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
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.

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PD-1 blockade promising in MMR deficient GI cancers

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, mismatch repair deficient tumors harbor thousands of mutations, and this led to the hypothesis that 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.”

Le and colleagues enrolled three cohorts of patients; cohort A included patients with mismatch repair (MMR) deficient colon cancer, cohort B included patients with MMR proficient colon cancer and cohort C included patients with any MMR deficient solid tumor. All patients were treated with Keytruda (pembrolizumab, Merck) at 10 mg/kg every 2 weeks and were tested for MMR status using standard immunohistochemistry for MMR deficiency or a PCR test for microsatellite instability.

Previous data from this trial was presented at ASCO 2015, which “showed a fair number of patients with responses that appear durable,” Le said. “Since that time we’ve expanded the protocol to allow more patients to enroll in cohort C and today I’m presenting the data on the 17 patients with non-colorectal GI cancer with [MMR] deficiency.”

The median age of these patients was 60 years (range, 34-92 years), 29% were female, 29% had an ECOG performance of 0, four patients had pancreatic cancer, four had ampullary cancer, three had biliary cancer, three had small bowel cancer and three had gastric cancer. All patients had metastatic disease, 65% had liver metastases and the median number of prior regimens was two.

Treatment-related adverse events were comparable to prior pembrolizumab studies; 76% of patients developed treatment-related adverse events, most of which were low grade, while 12% of patients developed grade 3/4 events. Fatigue, thyroid and dermatologic disorders were the most common adverse events.

**Perspective**

This oral abstract, looking at the significance of mismatch repair deficiency in immunotherapy for gastrointestinal malignancies, was particularly exciting. Immunotherapy is taking center stage in all of oncology, really, and is just now coming to gastrointestinal oncology. One of the key questions is how to predict the patients in which immunotherapy might be effective.

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
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**Disclosure:** Picozzi reports stock and ownership interests in AbbVie, Amgen and Johnson & Johnson; honoraria from Celgene; consulting or advisory roles for Halozyme and Taiho Pharmaceutical; and research funding from Aduro Biotech, Clovis Oncology, FibroGen, Immunomedics, Incyte, OncoMed and Theranostics Health.
Advanced gastric cancer patients may have better overall survival with mFOLFOX7 followed by mFOLFIRI

Fist-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 measurable metastatic or recurrent gastric adenocarcinoma who had not received prior treatment. First-line mFOLFIRI was received every 2 weeks by arm A (n = 54) for whom mFOLFOX7 was the second-line treatment, and vice-versa for arm B (n = 74). PFS served as the primary endpoint, while overall survival, disease control rate and toxicity served as secondary endpoints.

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, 6-13.5] 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 mFOLFIRI 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).

Both regimens were well-tolerated and toxicity was acceptable, Bi said. Grade 3/4 adverse events occurred in 53.2% of arm A and in 55.4% of arm B.

“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.
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-program death-1 immunoglobulin G4 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 multitumor 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 locoregionally advanced or metastatic gastric [gastroesophageal junction] cancer who received nivolumab monotherapy.”

Fifty-nine patients from the U.S. 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 five 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).

**Perspective**

The CheckMate-032 and KEYNOTE-028 trials study single-agent, anti-PD-1 antibodies against patients with refractory metastatic adenocarcinoma of the stomach or the gastroesophageal junction and esophagus.

The major take-home point is that this class of drug is active against these types of cancers. Where the response rate is going to sort out after several hundred patients are treated is yet to be seen, but we think that it’s reasonable to assume that there’s a response rate in the 10% to 20% range, at least. That means that these are really worthwhile drugs to study and hopefully go on to registration in this setting.

The main take-home points are that:

A. Not everybody is responding.

B. We don’t know why some people are responding and some people aren’t responding. PD-L1 expression doesn’t seem to be a robust biomarker in these patients and further research is necessary to figure out who is responding and who isn’t responding.

C. We need long-term follow-up to see if the data are going to be anything like melanoma, where there’s a subset of patients who respond for many, many weeks.

There are some phase 3 studies underway in this setting and we very much look forward to those results.

**David P. Ryan, MD**

Massachusetts General Hospital
Harvard Medical School

**Disclosure:** Ryan reports honoraria from UpToDate, consulting or advisory roles for Medimmune, and patents, royalties and other intellectual property from McGraw Hill Chapter Royalties.

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**Nivolumab continues on page 11**
Treatment 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, 177Lutetium-DOTATATE (Lutathera, Advanced Accelerator Applications) therapy demonstrated a trend toward improved OS.

“The 79% improvement in PFS is the largest that we have seen in a randomized neuroendocrine tumor trial,” 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 deaths on 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 177Lutetium-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).

“The 79% improvement in PFS is the largest that we have seen in a randomized neuroendocrine tumor trial.”

— JONATHAN R. STROSBERG, MD
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 NEOSCOPE 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 and colleagues randomly assigned 85 patients (median age, 65 years; 81% men) from 17 centers in the UK to receive either regimen between October 2013 and February 2015.

The CarPac group received AUC2 carboplatin and 50 mg/m² paclitaxel on days 1, 8, 15, 22 and 29, and the OXCAP group received 85 mg/m² oxaliplatin on days 1, 15 and 29 and 625 mg/m² capecitabine twice daily on 6 to 8 weeks after neoadjuvant chemoradiotherapy.

PERSPECTIVE

The NEOSCOPE trial evaluated induction capecitabine and oxaliplatin, followed by a randomization to concurrent capecitabine and oxaliplatin with radiation vs. concurrent carboplatin and paclitaxel with radiation. This is an important evaluation, as capecitabine and oxaliplatin with radiation and carboplatin/paclitaxel with radiation have emerged as two of the more commonly used chemoradiation strategies for esophageal and GE junction cancer. The concept of using a fluoropyrimidine with oxaliplatin has really come to light with the publication of the PRODIGE trial, which showed that it was the same in efficacy as cisplatin and 5-FU but with substantially less toxicity, while carboplatin and paclitaxel has gained acceptance based on the landmark CROSS trial, which demonstrated 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 ALIANCE was evaluating the response based on PET scan to the induction chemotherapy and making a decision then, based on the PET response, as to whether one should continue regimens or switch regimens with the radiation phase. These results are eagerly anticipated.

In the meantime, I think that carboplatin and paclitaxel remains a very good, neoadjuvant chemotherapy strategy with radiation. Further evaluation of capecitabine and oxaliplatin — or what’s more commonly used in the United States, FOLFOX, using the infusion form — rather than the oral form will remain important for further evaluation.

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Disclosure: Hong reports receiving research funding from Novartis.
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 radical resection 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. 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 FOLFOX4 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 5-FU, 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.

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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.

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.

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Disclosure: Krishnamurthi reports no relevant financial disclosures.
Radical resection remains the only treatment with curative intent for malignancy of the hepatopancreato-biliary.

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 injure 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 with external radiation or systemic chemotherapy. Until recently, there has been a lack of data on early outcomes (eg, perioperative morbidity and mortality rates, effectiveness of ablation) and long-term survival of patients with nonresectable 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 modality (“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 had previously shown that, in 54 patients with locally advanced pancreatic cancer, addition of IRE can improve local PFS (14 vs. 6 months), distal PFS (15 vs. 9 months) and OS (20 vs. 13 months) compared with chemoradiation alone.

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. Those 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
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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, one with ampullary cancer and one with cholangiocarcinoma.

“The PFS 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 reports research funding and speaking honorarium from Merck. Please see the full abstract for a list of all other researchers’ relevant financial disclosures.

Lutathera
continued from page 7

Among the 201 patients who remained evaluable for tumor response, researchers reported 10 (18%) partial or complete responses among those assigned 177Lutetium-DOTATATE vs. three (3%) in the control group (P < .0008).

“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 < .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, Merrimack, Novartis and Pharm-Olam.
Despite the fact [that] the trial in the UK, the toxicity of the chemoradiation regimens, postoperative morbidity and mortality, and other efficacy parameters.

Overall, 85% of patients had WHO Performance Status 0, 86% had T3 tumors, 67% had node-positive disease, 84% had lower third or gastroesophageal junction tumors, and the median tumor length was 5.8 cm.

Pathological complete response was achieved in 11.9% of the OXCAP-RT group (13.9% of resected patients) compared with 27.9% of the CarPac-RT group (29.3% of resected patients).

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

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

“… Both OXCAP-RT and CarPac-RT were well tolerated regimens. The postoperative mortality was low. The rate of postoperative complications was similar to that reported in literature. Induction chemotherapy may have contributed to the unexpected high incidence of grade 3/4 neutropenia seen in the CarPac-RT arm. CarPac-RT passed the prespecified efficacy criteria for taking forward to a phase 3 trial. OxCap-RT failed to meet the same criteria,” he concluded.

— SOMNATH MUKHERJEE, MD

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.

If this survival benefit is confirmed with longer follow-up, it might ultimately result in change to the clinical practice,” Wyrwicz said in the release.

A comparable proportion of patients in the experimental and control arms achieved 3-year DFS (53% vs. 52%) and experienced local failure (22% vs. 21%).

The researchers hypothesized that this shorter course of radiotherapy may be especially beneficial to patients with rectal cancer that has metastasized to the liver or lungs who are candidates for disease resection at all sites. This would allow patients to start chemotherapy to control those metastases sooner.

“This method is implemented in the treatment strategy of our patients,” Wyrwicz said in the release. “[It] seems to be feasible and effective in this rare subgroup of patients.” — by Anthony SanFilippo

Reference:

Disclosure: The researchers report no relevant financial disclosures.