Hello.

My name is Becky Campbell,

and I'm the senior manager of medical content here at PCF

Today I'm speaking with Dr. Zachary Klaassen about some interesting updates

coming out of a major medical conference held earlier this month.

Dr. Klaassen attended the European Association

of Urology annual meeting and has some updates to share with us

that are going to be important for patient care.

So Dr. Klaassen, thank you for joining me and for sharing your insights today.

Of course.

Always happy to join for PCF.

Wonderful.

So I'm just going to briefly introduce you.

And then I'm going to turn it over to you to, to share your, your findings.

Dr. Klaassen is a urologic oncologist and associate professor

in the department of neurology at Wellstar MCG Health in Augusta, Georgia.

He specializes in treating patients with urologic malignancies,

including prostate and bladder cancer, as well as other types of urologic cancer.

His research interests include mental health and cancer survivorship.

Epidemiology of Urologic cancers, clinical trials, and research focusing on biomarkers

for early detection of cancer and predictors of response to treatment.

He also is committed to educating both physicians and patients

about the latest developments.

He is the lead contributor to UroToday, which is a physician education

website or I should say, a provider education website.

And he develops content for the Prostate Cancer Patient Voices

website and is lead reviewer for PCF's Patient guides.

So sometime between doing

all that, you found time to travel to Paris to attend this meeting.

yeah. Didn’t have to twist my arm too hard.

But it was a great meeting for sure.

So I'm not sure if our listeners

are necessarily familiar with these large conferences.

Tell us a little bit about what happens with these meetings

and how ultimately that information gets disseminated out to, to clinicians.

Yeah, absolutely.

So the goal of these conferences, usually they're annual

and we have one in the United States, the American Urological Association

meeting, which is coming up in May of 2024.

But the European Association of Urology has a very similar

and a very excellent meeting, annually as well.

And usually it's in March this year was April 5th to 8th in, in Paris, France.

And so what happens at these meetings typically is we get together

as clinicians and providers and we share, new data.

We have review lectures.

And so it's really an opportunity for providers to go and learn about

what's new coming in prostate cancer, but all sorts of urology in general,

and then also to, to collaborate on, on future research projects.

So it's a very, international meeting.

I'm not exactly sure how many countries represented,

but certainly upwards of 9000 people attend this meeting.

And so it's fun.

It's, educational

and it's, an ability to just keep on top of the latest,

when we're talking to our patients in the clinic.

Amazing.

So you're going to help.

I know you shared that information with physicians and providers, nurses

on UroToday, and you're here to share this information

with patients and advocates today on PCF.org.

So I'm going to let you take it away and know you've got some great slides.

So, please, invite you to share.

Thank you. Okay.

Thank you very much, Becky, for the kind intro.

So I'm assuming you can see my slides there.

And, so again, thank you for the kind introduction

and to the listeners for taking the time to, to attend this webinar.

So, I'm going to run through several of the key studies

in prostate cancer that were presented at the European meeting.

And this was again in Paris from April 5th to 8th.

And so, I'm going to start off with a just a brief overview.

We'll look at some highlights

of some of these studies and trials for screening for prostate cancer.

We'll talk about localized prostate cancer, metastatic hormone sensitive

prostate cancer, metastatic castration resistant prostate cancer,

and an important study that was presented regarding survivorship.

And then we'll summarize, with a few takeaway points.

And for those that are interested in reading a little more in detail,

not just of the studies we talked about, but over different articles,

that we wrote and summarized, for the meeting.

This is at Urotoday.com, and you can follow the link here for the

prostate cancer section,

as well as other cancers such as, bladder cancer and kidney cancer.

I'm going to acknowledge my friend and colleague Dr.

Rashid Sayyid, who is a urologic oncology fellow

at the University of Toronto who contributed several of these articles

and whose summaries I used to put

some of these slides together.

So we're going to start with screening for prostate cancer.

And I thought

when I was putting this together, folks that are listening to this discussion

probably are advocates for, people that ask some questions about prostate cancer.

If they're a prostate cancer survivor, they're probably

speaking to people in their community

about when to get screened for prostate cancer.

And so I think these

are several important highlights as we look at some of these big trials

that are going on in Europe with regards to screening for prostate cancer.

So the first trial was from Auvinen and colleagues.

This is results from the first screening round of the ProScreen trial of PSA, kallikrein panel, and MRI.

And so this study

basically took a very sequential look at how to standardize screening.

And they, basically off of a first PSA, an initial PSA,

if that PSA was more than or equal to three,

they received this 4-kallikrein panel, which is a panel of proteins

that discusses risk of prostate cancer.

If that score was greater than 7.5%.

These patients were assigned in multi parametric MRI.

And if that multi parametric MRI had a PIRADS score of greater

than or equal to three, they were then referred for a prostate biopsy.

So typically we may get a PSA before screening.

And then we may get an MRI or may get a biopsy.

This group took a very sequential aspect to looking at

screening for prostate cancer.

And so based off of that first PSA,

if it was greater than or equal to three, they would be rescreened in two years.

If it was 1.5 to 3, they would be rescreened in four years.

And if it was less than 1.5 they'd be rescreened in six years.

And so this is a big ongoing trial. At the EAU, they presented the results of the initial cohort of just over 60,000

men, with about 15,000 in the screening arm, 45,000 in the control arm.

And these were patients from Helsinki and Tampere, Finland.

So we can see here looking at the results.

This is looking at the screened men, the screening arm and the control arm.

And so the control arm is those 45,000 men

that did not, that were not offered screening.

The screening arm is all the men that were offered screening.

And the screened men were the men that were offered

screening that ended up undergoing screening.

So it's three different….

it's two arms, but it's three different columns based off

of whether they actually accepted a screening invite or not.

And we can see here for Gleason Grade Group 1 prostate cancer, one case per 900 men invited, and for Gleason grade Group 2-5, one case

per 200 men invited in the screening arm versus the control arm.

If we break this down a little bit further,

by Gleason Grade Group, you can see here on the right the breakdown

for Gleason Grade Group 1,2,3 as well as 4 to 5.

And so I think the take home message from this trial for patients

is higher detection of high grade and low grade.

Excuse me, high grade rather than low grade cancer

at the first round of screening,

which was also seen in the control arm with no screening.

And so I think, a targeted

systematic screening protocol that they're using, helps with patients understanding

when their next test is going to be, take some of the guesswork out of it.

And this is an ongoing trial, probably for the next several years.

And in the second and third round of the screening,

which will present at future studies or future meetings, they're going to talk

more about the impact of the Kallikrein panel as well as multi parametric MRI.

The second study that looked at screening

was the risk adapted study out of Germany called the PROBASE study.

And this is really screening in young men.

And so this is 46,000 men that will be enrolled

between 2014 and 2034 in Germany.

And all men in this study will receive a baseline PSA

at the age of 45 or 50.

And if you shift over here to the right,

you can see that

when they get this baseline PSA similar to the last study we discussed,

they'll then be triaged into three different groups.

So if it's less than 1.5, a repeat PSA will be done

every five years, as long as the PSA remains less than 1.5.

If it goes to 1.5 to 2.9, there will be changed to every other year of screening.

And if it goes to greater than 3, they'll end up having

a multi parametric biopsy.

So you can see that if they move to a to the two year screening

they then go to MRI. If it becomes more than 3.

If it's more than 3 right off the bat they go to immediate MRI and biopsy.

So again a very strategic way of thinking about screening.

And then subsequently MRI.

This is some of the data they presented looking at some of the baseline

PSA values for men at the age of 45 as well as age of 50,

we can see 45 years of age on the left and 50 years on the right.

In terms of men that had a PSA less than 1.5

at the age of 45 and 89.9%, compared to 82.4% at the age of 50.

for PSAs 1.5 to 2.9, 9.8% for men, less than, at 45 years of age,

compared to 15.3% for men at age 50, and again for higher risk.

PSA equal to greater than or equal to 3.

2.3% for men at the age of 50 compared to 0.8% for men at the age of 45.

So this is again very early results from this trial.

And so some of the take home points from a patient standpoint,

a PSA at a young age that they're looking at in this in this study,

allows for stratification for subsequent PSA screening follow up.

And so I think,

they're really trying to, again, stratify men that are at higher risk

at a younger age versus those that are at lower

risk and can be screened a little bit less frequently. In some of the other work

they've done, which they discussed as well,

which is not discussed in this specific presentation.

I think it's important to know that men that have a PSA at the age of 45, less than 1.5, are very low risk of developing prostate cancer in the next five years.

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So let's shift gears to localized prostate cancer.

There was an important study, looking at it called the ARNEO trial,

which is a phase two randomized trial

looking at oncological outcomes of neoadjuvant Degarelix plus or minus

apalutamide before radical prostatectomy for high risk prostate cancer.

So neoadjuvant means a planned treatment

before a definitive therapy, such as a radical prostatectomy.

So especially in these high risk men

where we know they're going to be high risk of recurrence after surgery,

there's been a lot of work looking at

what can we give them before they even have surgery,

to decrease their risk of having recurrence and progression of outcomes

down the road after their operation.

So that's what neoadjuvant means.

So in a previous study, the previous, report of this study,

They found that neoadjuvant degarelix plus apalutamide, these are two treatments

we give for typically for advanced prostate cancer

had a higher proportion of minimal residual disease,

which means that there was less disease

in the prostate when they took the prostate out compared to the control arm.

And this was 38% achieved in that

in the combination group versus 9% in the control group.

You can see the trial design here.

So this is men that either had two intermediate risk factors or high

risk factor, one factor in the high risk group and had negative staging.

And the staging was done in this situation with a PSMA MRI.

They then randomized to degarelix plus apalutamide

versus degarelix for placebo.

So really looking at what the impact of apalutamide is doing before the operation,

before they had their radical prostatectomy,

they had another gallium PSMA MRI, had surgery

and then were followed every six months for up to three years.

And so what was presented at EAU 2024 was the assessment

of the oncological outcomes and specifically, biochemical recurrence.

And so the follow up for

these patients was a PSA and testosterone every six months.

At the time of PSA recurrence, they had a PSMA PET/CT.

And if this was negative, then they received salvage radiotherapy.

On the right here we can see

the biochemical free survival stratified by the randomization arm.

And so degarelix + placebo is in green; degarelix + apalutamide is in red.

And we can see from a statistical standpoint there's no significant

difference between these two arms for biochemical recurrence-free survival.

Although we do see from an absolute number there was more recurrence

events in the control group versus the degarelix + apalutamide group, 16 versus 10 events.

Although the sample size is small.

So we see a bit of a signal here; Statistical significance was not achieved however.

A couple of other outcomes from this.

So they looked at biochemical free survival, stratified by those

that either did or did not receive minimal residual disease.

So this is a decreasing of the disease in the prostate gland itself.

And basically there was no difference in biochemical free survival

when stratified by minimal residual disease or no minimal residual disease.

On the right, We do see some interesting data here.

So this is men that received

received either treatment

and were then stratified by whether they had T2 disease

at the time of their prostatectomy or T3 or higher disease.

And we can see here that those that had T2 disease had less

biochemical recurrence compared to those that had more advanced disease.

which makes sense from a, from a pathological standpoint,

if they're able to keep the disease in the prostate versus an extension

to the capsule and outside the capsule, these men had less biochemical recurrence.

So I think the take home message from this study is

although there's a lot of resources and trials going on for neoadjuvant

therapy prior to radical prostatectomy for these high risk men specifically.

So these are the Gleason 8, 9, and 10 patients, high PSA,

Although this improves local control outcomes such as minimal residual disease.

This has yet to be a proven strategy to improve the downstream oncological outcomes.

For instance, in this study, biochemical recurrence-free survival.

Okay, moving on to metastatic hormone sensitive prostate cancer.

We'll talk about a couple of studies in this section.

The first one is called the STORM trial.

This was salvage treatment of oligo recurrent nodal metastases

and looking specifically at 24-month toxicity results.

And so oligo means few, so few meaning, in this study,

less than 5 nodes positive. Recurrence means after primary therapy.

So basically this is men that had a primary treatment that then had

PET/CT-detected less than or equal to 5 nodes positive on their imaging.

And then what do we do with these patients afterwards?

So this study initially found that there was no meaningful difference

in worse grade 2 acute GI or genitourinary toxicity or in quality of life

between those receiving metastasis-directed therapy

and nodal pelvic radiotherapy during three months of follow up.

So this was the initial results of three months.

This study presented at EAU is looking at 24-month toxicity results.

And so the way these patients were allocated, they were randomized 1 to 1.

Arm A was metastasis directed therapy,

which was defined as salvage lymph node dissection or radiotherapy, plus six months of ADT or

Arm B, which was a little more of a… escalation in care.

This included metastasis directed therapy with either salvage lymph

node dissection or a focal radiotherapy boost

plus whole pelvic radiotherapy plus six months of ADT.

So similar arms but some treatment intensification in Arm B.

and what this

key secondary endpoint in this trial was 24- month late toxicity.

We see there's 190 patients, 97 that received metastasis directed therapy,

93 that received elective nodal therapy.

And we can see for the GI toxicity.

So these are mostly to the rectum and the colon.

These sort of toxicities, diarrhea, constipation, blood in the stool.

We see very comparable and relatively low rates of grade two and three

adverse events for these patients, roughly around 5.3 to 6.6%

When we look at the GU toxicity…So these are urinary frequency, urinary discomfort, blood in the urine.

We see slightly higher effects compared to the GI toxic effects but very similar again between the two groups

roughly low 20% grade two and three adverse events.

So the take home point for this study

is that both elective nodal therapy and metastasis-directed therapy

show appropriate grade 2+ toxicity

for oligorecurrent nodal metastases, with extended follow up.

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The next study in the

metastatic hormone sensitive setting is the PIONEER trial,

which is a development of predictive model for death among patients

with metastatic hormone sensitive prostate cancer using big data.

And basically the …authors for this study

collected a bunch of patients from observational studies within Europe.

You can see here a big number is 94,000 men with metastatic hormone

sensitive prostate cancer, of which over 77,000 received treatment.

The table, or the figure on the right, looks at number of deaths

by index year after the date of diagnosis, so the first column is within one year of diagnosis.

Second column 1 to 2 years after diagnosis, 2 to 3 years.

4 to 5 years.

Excuse me 3 to 4 years, 4 to 5 years, and 5 to 20 years.

And you can see that the majority of mortalities in this study

occurred within the first two years after the time of diagnosis.

So it's important here is what increases the odds of mortality. In this study, the factors that increased odds of mortality were age

more than 90 years, non-adenocarcinoma variants (So this is some of these less common more aggressive variant histology

rather than the sort of garden-variety prostate cancer)

M1c disease which means visceral metastases, So this is metastases to the lungs, the liver, the brain, the soft tissue organs

as well as liver metastases independently by itself

also was associated with increased odds of mortality.

This figure on the right is the model to predict death with certainty.

And, and really, this is mostly

related to the first year mortality…first year after diagnosis.

So this is a, a number of 0.743.

Basically what this means is if it was 0.5, it's basically a coin flip, chance Whether it could predict mortality,

if it was 1, it would mean 100% that they could predict it.

So it's somewhere in the middle at 0.743

and the model is not quite as good after year one for predicting mortality.

So the take home message here,

I think this is important, is that in the real-world setting.

So not in the clinical trial, just just across the board, in real world

community practices, 60% of deaths

in the metastatic hormone sensitive prostate cancer

setting occur within the first two years after diagnosis.

And what this really underlines is the importance

of treatment intensification.

So this means not just treating men with ADT alone,

but treating them either with doublet therapy - this could be ADT + enzalutamide.
It could be ADT plus apalutamide. It could be ADT plus abiraterone, or triplet therapy, which could be ADT plus darolutamide plus chemotherapy or ADT plus chemotherapy plus abiraterone.

And so this is really the crux of the take home message from this study

is that we know that the mortality risk is high within two years.

So we really have to treatment-intensify these patients at the time of diagnosis.

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All right.

We're going to switch gears now to metastatic castrate-resistant prostate cancer.

And this there's one study from the meeting that was important here.

And this is by my colleague.

Rashid Sayyid, who is a contributor to UroToday and who I acknowledged earlier.

And so this was a, a meta-analysis and a systematic review

to look at the importance of combinations of PARP inhibitors

and ARPIs for first line metastatic CRPC.

So a systematic review is exactly what it suggests.

It's a very delineated search strategy to try to identify

all the pertinent trials for a certain topic that someone's interested in looking at.

And then a meta-analysis takes all the data from these trials selected

and then makes conclusions based off of having more patients

to analyze based on combining data from these trials.

So for this, analysis, the systematic review for all phase three trials looking at PARP

inhibitors plus ARPI combinations in first line metastatic cancer

resistant prostate cancer, there was three trials identified.

Some of these may be familiar to the audience.

This was the PROpel trial which was olaparib plus abiraterone,

the MAGNITUDE trial, niraparib plus abiraterone

and the TALAPRO-2 trial, which was talazoparib plus enzalutamide.

And so what all these funny figures here

on the right are essentially called forest plots.

And what this is telling us is that in the overall cohort.

So all the men that were included in these trials,

there was a benefit hazard ratio of 0.65.

So a 35% reduction in radiographic progression free survival

for any of these combinations versus the control arm.

Where we really see benefit is in men that have a DNA mutation

called an HRR mutation, we see a hazard ratio of 0.55

So a 45% reduction in radiographic progression free survival,

even in the men that did not have the special DNA mutations,

we still see a benefit hazard ratio of 0.74

So a 26% reduction in radiographic progression free survival.

These treatments do come at a cost in terms of side effects.

So we can see here looking at grade 3+ treatment emergent adverse events.

The risk ratio is 1.45

So a 45% increased risk of an adverse

event for this combination therapy compared to the control arm.

and then we also see specifically

these PARP inhibitors can cause anemia.

And we do see a risk ratio of 6.22

So significant increased risk of anemia with these combinations

of PARP inhibitor plus ARPIs.

So the take home message is these work well in the first line mCRPC, meaning the PSA or radiographic

progression is occurring despite being on hormone therapy.

These work well in that setting, especially those with these DNA mutations

called HRR mutations or the BRCA 1 & 2 mutations; they work particularly

well in these BRCA 1 & 2 mutations.

But as we just discussed, this combination does lead to more adverse events,

including anemia, as we've seen here with the risk ratio of 6.22.

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The final section is, survivorship.

I think this is a very important study.

I was excited to read this one.

And we covered this for, the conference

This is looking at providers.

Excuse me, of of patient, significant others.

So people that are living with prostate cancer patients.

So this is a real-world evidence study from the EU-PROPER study. What this comprised of was a 20-minute online

survey, 80 questions for prostate cancer patient partners.

And they received over 1100 responses from 25 countries in Europe,

with a median partner age at the time of survey of 68 years.

Here's some of the key results from this.

And this is important.

all these bold points I think are very fascinating and very important.

89% of partners discuss prostate cancer with their spouse, which I think is good.

46% of partners say that the

prostate cancer influences their relationship with their spouse.

Now 43% said it brought them closer together.

However, 20% of the partners said they felt lonely

and 15% worried about the relationship with their prostate cancer survivor, significant other.

Additional key results

32% said that the prostate cancer diagnosis affected their social life,

27% said they were satisfied with their sexual life.

I did pull out some additional data

regarding sexual function, which I think is interesting as well.

And this really highlights the importance

of erectile dysfunction for these patients and their partners.

Now this is the survey,

answering questions regarding the partner.

So only 13% of partners said that the erection was firm enough for intercourse.

13% said it was firm enough for masturbation and foreplay.

Only…and 18% said it was not firm enough for any sexual activity.

That's 1 in 5 partners Where there is not a firm enough erection to have any sexual activity whatsoever

regarding incontinence. Roughly 50%

Note that their partner that has prostate

cancer has incontinence, and roughly one third of patients

partner state that their partner uses pads for their incontinence.

What's particularly interesting.

And one thing we as providers and as patients

and their significant others and family members and advocates

can, can really focus on, is that 1 in 6 partners

were not aware of the consequences of prostate cancer treatment.

So I think that really underlies the fact that we know that partners

are affected by their spouse's prostate cancer diagnosis.

And the final bullet point, I think, is important.

Both the patient and their spouse

need to ensure that physicians are explaining side effects of treatment

and have a survivorship plan early in the prostate cancer journey

so that we can improve on the education and the shared decision making that goes

along with choosing treatment between the physician as well as the patient, Their partner, advocate, significant other, family member.

So in summary, there are several large European prostate cancer screening

trials that are working to fine tune stratified screening strategies.

Trials of high risk localized prostate cancer have shown

that neoadjuvant treatment, which is before definitive treatment,

such as radical prostatectomy, that these approaches

improve pathologic outcomes,

but are yet to show improvement in long term oncological outcomes.

In the real world setting, 60% of mortalities in newly diagnosed patients

with metastatic hormone sensitive prostate cancer occur within the first two years

after diagnosis, and this highlights the need for treatment intensification.

And finally, data from prostate cancer patient partners

highlights the impact on spouses and the need for more rigorous

counseling in the pretreatment setting.

So thank you very much.

And I'll, turn it back over to Becky for some closing comments.

Well,

Dr. Klaassen, I really want to thank you for this tremendous presentation.

clearly, you've shared so much, important and new data

from screening to localized all the way through advanced disease.

And then, of course, our survivors and I know

that's another area of your of your research interests.

So some really powerful findings there.

And thank you.

You've given us so much to think about.

so and I also want to thank those who are listening today.

I hope that you got a sense of just how much research

and how much, investigation is going on

into helping patients with urologic cancers and,

that this sparked some discussions with your doctor about your treatments,

side effects, survivorship issues, anything that's on your mind.

So thank you again, Dr. Klaassen.

Thanks again, Becky.

And thank you to those, with PCF that are listening to this recording.

And I hope, I hope everybody finds it helpful.

Thank you very much for the opportunity. Thanks again.