Q&A Session with Dr. Mario Lacouture on Managing Dermatologic Side Effects from Cancer Treatments

with Dr. Jack West

Dr. West:
Hi -- this is Jack West, Seattle-based medical oncologist and Founder and CEO of GRACE, the Global Resource for Advancing Cancer Education.

This is part two of a webinar done by GRACE in partnership with LUNGevity Foundation, featuring Dr. Mario Lacouture, dermatologist and faculty member at Memorial Sloan-Kettering Cancer Center in New York City. As probably the leading figure in management of dermatologic side effects of cancer treatment, Dr. Lacouture presented a webinar on this subject, followed by the following question and answer session.

What do you recommend that the oncologists, or I don't know if you have an initial consultation with many patients as they start in EGFR inhibitor, but what do you recommend that people walk out with when they are starting one of these agents in terms of supportive medications? Do you give people Cleocin T Gel and Hydrocortisone creams? Do you give them any oral drugs? And how do you advise them to manage this versus when to come in for re-evaluation?

Dr. Lacouture:
Yeah, that's a great question. You're referring to when they're starting Tarceva or drugs like this?

Dr. West:
Exactly.

Dr. Lacouture:
Yes, okay. So, these drugs provide such a great benefit to many people but as you say about 90% of people develop a rash. So, the important part about this is that for those people who develop a rash we treat everyone. I see everyone if possible before they start them and many people are started on oral antibiotics because we know that oral antibiotics work for these conditions, and a topical anti-inflammatory medicine such as Hydrocortisone 2.5% and an oral antibiotic such as Doxycycline or Minocycline which are used widely for the treatment of skin conditions such as acne and rosacea.

We know that the rash to these drugs like Tarceva, it's usually worst within the first two to four weeks affecting about 80% of people. So, what we do is we treat people for the first six weeks and if they have improved or the rash is not significant then we stop the antibiotics and we use the cream as needed.

Importantly, after the rash has subsided is when you may have other conditions such as dry skin with the fissures in the fingertips, the cracks in the heels which would benefit from Desitin, and also the scaling or very dry skin on the body which can benefit from an exfoliant such as Amlactin.

It is not infrequent that when people are for many months or years on drugs like Tarceva, that they develop secondary skin infections and these secondary skin infections can be easily treated

with oral antibiotics. So importantly whenever your skin hurts or has any redness or yellow pus containing areas, to inform your oncologist so that an appropriate treatment can be done with antibiotics.

Dr. West:
We have a series of questions that have come in -- very practical ones. One now is, "Can you use Biotin while taking Tarceva and does that potentially interfere with the effect of the drug?"

Dr. Lacouture:
That's a great question. Most studies so far have shown that – have been done but it is unlikely that Biotin will affect the effect of Tarceva. I would suggest starting with one of the topical measures; the nail strengtheners, the Shellac and the nail polish and if someone tries that and is not happy with the way that's working then consider using the vitamins.

Dr. West:
Okay. Another question is, "Do you have any recommendations just for general skin care practices?"

Dr. Lacouture:
Yes. So, for general skincare practices we recommend depending on the location to use of course some protective clothing, to use a broad spectrum sunscreen with an SPF of at least 15 to be applied every two hours. Also gentle skincare with the use of a gentle soap such as Dove soap, Cetaphil or Basis, and the use of a fragrant free detergent that will be gentle on the skin such as Tide or All Free.

Using a moisturizer in wherever areas are dry such as the ones I mentioned before. If patients or if people are to be starting EGFR inhibitors, it is important to start therapy. Even at the initiation we would recommend to use a topical cream such as a topical corticosteroid cream on the face and chest and to use an oral antibiotic such as doxycycline or minocycline for the first six weeks.

For other treatments we do not have – because the incidence of skin side effects is much lower, about 20 to 30% depending on the drug, we don't start prophylactic treatment with anything, but what is important however is that as soon as something in the skin appears it should be treated and people should notify their doctor.

Importantly, when this notification occurs it should be done early on so it is important when you leave your doctor's office to always have a phone number that you can call so you can reach them and if possible, if your doctor informs you that the drug may be associated with skin problems, to start looking for a dermatologist that is familiar with these conditions associated with these drugs early on.

Another common condition is the legs, the swelling or redness of the legs with Pemetrexed or Alimta that is used frequently in lung cancer and for this what is commonly done is the use of oral steroids or Prednisone and this usually does not lead to the modification of the drug. Although it looks like a skin infection, this is not responsive to antibiotics or unlikely to be the case so leg elevation if that occurs, compression stockings, and oral steroids are usually effective strategies.

Dr. West:
Great. Is there any preventive or particular treatment approach that you recommend for skin related changes and burns in the setting of radiation?

Dr. Lacouture:
So, that is a great question because this is something that is usually not something that is brought about frequently. There have been many studies now that have shown that the only topical cream that works to prevent radiation burns or the itching and pain and the redness associated with radiation are topical cortical steroids or topical anti-inflammatory medicines.

What are these? These topical anti-inflammatory medicines are drugs that are available through a prescription and what these drugs do is they decrease the inflammation from the damage that is caused by the radiation. The most commonly used of these drugs or the one that has shown the greatest effectiveness from a study coming from Mayo Clinic recently is called Elocon Cream. It has been shown to decrease radiation burns and the sensitivity to the radiation in the majority of treated patients.

It is also frequent for people receiving radiation to develop secondary skin infections. In these cases pain, fluid coming out from the area or what is called moist desquamation, which means peeling of the skin that is also moist. In these cases it is important to inform your doctor so that appropriate antibiotic therapy can be started with either oral medications, antibiotics or topical antibiotics.

Dr. West:
Another question: obviously hair loss is a big issue with many of our anti cancer treatments; are there any supplements or other interventions besides the cold cap that can help with the thinning of hair?

Dr. Lacouture:
It is not infrequent that people suffer from this problem and it's one of the major problems that people report, so what to do about this. In addition to the Biotin 2.5 milligrams a day, there is also a supplement of orthosilicic acid which stimulates collagen formation and is believed to strengthen the nails and also to stimulate the hair growth.

This goes by the brand name of Biosil. It is available at most vitamin stores and one capsule twice daily is the recommended dose. In addition to this, it is important for people that are undergoing therapy and that have hair loss to have their thyroid hormone and their iron stores in the blood checked through a simple blood test. As this can be replaced easily and both deficiencies of these levels have been associated with hair loss and it's something that can be fixed.

In addition to this, there are several hair thickeners that can be obtained online or in certain salons and these products that are either sprayed or applied on the hair that give a fuller appearance. And there are companies specially dedicated to this and some people have used them and really love these. There are – DermMatch Topical Shading is one of them preferred by people and also Bumble and Bumble has a hair powder that is matched specifically to the color of the hair that gives an appearance of a fuller hair and will help during this difficult time.

These products most of them are available in different colors; gray, blond, brown or black.

Dr. West:
Great. A general question, many of the people in our audience are aware of the question and the association of skin rash with efficacy of EGFR inhibitors and the question comes up if a rash is initially manifest and then subsides, does that translate to an EGFR inhibitor being less effective?

Dr. Lacouture:
Jack, I can tell that the audience really knows very well about these topics, and that is an important question and a very distressing one at the same time. The association between rash within the first months or during the duration of therapy has been well established -- however, the fact that the rash goes away does not indicate that a drug is no longer working.

For some reason, the skin becomes accustomed to damaging effect of the EGFR inhibitors in the skin and this will in turn result in the improvement of the rash. So, the fact that the rash goes away with time does not mean that the drug is no longer working, and also in people that don't have a rash it does not mean that the drug will not work.

Ultimately, what will dictate whether the drug is or is not working is going to be the oncologist's determination based on the scans and the overall examination of the person receiving the drug and how the person is feeling. So ultimately the oncologist's impression based on their clinical exam and radiological evaluation will dictate whether the drug is working and not a rash.

Dr. West:
Well, what I often tell people in my own clinic and on the GRACE web site is that these results that are seen are on a population level, but on an individual basis we see it's neither necessary nor sufficient. I have some patients, and I'm sure you have some who you've seen who have terrible rashes who end up not doing that well with these agents. And I have some patients who you might never see who don't have any real side effects but do extraordinarily well with them.

So, even though the associations are there, on an individual patient basis I don't think that there is any kind of truism about the purity of that correlation.

Dr. Lacouture:
Agreed. That's a great way to explain this.

Dr. West:
A couple of other questions about chronic use, and that is well for the cracks in the skin especially at the fingertips, one of the tips we've gotten from at least one of the people on the web site was about Cordran Tape, the steroid impregnated tape, but potentially that chronic use could be a problem. I don't know if you've used that and might recommend that or think that's a poor choice.

Dr. Lacouture:
I think actually that's a good choice. We – I recommend several things and the difficulty here is that some people feel very strongly about – because it is up to people to apply them and some of them like it and some don't. But, the best thing for those cracks is to apply a barrier such as Desitin Maximum Strength, and that is a zinc oxide 40% ointment and the important thing is that it needs to be applied frequently; at least two to three times a day.

And at night ideally some people obtain the most benefit by sleeping with these cotton white gloves they sell at drugstores providing a better occlusion. If the tracks are painful people can fill them with liquid band-aids that can be obtained in the pharmacy or online as the brand New-Skin. They just seal the areas and let the liquid dry and then it's no longer a problem.

The Cordran tape is good, because whenever the areas are red and inflamed, it delivers, as you say, a strong anti-inflammatory, decreasing the inflammation and helping the area to seal. The skin the palms is so thick that we really don't worry about those long term side effects we would

worry about in other parts of the body. So, I think it is a good option, but other people may prefer either the Desitin with gloves when they go to sleep or also the sealing of the cracks with liquid band-aids also is very good.

Dr. West:
That was a question I had, because liquid band-aids or super glue type products have also been a suggestion. And is there any particular topical antibiotic that you strongly favor in this situation if there is a concern of infection?

Dr. Lacouture:
That's a great point because some antibiotics such as Neosporin that you can obtain over the counter in a pharmacy, dermatologists don't like to use because they have neomycin, which many people are allergic to. So, the antibiotics we like to use are either Bacitracin that can be obtained over the counter or if not antibiotics that your oncologist can write a prescription for or your dermatologist which include Mupirocin or Bactroban is the other name, or Polysporin.

The good thing is that these protect against the most common type of bacterial infections which are the staph aureus that occurs in people with these medicines. Interestingly we published a paper several years ago and we found that up to a third of people treated with EGFR inhibitors or the targeted therapies, had skin infections at the areas of their side effect and the most common culprits were bacteria especially the staphylococcus aureus bacteria that is susceptible to the antibiotics that I mentioned, the Bactroban and the Polysporin.

A very common problem, and I have to thank you for bringing out this point, that occurs in people treated with Tarceva is that they develop very crusty and in some cases bleedy inside of their nose with pain inside of their nose. And people refer to this as, "My nose is very dry, it forms a lot of crusts." I used to do a lot of bacterial cultures of the area when people told me this, and I found uniformly that everyone had staphylococcus aureus, which is already present in about 30% of people not receiving these medicines.

So, what I think is happening is that these drugs cause the skin to become so dry that is becomes – the bacteria inside the nose tend to grow more causing those symptoms of inflammation and crusting. So, they recommend to use Mupirocin or the Bactroban twice a day inside the nose for about two weeks whenever this occurs and then I usually maintain people on this therapy for – and I ask them to apply them only on the weekends.

Keep in mind that when people are receiving Tarceva and some of these other drugs, the skin becomes very fragile so it is very, very easy to become infected. Any redness or pus bump, any pimple can indicate an infection so that needs to be brought to the attention and ideally if one is to determine an antibiotic what I tend to do I do bacterial cultures in many people that have any type of skin finding.

Dr. West:
A last question which is from somebody who was a patient of yours in Chicago, says hello, but also is there anymore understanding of why perimenopausal women have more of a reaction to agents, to oncology drugs as was her case?

Dr. Lacouture:
That's a great question and hello, nice to hear from you. Is this very common? What we have found in several studies for other skin problems is that people tend to have more side effects with age, that's why I was mentioning about the ageing and all the impact of that. And also, although it

is not exactly known, for hand-foot syndrome with other drugs we see this frequently and also importantly I think it's a function of the ageing of the skin.

It is also more common in Caucasian women because they have had their skin damaged from sun exposure. We know that fair skin is more easily damaged by sun exposure and also perhaps it could be a function I think usually in women that are thinner with age we tend to see the more severe side effects. It probably has to do with the amount of the body that is receiving the drug.

So, although we don't know the exact cause, certainly I think we should be more aware in people with increasing age and women seem to suffer more from these types of side effects.

Dr. West:
So, with that we'll wrap up, and I'd like to again offer our deep thanks to Dr. Lacouture for doing a great job. And I also want to thank our co-sponsor, LUNGevity Foundation.

Thanks, and take care.