PD-1 blockade in MMR deficient cancers
GI tumors ‘highly responsive’ to checkpoint blockade

Modified FOLFOX7, FOLFIRI in advanced gastric cancer
Comparable PFS, disease control seen with both regimens

Short-course chemoradiation in advanced rectal cancer
Regimen effective, less toxic than standard 5-week regimen

Preoperative chemoradiation in resectable esophageal cancer
Trial compares carboplatin/paclitaxel with oxaliplatin/capecitabine
PHASE III

BRIGHTER Trial

A Study of Napabucasin Plus Weekly Paclitaxel to Treat Gastric and Gastroesophageal Junction (GEJ) Cancer

Eligible Patient Population

• Unresectable metastatic Gastric or GEJ adenocarcinoma
• One prior line of platinum/fluoropyrimidine-based therapy in advanced setting
• Neoadjuvant taxane allowed if progression occurred ≥6 months following completion of therapy
• PS 0 or 1

Primary Endpoint

Overall survival

Secondary Endpoints

• Progression-free survival
• Objective response rate
• Disease control rate
• Safety

1:1 RANDOMIZE

Napabucasin* + Paclitaxel**

Placebo + Paclitaxel**

*Napabucasin 480 mg PO BID.
**Paclitaxel 80 mg/m2 IV 3 out of 4 weeks.

Key Inclusion Criteria

• Cytologically or histopathologically confirmed advanced gastric or GEJ adenocarcinoma that is metastatic or locally advanced and unresectable
• Failed treatment with one regimen containing at least a platinum/fluoropyrimidine doublet for unresectable or metastatic disease. Treatment failure is defined as progression of disease (clinical or radiologic) during first-line treatment for unresectable or metastatic disease, or ≤6 months after last dose of first-line treatment
• Paclitaxel therapy is appropriate for the patient and is recommended by the Investigator

Study Locations

Global sites currently include Australia, Belgium, Brazil, Canada, Czech Republic, Estonia, France, Germany, Hungary, Israel, Italy, Japan, Korea, Lithuania, Poland, Romania, Russian Federation, Spain, United Kingdom, and the United States.***

About Napabucasin (formerly BBI608)

Napabucasin is an orally administered investigational agent not approved by the U.S. FDA, designed to inhibit cancer stem cell pathways by targeting STAT3.

Boston Biomedical’s mission is to develop the next generation of cancer therapeutics by creating drugs designed to target cancer stem cell pathways.

For additional information please see www.clinicaltrials.gov/show/NCT02178956 or contact us at info@bostonbiomedical.com.

WEB WATCH

Visit Healio.com/Hematology-Oncology for in-depth coverage of colorectal cancer in the At Issue: Colorectal Cancer resource center, dedicated to providing coverage of the most important issues in the management of this disease. The resource center provides exclusive video perspectives from key opinion leaders regarding trends in patient care, recent study findings and progress in colorectal cancer research.

Findings from Gastrointestinal Cancers Symposium focus on therapeutic developments, directions for research

Advances in the treatment of colorectal, esophageal, gastric, gastroesophageal junction and neuroendocrine cancers were highlighted during this year’s Gastrointestinal Cancers Symposium, held in San Francisco under the theme “Insight on novel mechanisms and precision care.” Gastroenterologists, oncologists and surgeons gathered from January 21-23 for lectures on immunotherapy in GI cancers, the role of chemoradiation in rectal and esophageal cancers and the treatment of gastric cancer and midgut neuroendocrine tumors.

Results of the CheckMate-032 trial demonstrated that nivolumab monotherapy was well tolerated and effective in patients with advanced, metastatic gastric or gastroesophageal junction cancers who were heavily pretreated. The NEOSCOPE trial, a phase 2 investigation in patients with resectable esophageal adenocarcinoma, showed a superior pathological complete response with pre-operative carboplatin/paclitaxel-based chemoradiation compared with oxaliplatin/capecitabine-based chemoradiation.

This HemOnc Today supplement provides readers with an overview of the most noteworthy findings presented at the Gastrointestinal Cancers Symposium. Perspectives from physicians in the gastroenterology and hematology/oncology communities provide further insight into the impact these findings may have in everyday practice.

— The Publishers of HemOnc Today

Visit Healio.com/Gastroenterology to hear more from Daniel V.T. Catenacci, MD, a GI medical oncologist at the University of Chicago, and other experts in GI oncology.

The Yonsei University Gastric Cancer Prediction Tool is “a new nomogram for helping to determine patient risk of recurrence after surgery.”

— DANIEL V.T. CATENACCI, MD

© Copyright 2016, SLACK Incorporated. All rights reserved. This part of this publication may be reproduced without written permission. The ideas and opinions expressed in this HemOnc Today* supplement do not necessarily reflect those of the editor, the editorial board or the publisher, and are not intended to substitute for the advice of the editor, the editorial board or the publisher.

SLACK* Publishing the best in health care information and education worldwide

© 2016 Boston Biomedical

Syntime Discovery Pharma Global Oncology
www.bostonbiomedical.com
Programmed death-1 blockade demonstrated promising activity in mismatch repair deficient gastrointestinal cancers in a phase 2 trial, according to data presented at the Gastrointestinal Cancers Symposium.

"Mutations have been shown to encode proteins that can be recognized and targeted by the immune system. The average tumor has dozens of somatic mutations. However, mismatches repair deficient tumors harbor thousands of mutations, and this led to the hypothesis that the immune augmentation with PD-1 blockade could be highly effective in mismatch repair deficient tumors," Dung T. Le, MD, from the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, said during her presentation.

"The frequency of mismatch repair deficiency varies depending on the reports for different histologies, but in certain histologies there is a higher proportion, including colorectal cancer, endometrial cancer, gastric, ampullary and small bowel cancer," Dr. Le and colleagues looked, in a very small group of patients of various types, at the frequency of so-called mismatch repair deficiency, which relates to the degree of genetic abnormalities and, ultimately, the degree to which cancers can generate an immune response.

What they found was a very striking correlation between this finding of mismatch repair deficiency and the ability of immunotherapy, in the form of PD-1 blockade, to work.

This is going to provide an important clue, going forward, in terms of what patients might be amenable to immunotherapy, how immunotherapy might work and what types of immunotherapy might work. I think it will be very foundational information to advancing this field within gastrointestinal oncology.

Vincent J. Picozzi, MD
Virginia Mason Medical Center

Disclosure: Picozzi reports stock and ownership interests in AbbVie, Amgen and Johnson & Johnson; honoraria from Colpex, consulting or advisory roles for Halozyme and Taiho Pharmaceutical; and research funding from Adura Biotech, Clavis Oncology, FibroGen, Immunomedics, Incyte, Oncology and Therapeutics Health.

Advanced gastric cancer patients may have better overall survival with mFOLFOX7 followed by mFOLFIRI

First-line treatment with modified FOLFOX7 or modified FOLFIRI chemotherapy resulted in comparable progression-free survival and disease control rate among patients with locally advanced gastric adenocarcinoma, while a subgroup of patients who received mFOLFOX7 followed by mFOLFIRI had better overall survival, according to phase 2 study results presented at the Gastrointestinal Cancers Symposium.

"In this clinical trial we wanted to compare FOLFIRI and FOLFOX in advanced gastric cancer," Feng Bi, MD, chairman of the committee of molecular targeted therapy and professor of oncology at West China Hospital of Sichuan University, said during his presentation. The primary endpoint was PFS, and secondary endpoints were OS and disease control rate, he said.

Aiming to compare mFOLFIRI and mFOLFOX7 as first-line therapies, Bi and colleagues performed an open, randomized study of patients with metastatic gastric cancer to modified FOLFOX7 vs. modified FOLFIrI, and for patients who progressed, second-line treatment was then the opposite regimen that was initially received. This was a phase 2 randomized trial that randomized patients with advanced gastric cancer to modified FOLFOX7 vs. modified FOLFIRI, and for patients who progressed, second-line treatment was then the opposite regimen that was initially received. The primary end-point was OS and disease control rate, and secondary endpoints were OS and disease control rate, he said.

The researchers found there was no significant difference in progression-free survival between groups. The median progression-free survival rate was 2.9 (range, 1.9-4.1) months for arm A compared with 4.1 (range, 3.2-4.8) months for arm B (P = .109).

Furthermore, there was no significant difference in disease control rate between groups (59.3% vs. 66.3%; P = .85).

The median overall survival was also not significantly different between groups (9.9 [range, 6.3-13.5] months vs. 12 [range, 10.3-13.7] months; P = .431).

However, in the subgroup of patients who completed both treatment lines per protocol, median overall survival was 11 (range, 5.1-16.9) months for those who received first-line mFOLFOX7 and second-line mFOLFOX7, compared with 20.2 (range, 13.4-26.6) months for those who received first-line mFOLFOX7 and second-line mFOLFIRI (P = .03).

"In conclusion, there was no significant difference in the PFS and disease control rate for FOLFOX7 and FOLFIRI as first-line treatment for advanced gastric cancer," Bi said. However, modified FOLFOX7 followed by modified FOLFIRI might have a better OS, which needs a large sample to validate." – by Adam Leitenberger

Reference:

Disclosure: The researchers report no relevant financial disclosures.

Perspective

This was a phase 2 randomized trial that randomized patients with advanced gastric cancer to modified FOLFOX7 vs. modified FOLFIRI, and for patients who progressed, second-line treatment was then the opposite regimen that was initially received. About 200 patients were enrolled and about 130 patients were ultimately included for analysis.

The main findings of the trial showed that, really, there was no difference in terms of protocol adherence or in terms of ultimate survival. However, on subgroup analysis, for patients who completed both first-line and second-line chemotherapy regimens, they actually found an improved median overall survival for patients who started with modified FOLFOX7 and then received modified FOLFIRI vs. patients who started with modified FOLFIRI and then received modified FOLFOX7.

The median survival was 20 months vs. about 11 months. That is certainly a large difference in overall survival, and these results, at this point, are at best hypothesis generating, but certainly reinforce the standard of care starting with FOLFOX chemotherapy, with FOLFIRI as a salvage regimen. I think further testing will be needed to determine if this superior survival is indeed true.

Daniel Chang, MD
Stanford University

Disclosure: Chang reports no relevant financial disclosures.
Nivolumab monotherapy was well tolerated and showed antitumor activity in patients with advanced and metastatic gastric or gastroesophageal junction cancers who received heavy pretreatment, according to initial results from the CheckMate-032 trial presented at the Gastrointestinal Cancers Symposium.

“Nivolumab is a fully human anti-CD80/CD86 monoclonal antibody with a favorable safety profile and demonstrated efficacy in multiple tumor types,” Dung T. Le, MD, from the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, said during her presentation. “The phase 1/2 randomized, open-label CheckMate-032 trial is a multimarker cohort study including patients with lung, breast, bladder, pancreatic and ovarian cancer who received nivolumab monotherapy or in combination with ipilimumab. The results presented today are the preliminary results for patients with advanced gastric and gastroesophageal junction cancer who received nivolumab monotherapy.”

Fifty-nine patients from the US and European Union received nivolumab monotherapy (Opdivo, Bristol-Myers Squibb; 3 mg/kg IV every 2 weeks) until disease progression or intolerable toxicity. PD-L1 positivity was not mandated for inclusion. A median of 2 doses were administered (range, 1-31).

Overall, 76% of patients were men, median age was 60 years (range, 29-80 years), 83% had been treated with at least two prior regimens, 15% had esophageal cancer, 53% gastroesophageal junction cancer, and 31% gastric cancer.

Objective response rate served as the primary endpoint, while adverse events, overall survival, OS rate, PFS, progression-free survival rate and duration of response served as secondary endpoints.

At the end of the study period (median follow-up, 4.6 months), 7% of patients remained on active treatment, while 78% patients discontinued treatment due to disease progression, 5% due to drug toxicity and 10% for other reasons.

Overall response rate was 14% — with one patient achieving a complete response and seven achieving a partial response — and 11 of the patients had stable disease, with a disease control rate of 32%.

Median time to response was 1.6 months; median duration of response was 7.1 months (95% CI, 0.0-13.2).

Lutathera improves outcomes in metastatic midgut neuroendocrine tumors

T
reatment with 177Lutetium-DOTATATE appeared to improve the overall response rate and prolonged PFS compared with octreotide among previously treated patients with advanced midgut neuroendocrine tumors, according to early results from a phase 3 trial.

Further, “Lutetium-DOTATATE (Lutathera, Advanced Accelerator Applications) therapy demonstrated a trend toward improved OS,” Jonathan R. Strosberg, MD, medical oncologist at Moffitt Cancer Center, told HemOnc Today. “Moreover, there is a very strong suggestion of improvement in OS, with 22 dead in the octreotide arm vs. only 13 with Lutathera. The safety profile of the drug is highly favorable.”

The agent is part of a new class of drugs known as peptide receptor radionuclide therapy, which combines radiotherapy and hormone therapy. In 177Lutetium-DOTATATE, a somatostatin analog attaches to a radioactive molecule, allowing for targeted delivery of radiation to the tumor.

Patients with metastatic midgut neuroendocrine tumors usually receive hormone therapy with a somatostatin analog, such as octreotide or lanreotide.

Because there are no effective second-line treatment options for patients with tumors that stop responding to somatostatin analogs, Strosberg and colleagues sought to compare Lutetium-DOTATATE to octreotide LAR in patients with inoperable and progressive disease.

By February 2015, the investigators identified 230 patients from 51 international sites with grade 1 or grade 2 metastatic midgut neuroendocrine tumors. Researchers randomly assigned them 1:1 to receive four administrations of 177Lutetium-DOTATATE (7.4 GBq) every 8 weeks or octreotide LAR (60 mg) every 4 weeks.

PFS served as the primary endpoint. Secondary endpoints included objective response rate (ORR), OS, toxicity and quality of life.

At the time of the analysis, there were 23 confirmed disease progressions or deaths in the experimental arm vs. 67 in the control arm. The median PFS was not reached for 177Lutetium-DOTATATE, although researchers are estimating that it will reach 40 months, Strosberg said. Median PFS was 8.4 months (95% CI, 5.8-11 months) in the octreotide arm (HR = 0.21; 95% CI, 0.13-0.34).

Lutathera continues on page 14

The presentation by Strosberg and colleagues from the Moffitt Cancer Center is of particular interest and particular value to clinicians. This was a comparison in more than 200 patients of a radioactive form of octreotide with the standard form of octreotide used to treat patients with midgut neuroendocrine cancers. This is a treatment that’s been tested in Europe for the past few years. It’s just now coming to the United States for testing.

In this rather large trial, there was a striking difference in the disease control and time to progression using the radioactive compound as opposed to the standard compound. It is hoped this trial will ultimately show an overall survival advantage to the patients receiving the radioactive compound.

This, I believe, presents an exciting new option for therapy for around the world, but particularly here in the US. The hope is that this agent can be licensed in the near future and made available to our patients.

Vincent J. Picozzi, MD
Virginia Mason Medical Center

Disclosure: Picozzi reports stock and ownership interests in AbbVie, Amgen and Johnson & Johnson; honoraria from Celgene; consulting or advisory roles for Haloysm and Teuto Pharmaceuticals; and research funding from Asturo Biotech, Clovis Oncology, FibroGen, Immunomedics, Incyte, OncosMed and Therametsics Health.
Despite current advances in cancer therapy, tumor recurrence and metastasis remain a clinical challenge.1 Cancer stem cells are a subset of the total cancer cell population that is highly tumorigenic.2,3 Chemotherapy and radiation have been shown to affect the primary tumor, but not the cancer stem cell.4 Many patients with cancer, even though diagnosed early, succumb to the disease because of recurrence and metastasis.5,6 Cancer stem cells are thought to contribute to this recurrence and metastasis.7

Another characteristic of cancer stem cells is that they possess stemness. Stemness distinguishes cancer stem cells from ordinary cancer cells by their ability to continually self-renew, differentiate into cancer cells, migrate, and regrow the tumor.8 Most chemotherapeutic strategies target actively proliferating cancer cells, resulting in bulk tumor shrinkage. Cancer stem cells, however, may be highly resistant to these therapies and may not be eradicated during treatment, resulting in recurrence and metastasis.4,7 Moreover, chemotherapy and radiation have the potential to induce stemness properties in non-stem cancer cells.2,4 Several signaling pathways are involved in the induction and maintenance of stemness in cancer stem cells, including JAK/STAT, Wnt/β-catenin, Hedgehog, Notch, and Nanog.6,10-12

Targeting these aberrant signaling pathways may result in cancer stem cell apoptosis, while reducing the toxicity to normal tissues that is associated with chemotherapy.4

CarPac preop chemoradiation benefits patients with resectable esophageal cancer

After induction therapy, patients with resectable esophageal adenocarcinoma achieved superior pathological complete response with preoperative carboplatin/paclitaxel-based chemoradiation compared with oxaliplatin/capecitabine-based chemoradiation, according to phase 2 study results presented at the Gastrointestinal Cancers Symposium.

“The main objectives of NEO-SCOPE were to evaluate the toxicity and postoperative morbidity and mortality of [carboplatin/paclitaxel and oxaliplatin/capecitabine] based [neoadjuvant chemoradiotherapy] regimens,” Somnath Mukherjee, MD, of the department of oncology, CRUK/MRC Institute for Radiation Oncology, University of Oxford, said during his presentation. “We also wanted to demonstrate the feasibility of recruiting to our neoadjuvant chemoradiation trial in the UK, where neoadjuvant chemotherapy is considered standard of care.”

Aiming to compare the toxicity and efficacy of two preoperative chemoradiation regimens — carboplatin/paclitaxel (CarPac) vs. oxaliplatin/capecitabine (OXCAP)-based chemoradiation — among patients with resectable esophageal adenocarcinoma (stage ≥ T3 and/or ≥ N1), Mukherjee described a survival benefit in the neoadjuvant setting for potentially resectable, locally advanced esophageal cancer.

However, no direct comparison has been done to this date regarding these two concurrent regimens. In looking at the outcomes from this trial, there is a suggestion that perhaps the use of carboplatin and paclitaxel was associated with a higher pathologic complete response rate and an improved R0 resection rate. However, there was more neutropenia seen with the use of carboplatin and paclitaxel when compared with capecitabine and oxaliplatin.

I think that these data are intriguing, but I think that the small numbers render a direct comparison difficult, and it remains difficult to declare a winner, as the small numbers lead to very wide variance in what the true pathologic complete response rate may be. One strategy that was employed by the ALMANACE was evaluating the response based on PET scan to the induction chemoradiation and making a decision then, based on the PET response, as to whether one should continue regimens or switch regimens with the radiologic phase. These results are eagerly anticipated.

In the meantime, I think that carboplatin and paclitaxel remains a very good, neoadjuvant chemoradiation strategy with radiation. Further evaluation of capecitabine and oxaliplatin — or what’s more commonly used in the United States, but these results may lead to increased usage of this method of radiation.

The analysis included data from 515 patients with stage III or stage IV rectal cancer. Researchers randomly assigned 261 patients to 5x5 Gy of radiation and three courses of FOLFIRI oxaliplatin chemotherapy after 1 week of rest. The other 254 patients were assigned to a control group. They received a standard regimen of 50.4 Gy radiation delivered in 28 fractions given simultaneously with F-U, leucovorin, and oxaliplatin.

Researchers noted the addition of oxaliplatin to 5-FU in the control group is not standard practice in the United States due to an increase in toxicity.

Patients in both cohorts underwent surgery approximately 12 weeks after radiation initiation and about 6 weeks following neoadjuvant treatment.

The rate of curative resection served as the study’s primary endpoint. Median follow-up was 35 months.

Fewer patients in the experimental group experienced acute toxicity (75% vs. 83%; P = .006). The rate of grade 3 or worse toxicity was 24% in both groups.

The most common toxicities associated with radiotherapy included diarrhea, inflammation of the bladder and/or rectum and local skin radiation response.

The rate of curative resection was 77% in the experimental group vs. 71% in the control group. The rate of pathological complete response was 16% in the experimental arm and 11.5% in the control arm.

The short-course chemoradiation regimen effective, less toxic for advanced rectal cancer

A short-course 5-day radiation regimen followed by consolidated chemotherapy prior to surgery appeared as effective as, and less toxic than, the standard 5-week chemoradiation course for patients with advanced rectal cancer, according to phase 3 study results. However, the short-course regimen failed to achieve a superior radiologic complete response rate compared with standard chemoradiation.

“There is a great need for improvement of preoperative strategies for patients with locally advanced rectal cancer,” researcher Lucjan Wyrwicz, MD, PhD, head of the medical oncology unit in the department of gastrointestinal cancer at Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, Poland, said in a press release. “The new regimen has similar efficacy but causes fewer side effects and is more convenient for patients. It is also less costly compared to standard chemoradiation, so it may be especially valuable in limited-resource settings.”

Chemoradiation — a standard approach in the United States to shrink tumors and reduce risk for recurrence prior to surgery — consists of 5 weeks of radiation, with concurrent chemotherapy in weeks 1 and 5.

Wyrwicz and colleagues evaluated an experimental regimen that included 5 days of radiation and 6 days of chemotherapy delivered over 7 weeks.

This study demonstrates that short-course radiation followed by chemotherapy can achieve reduction in tumor, as seen in a pathologic complete response of 16%, which is equal to that of chemoradiation. The short course has less acute toxicity than the chemoradiation.

However, we must keep in mind that the chemoradiation included oxaliplatin, which has been shown to increase toxicity of the regimen and is no longer a part of standard chemoradiation. Two previous comparisons of short-course vs. long-course radiation for rectal cancer found no significant difference in later toxicities; however, one study found a small increase in local recurrence in short-course radiation, particularly for distal rectal cancers.

In the current study, the more convenient short course had equal DFS and local failure rate compared with chemoradiation, and there was a trend toward improved OS. The short-course radiation has been more popular in Europe than in the United States, but these results may lead to increased usage of this method of radiation.
Guest Commentary: Update on use of irreversible electroporation for locally advanced pancreatic cancer

Editor’s note: In this guest commentary, Marcovalerio Melis, MD, FACS, discusses irreversible electroporation for locally advanced pancreatic cancer, following a presentation on the topic delivered at the Gastrointestinal Cancers Symposium by Robert C.G. Martin, MD, PhD, FACS, from University of Louisville.

Radical resection remains the only treatment with curative intent for malignancy of the hepato-pancreato-biliary tract. Unfortunately, pancreatic cancer is resectable in only about 10% to 20% of the cases. The vast majority of those malignancies present instead at a locally advanced stage, where metastases to other organs or invasion/proximity of the tumor to vital structures prevents resection with negative margins.

Of the nonresectable pancreatic cancers, nearly half present with involvement of the celiac axis or the superior mesenteric artery, which preclude curative treatment. Locally advanced unresectable pancreatic cancer is associated with poor prognosis (median OS is about 12 months) despite use of chemotherapy and/or conventional radiation therapy. Even many of those patients who are potentially candidates for surgery will present with tumors that, at the time of diagnosis, are abutting mesenteric or celiac vessels. Those tumors, defined as “borderline resectable,” are at high risk for resection with positive microscopic margins. For this reason, borderline resectable cancers are treated with chemotherapy and/or radiation therapy prior to attempting radical resection. Even after neoadjuvant treatment, however, risk for positive resection margins remains significant.

At this time, there is a relevant need for alternative treatments for pancreatic cancer not amenable to radical surgical treatment. Conventional thermal ablation techniques — radiofrequency and microwave — rely on the indiscriminate use of thermal energy to induce necrosis of tumor cells, a process that can result in damage to nearby structures including blood vessels, bile ducts and nerves. In addition, the blood flow of large vessels creates a heat-sink effect that severely inhibits the ability to ablate cancer cells in the vicinity of large vessels. These limitations are especially relevant to the malignancies of the pancreas, which typically lie immediately adjacent to the superior mesenteric vessels, the portal vein and the common bile duct.

Further, the use of ablative therapies in the pancreas has largely been avoided altogether due to the possibility of thermal injury–induced pancreatitis.

Irreversible electroporation (IRE) is a novel ablation technique that uses targeted delivery of high-voltage millisecond electrical pulses, resulting in permanent disruption of the cellular membranes and subsequent apoptosis. This process leads to cell death, but does not involve the extracellular matrix, thus allowing cellular tumor ablation while preserving structural components of tissues; therefore, collagen-based structures such as vessels or the pancreatic duct are not disrupted.

Further, because IRE is not based on thermal damage of cancer cells, the heat-sink phenomenon is not a concern, and even lesions abutting large vessels can be ablated with radical intent. Preliminary studies on swine and then humans have shown the feasibility and safety of this procedure on the liver and pancreas, with no damage of major vessels and pancreatic duct, and no incidence of pancreatitis.

IRE could be an alternative therapy when neither surgery nor traditional ablation can be used for tumors of the pancreas. IRE may offer an additional treatment option to patients who otherwise would have no hope for long-term survival and would be traditionally treated with palliative intent or external radiation or systemic chemotherapy. Until recently, there has been a lack of data on early outcomes (eg, peripерiportal morbidity and mortality rates, effectiveness of ablation) and long-term survival of patients with unresectable pancreatic cancer treated with IRE.

During the recent Gastrointestinal Cancers Symposium in San Francisco, Martin presented his experience with IRE, a technique of which he has been a pioneer. He has developed a new clinical algorithm that includes use of IRE in both patients with borderline resectable and patients with unresectable pancreatic cancer (see Figure).

For patients with unresectable pancreatic cancer, IRE is used as the main treatment strategy (“in situ” ablation). For patients with borderline resectable pancreatic cancer, IRE can be used in addition to surgical resection to “sterilize” from any remnant cancer cells the peripancreatic structures and connective tissues that are not removed by the surgeon.

Martin has now accumulated multi-institutional data on 200 patients with locally advanced pancreatic cancer. In this new report, OS was 28.3 months for patients with borderline resectable pancreatic cancer and 23.2 months in patients with unresectable pancreatic cancer. These numbers compare favorably with the survival of patients treated with chemoradiation alone, which is 13 months in historical controls.

In summary, IRE appears to be a very promising technique that may be used as part of a multidisciplinary treatment strategy in properly selected patients with pancreatic cancer. The initial favorable results of IRE presented by Martin need to be validated in upcoming randomized trials.

Currently, IRE is offered in few tertiary referral centers, including the Perlmutter Cancer Center at NYU Langone.

Reference:

For more information: Marcovalerio Melis, MD, FACS, is associate professor of surgery at NYU Langone’s Perlmutter Cancer Center and chief of surgical oncology at New York Harbor Healthcare System VAMC. He can be reached at marcovalerio.melis@nyumc.org.

Disclosure: Melis reports no relevant financial disclosures.
**PD-1 Blockade**

The objective response rate was 47%; 24% of patients had a complete response while 24% had a partial response, 29% had stable disease, the disease control rate was 76% and median follow-up was 5.3 months. There were responses in patients with gastric, ampullary, small bowel and pancreatic cancers and cholangiocarcinoma, and complete responses occurred in two patients with gastric cancer.

“...PD-1 blockade is non-estimable because it has not been reached. The overall survival is 21 months with an 18-month survival of approximately 86%,” Le said. “In conclusion, [MMR] deficiency is easily determined using existing commercially available tests, and [MMR] deficient GI tumors are highly responsive to checkpoint blockade with anti-PD-1. Clinical benefit is noted across tumor sites with [MMR] deficiency including colon, stomach, duodenum, pancreas, ampullary and bile duct cancers, and biochemical response correlates to the radiographic response.” – by Adam Leitenberger

**Reference:**

**Disclosure:** Le has received research funding and speaking honoraria from Merck. Please see the full abstract for a list of all other researchers’ relevant financial disclosures.

**Nivolumab**

Median OS was 5 months, 6-month OS was 49% and 1-year OS was 36%.

Overall, 39% of tumor samples were PD-L1 positive (1% expression cut-off). The OS rate was 27% among patients with PD-L1 positive tumors compared with 12% among patients with PD-L1 negative tumors.

“Treatment-related [adverse events] were similar to prior nivolumab mono-therapy studies,” Le said. No grade five or treatment-related adverse event or serious adverse event deaths occurred.

Treatment-related adverse events occurred in 69% of patients, most of which were fatigue. Seventeen percent of patients had a grade 3/4 treatment-related adverse event, while 10% of patients had a treatment-related serious adverse event.

“In conclusion, nivolumab monotherapy was well tolerated in patients with metastatic gastric, esophageal or gastroesophageal junction cancers,” Le said. “The [adverse event] profile was similar to those seen in patients with other tumor types. Confirmed response was 14% in heavily pretreated patients in a patient population that consisted of both PD-L1 positive and PD-L1 negative patients; 49% and 36% of chemotherapy refractory patients were still alive at 6 and 12 months, respectively.” – by Adam Leitenberger

**Reference:**

**Disclosure:** Le has received research funding and speaking honoraria from Merck. Please see the abstract for a full list of all other researchers’ relevant financial disclosures.

**Lutathera**

Among the 201 patients who remained evaluable for tumor response, researchers reported 10 (18%) partial or complete responses among those assigned “Lutathera-DOTATATE vs. three (3%) in the control group (P < 0.008).

“That 18% is a pretty impressive number since these tumors are typically unresponsive to systemic therapy,” Strosberg said during a press briefing. “Those numbers are usually in the single digits.”

OS data were not mature at the time of analysis; however, there were 13 deaths in the experimental group and 22 in the octreotide group, which indicates a trend toward improvement in OS (P < 0.019 at interim analysis).

“The new therapy is ... more convenient. It requires only four treatments, as opposed to medications that patients have to take daily over long periods of time,” Strosberg said. “Based on this trial, we hope that Lutathera will be FDA approved and available for treatment of patients in the United States in 2016.” – by Anthony SanFilippo

**Reference:**

**Disclosure:** This study was funded by Advanced Accelerator Applications. Strosberg reports no relevant financial disclosures. Two other researchers report consultant/advisory roles with, stock or other ownership in and research funding from Advanced Accelerator Applications, Genentech/Roche, Guardant Health, Ipsen, Lexicon, Merck, Merinmac, Novartis and Pharm-Olam.

**CarPac**

“The primary endpoint of the study was the rate of pathological complete response,” Mukherjee said. “Secondary endpoints included feasibility of recruiting to our nCRT group; 30-day postoperative mortality was 2.8% and 2.4%, respectively. "About half experienced any postoperative complications," Mukherjee said.

“... Both OXCAP-R-RT and CarPac-R-RT were well tolerated regimens. The postoperative mortality was low. The rate of postoperative complications was similar to that reported in literature.”

— SOMNATH MUKHERJEE, MD

**Common Terminology Criteria for Adverse Events grade 3/4 toxicity rate during chemoradiotherapy was 42.1% for the OXCAP-R-RT regimen and 52.4% for the CarPac-R-RT regimen (P = .358).**

In the OXCAP-R-RT group, 85.7% of patients underwent surgery compared with 95.3% in the CarPac-R-RT group; 30-day postoperative mortality was 2.8% and 2.4%, respectively. “About half experienced any postoperative complications,” Mukherjee said.

**Reference:**

**Disclosure:** Mukherjee reports consulting and advisory roles and receiving honoraria, research funding, travel accommodations and expenses from Celgene. Please see the abstract for a full list of all other researchers’ relevant financial disclosures.

**Short-course**

“Despite the fact [that] the trial was negative — superiority in radical resection rate has not been shown — short-course radiotherapy combined with three cycles of chemotherapy can be recognized as a new standard of treatment of advanced rectal cancer with threatened resection margin,” Wyrwicz said during a press briefing.

“Seventy-three percent of patients in the experimental arm achieved 3-year OS compared with 65% of the control arm (P = .046).

**Reference:**

**Disclosure:** The researchers report no relevant financial disclosures.