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Case Consult: PD-L1–Guided Treatment Decisions in Platinum-Resistant Ovarian Cancer

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Dr. Salani:
Welcome. This is CE with GLC. I'm Ritu Salani, a GYN oncologist at UCLA, where I'm Division Director.

Dr. Moore:
Hi, and I'm Dr. Kathleen Moore. I'm also a GYN oncologist, Deputy Director, and Director of Phase One at the Buffett Cancer Center in Omaha, Nebraska.

We're going to start this discussion with a case. So, this is a patient who was diagnosed with high-grade serous ovarian cancer in October of 2024. She had stage IV disease, excellent performance status, no baseline issues like neuropathy.

We got a biopsy and she was *BRCA* wild-type, HRD test-negative, PD-L1 was 2, and her folate receptor alpha is high.

She received neoadjuvant chemotherapy for 3 cycles, had a great response, had an interval cytoreduction to no gross residual, and then I did 4 more cycles of paclitaxel and carboplatin, and I added bevacizumab in cycle 5. And then I started bevacizumab maintenance in April of 2025.

And unfortunately, she had a recurrence in January of 2026 with both CT evidence of disease and a CA-125 of 60. And so she was started again on carboplatin and pegylated liposomal doxorubicin, and at first restaging CT after three cycles, she has progression. She's got liver metastases, small volume ascites.

So now her tumor is declared platinum resistant, defined by progression either on or within 6 months of her last platinum. Still good performance status for now, and her biomarker profile gives me some options. And so these are the things we'll be talking about in this next section. Her 3 options would be: The first, B96, which is weekly paclitaxel plus bevacizumab plus pembrolizumab, as gated by the CPS greater than 1. Two is mirvetuximab. She's folate receptor alpha high, as gated by MIRASOL, which we'll talk about in this series of lectures. And then 3 is ROSELLA, which is nab-paclitaxel and relacorilant.

All 3 of these are FDA approved for this setting, and we'll talk about why we might pick one or the other.

And so, with that, I'll turn it back over to Dr. Salani to review the pivotal data that support the use of the B96 regimen in this setting and

in platinum-resistant ovarian cancer in general.

Dr. Salani:
Yeah, a great case. And I think you highlight where we have options, and I think that's really important.

And immunotherapy in ovarian cancer has really kind of done a turn-face here. We kind of didn't really see a role for it, and these are 3 studies that are listed here: JAVELIN Ovarian 200, which looks at avelumab compared to pegylated liposomal doxorubicin; the NINJA trial, which looks at nivolumab compared to gemcitabine or PLD; and then the VBL-OVAL trial, which looked at weekly paclitaxel compared to weekly paclitaxel and this novel kind of gene therapy that elicits the immune system. But all 3 of these trials were actually negative trials.

And then along came KEYNOTE-B96. This is a phase 3 randomized double-blinded trial looking at weekly paclitaxel with or without bevacizumab. And then the study arm included pembrolizumab given every 6 weeks versus placebo. And you can see that this was for patients who had recurrent ovarian cancer, and they had to have one or two prior lines of systemic therapy. The primary endpoint was PFS, with a secondary endpoint of overall survival.

Here is the primary endpoint of progression-free survival in those patients who had a CPS greater than or equal to 1. And here you can see that pembrolizumab added a benefit to PFS with a hazard ratio of 0.72, so almost a 30% benefit or improvement in the rate of preventing cancer from coming back at this time. You can see here the PFS in the intention-to-treat population was pretty comparable, so this is including those with lower CPS, although that was a small percentage of patients, and 12-month rate of 33% versus 21% with the addition of pembrolizumab.

And then here you can see the Interim Analysis 2. So the data I just showed you was the Interim Analysis 1, and you can see we continue to see this benefit with the addition of pembrolizumab, both at 12 months and 18 months, in both the CPS greater than and equal to 1 and the intention-to-treat population.

And then what I think was notable was that the overall survival in the CPS greater than or equal to 1 population continued to hold out. So we had a sustained benefit: 12-month overall survival, 69 versus 59%, and at 18 months, 51 versus 38%. And I just like to highlight, in platinum-resistant ovarian cancer, 18 months is actually a pretty high bar. So this is really impressive data.

Objective response rate is always a nice metric, and I think patients can really relate to this. And you can see here that both for partial and complete response, we saw a higher objective response rate with the addition of pembrolizumab to weekly paclitaxel when compared to placebo. And so I think this kind of highlights that, and then I think you can also see a nice duration of response with the addition of pembrolizumab in this study.

So one of the important things about any trial is the evaluation of adverse events. And you can see across the board it's not uncommon that patients will have some toxicities from chemotherapy and immunotherapy, but truly treatment-related adverse events associated with immune-mediated therapy is quite low.

And here you can see another kind of depiction of treatment-related adverse events across the board, with hematologic toxicities, neuropathy, not surprisingly using a taxane-based regimen, and other side effects, including diarrhea being present here.

Here specifically are the immune-mediated adverse events, and you can see hypothyroidism, which we are well aware of, and checking for TSH continues to be one of the high ones. But it's important to recognize that infusion reactions, pneumonitis, and colitis continue to be significant as well, although low rates that can be impactful for our patients.

And soon after this study was presented and published, we then received FDA approval for the addition of pembrolizumab to weekly paclitaxel for patients with platinum-resistant ovarian cancer with a CPS greater than or equal to 1.

So now, Dr. Moore, I'd like to kind of turn it over to you. What are your thoughts about how you're going to incorporate immunotherapy into platinum-resistant ovarian cancer?

Dr. Moore:

I'm certainly testing everyone. We actually had scores on a lot of our patients so we could see who was eligible. But if I had patients who I don't know the CPS score, I'm making sure that I have that now.

I'm trying to pay attention to the overlap. How much overlap is there really between folate high and CPS 1? Because that's going to be a tension point of which one of those I use first in this particular patient. Both of them are microtubule toxins. Both have neuropathy risks. Stacking them could be problematic. So I'm thinking about that.

So right now I am glad to have it. I'm testing all of my patients. I'm talking to them about this option, especially when they're within that one to two priors that is the label, and I'm glad to have an option that, with currently available therapies, improves overall survival. I think we're all familiar with how to use pembrolizumab, so there's not a big learning with that.

But what are you doing? Like, what's your thought here?

Dr. Salani:
Yeah, I think it's a similar approach. I think one of the challenges is kind of deciding which regimen is maybe ideal, because we do have several regimens that are at least taxane derivatives or taxane-based, and so sometimes sequencing those one after another may be not ideal for a patient's tolerability.

But just similar to what you're doing, we are getting CPS score. It also can be done in-house pretty readily if you don't have it, so that's another thing about the testing. So I am testing it. I'm noting it down in my little notes for patients for future possibilities.

It is one to two prior regimens, so it is a little bit restrictive in that regard because patients may have seen multiple regimens, but it may be ideal for certain patients. I think there's a lot of excitement around immunotherapy, and at least in the patient world, so I think it's something that spills over, and I think it's a good option to think about.

And I think one of the things is that we're pretty familiar with managing it, and so I think from a physician— selfishly, from a physician standpoint, it's easy to incorporate and understand.

Dr. Moore:
Yeah, I think the issues around tolerability, though, are really key with these microtubule toxin regimens, not just because of neuropathy, but also just the weekly burden. But with an OS advantage, at least I think there's that added benefit that you could explain to patients as to why you might prefer this one over other options.

Dr. Salani:
Agree, and especially looking at its toxicities.

Well, great discussion. We've reached the end of our discussion. I want to thank you so much for your time and attention on this important topic.

Dr. Moore:
Thank you for having me.

Announcer:
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