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Improving Outcomes in Patients with Ovarian Cancer: Multidisciplinary Patient-Centered Care

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Improving Outcomes in Patients with Ovarian Cancer: Multidisciplinary Patient-Centered Care” is provided by Prova Education.
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Dr. Backes:
Hello, I'm Dr. Floortje Backes from the James Cancer Hospital at the Ohio State University, and I'd like to welcome you to our Patient-Clinician Connection on advanced ovarian cancer. As healthcare models evolve to become more patient centered, so should care provided to patients with advanced ovarian cancer, especially in relation to managing adverse events from PARP inhibitors. Clinicians are responsible for the health literacy of their patients because clinicians set the tone, content, and mode of information delivered to patients during counseling sessions and appointments.

Today I'll be illustrating my approach to patient-centered care through clinical vignettes with a patient who has stage III ovarian cancer. Let's get started.

Rebecca is in my office to discuss initial treatment options for her recently diagnosed ovarian cancer. She is 58 years old and has stage IIIC high-grade serous ovarian cancer. She underwent a primary debulking surgery followed by 6 cycles of carboplatin and paclitaxel. Her end-of-treatment imaging showed a complete response to chemotherapy. Her tissue was sent for tumor testing and showed a homologous recombination deficiency, or HRD. Her ECOG performance status is 0.

Hi, Rebecca, how are you today?

Rebecca:
Overall, I'm feeling pretty good, anxiously awaiting my results.

Dr. Backes:
Oh, I'm so glad to see you, and even more so to give you good news today. Because the CAT scans from your chest, your abdomen, and pelvis showed that there was no signs of cancer.

Rebecca:
That’s good news!

Dr. Backes:
Oh, congratulations.

Rebecca:
Should I be worried about the cancer returning?

Dr. Backes:

Well, this is the hard thing about ovarian cancer. There's always a high risk that the cancer does return. And that risk is about 80% to 90%. But the good news is, is that we have something called maintenance therapy that we can use to decrease the risk of the cancer returning and hopefully even to keep the cancer away for good.

Rebecca:
What are my options?

Dr. Backes:
Well, your option for maintenance therapy depends on 2 things. We look at your tumor and whether the tumor or in your genes you have something called a BRCA mutation. The other thing that we look at if there's a certain change called homologous recombination deficiency, or HRD.

Well, we tested your tumor, and based on those biomarker testing, we can see that your tumor is HRD positive. So that means that there's an option that's out there for you called PARP inhibitors. And there are 2 drugs currently FDA-approved that are called niraparib and olaparib that are pills that you would use on a daily basis as maintenance treatments.

There's one more option out there called bevacizumab. And that is an infusion that works on blood vessels to the tumors. And often if we use that in combination with your chemotherapy, we can continue that afterwards as a maintenance therapy. We didn't use that in your case, so for you, we would consider PARP inhibitors like niraparib and olaparib. And I'd be happy to tell you more about that.

In the first-line maintenance setting for patients who did not use bevacizumab and is BRCA or HRD positive, there are 2 approved PARP inhibitors, niraparib and olaparib.

From the PRIMA data, we know that those patients who are HRD positive and took niraparib versus placebo, their progression-free survival was almost 22 months, versus 10 months with placebo.

So in the PAOLA-1 data, those patients who were HRD positive and were on olaparib with bevacizumab, their median progression-free survival was 28 months, versus almost 17 months with bevacizumab alone.

Overall, niraparib alone and olaparib alone or with bevacizumab are useful options for the first-line maintenance treatment of adults with HRD-positive advanced ovarian cancer who are in complete or partial response to first-line platinum-based chemotherapy.

Let's return to our discussion with Rebecca to go over the efficacy and the safety of these options.

Rebecca:
Can you tell me more about these 2 options? Are they safe? And what can I expect about taking these medications?

Dr. Backes:
So for starters, both olaparib and niraparib have been shown to be very effective for reducing the risk of the cancer coming back. So that's good, but we do need to monitor you closely because there are some side effects that we can see with these PARP inhibitors. And we see those across all of them. Most commonly we see fatigue, nausea, and vomiting. But the good thing is that we have medications that we can use to help that you can take before you take the pills. And most of these side effects also improve or even go away after the first 3 months of treatments.

Rebecca:
Are there any other side effects that I should be worried about?

Dr. Backes:
Yes, there are some other side effects that we have to watch for. There can be some hematologic side effects. So those are the side effects that affect your blood counts, like your red blood cells, your white blood cells, and your platelets. And so to minimize those risks, we will monitor your blood counts really closely.

PARP inhibitors have a distinct adverse event profile not only as a drug class, but also as individual agents. Common nonhematologic adverse events of PARP inhibitors include fatigue or asthenia, nausea, and vomiting. Hematologic AEs are also a drug class effect and occur at higher severity and remain the main cause of treatment discontinuation.

If we look at the side effects listed from the PRIMA trial, where niraparib was used, we see that most of the hematologic side effects, as well as nausea, constipation, fatigue, are all very common. And that means greater than 30% of the hematologic side effects occur even in greater than 45% to 65%. So anemia is common, but fortunately also, most of the time, these are not severe events. We see that grade 3 anemia and thrombocytopenia still can be seen in 30% to 45%, but has been much improved with the introduction of the weights and plates rules.

In the PAOLA-1 trial, where olaparib and bevacizumab was used, again, the most common side effects with greater than 50% of occurrence were anemia, nausea, fatigue; we also saw some thrombocytopenia. But fortunately, again, the grade 3 overall side effects were much lower, and for most of the side effects, less than 10%.

When thinking about selecting treatment, it's important to discuss potential toxicities, as these are oftentimes deciding factors based on patient preference. And in that case, we're thinking about thrombocytopenia, for example, during the first month, hypertension and insomnia that can be seen with niraparib, upper respiratory infection symptoms and also a rising creatinine that can be seen with olaparib.

Of course, we always need to discuss with the patient that there is a risk of AML and MDS for all PARP inhibitors. Fortunately, that risk is low when we use it in a primary setting; the risk is approximately no greater than 1% to 2%. Once a patient understands the potential risks of each drug, it's important they know other differences that may sway their treatment selection.

Let's return to Rebecca as I discuss the differences between the niraparib and olaparib, including dosing and patient instructions.

Rebecca:
Are there any differences between the 2 treatment options that I should know about before making my decision?

Dr. Backes:
There's a couple of differences. Overall, the safety and efficacy between both niraparib and olaparib are fairly similar. One of the differences is that niraparib is taken once a day. So it's either a 200-mg or a 300-mg tablet that you would take once a day, whereas the olaparib is a tablet of 150 mg that you take 2 pills twice a day. So about 600 mg daily.

Rebecca:
Twice daily? Seems like a lot, doctor. I already have enough medications to keep me on track on a daily basis. But how long will I be in this maintenance phase?

Dr. Backes:
So for niraparib, we would continue the maintenance pills for 3 years. And for olaparib, that would be 2 years.

Of course, if your cancer comes back before that, or if you're not tolerating the treatment well, then we would stop earlier.

When discussing dosing and adverse reactions with your patients, you should understand the recommendations for dose reductions if these events occur.

Let's go over some dose modifications for niraparib. So the starting dose of niraparib is 300 mg once daily. The first dose reduction is 200 mg, and a second dose reduction would be 100 mg once daily. So based on weights and plates, if the patient's weight is less than 77 kg or the starting platelets are less than 150,000, in that case, you start the patient on 200 mg once daily rather than 300 mg once daily. If hematologic side effects still occur, such as thrombocytopenia, neutropenia, or significant anemia, in that case, you hold the drug, wait for recovery, and then resume at either the same or a once-reduced dose. If there's nonhematologic toxicities, such as fatigue or nausea, that doesn't resolve with conservative medicines or antiemetics or other supportive medicines, then, again, hold the drug, wait for recovery, and resume at a reduced dose.

We see similar adjustments for olaparib. Olaparib is dosed at 300 mg twice daily. The first dose reduction is 250 mg twice a day, and the second dose reduction is 200 mg twice a day.

Again, for hematologic and nonhematologic side effects, you would hold the dose, and then once it is recovered, you resume at a one-dose level lower.

There are a couple of differences between the 2 drugs. If the patient has renal impairment with a creatinine clearance, for example, of between 30 to 50, no dose reduction is needed for niraparib. But with olaparib, we would need to reduce the dose to 200 mg daily. For severe renal impairments with a creatinine of less than 30, there's no data that has been evaluated for olaparib.

We also want to look at hepatic impairment. For mild hepatic impairment, neither drugs need dose reduction. However, for moderate hepatic impairment, you want to reduce the starting dose of niraparib to 200 mg daily, but for olaparib, there's no dose reduction needed. And in severe hepatic impairment neither drug has any data established.

Lastly, if the patient is on other medication, which is very important to review as you choose your drugs and you choose your dosing, it's important to look at CYP3A inhibitors. If the patient is on a strong or moderate CYP3A inhibitor, you want to avoid the use of olaparib and consider alternatives. If this cannot be avoided, then dose reduce olaparib to 150 mg twice a day if the patient is on a moderate CYP3A inhibitor, and if they are on a strong CYP3A inhibitor, you want to dose reduce further to 100 mg twice a day. This dose

adjustment is not needed for niraparib, though.

Now let's go back to our patient, Rebecca.

Dr. Backes:
Now Rebecca, we also consider a couple of the other things when we're trying to choose between these 2 options. Your blood pressure and heart rate have been good, but sometimes those can be raised by niraparib, so that would help in our decision. And then blood counts such as your platelets are a little bit more likely to decrease with the niraparib, but that has not been a concern for you.

Lastly though, olaparib is approved for patients with a BRCA mutation. And your tumor or your genes did not have that BRCA mutation, but your tumor was HRD positive, which means that niraparib would be the best option for you.

What do you think about this? How do you feel about all the information I've given you so far?

Rebecca:
That option seems good, because I really didn't want to be committed to another medication twice daily. I like that one. I'd rather do that, once a day.

Dr. Backes:
Good. So let's go with niraparib then. Based on your weight and your starting platelets, we would start you on the 200-mg tablets rather than the 300-mg tablets. And that's to reduce the risk that your platelets are going to go really low. So you can take it anytime of the day. You can take it at night or in the morning, with or without food, but you want to take it mostly at the same time of the day. And so sometimes people, if they have issues with nausea during the day, they prefer to take it at night. But sometimes people see some insomnia also or difficulty sleeping. So if that's the case, then maybe you want to try and take it in the morning. But we'll just kind of have to see how you feel as you start taking this medication and make sure that we get you on a good schedule.

Rebecca:
That's good to know. So where do we go from here?

Dr. Backes:
So during the first month, we have to check your blood counts, specifically your red blood cells, your white blood cells, your platelets, every week for the first 4 weeks. And as long as that's good, then we'll spread out those blood draws and the visits to once a month for the first year. We'll also be monitoring your blood pressure. So you'll have to take your blood pressure at home and check your heart rate at home, because the niraparib can also raise your blood pressure and your heart rate. So we need to monitor that closely, too.

Rebecca:
Thank you, Dr. Backes, for discussing both these options with me. I'm ready to get started with a new phase of treatment.

Dr. Backes:
My pleasure. You're welcome.

I think the model presented in these vignettes can be adapted to address many scenarios we face daily in our medical practices. I hope you'll find it useful when discussing treatment and adverse event profiles for PARP inhibitors in the first-line maintenance setting post platinum-based chemotherapy with your patients. When prescribing PARP inhibitors for these patients, in order to maximize efficacy, it's important to apply shared decision-making and consider patient preference, potential advantages, and challenges to treatment adherence.

Thank you for joining me for our Patient-Clinician Connection vignettes on improving outcomes in patients with ovarian cancer.

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