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CLINICAL

VTI's CMO Dr. Ashley Tuan On NaturalVue and the PROTECT Study

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Review of Myopia Management's Editor-in-Chief John Sailer recently sat down with the Chief Medical Officer of **Visioneering Technologies Inc.** (VTI), Ashley Tuan, OD, PhD, to learn the latest information on the company's myopia management efforts. They discussed VTI's PROTECT (**PRO**gressive Myopia **T**reatment **E**valuation for NaturalVue Multifocal **C**ontact Lens **T**rial) study, a multi-center, randomized, double-masked clinical trial with participating investigators in centers in Canada, the United States, and Hong Kong. Dr. Tuan also shared insights into VTI's real-world data on the NaturalVue multifocal lens to support its use in myopia management and how her experiences in the eye care industry brought her to VTI.

Dr. Ashley Tuan

John Sailer: Can you tell us about your background and what drew you to Visioneering Technologies?

Ashley Tuan, OD, PhD: Certainly, John. I am an optometrist. I practiced in private practice for nine years, and I also decided to be trained as a vision scientist. I was taught both at Ohio State and UC Berkeley. So, after graduate school, I got into the eye care industry, and I was very interested in helping the development of new technologies for vision. I've worked on a spectrum of presbyopia solutions that included presbyopia optics on intraocular lenses, refractive surgery, and contact lenses. Besides that, I also had the privilege and opportunity to bring the first relative plus soft contact lens to market in myopia management. So, when I talked to VTI, I could appreciate what kind of exceptional optics VTI has for the NaturalVue Multifocal. Therefore, I just had to join the company and help bring NaturalVue Multifocals to the myopic pediatric population because this is an immense opportunity.

John Sailer: Very impressive background. So, now, for eye care professionals interested in learning about particular

treatments, what type of data do you believe is necessary for ECPs to feel that they can be assured of an intervention's efficacy?

Dr. Tuan: I believe that ECPs want systematically collected data to analyze the outcome scientifically, and the information can be generalizable to the patients in their chair. That means that the treatment outcomes need to be proven under a well-controlled RCT study and in the real-world environment because they want to help every myope that comes to them for help.

In the evidence-based medicine pyramid, the type of study considered high quality – high quality means that the outcome has the highest chance of being generalizable to the public – is the meta-analysis. This is because the meta-analysis summarizes multiple high-quality study results. So, in the end, we know the chance that this information can be generalized to the population that you will see in the clinic is the highest.

And among the individual studies, the highest quality is the RCT study because the randomization and the built-in control group can best eliminate known and unknown confounding factors. However, the RCT study is sometimes not feasible because of the cost of conducting such a complex study. So, the study tends to be a smaller population. Because the population is so controlled, a very specific range of people can participate in the study. Even though the RCT study is considered the highest quality and is used for regulatory submission, an after-market approval post-market study is needed for everyone to get a complete picture of how this treatment can benefit the general population.

Back to the pyramid, after the RCT, the next level down is called the cohort study. The cohort study of MiSight is an RCT study. The previously published VTI post-market study is also considered a cohort study because this six-year retrospective study is paired with a published virtual control group. We used the virtual control group that drives our meta-analysis. So, now you have a meta-analysis virtual control group with retrospective data, making a cohort study. And the results, we believe, can be generalized to the population that walks into the ECPs' offices every day.

John Sailer: So, you mentioned VTI has six years of real-world efficacy and safety evidence on NaturalVue Multifocal to support its use in myopia management. How will the data from the PROTECT study be different from that data, and why is that needed?

Dr. Tuan: Well, the six-year data gives us a lot of confidence in how it [NaturalVue Multifocal] will behave in the real world. However, as we talk about the [evidence] pyramid, it's not considered the "highest quality" because there's no built-in control arm. Also, each clinic has different methods of measuring refractive error and axial length. Some eye care practitioners who are used to seeing rigorous RCT data feel that something is still missing; therefore, our RCT trial is meant to address their needs.

We wanted to have high-quality data from a well-controlled, well-designed RCT study, and with that, we can have the built-in control group to control confounding factors. We can standardize the measurement for the outcome that is refractive progression over time and axial length elongation. With this kind of information, we believe we can

bridge that gap that people need — high-quality results that give them confidence when they make their informed decision. Whether it is a practitioner or parent, when they make their informed decision of what they want to use for the child's myopia care, we can provide enough information to make that decision.

John Sailer: Can you briefly describe the design of the PROTECT study? How is it structured to obtain quality data that will inform VTI's R&D program? What are the key endpoints, and when can we expect the first data readout?

Dr. Tuan: PROTECT is a multinational, randomized, double-masked, three-year follow-up study. We are looking at 144 myopic children from multiple countries, some are in the Americas, and some are in Asia, covering a range of ethnicities, lifestyles, and living environments. We will have a control arm and a treatment arm, and both the wearers and the practitioners will not be able to tell which arm they are in, thus the double-masked approach. We are looking at refractive error change over time and axial length change over time.

We designed this study closely mirroring two significant myopia progression control RCTs: the BLINK study and the MiSight study. We believe that PROTECT will generate very high-quality data and will also corroborate our six-year real-world data. We expect to have a one-year readout in mid-2023. That one-year outcome will be a strong predictor of our treatment effect, and we expect to release longer-term data as it comes.

John Sailer: We can look forward to that data. And now, who are some of the principal investigators and institutions participating in the PROTECT study, and what's the significance of their involvement?

Dr. Tuan: We plan to start between eight and nine study sites. Our first site is in Toronto — Toronto Eye Care, in Canada, with Dr. Barbara Caffery. She is the principal investigator.

We are looking for a balance between academic institutions and private practices when we select these sites because we want to have a diverse population from diverse settings. These PIs are well-respected members of the optometric and ophthalmology academic arenas. They are the key opinion leaders in the field of myopia progression control. They each have experience in conducting clinical trials and intriguing pediatric populations. As you can tell, doctors of this kind of caliber don't need to be in our study. The fact that they wanted to be part of the PROTECT study means they believe in myopia control research and want to be part of it. Indeed, they know about VTI's product, so they wanted to be part of it to see the outcome.

John Sailer: So, now you've reached a milestone — VTI has enrolled the first patient in this international study to test the merits of NaturalVue Multifocal contact lenses in myopia management. Can you explain why this is such a significant milestone?

Dr. Tuan: The PROTECT study demonstrates VTI's commitment to myopia progression control. VTI has invested significant time and resources in planning this study. The first patient in signifies that most of the planning is behind us. That includes the protocol design, the regulatory approval, site selection, etc. Therefore, this is an exciting milestone for us, and we anticipate that six months from now, we will finish our enrollment, and a year from there, we can share our one-year results with everyone.

John Sailer: What do you expect from the PROTECT study, and what are those expectations based on? For example, previously generated data?

Dr. Tuan: In our early clinical studies and large-scale post-market surveillance data, we have seen repeatable outcomes that the NaturalVue Multifocal is safe and significantly slows myopia progression in children wearing them. We are confident that the PROTECT study will produce support and validate NaturalVue Multifocal's use in myopia management.

John Sailer: How will the data be used globally, and how will that impact the company's global position as a leader in myopia management?

Dr. Tuan: The PROTECT study is designed to be a multinational study so that we can have a diversity of geographical locations, ethnicities, etc. Therefore, we believe the data we will get from PROTECT will reflect real-world situations afterward. This study design also allows head-to-head comparisons to other similarly designed RCT studies. That can help practitioners make informed decisions and justify our leadership position in myopia management.

John Sailer: Why is VTI dedicated to creating novel solutions for the management of myopia progression? For example, what do you consider to be the medical need?

Dr. Tuan: Some practitioners, or at least when I went through school, were trained to view myopia as a benign condition, and your treatment is to correct the refractive error only. We have been more understanding nowadays that myopia is not just a simple condition but rather an eye health issue. And it can impact visual loss long term. As the patient gets older, they will have an increased risk for more debilitating conditions because of their retinal health. The World Council of Optometry has declared myopia management the standard of care. Right now, there are over two billion myopes out there. By 2050, we expect to have five billion in the population. This is a significant public health issue. We believe in VTI's multifocal optics because of its uniqueness and effectiveness. We believe that we need to get our product out there to help the practitioner treat their myopic children and control their myopia progression. That will be our contribution to this pandemic.

John Sailer: Those are very important reasons. So, how do NaturalVue Multifocal contact lenses fit into VTI's overall strategy for providing treatments for pediatric myopia?

Dr. Tuan: We believe that for myopia management, there needs to be a lot of tools in [the practitioner's] toolbox to cover a spectrum of needs — lifestyle, particular personality issues, and preference. We believe the soft contact lens is among the essential tools, and therefore, the NaturalVue Multifocal is our most significant contribution to myopia management. But there's orthokeratology, there are low-dose atropine eye drops, and there are also specialized spectacles. We would look into expanding our product line in the future to address more of the population.

John Sailer: Dr. Tuan, my final question. From a commercial perspective, why is this such a compelling market opportunity?

Dr. Tuan: This is a growing market because there are growing needs. As we understand more, myopia impacts everyone — the majority of the population, especially in Asia. With this ever-increasing pandemic, the Chinese government is already addressing it from the top down. They have implemented programs to address the myopia epidemic in China. Singapore is going towards that. And the industry is going there — all trying to help in this pandemic. Therefore, it is a commercial opportunity, but it is also an obligation for eye care practitioners and policymakers who know what to do for myopia management. We believe that the study we are doing right now — the PROTECT study — will provide us with quality information so that you can give practitioners the necessary information for decision-making. Also, we can increase the collaboration in the communities in this myopia management field.

John Sailer: Thank you, Dr. Ashley Tuan, Chief Medical Officer of Visioneering Technologies Inc. Thank you, VTI, for sponsoring this interview.