KELOWNA PROSTATE CANCER SUPPORT & AWARENESS GROUP

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MERRY CHRISTMAS

Yvonne and I would like to take this opportunity to wish everyone a Very Merry Christmas and all the best in 2022. It will be two years in February since we have held an in-person meeting of the Kelowna Prostate Cancer Support & Awareness Group.

We hope that everything will be getting back to normal sooner rather than later. There is the very slight possibility that we may be able to have regular in person meetings beginning in January. However, if and when these meetings begin, they will be a little different than what we have had in the past. Unfortunately, there will be no coffee, so bring your own, and everyone attending the meeting will have to show proof of being at least double vaccinated by showing a copy of the Provincial Vaccine Card, and everyone attending the meeting will have to wear a mask during the meeting.

Unfortunately, if you are unable to show proof of vaccination, you will not be able to attend our meetings.

If anyone has any concerns that I may be able help with, please feel free to contact me either at the above email or phone number.

Dr. Kim Chi on the Design of the AMPLITUDE Trial in Metastatic Castration-Sensitive Prostate Cancer –

The following is an excerpt of an interview of Dr. Kim Chi by Ryan Scott for *OncLive®* The information was obtained from the Internet and was published on October 4, 2021.

Dr. Kim Chi, MD, Senior Research Scientist, Vancouver Prostate Centre, Chief Medical Officer, Vice-President & Medical Oncologist BC Cancer, and a Professor, Department of Medicine, The University of British Columbia discusses the AMPLITUDE study trial in and how this research could help inform the of PARP inhibition in patients with HRR gene-mutated mCSPC.

PARP Inhibitors are a group of pharmacological inhibitors of the enzyme poly ADP ribose polymerase (PARP). They are developed for multiple indications including treatment of heritable cancers. Several forms of cancer are more dependent on PARP than regular cells.

Although the efficacy of PARP inhibitors has been established in patients with metastatic castration-resistant prostate cancer (mCRPC) in previous studies, the use of these agents earlier on in the disease process has yet to be evaluated, according to Kim N. Chi, MD.

To address this knowledge gap, the ongoing phase 3 APMLITUDE trial has launched to evaluate the standard androgen deprivation therapy (ADT) plus abiraterone acetate (Zytiga) and prednisone with or without the PARP inhibitor niraparib (Zjula) in patients with ***homologous recombination repair*** **(HRR)** gene-mutated metastatic castration-sensitive prostate cancer (mCSPC)

"Overall, the proven efficacy of olaparib [Lynparza] in CRPC has really opened up a new era of precision oncology for patients with advanced prostate cancer," Chi said. "However, there is still room to improve outcomes – particularly in those with castration-sensitive disease and particularly in those with HRR-defective disease. The AMPLITUDE study provides an exciting opportunity for us to evaluate the efficacy of PARP inhibitors much earlier on in the disease process."

OncLive® **Can you speak on the current standard of care (SOC) for patients with mCSPC and its evolution**

Chi: - For decades, the SOC (for this disease) has been ADT, otherwise known as castration therapy, which can be performed either medically or surgically. Although it is initially effective in most of the patient population, eventually, prostate cancer progresses [and develops] castration resistance; this occurs at a median time of approximately one year.

Over the past five years, however, intensifying ADT with additional [agents], specifically docetaxel or androgen receptor pathway inhibitors like abiraterone acetate [Zytiga], apalutamide [Erleada], and enzalutamide [Xtandi], has improved progression-free survival [PFS] and overall survival [OS], and has delayed the time to castration resistance. By bringing these treatments [into the mix] earlier, at the time of ADT initiation, OS improve, with a risk reduction ranging from 30% to 40%.

How does your treatment approach for HRR gene-mutated mCSPC differ from that of wild-type disease?

Several studies have suggested that prostate cancers that have alterations in genes associated with HRR are more aggressive; these alterations are enriched in patients with metastatic disease. Approximately 20% to 30% of

patients with mCRPC often have these alterations, particularly the *BRCA2* gene. It is also known that these kinds of cancer can respond very well to PARP inhibitors. [We also know that in patients with mCRPC who have progressed after an androgen receptor pathway inhibitor, the PARP inhibitor olaparib can improve PFS and OS].

What was the rationale for the AMPLITUDE trial? What methods are being utilized?

The AMPLITUDE trial is further testing the concept of taking treatments which benefit patients in the mCRPC setting and utilizing them earlier on in the disease process when cancers are still castration sensitive. Patients with a gene alteration in a prespecified list of HRR-associated genes, including *BRCA2,* are eligible for the study.

On the study, all patients will receive standard therapy with ADT plus abiraterone and prednisone, but they will also be randomized to receive either niraparib, a potent and highly selective inhibitor of PARP, vs placebo.

The primary endpoint of the study is radiographic PFS, and an important secondary endpoint is OS. Other endpoints [are focused on] progression, time to castration resistance, response assessments, and patient-reported outcomes [PROs].

This is an international, multicenter, randomized, double-blind, placebo-controlled trial, which is already accruing.

What makes this trial stand out from prior trials that have been done with PARP inhibitors in this disease?

This is the first trial looking at PARP inhibitor in patients with mCSPC. The trials that have been previously performed and reported involve PARP in patients with mCRPC. [As such, this trial is evaluating these kinds of agents] several years earlier in the disease process, where we will hopefully see a greater benefit.

WITT'S WIT (ON THE LIGHTER SIDE) –

Yesterday my husband thought he saw a cockroach in the kitchen. He sprayed everything down and cleaned thoroughly. Today I'm moving the cockroach to the bathroom!!!

ESSA Pharma Announces a Clinical Collaboration with Bayer to Evaluate EPI-7386 With Darolutamide in Patients with Metastatic Prostate Cancer

The following is an excerpt of a news release by ESSA Pharma and is further to other articles I published in this newsletter in March, and June 2021 regarding ESSA Pharma and EPI-7386.

Essa Pharma, a clinical-stage pharmaceutical company focused on developing novel therapies for the treatment of prostate cancer has announced that the Company has entered into a clinical trial collaboration and supply agreement with Bayer to evaluate ESSA's lead product candidate, EPI-

7386, a first-in-class N-terminal domain androgen receptor inhibitor, in combination with Bayer androgen receptor inhibitor, darolutamide, in patients with metastatic castration-resistant prostate cancer ("mCRPC").

Under the terms of the agreement, Bayer may sponsor and conduct a phase 1 - 2 study to evaluate the safety, pharmacokinetics, and efficacy of the combination of EPI-7386 and darolutamide in mCRPC patients. ESSA will supply EPI-7386 for the trail and will retain all rights to EPI-7386. The clinical trial is expected to start in 2021.

"We are delighted to collaborate with Bayer to explore the potential clinical role of EPI-7386 in combination with Bayer's darolutamide in patients with metastatic castration-resistant prostate cancer, who have progressed on androgen deprivation therapy," said Dr. David R. Parkinson, Chief Executive Officer, ESSA Pharma Inc. "Combining our two therapies will simultaneously target both ends of the androgen receptor, and potentially allow for a more potent approach to suppressing androgen activity. We look forward to investigation the combination of these therapies and their potential role together in the treatment of prostate cancer."

The addition of Bayer's Darolutamide in combination with EPI-7386, increases the clinical collaboration that ESSA Pharma has with other pharmaceutical companies including Janssen and the use of EPI-7386 in combination with apalutamide as well as the combination of EPI-7386 with abiraterone acetate plus prednisone in patient with mCRPC. ESSA Pharma has also collaborated with Astellas to explore the use of EPI-7386 in combination with enzalutamide for patients with mCRPC.

The Kelowna Prostate Cancer Support & Awareness group does not recommend treatment modalities or physicians: However, all information is fully shared and is confidential. The information contained in this newsletter is not intended to replace the services of your health professionals regarding matters of your personal health.

The Kelowna Prostate Cancer Support & Awareness Group would like to thank Janssen - and TerSera for their support and their educational grants towards our newsletters and our support group.

UP COMING MEETING DATES FOR 2021 –

Due to the COVID-19 virus we are still NOT holding monthly in person Support Group Meetings.

NOTE: I will be in touch with everyone whenever it is safe to get back to holding regular meetings.

NOTE: Many of our past newsletters are available for viewing and printing through our website. - www.kelownaprostate.com

- A big *Thank You to Doris at Affordable Web Design for all he*