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Who is the older adult patient?

Dr Colloca: Good afternoon. Thank you to inviting me to this talk, and to permit me to talk about the geriatric point of view in the assessment of elderly patients with cancer. I try to give you just a few points, a few key-points, when we start an assessment of the older cancer patient, the older cancer patients itself. First of all, when we talk about elderly patients, or elderly individuals, we have to take in consideration that currently we have many different patients compared to past, and consequently, we have a change in needs. So, if we start our assessment just taking a view of the evidence-based medicine, we have to take in consideration that we have really missed the target. The evidence-based medicine is strongly related, in oncology, strictly related to the randomized clinical trial. Randomized clinical trial, so, often, when we talk about older individuals, are not the real world, are not able to cover completely the patients that we have in front of us. The second point when we talk about older patients is the frailty condition. Why it's so important for the titration the frailty condition, the frail topic? Just because when we talk about older patients and older cancer patients, we have a different scenario, and a scenario in which the patients have not just an index disease, but may have different syndrome, different condition, different features that may interact with the treatment, interact with the index disease, the core disease, interact with the scenario surrounding the patients. In other words, when we talk about the modern patients, the older patients, the frail patients, we have to take in consideration that may we can fudge a reaction syndrome, we can find such an economic situation that may interact with the treatment. We can find a new world, a new condition that is a multi-morbidity associated with a multi-drugs treatment. And on the top, there are two points, cognitive deficit and physical deficit, they are the basis of the frailty syndrome, the frailty condition. When we start to assess elderly patients, our focus is to try to detect the frail patients. Our focus is to detect the frail patients for two questions, two ways. The first way is just that if I know that the patient is frail, it's feasible to me to have a different approach and to start a different treatment in these patients. On the other hand, if I know that the patient is fit, we can do a standard treatment to this patient, or to treat the patients as a younger counterpart. Who is the frail patients? Frailty is just a key feature of a state of vulnerability to adverse health outcome. Frailty is strongly related to the negative outcomes. Frailty is a vulnerability, is just a vulnerability to stress. So, when we have in front of us an elderly patient, and older cancer patient, we have to take in consideration the scenario of frailty syndrome, in which we can have two different curves. The curves of normal aging, in which we have a progressive aging that we usually as geriatrician define as successful aging. On the other hand, we have the frailty phenotype. The frailty phenotype is a phenotype in which curve starts to bend deeper, starts to be more steep, and versus a complication state, in a state of disability in which, after a stress, the frail patient is not more able to come back to the previous condition. So, it's really important to try to understand the frailty or aim to detect the frail patient before to start every type of treatment in the geriatric field, just because, if we have a normal aging, we know that we can treat, we can follow the patient, versus a successful aging. But if we have a frail or preferably, vulnerable phenotype, for us it's really important to take in consideration that every stress may be strictly related to the loss of our self-subsistence, autonomy,

and to be related to the negative outcome to the patients. When we talk about the consequences of frailty, we have to take in consideration some points. From molecular point of view, we have oxidative stress, we have changing in DNA with DNA damage, or a mitochondrial environment. From a physiological point of view, we have just two points. Inflammation. So, define inflammation. Inflammation related to the aging. And change in the neuroendocrine regulation. From a physiological... clinical point of view, we have just one frail phenotype in which we can find, from physical point of view, five features that are defined, or usually they are defined as clinical phenotype, frailty, phenotype. That are slowness, weakness, weight loss, low activity and fatigue, and then, the clinician that it's able to define and understanding of frailty. So, when we talk about frailty, that is when we talk about frailty, we have to take in mind just this point. Frailty, it's related to the aging but it's not just aging. Frailty is related to the comorbidity, but it's not just comorbidity. Frailty may be related to the disease, disability, but it's not just disability. And most important point, frailty is something, really heterogeneous, multidimensional, that we have to assess in course of treatment, just because if our patient starts to be non-frail, it's a fit patient, maybe, during the treatment, after stress, if he's elderly, starts to be vulnerable to the stress and then, to frailty. So, the assessment has to be repeated during the treatment, just because frailty condition is something multidimensional, is something heterogeneous, is something dynamic. Frailty is most obvious under stress. So, in geriatric field, when we talk about cancer, when we think about cancer, we think that cancer is a sort of frailty stress test. If your patient is frail, for sure, if it's a frail patient with a cancer diagnosis, the frailty comes out and starts to be obvious once we have that. The second point of my talk is this one. When we talk about elderly patients, we have to take in consideration the frailty scenario, but we have to take in consideration also the age. Aging, it's extremely important in our elderly patients, and usually, we consider physiological age and chronological age. This is a study published some years ago in Lancet, and it's really interesting because it was able to define how aging process is different if we relate aging process to, say, economic and social conditions. So, for example, if we consider a 65-years-old features in a man and woman, it's possible to find these characteristics, these features in individuals of 75-80 years old in the west world, or in a high-income country, but it's possible also to find these features in a person, individuals 45-50 years old, if we consider a low-income country. So, it becomes more and more important when we're talking about elderly to take into consideration the age and how age it's strictly related to the country in which we're talking, and the social-economic condition of the patients. So, it's not so good to talk about chronological age, but it's also important to take into consideration just only the biological age of the patients. And talking about aging, we have to take in consideration another point, the life expectancy. Currently, the life expectancy for example of the millennials, people who were born after 2000, it's around 100 years old. But we have to take in consideration that the patients that we have in front of us probably are baby boomers, people that were born after the Second Word War, and so, have to be considered people that was born and lived in good socioeconomic condition, that have a high cultural level and that want to be treated as they need. And they want to be treated as people fit, if they are fit, and they want to understand if you decide to not treat as younger counterpart just for the age. So, the second point of my talk was related just the age, and to not consider just the chronological age itself. The third point of my talk, from geriatric point of view, are the comorbidities. We usually talk about comorbidity and we consider comorbidity a chronic condition that are over the index disease, in this case, the breast cancer. Currently, in geriatric field, we talk about multi-morbidity. And when we talk about multi-morbidity, we consider that all of the diseases, all they really interact with each other. We don't have just one index disease, but we have an index disease and our perspective is to shift from this index disease to multiple diseases that interact at each other, interact also during the treatment, and sometime, when we start a new treatment, for example, for a breast cancer, it's possible to have prime disease to start to re-acutize, or interact with drugs with other disease. So, we have to try to change our point of view from an idea of comorbidity to any idea of multi-morbidity. We start to treat the patient, we start to treat an individual in which we can find multiple diseases that interact with our index disease, in this case, breast cancer. And last but not least, currently in geriatric field when we talk about geriatric syndrome and frailty, we start to think about a new symptom, sarcopenia, that it's considered the cause of frailty syndromes. Etymologically,

sarcopenia means just losing muscle mass, but we see that with aging process, we have also a physiological loss of muscle mass, but also, a loss of strength, and muscle mass and strength are the features really important to report to the muscle and are strongly related to other points, other futures of our organism. As like, the immune system, and answer to the disease, stimuli and stress. In geriatric field, ontological signs, we find out how, for example, a loss of 30%-40% of muscle mass that we have find in an 80-years, 85-years-old woman, for example, it's related to a decrease in immune system, and it's related to negative outcome, as like in some case the loss of 40% of muscle mass to death. Sarcopenia, so, in our definition, is the loss of qualitative muscle mass. When we talk about quality, we have to consider muscle mass. So, low muscle mass and strength in term of physical performance, reduction in physical performance. When we talk about sarcopenia, we are not talking about cachexia. There are several differences between sarcopenia and cachexia. Sarcopenia is strictly related to the aging process. Sarcopenia may be reversible. So, we know now that sarcopenia is related to the negative outcome. Sarcopenia is strictly related to toxicity to the treatment and to adverse drug reaction. Sarcopenia is something that it's related to the aging process, but it's reversible. So, we have to detect the sarcopenia, because in this way, it's possible for us to detect a starting process of frailty condition, but also, to reverse this condition. So, my take-home message, when we talk about and we assess elderly patients, elder cancer patients, is just this one. The core point of the geriatric assessment, or the core point of the geriatric field, and the frailty condition. We have to try to understand the frailty condition, and to detect, to assess the patients in the way to better assess who is fit compared with [Audio Not Clear] or frail. Strictly relate to the frailty condition are two points, multi-morbidity, index disorder, surrounded with co-morbidities interact each other, life expectancy of the patients, and not age itself, chronological, biological age itself. Related to these two points, there is the quality of life the patients, the compliance. And the only way that we have in some way to assess, to understand better this scenario is to use a geriatric assessment. So, the key-message is, start to thinking at your patients in geriatric way, with some key-point of geriatrics, some key-futures, some knowledge of geriatric field. Thank you for your attention.

Dr Eniu: Good day, everyone. My name is Alex Eniu, I'm a breast medical oncologist currently working in Switzerland, and it is my pleasure to discuss with you an oncologist's point of view on who is the older adult patient. This is my disclosure information, but I also have another disclosure. I'm not an on-call geriatrician. I'm just a breast medical oncologist caring for older patients. So, what I would try to do in the next 12 to 15 minutes is to actually share with you some of our questions that we have in front of an older patient, some of the concepts that are inherited from our education, to try to set-up the scene for the discussion for more specialized persons that will be able to provide solutions and answer to the questions that we have. So, we know that we have paint the world in pink. We have painted the world in pink. As you know, breast cancer is now the most frequent cancer in most countries, as you can see in these data from 2018. What is more worrisome is that, due to the population change and due to the trends in the age pyramid, we will see important increases in cancer cases in older patients. The graph that you see is an estimated number of new cases from 2020 to 2040, that is in 20 years from now, for both sexes, aged from 70 to 85. So, we are looking at an increase, for instance in Asia, of more than a 100% of new cancer cases in the older population that is more than 70 years old. You look at Europe and you will see there's a 37 increase in the next 20 years. That accounts for about 240,000 new cancer cases in older patients, and that is a lot. There is an estimation that actually we will see mostly, so, 60 to 75% of the new cancer cases that an oncologist will see in the next years will be in older patients. So, this is just to make the point that we are facing an epidemic of cancer in older patients and we need to better understand how to treat them. Because now, when we are discussing a treatment proposal with an older patient, I think I've tried to summarize some of the questions that we have when we discuss with them the treatment proposal. The first one, of course, I think it's is she or he fit enough for the treatment? Is he fit enough to overcome toxicities? Will we need to reduce doses, and what would that mean for the efficacy of treatment? Is the treatment really going to help versus the added toxicity, especially in the adjuvant setting when we think about the benefits and competing causes of mortality? Will

the patient accept therapy? We have this issue with more and more patients, as you know, and for a good reason. What about the patient's other medical problems? Older patients, as we know, have a lot of comorbidities. How will that affect tolerability, efficacy, but also, perhaps, indirection between the various medicines that we are proposing? Then, the question is, what happens at home? How independent is the patient? How will he navigate this period of treatment at home? Will he be able to feed himself? Is he having cognitive issue, will be able to follow-up with the scheduling, to remember his appointments, to remember to take his medication, et cetera? These are important questions. And overall, what we want to understand is that, to have an answer to will we do more harm than good without treatment? So, of course, I think most of us have seen these kinds of pictures to highlight the idea that age by itself doesn't mean that much, and that although the woman on the left seems much more fragile than the woman on the right, my point is that looks aren't everything. Of course, we would like all to have older but fit patients, but we have to remember that actually there are many underlying conditions that do not directly relate to the looks of the patient. So, just judging at the looks is not enough to basically understand what are the chances of the therapy to help the patient. So, this is just to remind us that there are many, many other things that we need to take into consideration than age. But of course, let's be honest, age is the first parameter we take into consideration when we're discussing a tumour board, for instance, indications of treatment. And if we haven't seen the patient, or there's a patient that we have not seen yet, we have to rely on certain data, and age is a number that doesn't tell us that much. Of course, there is information that we can extract from, for instance, from meta-analyses. And this is just one table from the Oxford meta-analysis showing that perhaps only chemotherapy is helpful for patients that are older than 70-years of age. But you see the low number of patients that have been enrolled in this clinical trial, about 500 out of the 8,500 patients that were analysed in this analysis. So, indeed, there is some data there, but the quality of the data and the solidity of data is quite small due to very, very low accrual of patients in clinical trials, which also means that if we do not have enough toxicity data to judge what we should do with these patients. Now, another question is regarding the time lag. And if we are in the setting of an adjuvant treatment for breast cancer, we know that overall, the absolute benefit in survival of breast cancer mortality is in the area of one digit, and you need a lot of time to be able to see that benefit. So, the question is, will the patient have a long enough life expectancy to be able to expect the benefit that we are proposing to him, with the... for instance, with adjuvant chemotherapy? And for that we have, I think, there are many different tools that can help us assess what is the chance for one-year mortality in frailer patients. I do not want to go into the detail. This is just an example to say that this is something that we'd have to take into consideration. For the moment, we only use our experience, our gut feeling, but I think, we would need to have the help of tools to actually put more concrete data onto evaluations regarding, for instance, prognosis. Now, cardiac safety, for instance, with anthracyclines, with anti-HER2 treatment, of course is an issue in older patients. We, as you see here at the bottom of the slide, there are several risk factors for cardiac toxicity. Age, obesity, hypertension, all these three can be seen quite frequently. In older patients, of course, age is there, and the chance of developing cardiac toxicity from, in this slide, anti-HER2 treatment is much more increased if several factors are present. Therefore, this is a concern. So, should we propose intensive treatment to our older patients? And I had to go back to papers published while I was still doing my residency to actually put on this slide some information that we have that indeed dose, and dose-intensity, seems to be important in the adjuvant treatment of breast cancer, and you have here two old papers, but also, in the metastatic setting, it seems that there is a threshold effect. So, just doing a little bit of chemotherapy doesn't help your patient. So, this is an important message that is there, that in order to be able to provide the benefit that we have, we would have the tendency to offer the full dose treatment to our patients. Can we do more with less? And as we all know, there were several attempts to try to diminish the intensity of treatment in older patients, and you have here three examples of offering less. But unfortunately, according to these studies, less is not more for elderly patients. So, these de-escalated regimens did not prove to be as efficient as the standard treatment. In addition to that, some other analyses, for instance, this one published last year, showed that indeed for patients with, in this case, triple negative breast cancer, age 70 or older, chemotherapy seems to improve overall survival

after adjusting for age, comorbidity score and tumour factors. So, indeed, the message goes into the same direction, that in order to achieve the efficacy, we need to maintain the dosing. But the dosing will, of course, have an impact on the quality of life in older patients. And we all know that we diminish, for a while, the quality of life of older patients while receiving, for instance, adjuvant chemotherapy. And this is just some data showing that sometimes we see that while this decrease in quality of life is temporary, it will recover after the end of treatment. But this is still something that has a big impact on what is happening in clinical practice. Because we know that, from the beginning, there's a variation in the type of treatment that is proposed to older patients, and there's in many instances undertreatment, and this is some data to show that. Some patients are over-treated just because of the biology of the disease and not taking into consideration their co-morbidity, their frailty, et cetera. So, this is the true picture, that actually there's a lot of over-treatment, but also, probably more undertreatment, for the oldest older patients, and we have to put ourselves into the position to ask if we really are offering a service to our patient. In terms of oral therapy, and that has to do with, for instance, adjuvant therapy, but also in the metastatic setting with the advent of oral chemotherapy or CDK4/6 inhibitors, we know that the phenomenon of abandon of therapy for long-term treatment, that it is happening in the adjuvant treatment, but also, we have the issue in older patients with complying with scheduling. Multi-dose chemotherapy, to name a few, just oral vinorelbine or oral capecitabine, can be an issue to be managed with older patients. CDK4/6 inhibitors, again, especially, when they are taken together with an oral hormonal treatment, patients might confuse the two and not understand that they have different toxicity and different scheduling. And also, managing multiple medications and interactions among drugs, and you, sometimes, see the patient coming with this pill box to you and showing you how many medicines she has to take. That brings in the issue of trying to understand if there are interactions in between the several medicines that she's taking. So, compliance is extremely complex, it has to do a lot with the patients' previous experience, perhaps with his neighbours' opinion on the treatment, and we have to be aware of that. We have to be aware that not always our message is the first time to be retained by the patient. Therefore, a lot of discussion needs to take place in order to improve compliance. We do not have to forget that, although we are now offering a lot of oral treatment to our patients, these are not devoid of significant toxicity. And here, I'm mentioning just some cartoon on which signal transduction inhibitors, toxicity is highlighted, for instance, metabolic toxicities, et cetera, which have an impact on the quality of life and have a consequence for the other medication that the patient is taking. So, to conclude, and this is my last slide. I think always in our mind when we discuss with an older patient, we keep in our heads the Hippocratic Oath principle of primum non nocere, which means that we do not want to do harm to our patients. But this needs to be nuanced because, of course, we risk to do harm with our therapy, but we should not neglect that no therapy would not avoid the toxicity caused by the evolution of disease. So, it's a balance that we have to actually take into consideration all the time, and to put in this balance the different aspects of the tumour biology. From our medical side, we try to evaluate what is the chance of response to therapy, what is the risk of death of progressive disease, but also, we have to have long discussions with the patient to understand what is his disposition, how much he understands, what is his fear of symptoms, what are perhaps also the financial burden. In certain systems, this can be very important for the patient, how much he understands of the toxicity data, but also on the consequences of not doing the treatment. And we have to integrate that into our daily practice, and that represents a burden on the care team. So, therefore, caring for older patients also means that in order to be able to achieve good results, we have to invest more, which is a burden for the care team, but this is important in order to be able to offer our patients our best, best solutions. So, I will end here with saying that I don't offer you solutions, I just wanted to paint a picture with the different complexities seen from a practitioner point of view. And I'm looking forward, I think this is a very good opportunity, this conference is a very good opportunity to actually discuss and try to find solutions that will improve the fate of our older patients. With that, I thank you very much and I, on behalf of the scientific committee, I have the pleasure of inviting you to attend the ABC6 virtual meeting that will take place in a few weeks. Thank you very much for your attention.

Dr Wildiers: Hello, my name is Hans Wildiers, I was asked to give an onco-geriatrician point of view on the question, who is the older adult patient? Now, the first thing an onco-geriatrician needs to know is that cancer is a disease of older persons. This is a very elegant study showing that the number of new cancer cases among 65-plus patients will increase from 6.7 million in 2012 to 14 million in 2035, and by that time, 58% of all cancers will occur in 65-plus persons. The second very important aspect that you should know is that there is an extreme variability in health status in older persons. This is a landmark-study by Walter who showed that the life expectancy of an 80-year-old fit person is much, much longer than the life expectancy of an 80-year-old frail person, and this has an enormous impact on treatment and therapy decisions. Now, the best way to assess the frailty or the fitness of older persons is a geriatric assessment. And we should realize that this is a process, because many oncologists stop at the first or the second step. They do a geriatric screening, or they do a geriatric assessment and they find the problem, for instance, malnutrition. But then, it only starts. Then, you need to ask yourself, what should I do about the geriatric problems, what interventions are needed, and is the patient complying to the plan that we make? And to me, this is the most challenging part of taking care of older adults with cancer. The G8 screening tool is the first and important step, because these eight simple questions already allow you to have an idea of the most important domains of geriatric assessment, and the score by itself already has an enormous impact on prognosis, as you can see on the right side. So, a normal G8, which is a score more than 14 out of 17, is a much better prognosis in cancer patients than an abnormal score. Now, the question that I receive a lot from colleague oncologists, "Why do I need a geriatric assessment? Because I'm an oncologist I can see immediately if a patient is fit or frail." But there is in the meanwhile more than enough data that it has a lot of benefits. First of all, a geriatric assessment detects a lot of problems, geriatric problems, that oncologists are not aware of. Secondly, a geriatric assessment influences treatment choice. I will show in the next slide. Thirdly, a geriatric assessment has important prognostic information, and it tells you how long the life expectancy will be, independent of the cancer. So, if the prognosis of your cancer is better than the prognosis of the frail person, you should question whether a cancer treatment is necessary. Fourth reason is that it has a strong predictive value for morbidity, quality of life, and treatment toxicity, and there are very nice studies. The CRASH and CARG study showed that several tools of the geriatric assessment predict toxicity. And last but not least, you have the possibility to do something with the problems that you find. This is just an example of the second topic I mentioned. These are six nice studies that evaluated the impact of geriatric evaluation on treatment choice, and you can see that in many cases, oncologists decide to a less intensive treatment after the information of geriatric assessment becomes available. But in some cases, it can be the reverse, and sometimes, a oncology team can, after a geriatric assessment, decide to give a more intensive treatment. And I told you about the impact of geriatric interventions on outcome. We already have good data in the general geriatric world that this improves outcome and survival in some studies. But now, since ASCO 2020, we also have four very nice randomized trials in the older cancer population that evaluated different endpoints, and they were all positive trials showing that grade 3 to 5 toxicity, or health-related quality of life, or the post-op length of stay, all improved when some type of geriatric intervention was done. Now, data enough, but how do we implement this in oncology? This is the major challenge for an onco-geriatrician. And in an ideal world we could work, or the oncology world could be organized in geriatric oncology units, where you have a specialized team that cares for older persons with cancer, where geriatricians and paramedics are available. It has a lot of advantage that you can centralize geriatric expertise, but it also has major disadvantages, because you withdraw the patients from the familiar treating oncologists. You can only reach a limited number of patients this way, while I just showed you, that half of persons with cancer are old. And so, I think that this geriatric oncology unit concept is not the way to go forward for the majority of patients, and I think we need in some way to find geriatric consultation teams. Those are teams that come to the patient and that give advice to the oncologist, but the patient remains under supervision of the oncologist, but you will use the expertise of geriatric consultation teams. Now, I think, in Europe, most hospitals of oncology are close to geriatric hospitals. But in the U.S., for instance, I think, there is a great lack of geriatricians, and there are many standalone comprehensive cancer centers. And I think there, other ways of organization could be used.

Now, in my centre, we try to implement geriatric assessments by starting with a G8, to be performed by the treating physician, in all patients 70-plus with a new cancer or a progression where an important treatment decision is made. And if the G8 is low, normally the cut-off is 14, but for pragmatic reasons, we put the bar at 12 because those are the frailest persons, we refer them to the geriatric day hospital for geriatric assessment and advice. But this is the ideal strategy that we want to use, and some oncologists in my institute use this strategy, but many don't use it, and it's a major challenge to convince all colleagues to use this pathway. As a geriatric oncologist, you need to realize that the data we have are not representing the true elderly population. This is one example of the many trials available showing that the population in clinical trials, in breast cancer for instance, is much, much younger than the true U.S. population, and this is the case for most tumour types. Moreover, we need to realize that the same dose of chemotherapy may be differently metabolized by older persons. And there are many pharmacokinetic parameters that change with age, and that may have impact on the dose that the patient needs and on those other patients. And SIOG made several guidelines on this topic. Because I think we have to realize that we should not systematically give the same dose in older persons. For some drugs this is true, but for other drugs you may have too much toxicity when giving the young patient dose. And there are several guidelines by SIOG that you can read for the individual drugs. Now, there are problems in the reporting of side effects of drugs, and many publications conclude wrongly that new anticancer drugs are well-tolerated and feasible for older patients with cancer. But these manuscripts are often sub-studies from randomized trials, are often written by pharma, or co-written by pharma, and don't recognize that the older population in trials does not reflect the general older population. And there are several examples, that we provide in this paper, showing that the toxicity profile in the true elderly population may be very different from the ones in publications. Lastly, when you read as a geriatric oncologist, the reports from randomized clinical trials, you need to be aware of the endpoints used in these registration trials, because the classical endpoints used in these registration trials, disease-free survival, response-rate, are often no priority for older persons. We should develop studies with endpoints that are more relevant for older persons. Quality of life can be a primary endpoint. We could create co-primary endpoints or composite endpoints where you integrate the efficacy, also the toxicity and the fact if the patient was happy that he or she received the treatment. The last point I want to focus on is that oncologist have to realize that cancer biology may be different in older persons. We just finished a review on this, an extensive review in five tumour types, where we evaluated whether tumours in older persons are molecularly different from tumours in younger persons, and we found a lot of differences in terms of tumour subtype, in terms of mutational landscape, in terms of immune infiltrate, and we honestly don't know yet, well, what the impact is on the efficacy of all our treatments, and this is also related to the fact that the immune system is probably much different in older persons. And this brings me to the concept of immunosenescence, which is nicely shown in this figure, where you can see that the number of T-cells, of naive T-cells, decline significantly, that the B-cells become less functional, make less diverse crop of antibodies, and that a situation of chronic inflammation occurs, and all these aspects may have an important impact on how we have to target immune therapy and other therapies. So, this is all at the beginning. Our knowledge is not very advanced yet, but I'm convinced that we need to do more research into this domain. So, SIOG, the International Society of Geriatric Oncology established a paper, a top-priority paper, for the worldwide advancement of cancer care in older adults. It was coordinated by Martine Extermann, and it focuses on four domains where we have to do better in the future. The first one is education, the second is clinical practice. We need better guidelines, develop models of optimal care. We need better research, specific trials for older persons, and we need to have better collaborations and partnerships with pharma, but also, with the healthcare organizations, nationally and internationally. So, in conclusion, speaking as a onco-geriatrician, I think that older patients represent the majority and not the minority. We should acknowledge that there is an extreme variability in health status, and the geriatric assessment is the cornerstone for personalized care, and that there are major challenges for implementation. We have to be very careful when interpreting results from general population studies. The benefit of therapies may be less, and the toxicity higher in frail persons. We should acknowledge that the endpoints of clinical trials may be not relevant for older persons, and also,

that the cancer itself or the cancer biology may differ in older age. And my last most important message is that I am not more an onco-geriatrician than any of you. I think every oncologist should feel himself or herself as a geriatric oncologist. We all have to think, not only of the cancer, but of all the age-related aspects that are joining this cancer. Thank you for your attention.