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Journal Club: Dupilumab and Risk of Malignancy

#### Dr. Neal Bhatia:

Hi, I am Dr. Neal Bhatia. I'm Chief Medical Editor of Practical Dermatology, and welcome to another episode of the Atopic Dermatologist Journal Club. Here with my good friend, Dr. Matthew Zirwas. Matt is an Associate Professor at the Ohio University.

#### Dr. Matthew Zirwas:

Correct.

#### Dr. Neal Bhatia:

Correct.

#### Dr. Matthew Zirwas:

Yes.

#### Dr. Neal Bhatia:

For \$100, correct. So Matt and I have been gossiping about this article. Interesting topic, risk of malignancy associated with Dupilumab versus other treatments in atopic dermatitis. Just school me on this.

#### Dr. Matthew Zirwas:

Brand new study came out a couple of weeks ago online, not in print yet. It's in the *Journal of Allergy and Clinical Immunology in Practice*, so one of the big allergy journals. Fascinating. So the takeaway is Dupi substantially protects people from cancer. So they did it in the TriNetX database, so huge database. First, they compared people who were on Dupi to people with atopic dermatitis who were on other different immunosuppressants ... cyclosporine ...

#### Dr. Neal Bhatia:

Across the board.

#### Dr. Matthew Zirwas:

... Methotrexate, whatever, to try to compare bad AD to bad AD. And in that one, Dupi cut your risk of both solid malignancies and hematologic malignancies. But you're like, "Yeah, but they were on immunosuppressants. Those might increase your risk of cancer." So that wasn't the interesting part. The interesting part, they compared Dupi patients to patients diagnosed with AD who had never received a systemic.

#### Dr. Neal Bhatia:

OK.

#### Dr. Matthew Zirwas:

So they've only ever gotten a topical.

#### Dr. Neal Bhatia:

All naïve.

#### Dr. Matthew Zirwas:

Dupi still, for round numbers, I'm always a round number believer, 50% reduction in the risk of solid malignancies and hematologic malignancies. Didn't really affect skin cancer risk and that's an interesting thing in general. We've got new information on that as well

that's really cool.

**Dr. Neal Bhatia:**

Did they get any kind of mechanism into play or what do they say?

**Dr. Matthew Zirwas:**

Here's what they think. Dupi, unlike all the other drugs that we've got for AD ... Ebglyss and Nemluvio. Nemluvio's IL-31 and Ebglyss and Tralo IL-13. Dupi also gets IL-4. IL-4 pushes your immune system in a TH-2 direction and suppresses TH-1 immunity. It's why it's rare to see somebody with both atopic dermatitis and psoriasis, because basically the eczema treats the psoriasis. When you block IL-4, you actually up-regulate TH-1 immunity, and that is the suspected mechanism. Because TH-1 immunity is the primary.

**Dr. Neal Bhatia:**

That's the more protective side, more cellular side.

**Dr. Matthew Zirwas:**

It's the protective against viruses and cancer. And so it is fascinating. And then we already knew that this IL-4 induced shift was an important thing. Molluscum gets better. Warts get better. And we knew that it has some bad effects. So IL-4 blockade causes you to get arthralgias. It causes some people to get new onset psoriasis, causes some people to get this red face. So we knew that IL-4 was having this general immune effect. It just never ... If somebody had asked me three weeks ago, "You think Dupi might prevent cancer?" I would've been like, "I guess it's possible. And, boy, would Regeneron love that. But now I'm like, "I think it does." Now, we're going to need more data.

**Dr. Neal Bhatia:**

Oh, God, yeah.

**Dr. Matthew Zirwas:**

We'll get that. It just got its COPD indication, so now it'll be getting used in a lot of people who are old smokers.

**Dr. Neal Bhatia:**

I was going to say. And where's that going to leave them. That won't be a lung cancer issue.

**Dr. Matthew Zirwas:**

So that'll be interesting to see. Does it protect those people from lung cancer? It is just so fascinating.

**Dr. Neal Bhatia:**

So was there anything about a cumulative dose or a timeline that they would say, "You've crossed this line. Now you have enough immunity, enough protection?"

**Dr. Matthew Zirwas:**

No. And it's another interesting, does being on Dupi for a while have a long-lasting... If you were on it for two years and then your eczema is great and you came off it, is there a persistence to it? We don't know any of that yet.

**Dr. Neal Bhatia:**

Yeah, that's interesting too. Would you go backwards?

**Dr. Matthew Zirwas:**

It's crazy where we're seeing now with these drugs because Rinvoq, on the other hand, it now really looks like it is meaningfully cardio protective. So the more data we're getting, despite the boxed warning, the data actually looks like Rinvoq protects you from heart attacks and blood clots. So imagine this conversation with a patient. "So, hey, I've got these two drugs that are great. One will protect you from heart attacks, the other one will protect you from cancer."

**Dr. Neal Bhatia:**

Cancer, right.

**Dr. Matthew Zirwas:**

"Which one do you want?" "Both."

**Dr. Neal Bhatia:**

Isn't that something? And yet still dermatologists are on the ledge with all these drugs. That's the worst part about it.

**Dr. Matthew Zirwas:**

It's crazy. The JAKS, that boxed warning, there was actually another really interesting thing that just came out looking at the effect...

There was a boxed warning years ago put on SSRIs for causing pediatric suicidal ideation. So the FDA, "to protect kids", puts this boxed warning on. There's a clear dramatic increase in pediatric suicides after that boxed warning.

**Dr. Neal Bhatia:**

That's sad.

**Dr. Matthew Zirwas:**

Because doctors stopped prescribing it.

**Dr. Neal Bhatia:**

They stopped prescribing it.

**Dr. Matthew Zirwas:**

And people stopped, and so the depression went up and suicide. The FDA probably, by trying to be helpful and protective, hurt patients. And I think it's the same thing with the boxed warnings with JAKS. I get it. They're conservative. They want to make sure people understand the risk and the blah.

**Dr. Neal Bhatia:**

But there are so many derms, I mean, you and me in particular, we're on these other stages and we poke holes in this argument all the time, but still it's not changing trends. So we've got to use data like this to maybe see if we can wake some people up and get some eyes open.

**Dr. Matthew Zirwas:**

Yeah.

**Dr. Neal Bhatia:**

But that was really good. Thanks for giving us the primer on that article and we'll see what more comes down the road.

**Dr. Matthew Zirwas:**

Absolutely, man. It's fun to talk about.

**Dr. Neal Bhatia:**

It's fun to be with you.

**Dr. Matthew Zirwas:**

Yep.

**Dr. Neal Bhatia:**

And this is another episode of Atopic Dermatitis Journal Club, and we'll see you again.