILES ASSOCIATED WITH CLINICOPATHOLOGICAL CRITERIA AND SURVIVAL IN RESECTABLE PANCREATIC DUCTAL ADEOCARCINOMA	GLASGOW ROYAL INFIRMARY
19	AN ENGINEERED CHIMERIC, FC MUTATED, ANTI-CA19-9 SCFV-FC FOR IMAGING PANCREAS CANCER	UCLA
20	THE FOGOTTEN CORE PATHWAY: RNA-BINDING PROTEIN HUR SUPPORTS POST-TRANSCRIPIONAL REGULATION OF PANCREATIC CANCER CELL METABOLISM	THOMAS JEFFERSON UNIVERSITY
21	STAT3 MEDIATED CHEMORESISTANCE IS DEPENDENT ON ACTIVATED MAPK SIGNALING IN PANCREATIC CANCER	VANDERBILT UNIVERSITY
22	RETHINKING GEMCITABINE AND RADIATION THERAPY FOR PANCREATIC CANCER: TIMING DOES MATTER	THOMAS JEFFERSON UNIVERSITY
23	CORRELATION OF A PERSONALIZED PATIENT-DERIVED PANCREATIC ADENOCARCINOMA XENOGRAFT PROGRAM TO PATIENT OUTCOMES AFTER CURATIVE RESECTION	MD ANDERSON CANCER CENTER
24	FROM TEST TUBES TO CELLS: A SYSTEMATIC, RATIONAL DISCOVERY OF AN FDA	THOMAS JEFFERSON

	APPROVED DRUG FOR THE TARGETED TREATMENT OF PANCREATIC CANCER	UNIVERSITY
25	EMT IN AMPULLARY CANCER	UNIVERSITY OF FREIBURG, GERMANY
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27	ROBOTIC PANCREATIECTOMY: EXPERIENCE ON 80 CONSECUTIVE PATIENTS	UNIV OF PISA, ITALY
28	DUCT-T0-MUCOSA PANCREATICOGASTROSTOMY REDUCES POSTOPERATIVE PANCREATIC STUMP LEAK RATES AFTER DISTAL PANCREATECTOMY	HIROSHIMA UNIVERSITY, JAPAN
29	HEREDITARY PANCREATITIS: ENDOSCOPIC AND SURGICAL MANAGEMENT	INDIANA UNIVERSITY
30	THE UTILITY OF PANCREATIC PROTOCOL COMPUTERIZED TOMOGRAPHY SCANS FOR PREDICTING METASTATIC DISEASE OF PANCREATIC TUMORS: AN UPDATE USING CONTEMPORARY IMAGING TECNOLOGY	JOHNS HOPKINS
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33	PHYSIOLOGICAL AND PATHOLOGICAL EXOCYTOSIS IN ACINAR CELLS EXAMINED IN SITU IN HUMAN PANCREAS SLICES	UNIVERSITY OF TORONTO
35	ISLET CELL AUTOTRANSPLANTATION AND MORBIDITY AFTER OPERATIONS FOR CHRONIC PANCREATITIS	UNIV OF ALABAMA BIRMINGHAM
36	MINIMALLY INVASIVE OPERATIONS FOR ACUTE NECROTIZING PANCREATITIS: COMPARISON OF MINIMALLY INVASIVE RETROPERITONEAL NECROSECTOMY TO ENDOSCOPIC TRANSGASTRIC NECROSECTOMY	UNIVERSITY OF FREIBURG, GERMANY
37	SHORT AND LONG-TERM OUTCOMES FOR PATIENTS WITH AUTOIMMUNE PANCREATITIS TREATED WITH PANCREATIC RESECTION: A MULTI-INSTITUTIONAL STUDY	MAYO CLINIC (ROCHESTER, JACKSONVILLE), MASSACHUSETTS GENERAL HOSPITAL
38	AUTOIMMUNE PANCREATITIS (AIP): SHORT AND LONG-TERM OUTCOMES IN PATIENTS TREATED INITIALLY BY PANCREATICODUODENECTOMY, A COPARATIVE STUDY	INDIANA UNIVERSITY
39	DOES PANCREATIC STUMP CLOSURE METHOD INFLUENCE DISTAL PANCREATECTOMY FISTULA RATE	INDIANA UNIVERSITY
40	GREATER VOLUME RESUSCITATION DURINGTHE FIRST 24 HOURS AFTER ERCP IS ASSOCIATED WITH A LESS SEVERE COURSE OF POST-ERCP PANCREATITIS	INDIANA UNIVERSITY
41	TEMPORAL TRENDS IN THE USE OF DIAGNOSTIC IMAGING FOR PATIENTS WITH PANCREATIC CONDITIONS: HOW MUCH IONIZING RADIATION ARE WE USING?	UNIVERSITY OF CAGARY, INDIANA UNIVERSITY
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44	PANCREATICODUODENECTOMY AT HIGHT VOLUME CENTERS-SURGEON VOLUME GOES BEYOND THE LEAPFROG CRITERIA	UNIVERSITY OF SOUTH FLORIDA
45	READMISSION FOLLOWING PANCREATECTOMY: WHAT CAN WE DO BETTER?	BETH ISRAEL DEACONESS MEDICAL CENTER, UNIVERSITYOF PENNSYLVANIA
46	RESIDUAL TUMOR AFTER PANCREATICO-DUODENECTOMY: THE IMPACT OF A BRAND NEW STANDARDIZED TECHNIQUE TO EVALUATE RESECTION MARGINS STATUS	UNIVERSITY OF ROME, ITALY
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49	RADIOGRAPHIC DOWNSTAGING OF BORDERLINE RESECTABLE PANCREATIC CANCER IS RARE FOLLOWING NEOADJUVANT THERAPY	MD ANDERSON CANCER CENTER
50	INDUCTION CHEMOTHERAPY FOLLOWED BY RADIATION THERAPY IS ASSOCIATED WITH BETTER SURVIVAL FOR PATIENTS WITH LOCALLY ADVANCED PANCREATIC CANCER	JOHNS HOPKINS
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*Abstracts 7 and 34 were withdrawn		

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