Questions From the Audience

Speaker Key:

GD George Demetri

SB Sylvie Bonvalot

AT Angelo Paolo Dei Tos

Time code	Speaker	Text
00:00:00	GD	We have a couple of questions here. The first question is one I'd like to raise both to myself because it's about a drug, but it's also to you, Sylvie. It says, for recurrent desmoids or non-resectable desmoid tumors, what do you like to see?
00:00:28		Do you like to see sorafenib as a first line or do you like to see chemotherapy as a first line? And let me push that to you Sylvie, because, again, very often if something is unresectable, our surgeon, Shan Raud might say well, try to shrink it and we'll see. But generally, we still will not resect it unless it's very much endangering the plexus or something. How do you look at systemic therapy and do you have a preference?
00:00:57	SB	First, I will check the history of the local recurrence. Because sometimes you see patients who have been operated directly with [unclear] resection and they have a quick local recurrence. And, in fact, if you follow this patient, a lot of them will have a regression of the tumour because the surgery may bring some factors which are growth factors.
00:01:32		And when the surgery is inadequate on a tumour which could be regressive, you have a quick operation. And if you wait a little bit it will stabilise and then regress. So, first I look at the history because if it is really a patient with a quick recurrence, we follow the patient.
00:01:57		And if it decreases, of course, we will not treat the patient. If the patient has a progression of this recurrence and that, obviously, it's an aggressive tumour and that just surveillance is not enough, it depends on the location. If it is a good location, for instance,

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		abdominal wall or thoracic wall, I would say, we will operate the patient.
00:02:31		Because it's not too much [unclear] and most of the time it will be enough. If it is a bad location, for instance, in the limbs close to the vessels or the nerves or in the mesenteric, obviously, we will go for medical treatment.
00:02:55		And here it will depend on the comorbidities of the patient, of the age of the patient, on the risk in case of progression. It's obvious that if it is very risky to have a progression because you are close to the mesenteric vessels, you will choose the drug with the best objective response in the prospective studies or in the right prospective studies.
00:03:29		Because we lack prospective studies, of course, just two randomised studies. So, that's the strategy. We have to first look at the history of the recurrence and then, in case of progressive disease of this recurrence, we decide according to the location of the tumour.
00:03:59	GD	And the question about chemotherapy versus kinase inhibitor with sorafenib, our team always discusses that in what Paulo Casali always calls shared decision making. We say, well, we have this pill. Even though it's a pill, it still has its own side effects of skin problems and diarrhoea. Or we have this chemotherapy which, even though it's intravenous, can be very gentle. So, for example, liposomal doxorubicin is extremely gentle.
00:04:30		Lododoxorubicin can be very gentle. So, we actually talk patients through what feels like the best drug for them at any point in time. I don't think there's one that's better than another.
	SB	Yes, exactly. For the choice of the drug, it depends, really on the age of the patient, the expected morbidity and the long-term morbidity. For instance, for a young patient, you will choose a drug with the lowest long-term morbidity.
00:05:00		So, it depends, really, of the presentation, age, comorbidities. We cannot say that one is better than the other. First, because we do not have randomisation between all these regimens.

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	GD	One question… Let me move just for one second, this is a quick answer, I think. How do we monitor the neurocognitive effects of Avapritinib in patients like, say, with PGDF receptor alpha mutant GIST?
00:05:33		I think that's important because in GIST we use a higher dose than we use in the hematologic malignancies like systemic mastocytosis. We don't see a lot of neurocognitive problems at a low dose of Avapritinib. But in the GIST dosing, there are ten to 20% of people who do have some neurocognitive impact.
00:05:56		And frankly, the way our team does that is by talking to the patient and even more importantly, talking to somebody who lives with the patient. Because if somebody's having a neurocognitive deficit, they can look normal on the surface, but it's better to talk to their husband or wife or companion or family member to see if they think somebody's starting to have any kind of cognitive deficit. And it's a very interesting thing because if you just withhold the drug and come back in at a lower dose, we have not seen the cognitive deficit reappear.
00:06:30		So, I do think it's something that doctors need to be aware of and it is manageable, in my opinion. Again, full disclosure, I have never dosed any patient with Avapritinib. I'm on the board of Blueprint, so I firewalled myself off and I have no personal experience. I'm giving you the information I've heard from my team members and others across the world who have experience in dosing it. Just to be completely honest. Sylvie, we have another question about retroperitoneal. This time, dedifferentiated liposarcoma.
00:07:02		The question is, how long does the disease-free interval have to be to propose reoperating at the time of recurrence? If the patient has a disease-free interval of five years and has only one lesion and easy to take out, that's obvious. Do you have a minimal amount of time before you would suggest a reoperation for recurrent disease? And then, there's another question on top of that.

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00:07:30	SB	In case of recurrence of a liposarcoma, if it is a well-differentiated liposarcoma, you can wait to reoperate the patient. But if it is a dedifferentiated liposarcoma you shouldn't wait, because it may be high grade. Even if it was [unclear] at the first surgery.
00:07:58		So, if it is a dedifferentiated liposarcoma with a recurrence, if it is resectable, the patient should be operated. The discussion for this recurrence is if the patient was not irradiated at the time of the primary, there is a discussion according to the location to propose [unclear] radiotherapy. Because in Strass there is a senior in favour of radiotherapy for this patient.
00:08:26		So, if it is feasible at the time of the local recurrence there is a place to discuss reparative radiotherapy if it is really a local recurrence and not an [unclear] recurrence. But concerning the surgery, in case of dedif recurrence, the patient should be operated if it is resectable. The only patient where you can follow the recurrence, it is well-differentiated recurrence because it may grow during a few months or even years.
00:09:03	GD	The second question, relative to this, is how do you like to image such dedifferentiated liposarcomas to plan a surgical resection? Is it CT, is it MRI, is it some combination? Do you ever use FDG-PET?
	SB	No. We don't use FDG-PET except if we want to be sure that there is no metastasis.
00:09:32		From a technical point of view, we need the CT scan with a good imaging of the mesenteric vessels. And in case of doctor on invasion, for instance, of the muscle of the abdominal wall, an MRI is of course better.
00:09:55		And very often in these local recurrence, you may have an invasion of the oblique muscles or iliac muscle. And for this recurrence, obviously, MRI is better. So, very often, we ask for both. CT scan with a good opacification of the mesenteric vessels and iliac vessels.

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		And the MRI to check that there is no invasion of the oblique and oblique muscle and iliac vessels.
00:10:32		And, of course, if there is a recurrence in the pelvis, the MRI is better. So, very often, to have a good imaging preoperatively we ask for both CT and MRI.
	GD	Paulo, last question to you. Is there any kind of a national resource in Italy to do next-generation sequencing?
00:11:01		You mentioned that expert centres and expert pathologists like you are very good about giving expert opinions, but is there any easy way in Italy to do centralised molecular testing?
	AT	Well, actually, when an official [unclear] is considered, that's not a big thing. NGS, as you know, is quite expensive. What has been decided, for example, in my region where I coordinate the departments of pathology, which was centralised and just testing in three big places. And people who signed in the cases to one of these three places won't pay at all for the test, which is provided by basically the regional government. So, it's possible, it's available and people are encouraged to send material if they can afford it and can do properly in their place.
00:11:55	GD	We're out of time. I'd like to thank the audience for submitting the questions. I'd like to thank Sylvie and Paolo for sharing your expertise with the audience. And certainly, I'd like to thank our colleagues with PharmaMar for giving us this educational platform to share some good things that came out of 2020. And hopefully, even though ESMO decided today that it will be virtual, hopefully in 2022, our community will be able to get back together again in real life. Thank you all for joining us this evening.
	AT	Thank you, George.