

Contemporary Oncology®

Biomarkers, Pathways, and Targeted Therapies®

Articles

LUNG CANCER

Optimizing Immunotherapy in Lung Cancer

Angelica Welch

LYMPHOMA

Gene Expression Model Predicts PFS in Follicular Lymphoma

Jason Harris

PROSTATE CANCER

Degarelix May Reduce Risk of Cardiovascular Events in Prostate Cancer

Angelica Welch

UROLOGY

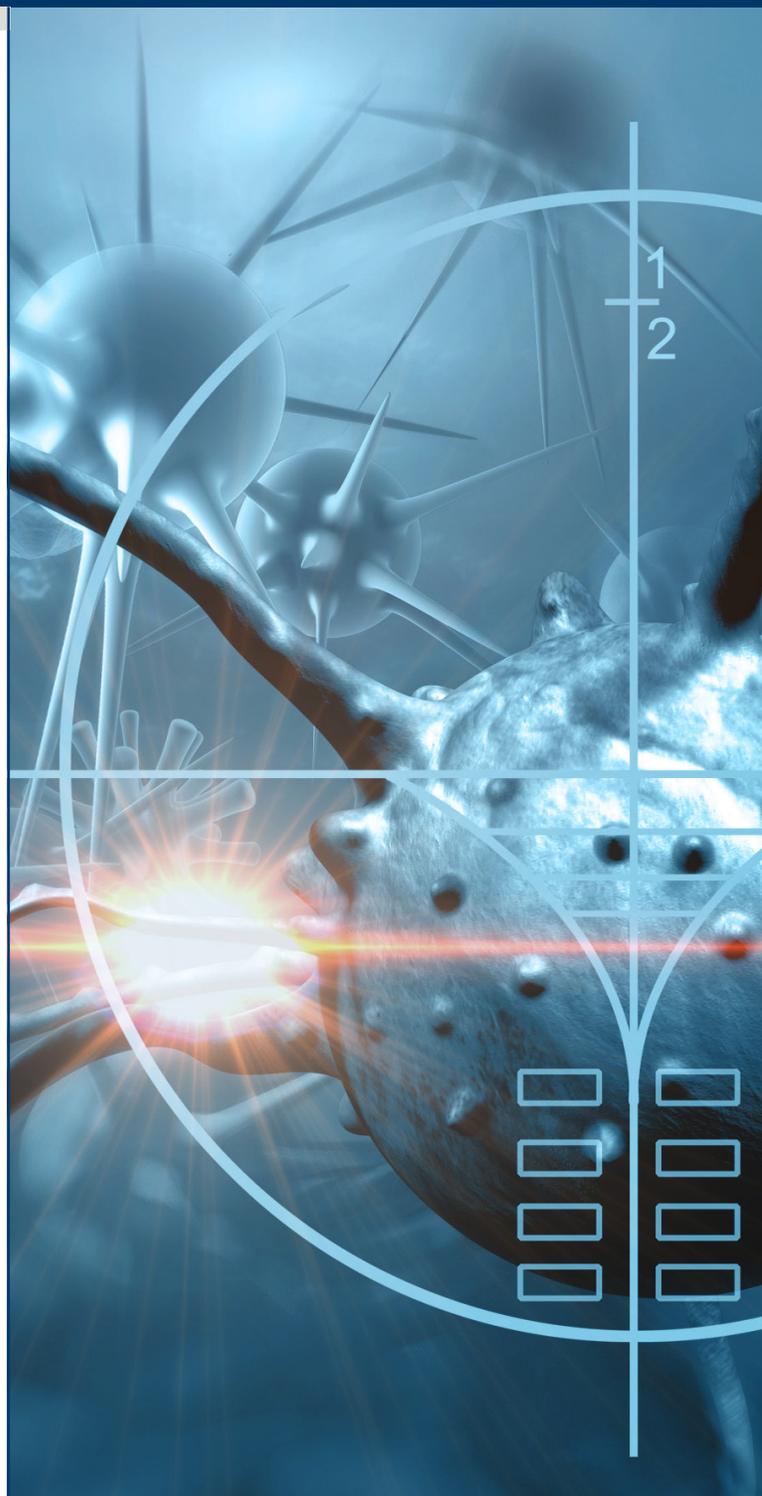
Urology Practice Succeeds With Transparency, Upfront Payment Model

Ariela Katz

ENDOMETRIAL CANCER

No OS Benefit With Chemoradiotherapy in High-Risk Endometrial Cancer

Jason Harris



Optimizing Immunotherapy in Lung Cancer

Angelica Welch

IMMUNOTHERAPY CONTINUES TO establish itself in the treatment of patients with non-small cell lung cancer (NSCLC), yet physicians continue to face challenges in later-line settings with resistance, hyperprogression, and optimal responders.

The second-line PD-1/PD-L1 agents in the landscape include nivolumab (Opdivo), pembrolizumab (Keytruda), and atezolizumab (Tecentriq) for patients who progress on platinum-based chemotherapy. The FDA recently approved durvalumab (Imfinzi) for treating those with locally advanced, unresectable stage III disease who have not progressed following chemoradiotherapy.

Moreover, frontline pembrolizumab is also approved by the FDA for patients with metastatic NSCLC who harbor $\geq 50\%$ PD-L1 expression and as a frontline treatment in combination with carboplatin/pemetrexed, regardless of PD-L1 status, for patients with advanced or metastatic nonsquamous NSCLC.

However, selecting patients for second-line immunotherapy can be challenging, says Claude Denham, MD, because PD-L1 and tumor mutation burden (TMB) are not as reliable as indicators of response. Patients with driver mutations often do not respond as well to immunotherapy in the second-line setting.

Although strides have been made in the past few years, some patients with NSCLC remain resistant to immunotherapy or potentially may experience hyperprogression. A subset of patients experience long-term remission with immunotherapy agents alone, but combinations with immunomodulatory drugs or anti-CTLA-4 agents might hold promise, says Denham.

In a presentation during the 2018 *OncLive*[®] State of the Science Summit™ on Non-Small Cell Lung Cancer, Denham, a medical oncologist at Baylor Charles A. Sammons Cancer Center, discussed the use of immunotherapy beyond the first-line setting in NSCLC. In an interview during the event, he dove deeper into the challenges with immunotherapy in this disease, as well as the promise of combination therapy.

***OncLive*: Can you give an overview of your presentation?**

Denham: My topic lays the groundwork for a lot of the others—it is the use of immunotherapy, largely anti-PD-1 therapy, for NSCLC. I reviewed the pivotal trials that have demonstrated that this is essentially the standard of care for most patients in the second-line setting for NSCLC, both adenocarcinoma and squamous cell carcinoma.

Also, I looked at some of the strategies being investigated that are incorporating other immunotherapies and immunomodulatory drugs, as well as incorporating more conventional cancer treatments such as radiation therapy and possibly chemotherapy.

Which patients will benefit most from immunotherapy in the second-line setting?

In the second-line setting, we don't typically use PD-L1 or TMB as a way to predict whether patients should get immunotherapy. The 1 thing that does seem to help us is that patients with driver mutations—*EGFR* mutations, *ALK* rearrangements—don't do as well with immunotherapy as others. Therefore, if a patient has a driver mutation, there are probably better strategies for second-line treatment, such as a rebiopsy, targeted therapy, or chemotherapy. There is a correlation between benefit and the TMB and PD-L1, however, so it can still be useful.

Is there enough evidence to warrant concern about hyperprogression?

I absolutely have concern because I have seen it. It is a very striking phenomenon that I don't think anyone fully understands, but fortunately, it is rare. One of the challenges is that many patients with NSCLC have a lot of smoking-related comorbidities that make separating out the more nonspecific inflammatory events of immunotherapy with hyperprogression or autoimmune-related adverse events somewhat complicated. I had a patient where I could see the trajectory of their cancer change markedly after their first dose of immunotherapy.

What about resistance?

Resistance is, unfortunately, pretty common. The majority of patients do not respond to therapy. We talked about single-mutation or driver-mutation patients, but in terms of what is happening to the others, I do not think we have a great handle on that right now. We do know that there are certain subsets of patients with certain mutations who don't seem to respond well to PD-1 therapy. It may be that those patients need an anti-CTLA-4 and anti-PD-1 therapy in combination.

What key ideas should be kept in mind as we explore later-line immunotherapies in the future?

Everyone who practices clinical oncology is aware of this new tool that we have in our tool kit. What is so great about it right now is that a patient

CONTINUED on page 8 ▶

Gene Expression Model Predicts PFS in Follicular Lymphoma

Jason Harris

A “ROBUST” 23-GENE expression-based model successfully predicted progression-free survival (PFS) for patients with follicular lymphoma enrolled in the phase III randomized PRIMA trial.

Investigators identified 395 genes that were associated with the risk for progression, 23 of which were included in a predictive model based on both B-cell biology and tumor microenvironment. In a multivariate Cox model for PFS adjusted on rituximab (Rituxan) maintenance treatment and Follicular Lymphoma International Prognostic Index 1 (FLIPI-1) score, the model independently identified patients at high risk for progression compared with those at low risk (adjusted HR [aHR], 3.68; 95% CI, 2.19-6.17; $P < .0001$). The 5-year PFS was 26% (95% CI, 16-43) in the high-risk group and 73% (95% CI, 64-83) in the low-risk group.

The predictor performances were confirmed in each of 3 individual validation cohorts. The aHR comparing high-risk to low-risk groups was 2.57 (95% CI, 1.65-4.01) in cohort 1, 2.12 (95% CI, 1.32-3.39) in cohort 2, and 2.11 (95% CI, 1.01-4.41) in cohort 3.

The median PFS was 3.1 years (95% CI, 2.4-4.8) for the high-risk group and 10.8 years (95% CI, 10.1-not reached) for the low-risk group ($P < .0001$) in the combined validation cohort. The risk for lymphoma progression at 2 years was 38% (95% CI, 29-46) in the high-risk group and 19% (95% CI, 15-24) in the low-risk group. In a multivariate analysis, the score predicted PFS independently of anti-CD20 maintenance treatment and of the FLIPI score (HR, 2.30; 95% CI, 1.72-3.07).

“This predictor can be used in routine practice and captures multiple aspects of the biology of the tumor and the heterogeneous composition of the tumor microenvironment,” Gilles Salles, MD, Service d’Hématologie Clinique, Centre Hospitalier Lyon Sud, Pierre-Bénite Cedex, France, and colleagues wrote.

“Together with clinical parameters such as the FLIPI index, this score might allow clinicians to better adjust existing therapeutic options according to the patient risk category. For patients at low risk of progression, short treatments with a low toxicity profile should be considered. For patients with high-risk FLIPI and 23-gene scores, having a 50% risk estimate of lymphoma progression at 2 years, new treatment options should be developed,” added Salles et al.

Salles and colleagues collected fresh-frozen tumor biopsies from 160 treatment-naïve patients participating in the PRIMA trial evaluating rituximab maintenance following

rituximab plus chemotherapy induction in patients with high-tumor-burden follicular lymphoma.

Patients were first treated with 1 of 3 regimens: R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), R-CVP (rituximab, cyclophosphamide, vincristine, and prednisone), or R-FCM (rituximab, fludarabine, cyclophosphamide, and mitoxantrone). After this induction phase, patients with a complete or partial response were randomly assigned to observation or rituximab maintenance for 2 years.

Investigators collected RNA from 150 patients. Formalin-fixed, paraffin-embedded biopsies were also available for 53 patients for the technical validation of gene-expression quantification on fixed tissue.

As mentioned above, the model generated from the training cohort was further evaluated in 3 independent validation cohorts of patients for whom formalin-fixed, paraffin-embedded biopsies obtained at diagnosis were available, including a distinct validation set of patients in PRIMA who were not part of the training cohort (cohort 1; $n = 178$), 201 patients from the University of Iowa/Mayo Clinic Lymphoma SPORE trial (cohort 2), and 109 patients from the Hospital Clinic University of Barcelona (cohort 3). Cohorts 2 and 3 consisted of newly diagnosed patients who were prospectively recruited in observational studies.

When investigators tested the 23-gene expression model in the independent cohorts, the digital gene-expression data met quality criteria for 460 (94%) of 488 formalin-fixed, paraffin-embedded samples, with performances ranging from 93% to 97% across the 3 cohorts.

“Despite recent progress in the stratification and management of patients with follicular lymphoma, a substantial proportion of patients are still underserved by existing standard treatment and have rapid progression of their disease,” wrote Salles et al. “Our gene-expression predictor could be valuable in the clinical setting to identify patients at high risk or low risk of progression so as to adjust the therapeutic strategy and enrollment for innovative treatments.” ■

REFERENCE

Huet S, Tesson B, Jais JP, et al. A gene-expression profiling score for prediction of outcome in patients with follicular lymphoma: a retrospective training and validation analysis in three international cohorts [published online February 20, 2018]. *Lancet Oncol*. doi: 10.1016/S1470-2045(18)30102-5.

Degarelix May Reduce Risk of Cardiovascular Events in Prostate Cancer

Angelica Welch

PRELIMINARY DATA SUGGEST that patients with cardiovascular disease being treated for metastatic prostate cancer may experience fewer cardiovascular events when treated with a GnRH antagonist, such as degarelix (Firmagon), compared with a GnRH agonist.

The currently accruing PRONOUNCE study is comparing the occurrence of major adverse cardiovascular events in patients with prostate cancer and cardiovascular disease receiving degarelix or the GnRH agonist leuprolide (NCT02663908). This is a multicenter, randomized, controlled trial of 900 patients with prostate cancer and concomitant cardiovascular disease.

Investigators will be assessing for major adverse cardiovascular events, such as myocardial infarction, stroke, or death. These patients will be randomized 1:1 to receive either degarelix or leuprolide according to label recommendations for a maximum of 1 year.

In an interview with *OncoLive*, Susan F. Slovin, MD, PhD, the co-principal investigator of PRONOUNCE and a medical oncologist at Memorial Sloan Kettering Cancer Center, discussed this multinational study and how the results may affect the treatment of patients with prostate cancer.

***OncoLive:* Can you first describe the difference between an agonist and an antagonist?**

Slovin: A GnRH agonist, such as leuprolide, essentially tells the brain not to send a signal to the gonads to make testosterone. Because there is a feedback loop between the brain and the gonads, the gonads immediately start to make more testosterone to try to get the attention on the brain and say, “Here I am. Tell me what to do.” Over a period of time, that connection just does not happen. The testes shut down, and it also has to do with follicle-stimulating and luteinizing hormones, but the point is that, at the end of the day, the testes do not receive that signal. They shut down, and the man goes through the equivalent of a chemically induced menopause.

The benefit of a GnRH agonist is that you don’t have that sudden surge of testosterone. Why we are concerned about that sudden surge of testosterone is because if someone has preexisting metastatic disease in the bone, or a huge prostate that is causing obstructive symptoms, that sudden outpouring of testosterone can cause the cancer to worsen. People could have pain in the bone, worsening of obstruction, and very often we have to give a second pill—an antiandrogen—in order to prevent that

testosterone from binding to the tumor cell and make it grow. This means we have to pretreat patients.

GnRH antagonists, such as degarelix, work very differently, as they bypass that time where that surge occurs. There is no surge [in testosterone] and castration can take place within the next 24 to 48 hours. With a GnRH agonist, it takes considerably longer. If patients come in and you want to treat them rapidly, you would use an antagonist. It seems to work much faster in getting that testosterone level down and it’s well tolerated. Again, it is user’s choice—we are not saying that one is better than the other in terms of getting the job done regarding castration. The mechanism of action is a little bit different, but they both get the job done in terms of castration.

Please provide some background on the PRONOUNCE study.

Cardiovascular disease is still a leading cause of death in men and women. Several years ago, it came under evaluation by a variety of physicians—including radiation oncologists and urologists—that there may be some increased risk of cardiovascular events, such as myocardial infarction and strokes, in patients who are receiving a GnRH agonist, such as leuprolide, which is currently being used for the treatment of metastatic prostate cancer.

This was taken very seriously in both in the United States and Europe, such that black box warnings were listed on the products to indicate that there may be a disadvantage in giving patients these drugs because it could increase cardiovascular events. This is not considering that men who have metastatic prostate cancer are often older, have preexisting cardiovascular problems, hypertension, and diabetes, in addition to having had some sort of previous cardiovascular event—these are people who are at high risk.

Therefore, we asked, “Is there any background to this—is this a real event or not?” This was largely based on observational and retrospective studies that were done by radiation oncologists and a variety of other physicians to indicate that there was a very high risk. Given now that we have new drugs, particularly a GnRH antagonist degarelix, preliminary data have suggested that the amount of cardiovascular side effects in men receiving a GnRH antagonist might be fewer than men who receive a GnRH agonist. Very simply put, is it better to take a drug that does not allow a flare in testosterone levels to occur?

This has nothing to do with marketing; it has everything to do with improving the care of men with known cardiovascular disease. Do we want to improve and make it safer for them? Or, is there something that we are doing that is exacerbating preexisting conditions?

Can you give an overview of the trial design?

The trial is currently ongoing. It is a prospective 900-patient trial, in which men are randomized to either a GnRH agonist or antagonist over the course of 1 year. It is open to patients who are newly diagnosed with metastatic disease. It is also open to patients who might be undergoing definitive radiation therapy and may need upfront neoadjuvant hormonal ablation. This is going to take a while to accrue—it is multinational, and there is a vigorous effort to complete this trial within the next 2 to 3 years.

This phase III trial of 900 men is really the first of 3 aspects. The first thing to do is a prospective comparison of a GnRH agonist versus antagonist. We must first look at biomarkers associated with cardiovascular events, including specific B-type natriuretic peptide and cytokines. This is the first study to look prospectively at what happens to the immune milieu and the immune cells under the influence of the GnRH agonist or antagonist. I can tell you that we know very little—the first few papers looking at the effects on the immune system using a GnRH agonist were probably in the 1970s. However, no one has ever looked forward—we've never had a clean slate in which we can evaluate it.

These 3 objectives are the first of their kind attempting to understand what is going on. This may also be important in terms of designing future trials from the immune system vantage point and other aspects. In fact, there are preclinical models with cardiovascular issues, such as atherosclerotic plaque formations, that under the influence of the GnRH agonist, is very different in terms of worsening compared with an animal that is given an antagonist. There are preclinical data showing that there may be something very different about the plaque stability in a patient who might be going on to receive an antagonist versus an agonist. This is very exciting for all of us; it is not going to be completed very fast, but at least it will answer an unanswered question of the last 30 years.

If someone is at risk for cardiovascular events, what would you recommend?

Either the GnRH agonist or antagonist is reasonable. Most of these people will come in already on medications to reduce the risk of having an event, so the question is, "Can those risks be worsened in any way?" For somebody who has an extremely high risk of metabolic syndrome, which is hypercholesterolemia and hypertension, weight

gain, and obesity, it is often prudent to speak with their primary doctor regarding concerns about cardiovascular risk. We actually have very strict criteria in terms of what we are looking at in the trial. We are looking at somebody in the trial who is on medication for their cardiovascular risk and who has had a myocardial infarction or a stroke. The idea is, are we preventing anything new from happening?

This is a very fair question being asked. Are we making anyone higher risk? The answer is probably not in terms of a major event. If someone is terribly ill and has [New York Heart Association] class 3 or 4—meaning that they are really a cardiac cripple—I would have a very long discussion with them, their primary doctor, and their cardiologist about the relevance of it. It is very rare that we see these patients though.

If this study is positive, how could it potentially affect treatment decisions?

If this is a positive study, it will likely result in a change in clinical practice. It is more than possible that people will be using a GnRH antagonist more routinely. There are concerns with the GnRH causing some local skin reactions that may not be tolerated by some patients, but the point is that it would change practice by not needing to use an antiandrogen before giving an injection of a GnRH agonist. It's one less pill to take, one less medicine to worry about, and you are guaranteed to get to castrate levels within 24 to 48 hours—which is much faster than a GnRH agonist. We are very eager to see how this pans out.

It is a very reasonable study, and the cardiac criteria are very stringently reviewed by Dr Matthew T. Roe, who is the co-principal investigator on the trial with me, and Dr Chiara Melloni, both of whom are from Duke University School of Medicine. They are extremely enthusiastic in terms of making sure that everyone who goes on the trial is an appropriate candidate. Each patient is reviewed very thoroughly before going into formal screening for the trial.

The most important takeaway message is that this is not a urology trial. This is a cardiovascular trial in patients who have prostate cancer. But, who sees the patients with prostate cancer? Radiation oncologists, urologists, and medical oncologists. ■

REFERENCE

Slovin SF, Melloni C, Mansor-Lefebvre S, Neijber A, Roe A. A multicenter, randomized, controlled trial comparing the occurrence of major adverse cardiovascular events (MACEs) in patients (pts) with prostate cancer (pc) and cardiovascular disease (CVD) receiving degarelix (GnRH receptor antagonist) or leuprolide (GnRH receptor agonist). *J Clin Oncol*. 2018;36 (suppl 6S; abstr TPS395).

Urology Practice Succeeds With Transparency, Upfront Payment Model

Ariela Katz

IT MAY BE TRUE that most people do not enjoy staff meetings, but the partners at Wichita Urology, the largest independent urology practice in Wichita, Kansas, have built their success over 60 years partly by holding frequent meetings, which they say build camaraderie and make it possible to address needs quickly.

Meetings, they say, create a transparency that prevents employees from being broadsided by any changes. “All the physicians come together at the board meetings. Even if you’re not yet a partner you still attend, and we hold board meetings 3 times a month,” said Twila Puritty, CEO of Wichita Urology. This makes the practice nimbler and, as a result, things that need doing don’t languish on the back burner. “We are able to accomplish a lot of things in a short period of time compared with other groups who don’t meet as frequently,” she said. This collaborative style also allows for everyone’s voice to be heard when practice-changing decisions are made.

Another pillar of the administrative structure at Wichita Urology is a collection model that ensures the physicians are fairly and efficiently paid for their hard work, Puritty explained. The practice requires payment upfront for elective surgeries—before the procedures take place. “We used to write off thousands of dollars for elective surgeries that patients didn’t pay for after receiving surgery. So, we adopted a policy that surgeries would be classified as either urgent or elective, and if they’re elective the surgery isn’t scheduled until the patient pays the out-of-pocket amount,” Puritty said. It was felt that these nonessential unpaid surgeries were not only an inefficient practice but also cost physicians time that they could have spent at home with their families.

Under the revised policy, the cost of the elective surgery is explained to patients, and numerous attempts are made to ensure payment is received upfront. The surgery will usually be rescheduled until that requirement is met. However, it sometimes happens that the practice will do an elective procedure without payment and accept the unpaid bill as a cost of doing business.

History of the Practice

Wichita Urology has grown organically, without merging with any other urology groups. It was founded by 3 urologists in 1955 and now has 9 physician partners. The support staff numbers 92 employees, including 84 who are full time and 8 who are part time. Although the

practice has many employees, its efficiency is high, and this enables clinicians there to see a high volume of patients, Puritty said. From 2016 to 2017 the group saw 19,427 patients.

Wichita Urology is spread out over 3 offices in the south-central Kansas metropolis. The main office on the east side of town is large enough to have 3 clinics operating at once. By contrast, their west-side office offers just 1.

Physicians at the practice see adult and pediatric patients with all stages of prostate, bladder, and kidney cancer. “We have individuals from first diagnosis to those who walk in with metastatic disease. We not only get referrals for end-stage disease, we see every type,” said Timothy A. Richardson, MD, a physician partner.

The urology group participates in many clinical trials for prostate cancer and a smaller number for patients with renal or bladder cancer. Wichita Urology also enrolls patients in trials for general urologic disorders, such as overactive bladder and benign prostatic hyperplasia. There are no medical oncologists on staff, but the practice works closely with a local medical oncology group to address patients’ needs for chemotherapy or other specialized cancer treatments. Following outside care, patients usually return to Wichita Urology to resume treatment.

The practice often can provide in-house treatment for a wide spectrum of a patient’s needs. For example, the practice can provide surgical interventions for patients with resectable cancers. “For prostate cancer, we take care of those patients from diagnosis. If they need chemotherapy, we send those on, but we still try to manage everything else,” Richardson explained.

In 2014, Wichita Urology opened an office that is dedicated to radiation therapy. The availability of radiation oncologists enhances the practice’s ability to treat patients in-house. The practice also has an outreach program for about 15 communities. Wichita Urology physicians travel to those offices regularly for clinics that may be held multiple times per week.

Wichita Urology’s commitment to these outreach clinics often stems from hospital requests for urology coverage, according to Puritty. It is not always possible to provide support for these outside clinics, either because of a lack of staff or because a location is too far from Wichita Urology’s offices. “We can’t always say yes,” she said.

CONTINUED on page 8 ►

No OS Benefit With Chemoradiotherapy in High-Risk Endometrial Cancer

Jason Harris

ADJUVANT CHEMOTHERAPY GIVEN during and after radiotherapy did not improve 5-year overall survival (OS) for patients with high-risk endometrial cancer in the phase III PORTEC-3 trial, although the treatment increased failure-free survival (FFS).¹

At a median follow-up of 60.2 months (IQR, 48.1-73.1), the 5-year OS was 81.8% (95% CI, 77.5-86.2) with chemoradiotherapy versus 76.7% (95% CI, 72.1-81.6) with radiotherapy (adjusted HR, 0.76, 95% CI, 0.54-1.06; $P = .11$). Five-year FFS was 75.5% (95% CI, 70.3-79.9) with chemoradiotherapy versus 68.6% (95% CI, 63.1-73.4) with radiotherapy (HR, 0.71, 95% CI, 0.53-0.95; $P = .022$).

“For each patient [with high-risk endometrial cancer], the cost in terms of increased toxicity and longer treatment duration should be weighed against the benefit in terms of improvement in failure-free survival,” first study author Stephanie M de Boer, MD, department of Radiation Oncology, Leiden University Medical Center, the Netherlands, and coinvestigators wrote.

PORTEC-3 was an open-label, international, randomized, phase III trial involving 103 centers collaborating in the Gynecological Cancer Intergroup. Eligible women had high-risk endometrial cancer with FIGO 2009 stage I, endometrioid-type grade 3 disease with deep myometrial invasion or lymph-vascular space invasion (or both), endometrioid-type stage II or III, or stage I to III with serous or clear cell histology.

From November 2006 to December 2013, patients were randomly assigned to radiotherapy alone with 48.6 Gy in 1.8 Gy fractions given 5 days per week ($n = 343$) or radiotherapy and chemotherapy consisting of 2 cycles of 50 mg/m² of cisplatin given during radiotherapy, followed by 4 cycles of AUC5 of carboplatin and 175 mg/m² of paclitaxel ($n = 343$). The intent-to-treat population included 660 patients, 330 in both groups.

Stage, histological type and grade, type of surgery, participating groups, lymph-vascular space invasion, and age were included with treatment in the multivariate analysis. In the presence of these factors, combined chemotherapy and radiotherapy significantly improved FFS. Most factors, except lymphadenectomy, were significantly correlated with FFS.

In multivariate analysis for FFS, only age group was found to be predictive of treatment effect, with a strong treatment-by-age effect ($P_{interaction} = .012$). Women aged 70 years or older derived the greatest benefit from chemoradiotherapy.

In a subgroup analysis, women with stage III endometrial cancer had significantly lower OS (HR, 2.41; 95% CI, 1.66-3.51) and FFS than those with stage I-II disease. Five-year OS for patients with stage III disease was 78.7% (95% CI, 72.2-85.7) in the chemoradiotherapy group versus 69.8% (95% CI, 62.4-78.1) in the radiotherapy group (HR, 0.71; 95% CI, 0.45-1.11; $P = .13$; adjusted $P = .074$).

Five-year FFS for stage III cancer was 69.3% (95% CI, 61.1-76.2) in the chemoradiotherapy group versus 58.0% (49.3-65.7) in the radiotherapy group (HR, 0.66; 95% CI, 0.45-0.97; $P = .031$; adjusted $P = .014$). Five-year FFS for stage I-II patients was 80.8% (95% CI, 74.1-86.0) in the chemoradiotherapy group versus 76.6% (95% CI, 69.5-82.2) in the radiotherapy group (HR, 0.85; 95% CI, 0.54-1.33; $P = .47$).

Patients assigned to chemoradiotherapy were more likely to experience grade 3 (45% vs 12%) and grade 4 toxicity (15% vs 0%). This chemoradiotherapy arm was more likely to experience grade 3/4 diarrhea (11% vs 4%), leucocytes (23% vs <1%), lymphocytes (33% vs 5%), and neutrophils (20% vs <1%).

“By contrast with the benefit conferred to stage III patients, the addition of chemotherapy did not improve outcomes for stage I or II patients,” Sean C. Dowdy, MD, and Gretchen E. Glaser, MD, wrote in an accompanying editorial.² “Although PORTEC-3 might have been underpowered to identify differences in failure-free survival in this subgroup, the small magnitude of benefit does not seem to justify the accompanying increase in adverse events, impairment in long-term quality of life, and longer treatment duration.

“Future trials should investigate regimens to maximize the local control advantages of radiotherapy with distant control improvements seen with chemotherapy for patients with high-risk endometrial cancer,” they wrote. “Continued assessment of toxicity, quality of life, and cost will be paramount to define optimal adjuvant therapy.” ■

REFERENCES

- de Boer SM, Powell ME, Mileshkin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial [published online February 12, 2018]. *Lancet Oncol*. doi: 10.1016/S1470-2045(18)30079-2.
- Dowdy SC, Glaser GE. Adjuvant therapy for women with high-risk endometrial carcinoma [published online February 12, 2018]. *Lancet Oncol*. doi: 10.1016/S1470-2045(18)30091-3.

▶ CONTINUED from page 8

can be completely refractory to chemotherapy and have dramatic benefit from these agents. Therefore, you no longer have the downcast look on your face when you walk into the room to tell a patient that they have progressed on first-line chemotherapy. This is a tremendous advance in the field of solid tumor oncology.

There is certainly still a lot of room for improvement. Immunotherapy has sort of disrupted a lot of our

paradigms that looked purely at performance status or age as a way of predicting who is appropriate for chemotherapy or systemic therapy for metastatic cancers. We have been thinking about this shift in the paradigm with the advent of targeted therapies, which have a dramatic effect in some patients that you wouldn't historically offer chemotherapy. We are having that same sort of challenge in decision making with the immunotherapies, as well. ■

▶ CONTINUED from page 6

Advanced Prostate Cancer Clinic

One of the most important additions to Wichita Urology is their advanced prostate cancer clinic, which they opened in 2017 to address the increasing complexity of advanced prostate cancer care. Richardson serves as the lead physician and “champion” of that clinic. “Advanced prostate cancer has become so convoluted and confusing. There are more therapies being approved every day.” To address patients’ need for access to quality care and Wichita Urology’s need for efficiency of operations, an advanced prostate cancer clinic was developed that could work with just 1 or 2 doctors, Richardson said.

Wichita Urology strives to offer patients cutting-edge technologies and treatments, but its doctors also want to ensure that patients get the most appropriate care. Puritty said an example of this is a current initiative to start dispensing catheters directly to patients. She said group discovered that a vendor they worked with previously was dispensing catheters based on what made good financial sense to the vendor rather than what was most appropriate for patients’ needs.

The physicians pay close attention to the many drugs in development and look forward to being able to give their patients therapies that offer better outcomes. “There are about 300 drugs in development now, and there are a lot of drugs on the horizon that are going to be approved for us to use earlier and in different situations,” Richardson said.

He anticipates that some of those drugs will become available as soon as the first or second quarter of this year.

Richardson and his colleagues also recognize the value that genetic counseling can bring to cancer treatment. They currently offer several genetic tests to patients with prostate cancer. The practice works with several genetic counselors, including one who is associated with a hospital in Wichita and another with whom patients can speak by phone.

The practice is also investigating telemedicine and how it can reduce the distances their physicians have to travel. Because they serve so many clinics across Kansas, including some that are hours away from Wichita, telemedicine would allow physicians to treat patients remotely who may not have been reachable before. “The travel burden on a busy urologist can be a killer on their productivity,” Puritty said.

Wichita Urology is vigilant about monitoring changes in payers’ payment policies, and practice members are confident that their in-house efficiencies will protect them from the potential revenue losses that can result from payment policy changes. “There are all these conversations about reimbursement, such as the Medicare Access and CHIP Reauthorization Act and the Meritbased Incentive Payment System, and how are we going to be impacted—negatively or positively.” Puritty said that internal policy changes can help to offset external pressures. The practice’s decision to aggressively pursue payment upfront for elective surgeries is one such example, she said. ■