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Case Consult: Treatment Strategies for FRα-Positive Platinum-Resistant Ovarian Cancer

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Dr. Moore:
Welcome. This is CE with GLC. I'm Dr. Kathleen Moore, Deputy Director and Director of Phase One at the Fred and Pamela Buffett Cancer Center in Omaha, Nebraska.

Dr. Salani:
Hi, I'm Ritu Salani. I'm a GYN oncologist at UCLA, where I'm also Division Director, and I have an interesting case for you today. So, let's go ahead and get started.

This is a 61-year-old patient who was diagnosed with stage IIIC high-grade serous ovarian cancer. She received neoadjuvant carboplatin and paclitaxel, and this was followed by interval debulking surgery, which is optimal. She then completes her first-line carboplatin and paclitaxel and has bevacizumab added afterwards. She achieves disease control and subsequently receives maintenance bevacizumab.

Unfortunately, at 15 months after completing her first-line therapy, she has recurrent peritoneal disease. She's initiated on second-line therapy with cisplatin, gemcitabine, and bevacizumab again, and she achieves a partial response and once again receives maintenance bevacizumab. She experiences progression within 3 months after completing second-line therapy while on maintenance bevacizumab. Her biomarker testing is shown here, and it shows folate receptor alpha testing positive of 80%, HER2 IHC of 1+. Mirvetuximab is initiated as third-line therapy, and a first assessment demonstrates evidence of ongoing clinical and radiographic benefit.

So, with this case, Dr. Moore, could you review the pivotal data that supports the use of mirvetuximab for platinum-resistant ovarian cancer?

Dr. Moore:
All right. Well, I'm going to take us through some of the pivotal data that led to support of use of mirvetuximab in the platinum-resistant ovarian cancer setting.

So just to level set, mirvetuximab soravtansine, which I'm going to call MIRV from now on, is a monoclonal antibody. It targets folate receptor alpha. It has a very stable linker in circulation, and its payload is a microtubule toxin. It's called DM4.

Folate receptor alpha is a target that we've been interested in in a lot of tumors, to be perfectly honest, but particularly in ovarian cancer

for well over a decade because it's so common. It's almost ubiquitous on high-grade serous ovarian cancer that we find some folate receptor alpha, but then different levels have different cut points. We also find it in low-grade serous ovarian cancer.

The FDA approval is based on the phase 3 clinical trial known as MIRASOL, which was a study of MIRV versus investigator's choice chemotherapy in patients with platinum-resistant ovarian cancer. They could have 1 to 3 prior lines of chemotherapy, and their tumors were determined by a central test to be folate receptor alpha-high expressing, which means that the tumor, when you look at it under the microscope, at least 75% of the cells have 2+ or greater staining intensity.

Once those tumors were determined to be folate receptor alpha-high, patients could be enrolled, and then they were randomized to either mirvetuximab or investigator's choice chemotherapy. And what you can see here are the demographics of the participating patients.

So progression-free survival, we saw a 35% reduction in the rate of progression events with the use of mirvetuximab versus investigator's choice chemotherapy. And for overall survival, we had a 33% reduction in the rate of death for patients initially randomized to mirvetuximab as compared to investigator's choice chemotherapy. And then on the bottom of this slide, you can just see the response rates: 42% for MIRV versus 16% for investigator's choice chemotherapy.

Now the distinction, other than it working very well to mirvetuximab is it does have a differentiated safety profile, which is good. We have very little hematologic toxicity. So across neutropenia, anemia, thrombocytopenia, nominal levels of significant impact with mirvetuximab, which is great for patients to rotate this in and give their bone marrow a break. Neuropathy is seen, though; less than with paclitaxel, but it is still something we have to monitor for closely with use of mirvetuximab. We do have nausea. It's moderately emetogenic, so you do have to premedicate. Diarrhea, low grade but about 30% of patients can have diarrhea, mainly grade 1 so you have to mitigate for that.

The main differentiator here is with ocular toxicities. These resolve over time with holding the medication and increase in use of steroid eye drops, and either we re-dose at the same dose and it doesn't happen again, or we dose-modify based on the severity of that medication. But that is a key side effect that we have to counsel patients about and provide mitigation for.

But that's the data, and that led to FDA approval of this medication in 2024.

And so with that, I'll turn it back to Dr. Salani, just to ask how you're thinking about use of mirvetuximab in your patients with platinum-resistant ovarian cancer.

Dr. Salani:
Yeah, that's a great overview, and I know you were instrumental in a lot of these studies that really brought this to our landscape. And I think it's something that we are testing, and you mentioned NGS testing in one of the earlier episodes, which we're getting off at the time of diagnosis, and oftentimes we'll add IHC testing, and so you actually get your folate receptor scoring at that time. And I remember when we first got this, it was positive or negative, and now we're actually looking at the percentages because we're learning more and more about kind of some of the expression here as different agents come into the market as well. But this is something that I will know pretty much right off the bat, and it's nice to have that information.

And then, if these patients do have folate receptor expression high or greater than 75% as with 2+ intensity or higher for the study, I will actually use this as kind of one of my target lines in the platinum-resistant setting.

I do agree that it's well tolerated, but the ocular toxicities are real. The mandate from the FDA was that every other cycle up to cycle eight, and then it's kind of as needed. But for patients who I personally, my anecdotal experience is patients who've been on it for a longer period of time do start developing more ocular toxicity, so I will often continue with eye exams pretty routinely for these patients.

Dr. Moore:
No, I mean, I think that's very true. It's when you're counseling a patient about this, talking about eye toxicity is a sensitive topic. We put our patients through a lot. They lose their hair, we hurt their nerves. We use GCSF, which gives them bone pain. Now we're giving them mucositis with these ADCs, and they just tolerate a lot from us. But messing with their vision is sort of a line that you cross with patients that really requires some sensitivity in the discussion and an ongoing assessment of this drug now that it's in the wild, as I like to say.

Dr. Salani:
Just to add to that, you can actually go on the website and actually get the information that's needed. They can take that to their eye provider, whether it's an optometrist, ophthalmologist, and then get that filled out and bring it back. So I think it kind of eases it. And then highlighting the use of the appropriate eye drops per the schedule. And I think you'll see great success with kind of patient compliance, education, and coordination of care. So it's a really great option for our patients, and I'm excited that we have it.

Dr. Moore:
Now, when I talked about MIRASOL just now, you emphasized that it is for folate receptor alpha high. The medicine works. There was a study before MIRASOL called FORWARD I, where we had medium and high, and it works there. We have NCCN approval for bevacizumab and mirvetuximab in any expressing folate: low, medium, or high. When, if ever, do you use that combination? When are you thinking about it? Are you not thinking about it for tumors maybe that are not folate receptor alpha high, but folate 60%?

Dr. Salani:
Yeah, it is something I have used per the NCCN label. It is something I've used, and I've seen success with. I think it's become challenging now that we have other options emerging into this landscape for platinum-resistant. Now, if they have folate medium expression or low expression and I have the relacorilant/nab-paclitaxel, or the B96 regimen, which is weekly paclitaxel, pembrolizumab, plus or minus bevacizumab, I think the eye gets a little bit more challenging, and then that's not even including all these other ADCs that are kind of headed into this space.

Dr. Moore:
Right. Well, I think we pivot all the time with every new approval, so we'll have to redo this probably in a year.

But that brings us to the end of this episode. Good luck translating this information into your everyday practice, and thank you for joining us.

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