Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/cme/taking-the-patient-centered-approach-to-mycophenolate-risk-mitigation-mycophenolate-risk-mitigation/16628/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Taking the Patient-Centered Approach to Mycophenolate Risk Mitigation, Mycophenolate Risk Mitigation

Announcer Open:
Welcome to CME on ReachMD. This activity titled: Taking the Patient-Centered Approach to Mycophenolate Risk Mitigation, is provided by Boston University Chobanian and Avedisian School of Medicine in partnership with Clinical Care Options LLC, and is supported by an independent educational grant from the Mycophenolate REMS Group. This activity is intended to be fully compliant with the Mycophenolate REMS education requirements issued by the U.S. Food and Drug Administration, FDA. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Ms. Simpson:
Hello, and welcome to Taking the Patient-Centered Approach to Mycophenolate Risk Mitigation. The program was provided by the Boston University Chobanian and Avedisian School of Medicine, Barry M. Manuel Center for Continuing Education, in partnership with Clinical Care Options, and is supported by an educational grant from the Mycophenolate REMS Group. I'm Jennifer Simpson, nurse practitioner, and I'm excited to be joined today by Dr. Cara Dolin from Cleveland Clinic, Lerner College of Medicine Case Western Reserve University School of Medicine in Cleveland, Ohio, and Dr. Diana Girnita from University of Cincinnati, and Rheumatologist on call in Irvine, California.

These slides list the faculty, steering committee, and patient involved in this program. Here are the disclosures. Here are additional disclosures.

Here are the learning objectives for today. Identify the pregnancy and fetal risks associated with mycophenolate use in female patients of reproductive potential; educate and counsel female patients of reproductive potential on the need for pregnancy prevention and planning during mycophenolate treatment; select safe mycophenolate alternatives for female patients who are pregnant or considering pregnancy; and promptly report pregnancies that occur during mycophenolate treatment to the Mycophenolate Pregnancy Registry. Through this discussion, we'll will follow the case of Lisa, who has a history of lupus as she begins mycophenolate therapy and then navigates family planning. So, we'll talk about getting started with mycophenolate treatment, navigating family planning with mycophenolate treatment, and then a collaborative approach to caring for mom and baby.

And now I'll be joined by Dr. Diana Girnita.

Dr. Girnita:
Thank you very much for the introduction. Today, I'm going to start about getting started with mycophenolate treatment. There are two forms of mycophenolate that are used today as immunosuppressants, mycophenolate mofetil and mycophenolate acid. Mycophenolate mofetil is indicated for prophylaxis of organ rejection in adult and pediatric recipients of allogeneic kidney, heart, and liver transplant in combination with other immunosuppressants, and it is available as an oral capsule, tablet, suspension, or injection. Mycophenolate acid is indicated for prophylaxis of organ rejection in adult recipients of kidney transplants but also in pediatric patients more than 5 years of age who are more than 6 months post kidney transplant, and can be used and should be used in combination with cyclosporine and corticosteroids. And it is available as a delayed-release tablet containing enteric-coated mycophenolate sodium.

Now, over the years mycophenolate was also used in many autoimmune diseases from uveitis, lupus or lupus nephritis, graft-versus-host disease, bullous pemphigoid, pemphigoid vulgaris, systemic sclerosis, autoimmune hepatitis, dermatomyositis, focal segmental glomerulosclerosis, and interstitial lung disease. All of these diseases are using mycophenolate as an off-label type of medication.

However, over the years, the FDA had to adjust for adverse pregnancy outcomes associated with the use of mycophenolate during

pregnancy. If initially the warning was for pregnancy or during labor or delivery or nursing mothers, today we are talking about adverse pregnancy outcomes reaction in pregnancy, lactation, and now for females and males of reproductive potential. So, there are some specific populations where we have to be very careful, including pregnancy, lactation, and as I said, females and males of reproductive potentials, where not only that we have to adjust for the life of the people that are using the medication, but we also have to educate patients about pregnancy testing, contraception, and the risk of infertility.

Now, we have to check for pregnancy status prior to initiating this type of treatment with mycophenolate, but we also have to monitor during the treatment. We have to tell patients about one pregnancy test with a high sensitivity that should be done immediately before starting the therapy with mycophenolate. But we also have to educate patients about another pregnancy test with the same sensitivity that should be done 8 to 10 days later. We have to repeat pregnancy tests that should be performed with every routine follow-up visit. And the results of those pregnancy tests should be discussed with the patient.

The pregnancy and fetal risk associated with the use of mycophenolate use during pregnancy, they've changed over the years. And regarding pregnancy loss, according to the National Transplantation Pregnancy Registry Report in 2006, there were 24 females that were transplant patients that reported 33 mycophenolate-exposed pregnancies. Out of those, 45% had spontaneous miscarriages and 22% had structural malformation. We also have data postmarketing in 77 females systemic treatment during pregnancy, where it was found that 32% had spontaneous abortion and 22% had a malformed fetus or infant.

If you look at these graphs, you're going to see that preconception and postconception, the number of patients that develop miscarriages is completely different. If you look at the first graph, you're going to see that if the mycophenolate was discontinued before the pregnancy, the number of miscarriages is significantly lower compared to patients that had the medication discontinued after conception. And the same kind of pattern we can observe for birth defects; if the treatment was discontinued before conception, the risk of birth defect is significantly lower compared to if the treatment was stopped after conception.

If we look even deeper, we're going to find out that mycophenolate exposure in females that received a kidney transplant, in a study that was retrospective was also prospective from the same database, it was found that about 30% of these patients that had a pregnancy, suffered a miscarriage. However, patients who discontinued mycophenolate more than 6 weeks prior to pregnancy did not show a significant difference in the risk of miscarriages, versus patients who discontinued before 6 weeks prior to the pregnancy. So, if you look at these numbers, if the patient discontinued the treatment less than 6 weeks prior to conception, you're going to see an odds ratio, or an increased risk of 1.12 – almost 1.12 compared to patients that discontinue the treatment more than 6 weeks after preconception. If they discontinue the treatment during the first trimester, the risk increases. But if they discontinue the medication during the second trimester, this risk is significantly higher, almost 10.

When we look for birth defects, the same study shows that 9% of those patients who were exposed to mycophenolate have experienced birth defects. And the same kind of pattern applies here. When we look for patients that discontinue the therapy less than 6 weeks prior to preconception, their risk is significantly lower compared to patients that discontinue during the first trimester or discontinue the medication during the third trimester where the risk was six times higher. If the patient had multiple pregnancy, the risk increases with the number of pregnancies.

Now, what are the types of birth defects that are associated with the use of mycophenolate mofetil during pregnancy? As you can see, ear and orofacial and ocular type of birth defects are the most frequent ones. And then we also have birth defects at the visceral level, heart, distal limbs, and central nervous system.

This is a picture of an infant with a cleft lip. And these are different types of cleft palates, birth defects that can happen in infants that were exposed to mycophenolate during pregnancy. And this is another common birth defect. This is an external ear abnormality in an infant that was exposed during pregnancy, to his mom's pregnancy, to mycophenolate mofetil.

Ms. Simpson:
Now, let's join Lisa's discussion with Dr. Girnita. Lisa is a 26-year-old woman diagnosed with systemic lupus erythematosus as a teenager. She's meeting with her rheumatologist, as her lupus has flared even with steroids, and she wants to know what her options are.

Dr. Girnita:
So, as we have discussed today, we will be starting mycophenolate mofetil to help control your lupus symptoms. I will review some very important information with you. I will also give you a guide and a list of other resources that you can always access more information about the medication. One important thing to discuss with you today is that this medication cannot be used in patients who want and who can become pregnant. Those patients using mycophenolate who can become pregnant must use contraception to prevent pregnancy.

Lisa:
I am sexually active but don't want to get pregnant. Why is it important to use contraception?

Dr. Girnita:
That is a great question. Contraception is required because there is an increased risk for miscarriage and birth defects. Studies have shown that there is a high risk for miscarriages especially in the first 3 months of a pregnancy. Data from National Transplant Registry found out that out of those 33 pregnancies in patients taking mycophenolate, almost half of them had miscarriages. In addition, 20 to 25% of babies in these studies, they have birth defects. And those birth defects could involve the ear, the cleft lip, cleft palate, defects in the arms, legs, heart, esophagus, kidneys, and nervous system.

Lisa
So, what do I need to do before starting this medication?

Dr. Girnita:
Before you start on mycophenolate, we will do a pregnancy test to ensure that you are not pregnant now. And then in 8 to 10 days after that, we will repeat the pregnancy test. We will also check pregnancy status while you are on this therapy for all your routine follow-up visits here at the clinic.

Lisa:
I definitely don't want to get pregnant and risk having a miscarriage or harming the baby. What type of birth control do you recommend I use? Are there some that are better than others?

Dr. Girnita:
That is a great question. Because not all methods of birth control are equally effective. And it is important to use the best types and to use them as directed. You will need to use these methods of birth control during your entire treatment with mycophenolate, and for at least 6 weeks after you stop therapy. And there are several options to consider. The first option, which is the most effective with less than 1 pregnancy per 100 females in 1 year includes intrauterine devices, tubal sterilization, or having your partner have a vasectomy. The second option is to use a hormonal birth control and a barrier method, for example, condoms. This results in 4 to 7 pregnancies in 100 females in 1 year. And it is important to use the barrier method with the birth control because mycophenolate can decrease the effectiveness of birth controls like your pills, the patch, the ring, the shot, and even the implant. And the third option is to use two barrier methods, but this is the least effective, resulting in more than 13 pregnancies per 100 females in 1 year.

Lisa:
I am already on the birth control pills and feel very comfortable with them. So, I'd like to add the barrier method also, but would like to discuss this with my partner.

Dr. Girnita:
So, as you can see, it is extremely important to educate females of reproductive potential, including girls who have entered puberty and all woman who have a uterus and ovaries and have not passed through menopause, because it's important to know that educating women of reproductive potential will increase the risk of first trimester pregnancy loss and birth defects. For pregnancy loss and birth defects associated with mycophenolate during pregnancy, it is important to offer patient education. It is important to refer them to medication prescribing information for different type of population and refer them to the most recent data on the risk of pregnancy loss and congenital malformation. And it is also important to provide patient education about pregnancy prevention and planning during mycophenolate treatment to discuss acceptable methods of contraception and appropriate duration of contraception. And not only that, but advise patients to let providers know if they are considering pregnancy. Patients can use REMS material and they can find out about the pregnancy risk and counsel them about the types of contraception and the pregnancy planning. It is important to provide the patients with treatment options if they are considering pregnancy, and also discuss about immunosuppressive efficacies and safety profile of available therapies that will replace mycophenolate. Through these programs, mycophenolate mofetil, we can offer patients with brochures, but we can also offer prescribers with a healthcare provider brochure.

Ms. Simpson:
So, let's discuss what we just heard about from Dr. Girnita. So, very important, we need to be discussing this at every visit with our patients. Wouldn't you agree, Dr. Girnita, that we need to make this a priority that our childbearing women who have the potential to get pregnant, we need to be touching with them on every level with this?

Dr. Girnita:
Yes, that's correct. We have to open the discussion and to continue the discussion with every visit that they have with us and remind them that there are options if they consider to remain pregnant.

Ms. Simpson:
And tell me what are your strategies of opening up this conversation with your patients? What do you say to them to, you know, help them feel comfortable that they can be discussing this with you?

Dr. Girnita:
I will always ask them if they change their mind, if they consider at this point to remain pregnant, especially females that are childbearing age, this is extremely important to remind them about the side effects of the medication, but also that there alternatives if they consider pregnancy.

Ms. Simpson:
Yeah, I think that's great to point out that they do have other options, that there are alternatives that we can offer them if their lifestyle or what they're trying to plan for in the future has changed, right? And I think definitely making them feel comfortable that there's – whatever they are foreseeing that to be is perfectly okay.

Dr. Dolin, do you have anything to add as far as if you're seeing a patient in the office that you know is on mycophenolate, they're using contraception, are you having conversations with them about the importance of that?

Dr. Dolin:
As a maternal fetal medicine subspecialist, I'm often seeing these people after they're pregnant, sometimes for preconception visits, which I think we're going to talk about a little bit later. But I love what Dr. Girnita is saying how she talks about this at her appointments as a rheumatologist. So, I think this discussion really needs to happen outside of the OB/GYN world, essentially, and I always teach my medical students who aren't going into OB, that if they take anything away from their rotation or the time they spend with us, it's that in their patients of reproductive potential to always ask about pregnancy plans. And so, at every visit, especially on a patient that's on a medication that isn't compatible with pregnancy, like mycophenolate, you should be asking, 'Do you plan to become pregnant in the next year?' And so that really opens the door? If they say no, 'Okay, what contraception are you using? Is it appropriate? And if you're not using contraception, can I prescribe you something? Or can I refer you to a gynecologist that can and counsel you and prescribe you appropriately?' And if the answer is yes, then it's like, 'Okay, let's review where you are with your disease. How can we optimize your preconception health? And how can we transition you to some medications that are compatible with pregnant?' And specifically, with someone that's on mycophenolate, it's having this conversation and making sure that they have a clear family planning plan in place. Because we do know that 50% of pregnancies are unintended. And so, it seems simple that people should be, you know, preventing pregnancy and thinking about their family planning, but oftentimes people aren't, even people with underlying medical conditions and on medications that aren't compatible with pregnancy. So, I think this is a really important discussion to have.

Ms. Simpson:
Well, and I think even taking that step just to ask them, you know, what are you planning? Where do you foresee yourself in the next year with that? And then what's your plan according to how that fits? Right? I think even just putting that in the minds of our female patients will help them to be like, 'Okay, I definitely need to be thinking about this. And I need to be aware of the risks, so that way I'm making the appropriate decision for myself and for, you know, my future children, too.'

So, now we're going to talk about navigating family planning with mycophenolate treatment. Here, Dr. Girnita will meet with Lisa for her follow-up visit after being on mycophenolate for a few months. So, Lisa and her rheumatologist meet for a follow-up visit after starting mycophenolate for her lupus management. And Lisa tells her doctor that she's feeling very well with no lupus flares and that she would like to start a family.

Dr. Girnita:
It is wonderful to hear that you are feeling better with your lupus symptoms on taking mycophenolate. And your labs are looking great. At our last visit, you mentioned that you were not interested to remain pregnant. Is that still your goal?

Lisa:
Actually, after talking to my partner about this, we would like to try within a year.

Dr. Girnita:
I understand. We can certainly make a plan together for this. Are you still using the recommended contraception to prevent pregnancy now?

Lisa:
Yes, I'm taking birth control pills every day at that time and we've been using condoms as well.

Dr. Girnita:

Great. It is important to continue to use both the birth control and the condoms while you are taking mycophenolate and for at least 6 weeks after you stop this therapy. This is to prevent potential side effects related to your pregnancy, like miscarriages or birth defects in your baby. When you are ready to start getting pregnant, you have to let me know because we will discuss additional options or alternative options. Are you planning to start getting pregnant in the next 6 weeks?

Lisa:
We're fine to wait a bit longer if that's what you recommend, but I would like to hear about the other medications.

Dr. Girnita:
Absolutely. We can discuss these options today. Since your lupus appears to be well controlled without any recent flare-ups, that will be a good time for us to consider to switch on something that is safer for your pregnancy, a medication like azathioprine. We would like to make sure that you remain safe and your lupus is controlled on this medication while you are trying to get pregnant. And in the meantime, I would like to refer you to a maternal fetal medicine specialist for preconception counseling and for high-risk obstetrical care.

Lisa:
That sounds great.

Dr. Girnita:
Finally, as a reminder, if you do become pregnant while taking mycophenolate or within 6 weeks of having stopped this therapy, please let me know. If that happens, we will also submit a report to the Mycophenolate Pregnancy Registry. I want to assure you that if we do make a report, any protected patient contact information or medical information to the Mycophenolate Pregnancy Registry is covered by a HIPAA waiver.

Ms. Simpson:
Please welcome Dr. Dolin.

Dr. Dolin:
Okay, so now I'm going to go through the contraception options and how to counsel patients on mycophenolate about reliable and effective contraception while they're taking this drug. So, as we just talked about, it's very important for all healthcare providers that are taking care of patients on mycophenolate to counsel them about their family planning intentions and appropriate contraception, and to let them know to communicate when they're ready to start a family or start to try to conceive and so they can be transitioned to the right medication that's going to be safe for pregnancy.

Any patient of reproductive potential who is sexually active with a man needs to be on a reliable and effective form of contraception for the entire treatment course while they're on mycophenolate and for 6 weeks after stopping the drug. This part's really important. So, this chart here goes through kind of three different levels of different contraception options that we're going to go through in a little more detail in the following slides, it's kind of just an overview.

Before we get into that, we do want to touch on emergency contraception. So, as I said, many pregnancies are unintended and sometimes things happen where people didn't have the appropriate contraception in place. And so, it's important that patients know that emergency contraception exists, and there's multiple options. And so, listed on the slide here are two options that are available just at the drugstore, so they don't need to see a provider. So, one is levonorgestrel, this is effective up until the LH surge, it's approved for use up to 72 hours after unprotected intercourse but can be used off-label for up to 120 hours after unprotected intercourse. It's available over the counter without regard to age, so there's no age restrictions. So, there really should be very few barriers to a patient obtaining this medication in the instance that they need emergency contraception.

Ulipristal is another medication that does require a prescription but is approved for use up to 120 hours after unprotected intercourse. Importantly, this one cannot also be used with other progestin contraceptives.

Another option for emergency contraception is the intrauterine device, or an IUD. So, this can be used for up to 5 days after unprotected intercourse but may actually be effective at any time before a positive pregnancy test. One of the benefits of this is that it's highly effective regardless of BMI. So, the levonorgestrel has less efficacy in the patients with obesity, and it can be used anytime within the menstrual cycle. A downside of this is obviously patients need to go in and see a clinician to have the IUD placed. But another benefit is that while working as emergency contraception, it can then be their long-term, reliable, reversible form of contraception. So, they're kind of getting, you know, they had this oops, they are treating it with their emergency contraception, and now they have a reliable form of birth control in place.

So, here are some of the other acceptable birth control options. So, on this first tier, Tier A, these are really our most effective options and really the ones that we should recommend for patients. It's important that when we're asking patients about their family planning

intentions, to ask if they're finished with their childbearing, maybe they already have a few kids or maybe they don't even want children. And then a form of permanent sterilization is always an option, and is very, very reliable and effective. And so, the two forms of that is the woman can get a tubal sterilization, or her partner can get a vasectomy.

If the patient does desire future fertility, but just not at this time, then IUD is a great choice. And really, this is our first-line number one recommended option for patients on mycophenolate. It works very well, less than 1 pregnancy per 100 women per year. Patients don't have to remember to take a pill every day, they don't have to come back for an injection, it's placed and it can stay for years. And then when it's removed, the return to fertility is actually quite quick. And so, usually once we remove it, if people are interested in becoming pregnant and we've transitioned to them to their safe medications, they can often achieve fertility pretty quickly, which is great.

So, on the second tier, Tier B, we have the different hormonal options. And so, these include progesterone only or combined progesterone and estrogen type options. This includes the progesterone-only injection, birth control pill, which can either be a progesterone only, or a combined progesterone/estrogen pill, the progesterone patch, the vaginal ring which is estrogen, and then the progesterone implant. Very important when it comes to these different hormonal methods is that when patients are on mycophenolate, it decreases the efficacy of these options. So, patients need to use an option from Tier B along with an option from C, and so these are the different barrier methods.

And then a final option is to use two barrier methods together. This is really not recommended. It is the least effective and we now all know all of the risks of being on mycophenolate and becoming pregnant, and so we really don't recommend this. But if a patient absolutely won't take a hormonal method or isn't interested in IUD or permanent sterilization, then obviously this is better than nothing, but they really need to use two to increase the efficacy.

This slide is really important. So, when it comes to estrogen-containing contraception, as well as the progesterone-only injection, people who have a history of a thrombotic event or have a high risk of thrombosis, really any estrogen-containing contraception is contraindicated because of that thrombosis risk. This also includes patients that have antiphospholipid antibodies, and we know that many of our patients with lupus also have these antibodies, which puts them at a higher risk of a venous thrombotic event. So, they really shouldn't be using these estrogen-containing contraception. Likewise, patients that had a higher risk of osteoporosis, maybe because of their other disease states or their age, should not be using the progesterone-only injections. And then also people who their disease is not very well controlled, who have very active disease also shouldn't be using an estrogen-containing contraception. So, this comes back to what I said on the last slide, really an IUD is the most effective, it's the safest, it's the most reliable, and really should be what we're counseling our patients to use if they're taking mycophenolate.

Obviously, if a patient has gone through menopause, then they are no longer at risk of pregnancy. But it's really important that menopause is clinically confirmed by a healthcare professional. And so, the definition of menopause is a permanent end of menstruation and fertility. And so, this can be diagnosed either by 12 months of spontaneous amenorrhea, so a patient not having her menses for 12 months. It can also occur from post-surgical, so if a patient has had a bilateral oophorectomy, so no longer has their ovaries. And it usually isn't confirmed solely on elevated FSH and LH, but this can be used to help make the diagnosis as well.

As we said earlier, it's very important to be monitoring for pregnancy when patients are on mycophenolate. Patients should have a pregnancy test with a high sensitivity done immediately prior to starting mycophenolate. And then that test should be repeated about 8 to 10 days later. And then they're going to need regular repeat pregnancy tests at all routine follow-up visits, or if at any time when they think they may become pregnant. And it's very important that obviously that we're telling the patients the results of these pregnancy tests, but that also if a patient takes a pregnancy test at home and finds out they're pregnant, that they let us know right away.

So, patients who want to get pregnant, very important to counsel patients on mycophenolate to let us know that they would like to become pregnant before they start trying, hopefully. This is a great time to determine whether there are other appropriate treatment options that have better – less teratogenic or have less potential for embryofetal toxicity. It's a time to refer patients for a preconception counseling visit with their obstetrician or a high-risk obstetrician, like a maternal fetal medicine or fertility specialist. And there needs to be continued multidisciplinary care with the patient's obstetric team, their rheumatologist, and their primary healthcare providers.

So, on this slide, we have the 2020 American College of Rheumatology guidelines for medications to use before and during pregnancy and during lactation. And I'm not going to go through all of this now, all of this will be available on the downloads that accompany this course. But you can see that there are multiple medications to choose from that are compatible with pregnancy that can be used as an alternative to mycophenolate. And so here are just some of those safe alternatives in a little bit more detail. Many, as you can see up here, hydroxychloroquine and sulfasalazine can be used preconception, during pregnancy, and breastfeeding. And so, if this is a medication that you can transition your patient to, these are great choices.

And then if a patient does become pregnant while taking any of these medications, these are the recommendations. And so, for the

majority of them, it's to stop. And as we've already touched on with mycophenolate, we want to stop it at least 6 weeks prior to conception, as well as not using it during pregnancy or during lactation. So, it's important to counsel our patients what to do if they do have a positive pregnancy test.

So, if there is a risk of maternal mortality after stopping mycophenolate, we can consider continuing it, especially if it's after the first trimester because that's when a lot of organogenesis happens. And so, if they're already past the first trimester, and we think the risk of them stopping this medication outweighs the risk to the fetus especially if any effect has already happened, then we can consider continuing it, but that needs to be in a multidisciplinary fashion with their maternal fetal medicine provider and their rheumatologist. If possible, we try to find an acceptable alternative to transition them to so they can stop the mycophenolate. And then we always discuss the potential risk to the baby. So, there's the risk of miscarriage but also those different risks of birth defects. And so, from our standpoint, as obstetricians, we may do additional ultrasounds or earlier ultrasounds so that we can find out if there is a congenital malformation or some issue sooner than later and be able to make a plan for the pregnancy. And then finally, as I mentioned, referring to maternal fetal medicine for that interdisciplinary care and counseling.

And so now, I'd love to open it up to the group to talk about what to do in cases of unplanned pregnancy.

Ms. Simpson:
Have you had this happen before, Dr. Dolin, where you've had a patient who had an unplanned pregnancy come in and was still taking their mycophenolate?

Dr. Dolin:
I have had this in the past. And with that patient, I was able to communicate with her rheumatologist, and together as a group decided that the patient, there were acceptable alternatives. And so, we had her stop right away, as soon as we found out, and transitioned to her to a medication that was compatible with pregnancy. And then we did do additional ultrasound surveillance to check on the fetus and make sure it was developing normally. And luckily, she actually had a great outcome. And I think that's a really important point. Because even though we put up those slides earlier that there's a high risk of miscarriage and a high risk of congenital anomalies, the majority don't. Right? And so, it is important to give those patients that reassurance once whatever has happened has happened, moving forward, that we're going to watch you in the baby closely, but that the most likely outcome is that everything's going to be okay.

Ms. Simpson:
That's good to reassure them. I'm sure that's a nerve-wracking situation for a mom to be in. So, I'm sure that's great to have their OB to help them kind of guide them through that situation.

Have you had that happen, Dr. Girnita, where you had a patient on mycophenolate who had an unplanned pregnancy?

Dr. Girnita:
Yes, I did. And I think, like Dr. Dolin said, it's very important for the patient to know that the risk exists, but not all the patients will have these outcomes. With the right planning and with the right team, the patients have the ability to overcome this very stressful period in their life. And I think that if we educate them that there are alternatives and switch the treatment as soon as we find out about the unplanned pregnancy, the risk is smaller, closer to the time of disclosing the pregnancy. So, it's important to have that open channel of communication and the team to support the patient going forward.

Ms. Simpson
Yeah, I definitely agree about open communication. I think, again, having that relationship with your patients where you can – they can feel comfortable asking you questions, and not feeling shame if something happens, you know, especially if you've been having this conversation with them, and saying, 'Hey, I want you to make sure you let me know if your plans have changed, if you're wanting to become pregnant in the next year.' And then it turns out that, you know, oops, whatever did happen, they do become pregnant, it wasn't planned, that they don't feel then, you know, shame that they can't come to you and say, 'You know, this is what happened, and, you know, I believe I'm pregnant.' And that way you can, you know, mitigate what's going on, get through the appropriate channels, get them over to the registry and make sure all of that is documented and then tracked going forward. And make sure they feel comfortable in that situation to have those conversations. It's one of the most important things I think we could do as the providers.

Dr. Dolin:
And enrolling in the registry is key. As we saw in the earlier slides, we have pretty small numbers. And so, really knowing about every pregnancy that is exposed to mycophenolate and being able to put all that information together really helps us with counseling patients in the future. So, it's super important. And in my experience, patients are really open to joining the registry, they really like to contribute to the science and the knowledge and be able to help other women that are in their similar situation in the future.

Ms. Simpson:

I agree with that. Dr. Girnita, would you say there's any specific strategies that you do when you're communicating with our OB/GYN colleagues in this situation?

Dr. Girnita:
I think the most important thing is to have that channel of communication to pick up the phone and find the colleague that will immediately see the patient and counsel the patient going forward. And telling the patient, like you said, there is no shame in that, things like this happen. As Dr. Dolin said, 50% of our patients will have an unplanned pregnancy. And there is nothing to be ashamed about. Things like that happen. And between us and patients, it should always be this way of communicating, that you are there to help them and it doesn't matter what happens, we will find something to help them or we will try to find the best things or the best methods that we can use to help them going forward. As a strategy to communicate, I think it's, you know, we have multiple channels of communications between us as medical providers, but, you know, finding one that is very comfortable to take these patients and counsel them forward, I think it's also important for the patient.

Ms. Simpson:
Dr. Dolin, would you say there's any specific strategies that you've employed in dealing with situation, like maybe if there was a situation where a patient had come to you with an unplanned pregnancy prior to them being able to have that conversation with a rheumatologist or maybe a different provider that had them on a medicine that had these risks?

Dr. Dolin:
I echo what was just said. I think the most important thing is having that relationship with your colleagues and being able to take care of these patients in a multidisciplinary fashion. And so, there's often times where I'll have that patient in front of me and say, 'Let's call right now,' you know, and I'll call up a colleague and, you know, ask. Because as a maternal fetal medicine physician, you know, though, while I'm aware of some of the safe alternatives, it's not really my area of expertise to transition them for their underlying disease process. And so, I will call up their physician that is the expert in that area and say, 'Okay, she's pregnant, what's our plan moving forward? What medication can we switch over to?' Because we want to do it right there as soon as possible; I don't want to wait until she has an appointment in 2 weeks with that provider, and then figure out a plan. And so, you know, I agree, it's, you know, just being proactive and reaching out to our colleagues. And we're all in this together to take really good care of patients and make sure that they have healthy pregnancies, and also that they, you know, stay healthy with their underlying disease process.

Ms. Simpson:
Yeah, and I think that's definitely a good point is like, hopefully that transition happens very smoothly, because I'm sure what we're all kind of worried about in this situation, too, is not just, of course, the harm to the fetus, but also this patient, and are they going to flare. Are they going to have a worse outcome, which of course is not going to be good for the pregnancy either. Which is why it's always important for us to be having this conversation with a patient prior to the pregnancy is that way, hopefully, they're in a good preconception health to, you know, not flare, have a safe pregnancy for mom and for baby. So, I think that is definitely highlighting that for our patients. And them understanding this is why this is important, is that we want you to be healthy, we want your future pregnancies to be as healthy as possible, and for you to have the best outcomes.

Dr. Girnita:
I think the best outcomes comes from a group effort like a multidisciplinary effort, because as Dr. Dolin said, if you have a patient that is not only having lupus, but has a high risk for thrombotic events because of antiphospholipid syndrome, or has other complications, like lupus nephritis, you have to be very careful and, you know, take care of the patient, but also foresee what is going to happen with the pregnancy. So, I think that all of us, we play a big role into the life of that patient, but without each of us, you know, that patient cannot have a good outcome, because we all have to come in with our heads together to optimize the health of the patient to have a good outcome regarding the pregnancy.

Ms. Simpson:
And now we'll talk about a collaborative approach to caring for mom and baby. Let's join Lisa as she meets Dr. Dolin. Per her rheumatologist recommendation, Lisa stopped taking mycophenolate mofetil and started taking azathioprine, which as we saw, is a safer option for someone considering pregnancy. Lisa's rheumatologist also referred her to an OB/GYN maternal fetal medicine specialist for preconception counseling and high-risk obstetrical care. Lisa has been receiving azathioprine for 4 weeks at the time of her appointment. Thankfully, she's feeling well and having no lupus flares.

Dr. Dolin:
Hi, it's wonderful to meet you. My name is Dr. Dolin. I'm one of the maternal fetal medicine physicians. Your rheumatologist has referred you to discuss your goal of becoming pregnant. I understand that you've been taking mycophenolate to treat your lupus, is that correct?

Lisa:

Yes, that's right. I met with my rheumatologist a few weeks ago to let her know that my partner and I have been wanting to try for a baby soon. And she thought that I should meet with you.

Dr. Dolin:
I agree. And I'm so glad you're here. I always love to meet patients like you preconception before you start trying so we can make sure we have a plan for a healthy pregnancy. I'm sure you and your rheumatologist have discussed the risk of becoming pregnant while taking mycophenolate for both mother and baby. With lupus, you're at increased risk for complications such as preeclampsia, gestational diabetes, or cardiovascular problems around delivery. And for the baby, mycophenolate has been known to cause pregnancy loss or miscarriage. And if miscarriage doesn't happen, there might be other serious risks for the baby, including birth defects. So, I'd love for us to work together to decrease risk for both you and your baby.

Lisa:
Yes, my doctor and pharmacist reviewed those risks with me. They definitely do make me nervous. And when I let my rheumatologist know that I wanted to get pregnant, we discussed other medications I could use during the pregnancy to treat my lupus instead. I'm taking hydroxychloroquine and we added is azathioprine. I started on that 4 weeks ago when I stopped the mycophenolate. So far, I've been doing well with no flares.

Dr. Dolin:
That is great to hear. And I'm so happy that those other medications that are more compatible with pregnancy are working to help keep your lupus controlled. Have you continued with your contraception as well?

Lisa:
Yes, I'm still on birth control pills and I'll use condoms also. How long will it be before I can start trying to get pregnant again?

Dr. Dolin:
You have about 2 more weeks left to go without the mycophenolate before we'd want you to start trying to get pregnant.

Lisa:
Okay, that sounds good. I definitely want to start trying soon.

Dr. Dolin:
This is a very exciting time. I have some other things I want to discuss with you to make sure that we have a plan for a healthy pregnancy and a healthy baby. But if you do happen to become pregnant before the next 2 weeks, please let me and your rheumatologist know, we can then work together to make a plan to make sure you have a healthy pregnancy and will also submit a report to the Mycophenolate Pregnancy Registry.

Lisa:
Thank you.

Ms. Simpson:
So, strategies for coordinating care among the care team, as we've talked about, kind of between a rheumatologist and their OB/GYN, is just it's developing relationships within the community and making sure we have those open lines of communication to be able to contact a colleague when we need to be able to get our patient in. And I think a lot of this is kind of setting the expectations for our patients as well, that they know how important it is ahead of time.

Dr. Girnita, do you have any thoughts on how you would incorporate nurse practitioners or PAs into this care team strategy?

Dr. Girnita:
I think that educating everyone around us about the risk of mycophenolate, it's the most important thing. You know, the patient is aware with every visit, if you remind them about the risk, they will be surely aware that there is a risk if there is an unplanned pregnancy, or there is a strategy that we need to apply for that case when they plan a pregnancy. But even in our team or colleagues of ours, including nurse practitioners, PAs, and our nurses, we – or our medical assistants, if we educate them, they also interact with the patient. And sometimes they do spend a little bit more time with the patient than we have during our visit. So, if they are able to reinforce these kind of strategies, it's extremely important for the team, that in that way the patient will see and will hear the same message from a team, not only from one person.

Ms. Simpson:
I think that's great feedback. Dr. Dolin, would you say that you have any experience dealing with pharmacists in this particular instance?

Dr. Dolin:

Pharmacists are definitely a key member of the healthcare team. I often reach out to a pharmacist to, you know, clarify dosage, drug-drug interaction, and impact on pregnancy and lactation. We're always available for the pharmacist to call and reach out if they have a question about a drug. I've had that experience with other medications.

And then I would just say that that preconception referral is so important. As a maternal fetal medicine subspecialist, I love seeing these patients before they're pregnant. You know, it's the opportunity not just to make sure that they're transitioning to drugs that are compatible with their pregnancy, but also optimizing their preconception health. And so, we know for example, patients with lupus, if they conceive when their disease is quiescent, they have much better pregnancy outcomes than when they conceive when they're disease's flaring and likewise with a lot of other autoimmune diseases. So, it's really important to see these patients before they even start trying to conceive, so we can work together as a team coordinating their care, optimizing their preconception health, you know, making sure that they're on their prenatal vitamin and that it contains folic acid, you know, those little things can be really important for a healthy pregnancy.

So, this is the information about the Mycophenolate Pregnancy Registry. So, very important to report any pregnancy that occurs while a patient is on mycophenolate treatment or within 6 weeks following discontinuation. It's important to inform the patient that you may report this pregnancy. And like I said, in my experience, patients are really open to this and supportive of it. We encourage our patients to participate in the registry too, themselves, and we always make sure that they know that these reports are covered by HIPAA, so all this information is kept confidential. This is the website to access the pregnancy registry online and you can also do it by phone at this phone number on the screen.

These are some additional resources for both healthcare professionals and patients. They can all be found at the Mycophenolate REMS website. For prescribers, they can complete the online training, obtain patient signatures on patient prescriber acknowledgement forms, there's the voluntary report to mycophenolate pregnancy exposures to the MPA Pregnancy Registry, as we just discussed. And so, all this is available on the website.

There are additional healthcare provider and patient educational resources available. The American College of Rheumatology has a Reproductive Health in Rheumatic and Musculoskeletal Disease guideline. The American College of Obstetrics and Gynecology has a clinical opinion article that goes through different immune-modulating therapies that can be used in pregnancy and lactation, which is a great resource when thinking about what medications are safe to transition your patients to who are currently on mycophenolate. Clinicaloptions.com/immunology has more information for both healthcare providers and patients, as well as the Boston University websites.

Announcer Close:
You have been listening to CME on ReachMD. This activity is provided by Boston University Chobanian and Avedisian School of Medicine in partnership with Clinical Care Options LLC, and is supported by an independent educational grant from the Mycophenolate REMS Group. This activity is intended to be fully compliant with the Mycophenolate REMS education requirements issued by the U.S. Food and Drug Administration, FDA. To receive your free CME credit or to download this activity, go to reachmd.com/cme. Thank you for listening.