Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/TKI-The-New-TKO-for-Retinal-Diseases/54099/

Released: 03/04/2026
Valid until: 03/04/2027
Time needed to complete: 35m

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

TKI: The New TKO for Retinal Diseases

Announcer:
Welcome to CE on ReachMD. This activity is provided by **Evolve Medical Education** and is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Weng:
Welcome to CE on ReachMD. I'm Dr. Christina Weng, and with me today is Dr. Katherine Talcott. Let's discuss some exciting developments in the treatment of exudative retinal disease. In particular, our focus today will be on tyrosine kinase inhibitors, also known as TKIs.

Dr. Talcott, we've had anti-VEGFs for 2 decades now. They're very effective. But we also know that not all patients are fully responsive, and there's also the need for longer durability agents, which TKIs may help address. Dr. Talcott, walk us through the mechanism of action of TKIs, and how does it differ from our current anti-VEGF therapies?

Dr. Talcott:
Sure, thanks so much for having me. So I think that's a great question is why should we use tyrosine kinase inhibitors in neovascular AMD and diabetic macular edema?

So unlike anti-VEGFs, which are certainly excellent tools to have in our toolbox, tyrosine kinase inhibitors, examples of which include EYP-1901, OTX-TKI, and CLS-AX, are really pan-VEGF receptor inhibitors that can inhibit signaling from all VEGF isoforms. So that includes VEGF-A, VEGF-B, C, and D. Tyrosine kinase inhibitors can also differentially inhibit signaling from other pathways relevant to retinal angiogenesis and other disease processes, which I'll cover in just a minute. And unlike the antibodies, which are really the mainstay of current existing treatments for retinal disease, these are small molecules. And these are really ideally made to be able to put in a sustained release-like formulation.

So small molecules, of which TKIs are an example, can really be formulated to be in a polymer matrix. And this can be designed to ensure drug delivery over a certain period of time. And they can be delivered in a more convenient fashion than something like surgery. So they can often be delivered by intravitreal injections, which can be really beneficial for us as we take care of patients in the clinic.

So as I mentioned, TKIs are really pan-VEGF receptor inhibitors. As we know, pathological angiogenesis and vascular instability really underlie retinal exudative disease processes. So VEGF receptors, as well as PDGF-like receptors, play important roles in this. And TKIs can really act intracellularly to prevent sort of pro-angiogenic signaling by altering the activity of both VEGF receptors as well as PDGF-like receptors, as well.

There's other receptors such as the JAK2 receptor that can play a role in mediating intraocular inflammation as well via IL-6. And one of these, EYP-1901 has actually been shown to be inhibitory to pro-inflammatory IL-6 signaling that's targeted by JAK1.

So although we often think about TKIs as a group and that they have a lot of similar properties, there has been some work done to be able to look at what are the differences between TKIs. So I mentioned this IL-6-mediated inflammation difference between the different TKIs, but overall there's a lot of similarities.

So each of the TKIs that I mentioned all exhibit pan-VEGF receptor inhibition, and they can inhibit receptor tyrosine kinase activity that's associated with angiogenesis, but there are some differences. If you look at the 3 different TKIs, actually OTX-TKI also was found to potently inhibit TIE1, which is actually essential for vascular stability as well. But overall, these findings that have been shown in preclinical studies really support the use of TKIs and the inhibition of angiogenesis that's observed both in diabetic macular edema as well as neovascular AMD. And they really have the potential to be able to extend treatment duration in patients with these diseases.

Dr. Weng:
That's a fantastic overview for our viewers, Kat. Thank you so much.

Well, to summarize, there are several TKIs in the pipeline. You mentioned the 2 leading ones being EYP-1901, or vorolanib, and OTX-TKI, or axitinib. These drug candidates offer a novel mechanism of action that distinguishes them from our current anti-VEGFs. Like you said, Kat, they work intracellularly to broadly target all VEGF receptors. It may also render benefits by inhibiting other targets like PDGF and FGF receptors. And like you mentioned, I like that you've highlighted that EYP-1901 was recently reported to also block JAK1 inhibitors, inhibiting the IL-6 inflammatory signaling, which has a budding interest right now, especially for diabetic macular edema.

And clinically, this might translate into being able to extend the treatment duration for patients with wet AMD and DME. And I'm also really glad that you pointed out that while there are many commonalities within the TKI class, there's nuanced differences between each TKI that are important to recognize and that we'll continue to learn about.

Well, this was brief, but so glad to chat with you, Dr. Talcott. I'm glad we had the chance to visit the mechanistic data on TKIs with you all. Thanks for listening, and we'll see you on the next episode.

Dr. Talcott:
Thanks, Christina.

Announcer:
You have been listening to CE on ReachMD. This activity is provided by **Evolve Medical Education** and is part of our MinuteCE curriculum.

To receive your free CE credit, or to download this activity, go to ReachMD.com/**CME**. Thank you for listening.