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Highlights of the Advanced Prostate Cancer Consensus Conference (APCCC) 2022

Prof Gillessen: So, yes, good evening and welcome everyone for this discussion about some of the highlights of the Advanced Prostate Cancer Consensus Conference this year from April, 2022, APCCC, and we are doing this discussion together with my friend and colleague Aurelius Omlin.

Dr Omlin: Welcome also from my side, and it's a great pleasure to discuss some of the highlights. I would also like to thank ESO for giving us the opportunity to present some of the findings that are not yet published. I think we start with conflicts of interests. These are mine, and which are potentially relevant to the questions that we'll discuss in the next 45 minutes. And these are professor Gillessen's.

Prof Gillessen: Yes. So, take a bit of time to look at it, and then, we go deep into the conference. So, Aurelius, if you would take the next slide. So, we are often asked because we have founded this conference quite some time ago now. So, almost 10 years, 2013, when we started to think about it, why do we actually need a consensus conference? And why do we need it for advanced prostate cancer? And I have to say we had obviously some input from our colleagues who do breast cancer that have since a long time a consensus conference for early breast cancer. And so, we had a bit the idea in a coffee break, that in reality, also in prostate cancer we have a lot of these questions that you know all from clinical practise where we don't have strong evidence or no evidence at all, where we have conflicting evidence. Right now, we have a very good example with the first line mCRPC setting, giving abiraterone plus a PARP inhibitor. So, this is really a very classic one. We have two trials that don't show the same results, but sometimes, it's also the same evidence that can be interpreted very differently. And I think that's very interesting very, very often, as you know, the evidence in studies, in trials, is generated only in a very selective population of patients that usually may be a bit better off than the patients that you see every day in clinical practise. So, I think important to say is that what we are doing with the APCCC are really more recommendations. So, it's not guidelines. It's really here for complement guidelines that are mostly based on stronger evidence. And our idea was actually that we take together a lot of experts, of oncologists, of radio-oncologists, of urologists who have a lot of expertise in prostate cancer. And then, give this expertise to other doctors, other physicians who may be having a much broader population of patients, not only patients with prostate cancer. So, if you can go to the next one, please, Aurelius. Perfect. So, for 2022, again, we have the meeting in April, end of April. We have developed more than 190 questions so, almost 200 questions. And obviously, Aurelius and I have started it. But we had a lot of experts from the APCCC expert panel. I show you afterwards the panel. And then, because of COVID, for logistical reasons, the voting this time took place prior to the conference with a survey. And the topics of this year's APCCC were intermediate, high-risk of locally advanced prostate cancers. You can read it here. Biochemical recurrence, metastatic hormone-sensitive prostate cancers, very important field, non-metastatic castration-resistant prostate cancer, and then, something that sometimes a bit may be under-evaluated, but very important, the importance of lifestyle and prevention of complications in patients with

advanced prostate cancer. Then, also, the management of metastatic CRPC. And a very high topic, oligometastatic prostate cancer. And with that, I show you the expert panel that is quite impressive. So, because we did everything this time more virtually because of COVID, we actually had also the opportunity to have much more panellists involved. So, you see here, we have more than hundred panellists from kind of all over the world. And as I said, very multidisciplinary. Aurelius.

Dr Omlin: Excellent. So, Silke, you mentioned, we started the first conference in 2015. We always published the results of these questions and we put them into context in, I think, very nice manuscripts, which are sometimes a bit long because we cover a lot of areas. So, we highlighted here the most recent publications from 2019, also one publication where we looked at areas where we did not find the consensus to identify areas of unmet research need. Then, we had a smaller virtual event in October, 2021, also, management of patients during the pandemic, and then a report on the 2021 consensus, which was virtual, covering also a bit of MHSCC but also a lot of molecular targets and PSMA. And I think with this, this is a reminder that you can ask a question in the Q&A button. You will see this slide more and more during the presentation, and we will always pause after a few questions and then, you have the opportunity to write them in the chat and we will try and address all your questions. And I think we will start here with the first set of questions, which are now directed to localised prostate cancer and the impact of next generation imaging. And by these specifically, in these questions that we summarise here, and we mean PSMA PET. And the experts voted on the question, whether they recommend PSMA PET, CT, or MRI in the majority of patients with clinically localised prostate cancer. You see how the votes for high-risk localised prostate cancer, we used the NCCN definition, 77%, yes and 23%, no. Then, with the category of intermediate unfavourable risk, it's about half-half. 52 voted yes. 48 of the panel voted no. And when we go to the intermediate favourable risk, it's a completely different picture. Only 8% voted for a PSMA PET CT and 92% voted no. In our consensus conference, you have a definition of 75% or more for one answer option as a consensus. So, we have a consensus for PSMA PET in high-risk localised, definitely not in intermediate favourable risk. And it's about half-half in the intermediate unfavourable risk patients. Okay, Silke, I hand over to you for the next question.

Prof Gillessen: Yeah. And I may be adding also, because for someone who doesn't know the context, we always assume that the panellists have everything available. Diagnostically, also as treatments. So, that really, they choose here the answer option that they would do when they could do everything. That is obviously, we all know, not the reality of everyone, but just to make that a bit clear. So, the questions, if not specified otherwise, are really the questions scientifically, what would you do if you would have everything available? So, the next question we asked about the PSMA PETS. So, if you do it as a staging in clinically localised prostate cancer, when do you recommend it? And I think also here, very clear. So, also, a consensus more than 75% of the panellists said you should do if you use it for staging in localised prostate cancer, use it upfront. So, I think that was quite interesting to see that no one would say, okay, we do first the conventional. And then, if it's negative, maybe, go to PSMA PET. So, really most would say go to upfront PSMA PET.

Dr Omlin: And I think we, here, already have time for discussion. Silke, I don't see the chat anymore because I shared my screen.

Prof Gillessen: Yeah, in the moment, there is no question. So, obviously, we were very clear, but I think take the opportunity because now it's really for you the time to make some questions that hopefully we can answer. In the end, we have to say, this is not our opinions. This is what have been the questions that have been voted on from more than the hundred panellists that you saw on the slide. So, it's actually really an expert opinion that you are getting here. So, no questions from the chat. So, maybe, do you have a question?

Dr Omlin: Yes. Silke, you have written a very nice editorial on the question of what next generation imaging, especially PSMA PET, we use it for localised disease, may have implications for patient management. I tell you an example, I've just recently been asked my opinion about a case with a PSA of six or seven. It was purely Gleason 6 in the biopsy, no extracapsular extension on the MRI or T3B. So, a localised prostate cancer

with a low PSA, Gleason 6, he had a PSMA PET for staging. I'm not saying that that was correct. With four potential lesions in the bone. And he was treated for metastatic prostate cancer, no local treatment, but systemic treatment only. And the question was, after six months the patient was getting a bit anxious because he was reading up and said, but I have a Gleason 6, and why do I do I not get local treatment? And... yeah. So, I think this is increasingly something we probably see at the tumour board.

Prof Gillessen: Yeah. Hopefully not for low-risk cancers. So, I think the first point is to point it out, totally correctly. Right? So, you have seen in what we have shown, the votings, that already for intermediate favourable risk patients, the panellists have a clear consensus to not do a PSMA PET CT. And I think this is really something that I totally agree with. Again, this was the kind of opinion of the panellists, but I would agree completely that it doesn't make a lot of sense in these patients where we usually wouldn't have made a conventional staging, now starting to do PSMA PET CT staging. These specific patients, we have kind of discussed a lot about that. So, in Switzerland, a lot of these, the tracer fluoride 1007 is used where we know it can have artefacts in the bone. So, it's really important that you have a good reader. So, I think you need a learning curve as a reader of PSMA PET CT. So, make sure everyone who listens to that, that you have your nuclear medicine of your trust, ideally, in your tumour conferences. If not, at least that you can call him and discuss all the images with him or her. I think it's quite important that we learn together as clinicians with the specialists from imaging, from nuclear medicine, to interpret really, really well these PSMA PET CT.

Dr Omlin: I couldn't agree more because the question is really some patients, we will inevitably overtreat because we think they're metastatic. When in fact it's probably artefacts in the bone and they get combined systemic treatment. We come to the HSSBC section later, and at the same time, they don't get the adequate local treatment of the primary, potentially. And I guess, all the trials that have been done, everything that has been done in localised prostate cancer was without PSMA PET so far and showing the evidence for prostatectomy or radiotherapy.

Prof Gillessen: And specifically in this patient. Right? So, to be honest, even you would believe that is a PSMA PET CT, but I don't personally, it would be a low volume patient even, and we at least, based on the STAMPEDE data, would not treat with ADT alone. If you now, really something that I wouldn't do, but if you have a patient who you would consider low volume, metastatic disease, I think the treatment you should give, and again, I wouldn't give it in this patient, but if you have a low volume metastatic hormone-sensitive patient, we usually discuss radiotherapy to the primary ADT plus usually a novel endocrine agent, an ARTA, however you want to call it. And I think, so this patient was treated quite interestingly, let's put it that way, but it's good he met you.

Dr Omlin: Absolutely. And I think that's it. You mentioned STAMPEDE and I think we can go to the next question.

Prof Gillessen: Yeah. There're no questions here from the audience. So, please, audience ask some questions. Otherwise, we do have to come up with all the questions ourselves, which is quite difficult. So, ask questions if you want. Is this mine or yours?

Dr Omlin: Oh, sorry. I think I should introduce this question. So, we move on to high-risk localised prostate cancer, meeting the STAMPEDE definition. So, these are patients that have two out of three criteria or more of locally advanced cancer, T3, T4, a PSA of more than 40, and a Gleason score of 8 to 10. They are non-metastatic on next generation imaging in this question. And we asked the experts what they recommend as systemic therapy in combination with local radiation. So, we already decided this patient goes for local irradiation of the prostate plus ADT. I think here, similar to what we have seen before, it's also consensus with 78%. The experts voted that in this case they would recommend ADT for two to three years. STAMPEDE is three years. Plus abiraterone for two years. A minority 21% would go for ADT alone and only 1% would add docetaxel in this situation. And I think already, we want to discuss here, is the STAMPEDE trial enough to change the standard of care? Certainly, you are on the STAMPEDE publication. You're also in the trial

management group. I know that the trial has been discussed differently and also, we don't know whether approval will be sought by the company and for abiraterone for these two years, I'm in this situation because it's generic and a lot of competition in the field. Is this something you have changed in your practise?

Prof Gillessen: Yes, I have. And yes. So, I think it's good you said it. It also was in one of my conflicts of interests slide, I think so. Yes. So, I'm quite biased because I'm part of STAMPEDE. But I think the interesting point is also that you could formally speaking also, say, because as you know, this is always one standard arm, but there was the arm with abiraterone alone and there was the arm with Enza. + ARPI. And these, in total three arms, were also kind of put into a manuscript together, reported together from raw data. So, in reality, it's almost like two trials, the one with the combination and the one with ARPI alone to show that there is a benefit even in the M0 patients. And I have to say, so, the benefit is quite relevant. So, for me, I have to say, yes. If I'm using it, I'm asking the health insurance, since it is generic, it's also getting less costly. I guess really here, I find that it makes a lot of sense to already use this treatment in patients. What are you doing?

Dr Omlin: Absolutely, absolutely the same. And I think the beauty is that you can stop after two years, it's not an indefinite treatment. And then, we have received a question by email. And I think that fits well with this, with this question by Dr Sabra. I don't whether he or she's online, this is a 65-year-old patient with high-risk localised prostate cancer, a PSA of 33. It looks like MRT 3B with invasion of the seminal vesicles. The Gleason score is 8. The patient received irradiation and two years of ADT. Has now a PSA of, call it undetectable, it's 0.005. So, in the very low range and a PSMA PET was done at this stage and the PSMA PET shows some uptake in the prostate. And the question is now, do we stop treatment? Do we biopsy? Is this an, I don't know, rest of the cancer that has not responded? I have to say it's a very unusual question. I've never seen that situation before. I don't know, Silke, whether you have, and what you would recommend. This is, I think, could be a STAMPEDE patient?

Prof Gillessen: Yeah. So, to start with, I guess I would have treated him with, as we saw here, with more like three years of ADT, if he would have tolerated it well, plus abiraterone because it is a high-risk patient also according to STAMPEDE so, he could have been included, but obviously, this was two years ago, so, maybe, the data was not out there. So, I guess, that's what we would do nowadays. I have to say, I have also no experience like you monitoring this PSMA PET CT in a hormone-sensitive setting. At least not a lot. I've seen PSMA PET CT or MRIs done, but in very, very few occasions. And so, I think the main thing is that we actually don't know what it means because most of the data that we have generated is not for monitoring after start of ADT. So, we know there is some increase. There can be some increase in PSMA expression by starting ADT or other hormonal agents. We don't know how long this is going to last. You don't know what it really means if you still have some, let's say spots, here and there. So, also here, probably, talk to your nuclear medicine physician, what he thinks that really means. And I think we should never forget that PSMA is not a functional kind of PET CT like the FDG PET that we know much better. So, it doesn't really show activity. It shows a protein. So, the question would be, what does it really mean? But interesting question. And I think we are going to learn a lot because there's a lot of studies ongoing that will test PSMA PET CT in that setting also for monitoring. But right now, we only have the data for the staging.

Dr Omlin: Absolutely. I think the recommendation would be to ignore it at this point in the context of a very, very, very low PSA and the patient received standard treatment of radiation plus two years. I mean, you could go to three years of ADT, but I don't think I would now, I don't know, overreact at this point with only a PSMA PET when we don't know what the activity means in the prostate.

Prof Gillessen: Yeah. The only thing what we discussed, maybe, talk to the radiotherapist, because there're some data out that if you're doing brachytherapy to lesions, I mean, maybe that hasn't been done and could be done. So, I think as you said, I wouldn't change my usual treatment, but maybe, have another look with

your radiotherapist, with your nuclear medicine guy. And especially, I think what is the problem is that you make patients very nervous with these scans. So, really think about it if you want to do that scan.

Dr Omlin: And I think we have, we will not show it tonight, but we have a lot of questions on recurrence after radiation of the prostate. And I think that the idea is then more to go for MRI, if you suspect a local recurrence and potentially do a biopsy. I think we move on to pN1. And I think this is your question.

Prof Gillessen: This is mine. Yes, you're right. Or mine too. So, here, this is another really, I think, very interesting topic that you see a lot in your clinic. So, you have patients, mostly high-risk patients that have been operated because we operate more and more, hopefully not we, but the urologists operate more and more of the high-risk patients. And now, you find in the pathology report that a patient has a pN1 disease. And our question here was, so, we had a lot of these questions, but this one was, if a patient has one or two pathologically positive pelvic lymph nodes in the surgery with an extended PLND obviously without evidence of metastasis on a preoperative stage. So, cN1 pN1 disease and a non-detectable postoperative PSA. What is your recommendation, again, provided the patient has regained continence? And we asked two very similar questions once when the patient had no other high-risk features like very high Gleason, PT3, or positive margins. And once with high-risk features. So, you see here for the patients who have no high-risk features, 81% of the panellists will do monitoring alone in pN1 and salvage, but early salvage therapy in case of PSA rise. So, this was a clear consensus. So, no adjuvant radiotherapy, no adjuvant radiation therapy plus systemic hormonal treatment. Clearly also, no systemic hormonal treatment alone. If the patient has high-risk features, so at least two out of the three, then, you see here gets more to a picture half-half again. So, half would also go for only monitoring and early salvage therapy if the PSA is rising, but the other half would go for adjuvant radiation therapy plus systemic hormonal treatment. So, I think that's quite interesting. And we saw really this just last week, we saw a patient like that with the second in our tumour-board. And as you see here, it's not very easy. But in the meantime, there was a retrospective study published, but again, retrospective, that seemed to show a benefit for adjuvant treatment in these patients with high-risk features.

Dr Omlin: Absolutely. The next slide would be the discussion, but maybe I can ask you here. So, okay. Some people voted for systemic hormonal treatment. These are the yellow options for in both groups. It's a small four-three and 5%. Do you think this is still adequate? We know this is a very old trial with node positive prostate cancer, a small trial, but this seems to be, I don't know, something that is stuck in our mind that some people, in this case, I mean, you see the PSA undetectable, one to two pathologically involved nodes. And would you really go for systemic therapy in any of these patients?

Prof Gillessen: No, alone. I mean, systemic therapy alone, no. So, that was the answer, was really systemic hormonal treatment alone. So, if you give adjuvant radiation therapy, then, I think it makes sense to give some systemic hormonal treatment with it. We are not going to go into details right now, but systemic hormonal treatment alone, but we see it also here. Right? It's dead. I mean, yes, we have this Messing study from years ago, but the operations were not really good. There was no PSA at that time. So, you couldn't do early salvage. So, I think that was really another generation decades ago. And I think we shouldn't, only because it is the only randomised trial that we have. Because I think less than 90 patients. So, it was really a small trial, I guess. Yes. So, now, I think this is outdated and you see that also in the voting of the expert.

Dr Omlin: Excellent. Are there any questions in the chat?

Prof Gillessen: No. No. I will let you know.

Dr Omlin: Okay.

Prof Gillessen: I know you're getting nervous because you can't see it. But...

Dr Omlin: In the interest of time, I would go to the next topic, which I think it's also yours.

Prof Gillessen: Yes, exactly. So, here another question, what we see a lot for the majority of patients with rising PSA after radical prostatectomy. So, this is now biochemical recurrence and the PSA doubling time of less than one year. So, quite fast PSA doubling time or a high Gleason grade again. And that's the defined definition of EAU high-risk biochemical recurrence. What management would you recommend? That was the question. And then, again, we made two questions, one with risk factors for local relapse. So, a pT3b or more stage, as we've seen before in that patient we discussed, and/or R1, or without risk factors. And you see here again, salvage radiotherapy 60%. So, there was clearly no consensus for patients with the risk factors, but also no consensus for the patients without risk factors. So, salvage radiotherapy or waiting until PSA is more than 0.2 and perform imaging then was quite half-half split. And interestingly, having risk factors or not didn't make such a big difference.

Dr Omlin: So, no consensus here. What do you do in your practise? Because the option two, and I think this is still something based on the older definition, when it was defined as the PSA, biochemical cancer, 0.2 and more and rising. And some people do PETs early at 0.10, 0.15, but then, often you don't see anything on the PSMA PET and you could argue both ways, do an early PSMA PET, not see anything and go for salvage treatment, or say, no, we wait a little bit longer because the chances are better to see something. But then, you may miss the option of curing patients because we know we should salvage early.

Prof Gillessen: So, I have to say, unfortunately, I see a bit too many patients who come with a PSA that is already much larger than 0.2, so, I think the more critical point is really, really that you do early salvage. And that's something that I'm seeing, especially, if the patients are then transferred at some time-point to the GPs, they think, oh well, the PSA is less than 0.2, right? And I totally understand because it's written on the report that below 2 is normal. And then, you think, oh yeah, that seems to be normal. But obviously, after prostatectomy, it should be really half, an undetectable PSA. So, I have to say, I go more for option number one. So, I do the PSMA PET quite early, also maybe sometimes before 0.2, even if you don't see these patients so much. And then, if you don't see any metastasis, go for salvage radiotherapy, obviously, if the patient wants to do that, if he's fit, if he has a long-life expectancy, outside of the prostate cancer, he has all these points. What we don't do so much that some people do, as you know, is waiting until you see something, then, only irradiate that, like metastasis directed therapy. And then, the next one, next one, next one. So, I have to say, I'm not so convinced about this kind of procedure.

Dr Omlin: Nor am I. Again, I've just seen someone yesterday who had so much radiation that now his haematological function is not normal anymore. He has platelets of around a hundred because bone, bone, bone, here, radiation. And I think at some point he will need his bone marrow function for future treatments and he has not even started systemic treatment yet.

Prof Gillessen: OK. Next one.

Dr Omlin: I think you covered this one as well.

Prof Gillessen: So, yeah, it's the same kind of topic, PSA recurrence. So, biochemical recurrence after radical prostatectomy. And so, in the majority of patients with an early rise of PSA after radical prostatectomy that you made for intermediate or high-risk localised prostate cancer, what is your preferred treatment option in conjunction with early salvage radiotherapy to the prostate bed? So, you have now an early rise. And here, we also made two questions out of that, one's with a PSA lower than 0.7, one's more than 0.7. And you see here for less than 0.7, salvage radiotherapy alone would be only done by about 10%. 61%, so the majority, would give salvage radiotherapy plus six months of systemic hormonal treatment. So, six months. Some panellists would give two years of systemic hormonal treatment and other people would do even a molecular test, something that's mostly done in the States for now, based the decision on systemic therapy, yes/no, duration, based on this result. And if you have a much higher PSA, you see here, even less panellists will do salvage radiotherapy alone, 63, so, again, the majority would do salvage radiotherapy plus six months of systemic hormonal treatment. And a bit larger portion would also give two years of systemic hormonal

treatment. But you see here, it's quite interesting that we don't find any consensus. And this question, and again, these are really frequent patients. So, I found it quite interesting that we couldn't reach consensus in any of these questions.

Dr Omlin: I guess we could say, if we combined the option orange and grey, with salvage plus systemic, we have quite a strong consensus in the PSA of more or equal to 0.7 for systemic treatment. I guess the problem is that the six months in the trials was classical ADT and the two years was bicalutamide 150. I don't know. Is this something that you still do? I don't do this 150 mg of bicalutamide here, but I guess it's still an option that is considered by some of the panellists, because it is also a trial, which has shown a significant benefit for these two years of bicalutamide.

Prof Gillessen: But talking to the panellists, I guess even the two years, even if the trial was done with bicalutamide, they would do it with LH. A lot of them, LH, or RH agonist, or antagonist, in extrapolation to the data with the bicalutamide. I think we have asked that question, I can't remember, 2021 or 22, and most people would go for LH-RH analogues.

Dr Omlin: Because also for a concern of excess toxicity with bicalutamide 150 on the cardiac side. But I think we will come to that.

Prof Gillessen: Yes.

Dr Omlin: When we come to the side effects. Any questions in the chat?

Prof Gillessen: No.

Dr Omlin: No. This is a reminder. You can ask questions and send comments any time. And if you don't, we go to change topic now. We leave the localised and recurrent setting. We go to the metastatic hormone-sensitive prostate cancer. And the first question doesn't need a lot of explanation. I think it's a very clear vote. 97% in the majority of patients with metastatic hormone-sensitive prostate cancer, the panel voted for combined treatment ADT plus systemic therapy and/or local radiation, but 3% voted for ADT alone for the majority of patients, assuming that all the options are available. I think the next question I leave to you.

Prof Gillessen: Yeah. So, this is also a very, very interesting question and very hype right now, triplet therapy. So, in which patients with mHSPC that are chemotherapy fit, would you recommend the triplet therapy ADT plus docetaxel plus AR pathway inhibitor? And again, we asked the question in two settings. Synchronous, so, de novo metastatic disease or metachronous or relapsed metastatic disease. And you see here, no consensus, but it's really only very few panellists would give it in the majority of patients, such a triplet independent of disease volume. And for synchronous metastatic disease, 70%, so, close to consensus would give it only in high-volume patients. Whereas in metachronous, these were only 58% of the panellists. And I usually do not recommend these combinations of triplet therapy. Never. You see here that synchronous will be a quarter of the panellists. And in relapse, even 37%. So, I think that that was quite clear, even if no consensus was reached, at least not quite. And I think that's interesting that quite a lot of candidates would not even consider giving triplet therapy.

Dr Omlin: Absolutely. And I think the next question is we ask the experts what combination they would use if they voted for triplet therapy. Now we specified synchronous because the PC1 patients were only synchronous mHSPC, chemotherapy fit, which AR pathway inhibitor, given that we have two trials, PEACE-1 and ARASENS, and you see, again, a split, almost half-half. 49% would go for abiraterone in combination with ADT and docetaxel. 46% would use darolutamide in the combination. 5% would use apalutamide.

Prof Gillessen: Okay. And the next question is a very easy one in that sense. So, how would you do that triplet therapy? And here was a clear consensus to do concurrent administration as was done in ARASENS PEACE-1 and ENZAMET.

Dr Omlin: I think this is an important message because I hear a lot of concern that physicians don't want to start ADT, docetaxel, and the additional endocrine therapy, but I think all these trials have shown, apart from ENZAMET, I think there was more toxicity, and ARASENS and PEACE-1 they worked really well, even if you give it all together.

Prof Gillessen: Yeah. It was also a bit more toxicity, but really manageable.

Dr Omlin: And the last question, I think, of this set is patients with synchronous low volume. And we asked, would you still consider the triplet therapy? Because we know all that there are some patients that we think by definition are low volume, but really, biologically because they don't fit in the definition, they actually have high volume disease. And so, clearly not in the majority, only 2% voted in the majority for triplet here. And 30% would consider the triplet in this borderline high-risk patients, Gleason 8 to 10, maybe 3 to 4 bone mets, extensive lymph nodes because lymph nodes do not make, formally, a patient high volume. But 68% do not recommend the triplet in these patients. Discussion of triplet therapy. I would like to get your opinion briefly. Do you use it only in synchronous patients, mostly high volume, or do you also consider the triplet for the later metachronous relapse patients with maybe high-volume disease?

Prof Gillessen: So, to say, I think it's always more discussion with the patient, right? Because we don't have really good data formally, as we all know, we have now data that adding the novel endocrine agent, as I still call it, it's not so novel any longer, to docetaxel and ADT is giving you a benefit. If really adding the docetaxel to the novel endocrine agents and ADT it's giving you a benefit, has not been validated, tested. So, we don't really know how much is the added value of the docetaxel. So, I think that the data are quite convincing. I discuss with fit patients, chemotherapy fit patients, specifically, high volume. And as you said, de novo, because there we have the strongest data. I mean, as you know, some of the ARASENS patients were metachronous, I think 14 or 16%. So, not a lot of them, actually. But high volumes that they don't have a very good prognosis, if they're metachronous and high volume, it's not better than low volume and de novo. So here, I guess, there are some patients that could profit and should be at least informed that this option exists.

Dr Omlin: Absolutely. I do it exactly the same. I think the trend was going more towards only endocrine combination. And I think now we have a very good rational to introduce chemotherapy early in the patients that clearly, if they go on ADT plus then ARTA, sometimes, are after six to nine months already in the CRPC situation, if they have really high-volume disease. Now, again, the option to ask questions.

Prof Gillessen: There are no questions.

Dr Omlin: No questions. We have three more questions, one that is close to your heart.

Prof Gillessen: So, yeah. So, because, Aurelius, worked with me for some time, and I personally, because we know that hormonal treatment can induce long QT, do recommend a baseline ECG. So, I just like to expose myself. So, to tell everyone, so we asked that question and then ECG also, I think it's a very, quite easy thing to do most of the time. But you see here, there is no clarity at all. So, a third would say, yes, do an ECG in the majority of patients. Then, a bit more than a third would say, yes, but only in selected patients with a history of major adverse cardiac events or risk factors. And then, a third of the panellists said, no, I would never do an ECG. So, it was quite interesting. Yeah, I don't know. I think we leave it there.

Dr Omlin: And very similar here. And we asked whether a cardiac evaluation apart from ECG, maybe even including an ECHO, is recommended in patients with mHSPC. Now, before they start an AR pathway inhibitor, Abi, Apa, Daro, or Enza in addition to ADT, no consensus. 14% would do it actually in the majority of patients. 57 would do it in patients with a prior cardiovascular history, especially a major one. And I think a third again, would say, no, not necessary. Maybe, we can discuss it at the end and I hand it over to you for the last question.

Prof Gillessen: Rapid. So, yes. So, that was the question also for monitoring of lipid profiles. Again, we know that ADT induces metabolic changes. We know that also some of the novel endocrine agents can cause hyper cholesterol, cholesterolemia, and you see here. Yes. So, here a bit more like 60% of the panellists would say, yes, we do a baseline lipid profile. And then, we do it regularly every 6 or 12 months or recommend it, right. Obviously, that can be done by the GP. Doesn't have to be done by the urologists or oncologists or radiotherapists, but at least about 60% would do it. And, and 24% would say no, you should never do that.

Dr Omlin: It's actually even and I think this is your merit, it's even in the EAU guidelines as a strong recommendation to do it at least once a year and profile it. I think we know that all these patients on systemic therapy for prostate cancer have an increased cardiovascular risk for, I guess, multiple reasons. But I think it's not asking too much if you want to keep your patient fit and healthy to do everything possible, especially, in someone who already has a history.

Prof Gillessen: And I guess, especially now where we obviously have prolonged the life of our patients with all these new treatments, with giving all these new treatments early, I mean, it's fantastic, right? We now have really patients surviving much longer, but obviously, also, then being able to suffer much longer from the side effects that are induced by the therapy. So, I think we should really concentrate now also on the survivorship and look at all these things because obviously it's really important and it can really have an impact on your quality of life if you have some cardiovascular event as a patient.

Dr Omlin: Absolutely. I think with this, we are almost perfectly on time. One minute over. And we would like to advertise the next APCCC. You probably saw it in the background of our Zoom recording, that there is a next conference in April 2024.

Prof Gillessen: So, be all there and then, ask a lot of questions.

Dr Omlin: And I think that, importantly, you can join. This is not a consensus behind closed doors, but this is a consensus with participation so everyone can join. And of course, the experts will do the voting.

Prof Gillessen: Right. And there's also a lot of talks, very short, very focused talks, very clinical talks. So, it's really worth going there if you're interested in prostate cancer.

Dr Omlin: Excellent. Thank you all for joining or for watching it later, and from my side, thank you very much.

Prof Gillessen: And also, from my side. Bye-bye and ciao, arrivederci.

Dr Omlin: Bye. It was a pleasure.

Prof Gillessen: As always. Ciao.