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Dr. Nima Mazinani:

Welcome to RheumNow. This podcast is sponsored by Augurex Life Sciences. My name is Dr. Nima Mazinani, Medical Science Liaison at Augurex Life Sciences. And today I'm joined by Dr. Walter Maksymowych, a professor, clinician, and medical scientist in the Division of Rheumatology at the University of Alberta, Canada. Dr. Maksymowych is an expert in arthritis research with a focus on biomarkers and imaging in rheumatic diseases.

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He is the founder and chief medical officer of CARE Arthritis and recipient of the 2012 Distinguished Investigator Award from the Canadian Rheumatology Association. He's also the co-developer of the SPARCC MRI scoring system, now an industry standard in clinical trials. Finally, he's authored in over 400 research articles and an active member of numerous global arthritis societies.

1:03

Dr. Nima Mazinani:

Thank you so much for joining us, Dr. Maksymowych.

1:07

Dr. Walter Maksymowych:

It's a pleasure, Nima. Very happy to be here.

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Dr. Nima Mazinani:

Today we'll be discussing the role of biomarkers in RA care, how they complement traditional markers, their value in seronegative RA, and their potential in ongoing disease monitoring. Biomarkers have become increasingly important in RA care, with many clinicians still relying primarily on RF, anti-CCP, and CRP. Can you speak to the broader role biomarkers play in optimizing disease management.

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Dr. Walter Maksymowych:

I'd be happy to. Biomarkers are crucially important because they allow us to make an early diagnosis first and foremost and we know from studies of a variety of rheumatic diseases

that better outcomes are observed in patients with an earlier diagnosis but we also want biomarkers that are going to inform us regarding prognosis and especially the development of damage, whether it's joint damage or organ damage. So in rheumatoid arthritis, we're particularly concerned that we optimize our treatment toattain low levels of disease activity and to ensure a good prognostic outcome with preservation of joint function and prevention of joint damage.

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Dr. Nima Mazinani:

Many rheumatologists are familiar with RF and anti-CCP and CRP but many may not be familiar with 14-3-3eta. How does it complement these traditional markers and why should clinicians consider it in routine practice?

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Dr. Walter Maksymowych:

Well, there are a number of very important gaps in the use of biomarkers that aren't filled by rheumatoid factor and anti-CCP. The first problem is that these are not modifiable biomarkers. We can't really use them, for example, in treat-to-target strategies to attain good disease control. We don't have modified prognostic biomarkers and 14-3-3 is a modifiable biomarker that informs us about prognosis. So when we use it in combination with rheumatoid fractor and anti-CCP and acute phase reactants, there are additional benefits. First of all, we do capture additional patients with a diagnosis of rheumatoid arthritis that will be negative for these biomarkers. And then as we use the 14-3-3eta for monitoring purposes, it helps us to inform which patients should be treated more intensively.

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So we know that normalizing 14-3-3eta is associated with better prognostic outcomes. And so together, using all of these biomarkers in the management of patients, we achieve better prognostic outcomes. And that is really something that we don't get from rheumatoid factor and anti-CCP.

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Dr. Nima Mazinani:

With the recent re-emergence of anti-MCV, can you comment on it and how it's different from 14-3-3eta?

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Dr. Walter Maksymowych:

Anti-MCV is a citrullinated biomarker and just like other citrullinated biomarkers, these are often strongly positive in patients with rheumatoid arthritis, don't really change a lot with treatment and so they're not really modifiable prognostic biomarkers. So we need something that is modifiable and is responsive to treatment and I think that's where 14-3-3eta has an important role and give physicians some degree of confidence that when they see normal levels of the 14-3-3eta biomarker, these patients are not likely to progress to joint damage. So that's a very, I think, helpful aspect of monitoring using the 14-3-3 eta biomarker.

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Dr. Nima Mazinani:

You touched on seronegative RA. Can you expand on that and what role 14-3-3eta plays in identifying and managing these patients?

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Dr. Walter Maksymowych:

So we're seeing increasingly in population data that the proportions of patients who are seronegative is increasing with time. And this is a very, very difficult group to evaluate. It's quite a heterogeneous category of patient. And of course, we want to treat these patients optimally, and we want to in particular identify whether they fall within the spectrum of patients with rheumatoid arthritis, as opposed to some other condition, for example, psoriatic disease or spondyloarthritis. And I think that’s where 14-3-3eta really helps us to understand that these patients do have first of all an inflammatory arthritis and secondly that this is within the spectrum of patients who have rheumatoid arthritis and I think this helps us to design appropriate treatment strategies.

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Dr. Nima Mazinani:

One of the largest challenges in RA management continues to be ongoing monitoring. How does 14-3-3eta help assess a disease progression and joint damage risk over time?

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Dr. Walter Maksymowych:

So this is a particular challenge in the ongoing management of patients with rheumatoid arthritis is evaluating prognostic risk risk over time. Radiographs are certainly not responsive enough, really don't change very much over time. And acute phase reactants are helpful to some degree, but are limited in the prognostic information they provide. They're particularly helpful in the setting of patients who are on conventional synthetic disease-modifying agents, but they lose their prognostic capacity once these patients are treated by biological disease-modifying therapies. So I think this is where 14-3-3eta steps in and helps us with prognostic risk assessment on an ongoing basis. And we have a very interesting study from the Sherbrooke cohort, which has followed up patients with early rheumatoid arthritis over time to see what the role of 14-3-3eta might be. And I think a key message from the analysis of this work, which has been published, a key message is that 14-3-3eta acts in a complementary fashion with other biomarkers, and in fact has other advantages, as I mentioned, over other biomarkers in that it is modifiable with treatment. And so I think you get more prognostic information when you add a 14-3-3 assessment to the assessment of acute phage reactants, rheumatoid factor, and anti-CCP, you get a more complete picture of the prognostic risk for that patient and what else needs to be done in terms of optimizing therapy to prevent joint damage.

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Dr. Nima Mazinani

For rheumatologists interested in incorporating 14-3-3eta at testing, what are some practical steps they should take?

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Dr. Walter Maksymowych:

Well, first of all, 14-3-3eta, I should mention, is a really robust assay. It's been thoroughly tested in respect to its stability at room temperature. It really doesn't really change, for example, on a diurnal basis. Some MSK biomarkers are elevated when patients first get out of bed in the morning. So it really is a robust biomarkers that are used to evaluate, diagnose, as well as monitor patients with rheumatoid arthritis. So it really is very straightforward to do the testing, either a 14-3-3eta on its own, but I think it's really particularly helpful when it's done in combination with the other available biomarkers.

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Dr. Nima Mazinani:

Dr. Maksymowych, this is all the time we have for today. Thank you for sharing your expertise and thank you for our listeners for tuning in. For those interested in learning more

about 14-3-3eta, please visit the RheumNow Therapeutic Update page for more helpful information and resources.