EUnetHTA JA3 WP4 - Other technologies, OTCA18
Review by external experts of the 2nd draft Project Plan for Regional hyperthermia for high-risk soft tissue sarcoma treatment

Comments should be submitted not later than Tuesday *05/03/2019*

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Comment from *Insert your name and organisation*	**Page number** *Insert 'general' if your comment relates to the whole document*	**Line/ section number**	**Comment and suggestion for rewording** *Please insert each new comment in a new row.*	**Character of comment** • 'major'[a] =1 • 'minor'[b] = 2 • 'linguistic'[c] =3 *Please indicate your choice by writing the according number in this field, e.g. for major choose "1".*	**Author's reply**
Stephan Bodis	5	Table 1-2	Add IT IS/Zurich (Prototype and Planing system developped) IT IS has no CE certificate in 2019 (maybe by 2020/20221)	2	As per EUnetHTA rules we can only include CE approved devices.
Stephan Bodis	8	7th para 1st line	With radiotherapy and **/ or** chemotherapy	2	Changed accordingly.
Stephan Bodis	14	@experts	Patients with Kaposi's sarcoma or melanoma should not be considered as population for this assessment	2	Ok
Stephan Bodis	14	@experts	I suggest to go ahead with ESMO definition. However any one of the criteria - tumours T2 –T4 (extremity, retroperitoneal sarcomas, head neck) WITH OR WITH OUT Grades 2 and 3 should be high-grade. For thoracic and abdominal STS , it could be T2a to T4c. Contact senior staff within NCI	1	We have adapted the description in accordance to the feedback from the other experts.

Please add extra rows as needed.

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			and FNCLCC for input		
Stephan Bodis	15	2nd last para	The suggested approach is fine. Below an alternative option of how to proceed.F/u for high risk sarcomas: f/u after one month; year 1 and 2 q 3 months; year 3 to 5 q 6 months	2	Given the consensus among the other external experts, we have opted to maintain the current approach.
Stephan Bodis	18	reference	add: Datta et al Int J Particle Ther 2016; Proton irradiation with hyperthermia in unresectable sotf tissue sarcoma	2	Added.
Frank Lohr AOU Modena	10		Melanoma and Chloroma can be excluded	2	We have excluded these terms together with other terms that were suggested by other experts.
Frank Lohr AOU Modena	12		Specific RT parameters in addition to those chosen: Beam Quality (Photons, Electrons, N, P), Overall treatment time	2	Added.
Frank Lohr AOU Modena	14		Kaposi to be excluded	2	Ok
Frank Lohr AOU Modena	14		Reclassification makes only sense when access to patient individual data is available. Maybe I overlooked it but looking at the most recent ESMO-guideline (10/18) I don't find a clear definition of "high risk". Or a cut off based on sarculator is chosen or everything that is not considered low risk (e.g. not requiring neo/adjuvant RT/Cht), which means everything but small, superficial low-grade tumors are defined as high risk.	1	We have added the following statement to the description of the patient population: …"This excludes studies that focus on low risk sarcoma which do not require radiotherapy or chemotherapy and which means small, superficial, low-grade tumours."
J.P.Poulsen	10	Table 2.3	I think that the following groups should be omitted: 5: Adenosarcoma,	1	We have excluded these terms.

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Oslo universitetssykehus			8: Carcinosarcoma, 9: Carcinoma, 28: Histioblastoma.		
J.P.Poulsen Oslo universitetssykehus	11	Table 2.3	Omit: 33: Leucosarcoma, 34: Leucolymphosarcoma, 35: Leucosarcomatosis, 37: Lymphoma, 49: Melanoma, 50: Ehs tumor, 51: Chloroma, 52: Myeloid cell tumor, 53: Reticulosarcoma, 54: Reticulolymphosarcoma, 55: Retotheliosarcoma, 58: Synovioma	1	We have excluded these terms, except for 58: given that this was not suggested for exclusion by the other experts.
J.P.Poulsen Oslo universitetssykehus	12	Table 2.4	I don't know what parameters one use for hyperthermia. For Radiotherapy is dose/fraction and numbers of fractions impotant. Total treatment time may be important too. For chemotherapy is it important to know which substaneces, dose per course and total dose. It is also important to know if there was any reduction in doses or if there was any delays due to side effects, neutropenia etc	1	We have consulted with the other experts for the hyperthermia related parameters and we have included the suggested parameters for radiotherapy and chemotherapy.
J.P.Poulsen Oslo universitetssykehus	14	Table 2.5	I would not consider patients with Kaposi's sarkom or Melanoma as a patient population of this assesment. The same is true with patients having the diagnoses that I omitted, mentioned from table 2.3. They are not "true soft tissue sarcomas"	1	Ok.
J.P. Poulsen Oslo universitetssykehus	14	Table 2.5	As you say, the 2 most widely used systems for grading sarcoma are the NCI system and the FNCLCC system. I think that they are partly overlapping, and it depends from what country the article (report) is coming,	2	We have further specified the description of high risk, taking into account the feedback from the other experts as well.

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			which system they use. I don't think it make any difference. The ESMO guidelines are very good too. The Sarculator is an "App" made by either French or Italian colleagues, and I don,t know how accurate it is or whether it has been evaluated properly against the other systems.		
J.P.Poulsen Oslo universitetssykehus	15	Table 2.5	The acute toxicity should also be checked if possible at 3 and 6 months after completing the treatment. After that I agree with follow-up time that you suggest, one year, one to three years and more than three years after the invention.	1	We have added 3 and 6 months as follow-up time categories.
J.P.Poulsen Oslo universitetssykehus	22-23	5.2	My answers are No for all questions except question 2.1. Does the introduction of the new technology and its potential use/non-use instead of the defined, existing comparator require organizational changes? Yes, it requires specialized centers for administration	1	We will assess the questions in this checklist during the assessment.

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