Speaker 1

Speaker Key:

SB Sylvie Bonvalot

Time code	Speaker	Text
00:00:10	SB	Thanks for the invitation. Update on sarcoma from the surgeon's point of view. So that's my disclosure. So, first, retroperitoneal sarcoma. We have the final results of STRASS, which randomised surgery and preoperative radiotherapy at the dose of 54Gy, followed by surgery, with a stratification by institution and performance status.
00:00:42		The primary endpoint was abdominal recurrence-free survival, which was calculated from the date of randomisation to the date of abdominal relapse or death, with parameters defined during or after surgery, local relapse after complete resection, peritoneal sarcomatosis, macroscopic disease left behind at laparotomy, R2 resection.
00:01:11		And parameters before surgery, tumours that's become inoperable between randomisation and surgery. And that was defined by becoming as a three. Development of distant metastasis while on preoperative radiotherapy, and local progression during radiotherapy.
00:01:32		So trial is globally negative. And the three years' abdominal recurrence-free survival was 60% in the preoperative radiotherapy group and 59% in the surgery group. However, in the sensitivity analysis, where local progression on radiotherapy is normally regarded as a primary event for the patients who were finally operated, there is a strong signal in favour of preoperative radiotherapy in the liposarcoma subgroup.
00:02:09		In the subgroup analysis by sarcoma subtype and grade, it suggests then in high-grade sarcoma and leiomyosarcoma there is no benefit of this preoperative radiotherapy, which is not surprising, because this high-grade sarcoma and leiomyosarcoma are mostly exposed to metastasis.
00:02:35		This is a TARPS retrospective study on retroperitoneal sarcoma. That's the reason why there is the next trial, which is randomisation for this high-grade liposarcoma or leiomyosarcoma, randomisation between surgery and

Time code	Speaker	Text
		neoadjuvant chemotherapy. And the trial is just open to the inclusion in January 2021.
00:03:06		So with all the limitations we have, Grade 3 dedifferentiated liposarcoma and leiomyosarcoma do not seem to benefit from preoperative radiotherapy, and these patients could be included in STRASS 2. And preoperative radiotherapy could be discussed in well-differentiated liposarcoma and Grade 1 or 2 dedifferentiated liposarcoma. And in the next ESMO guidelines, published in ’21, this is an option.
00:03:35		And a dedifferentiated STRASS will be done after five years’ follow-up. But at the current follow-up, there is no impact of radiotherapy on the overall survival. However, this retroperitoneal sarcoma must be treated in a referral centre from the beginning. Extremity sarcoma, we have the final results of the neoadjuvant chemotherapy trial in high-risk extremity soft-tissue sarcoma.
00:04:04		This trial randomised histology-tailored chemotherapy and standard chemotherapy, defined by epi-adriamycin plus ifosfamide, three cycles, followed by surgery with or without radiotherapy. And the main objective of the trial is disease-free survival.
00:04:26		As you see, the trial became negative because disease-free survival of the histotype-tailored chemotherapy is 10% better than the initial projected disease-free survival, where it was comparable to the standard, without chemotherapy, of a previous trial of the Italian group.
00:04:54		This trial, of course, cannot be interpreted that neoadjuvant chemotherapy is better than no chemotherapy. The overall survival looks better in the standard chemotherapy group. But it must be underlined that the trial was not stratified on the histological subtype. And, for instance, there is more UPS in the histotype-tailored chemotherapy.
00:05:24		And, as you know, this undifferentiated pleomorphic sarcoma has a worse prognosis. In the patients who have predicted overall survival more than 60%, according to Sarculator, there is no difference between the two groups on disease-free survival and overall survival.
00:05:51		For the patient who has a predicted overall survival less than 60%, according to Sarculator, there is a trend in favour of the

Time code	Speaker	Text
		standard chemotherapy group, but it is not significant. And concerning the overall survival, there is the same remarks than for the overall population concerning the fact that it is not stratified according to the subtype.
00:06:20		So the author concluded that on tetracycline and ifosfamide should remain the regimen to choose when a neoadjuvant chemotherapy is decided. However, it must be acknowledged that in the histotype-tailored chemotherapy the regimen could've been a little bit different, so the debate is still open.
00:06:51		And in the last guidelines from ESMO, which should be published in '21, neoadjuvant chemotherapy is still an option. Concerning this dogma, is systematic resection after unplanned R1 surgery always necessary? As you know, whole resection requires larger excisions than initially necessary.
00:07:20		And sometimes it's mutilating, demanding plastic reconstruction. Residual cells are found in 50% of cases. And, anyway, some patients will never recur. This is retrospective surgery on the French national database concerning 622 patients. Of course, the patients who had R2 resection or piecemeal resection were not included in this study.
00:07:49		Three groups were defined, the group R concerned R patients who underwent the systematic resection in a sarcoma centre. The Group B is patients who underwent the systematic resection but outside referral centre. And the Group C is patients who didn't have re-excision because it was not feasible or because it was the choice of the doctors.
00:08:19		As you can see, of course, the probability of local relapse is higher when the patient didn't have re-excision. And you can see that when re-excision was done in a sarcoma centre, the probability is lower than when it was performed outside a sarcoma centre. But the overall survival of the three groups are exactly the same.
00:08:47		So the question is, is it necessary to perform this re-excision at the time of the initial treatment or at the time of the local relapse? And recently there is this second study performed by the Italian group. They looked retrospectively at the patients who had resection, and they looked at the impact of the microscopic residual disease.

Time code	Speaker	Text
00:09:18		And you can see that the overall survival of the patients who have microscopic residual disease is exactly the same than when they do not have microscopic residual disease. So the debate now in ’21 is open. Is this systematic re-excision always necessary when there is no tumour rupture and no microscopic residual disease?
00:09:49		Probably there is a place for a randomised study or for a prospective database. So this debate is open in 2021. So desmoid, as you know, in this first study, evaluating surveillance for primary desmoid, the event-free survival after surveillance is the same than after as a whole surgery.
00:10:21		And this surveillance was applied, this concept was applied on various locations, retroperitoneal desmoid, extremity desmoid, breast desmoid. This is an example, on the right, of a mesentery desmoid. The patient was placed under active surveillance. And you can see a few years later, without any treatment, the residual disease, which is 4cm.
00:10:53		In retrospective national database of the French sarcoma group, half of the patients were operated and half of the patients were placed under surveillance. And this large national database confirms that in favourable locations the event-free survival of the patients who were not operated is the same than the patient who were operated. And it is worse in patients operated when it is unfavourable location.
00:11:26		And, finally, in this randomised study for advanced and refractory desmoid tumour, evaluating the impact of sorafenib, the patients were selected for initial progression or recurrence. And it is very interesting to look at the placebo group. 20% of the patients had disease spontaneous significant regression. It was a study which was blind. And two-thirds of the patients had stable disease or regression.
00:11:58		And the author concluded that this provides evidence for an initial period of observation. In recent meta-analysis, the proportion of patients with progressive disease is around 20%. And, finally, in the 2020 Consensus meeting, with Europe, US and Japan, active surveillance became the first-line strategy, outside any complication, of course.
00:12:31		GIST. In this posthoc study, which is based on adjuvant trial of ERTC, which randomised RCT, which randomised high- and intermediate-risk GIST between neoadjuvant treatment and

Time code	Speaker	Text
		imatinib, the objective was to assess the association or R1 resection with overall survival and recurrence-free survival.
00:12:59		As you can see, 162 patients had an R1 resection, and of them, 97 had tumour rupture. The overall survival of the patients who had an R0 resection is better than the patients who had an R1 resection, with or without imatinib.
00:13:26		However, when you look at the patients when tumour rupture were excluded, the overall survival of the R0 patients is the same than the patients who had an R1 resection, with or without imatinib.
00:13:45		So the conclusion is that the R1 margins, of course, without tumour rupture, is not a parameter which in decision-making about adjuvant treatment with imatinib. And patients who had an R1 resection shouldn’t be reoperated.
00:14:08		And, to conclude, this is the update of the adjuvant trial of the Scandinavian and German group. And this study confirmed that three years of adjuvant imatinib is superior in efficacy compared with one years of imatinib. Thank you.