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

Comments should be submitted not later than Thursday *07/03/2019*

Please use this form for submitting your comments and please return to Stijn Van de Velde:

1. Please put each new comment in a new row.
2. Please insert the page number and section number on which your comment applies. If your comment relates to the document as a whole, please put **'general'** in this column.
3. Please provide a description of your comment as specific as possible and preferably also provide a suggestion for rewording. If you wish to draw our attention to published literature, please supply the full reference.

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**
Nina L. Jebsen Haukeland University Hospital	9		«…versus the effect of studies that either ~~that~~ did not report temperature…» (superfluous word)	3	Corrected.
	10/11		Ad. Search terms for use in Medline: the list of diagnoses is very lengthy and includes rare tumour types which are not considered sarcoma entities (although carrying sarcoma in the label such as reticulosarcoma which actually represents a non-Hodkin's lymphoma). Also, outdated terms for sarcoma subtypes are listed, as well as subtypes of sarcoma for which regional hyperthermia is not indicated. I would suggest removing the following terms: 5, 8, 9, 10, 11, 13, 14, 15, 16, 17, 18, 19, 28, 29, 30, 33, 34, 35, 37, 47, 48, 49, 50, 51, 52, 53, 54 and 55. More commonly used terms such as synovial sarcoma (as opposed to synoviosarcoma), and important subtypes such as	2	We have excluded those terms for which we had consensus with the appointed external experts and the librarian will assess the need to add the other suggested terms.

Please add extra rows as needed.

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			undifferentiated pleomorphic sarcoma (UPS), epithelioid sarcoma, malignant peripheral nerve sheath tumour (MPNST), and undifferentiated sarcoma could be added instead.		
	10/11		"21. Neurofibrasarcoma" is misspelled – should be Neurofibrosarcoma		Corrected.
	14		Suggested change (new text in red): "Adults (>18yrs) who have a high-risk soft tissue sarcoma. We exclude adolescents or children ~~given that soft tissue sarcoma is a very rare disease for this age group.~~ since treatment in these age groups follows specific paediatric protocols.	2	Changed accordingly.
	14		Suggested change in red: «Soft tissue sarcomas ~~are~~ represents a type of cancer that ~~can start~~ arise in soft tissues…»	3	Changed accordingly.
	14		«Surgical excision of the tumour tissue is ~~an~~ the most important ~~part of the overall~~ treatment for patients with soft tissue sarcoma, but achieving a ~~clean~~ clear surgical resection is not always possible. In this assessment, we will include both patients with non-resectable tumours and with tumours that can be surgically resected. ~~because of the high risk of metastasis in this population.~~	3	Changed accordingly.
	14		High-risk soft tissue sarcomas ~~are tumours that have~~ harbor an increased risk of local recurrence ~~after being removed or a high risk for~~ and distant metastases following surgical resection, resulting in a high ~~and~~ tumour related mortality. We will use the criteria from the European Society for Medical Oncology (ESMO) guidelines, ~~we~~ define~~e~~ing high-risk sarcoma as tumours which are high-grade malignant, situated deep to the subcutaneous fascia and large (size > 5cm)	2, 3	Changed accordingly.
	14		Within this assessment we will include both ~~non-metastatic~~ localized and metastatic sarcomas (where	3	Changed in a way that matches with the provided feedback.

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			the cancer has spread from the main tumour~~s~~ to other areas). Cases treated with ~~We will also include~~ ~~both~~ either curative and palliative ~~patients.~~ intent will be included. "In the event of studies ~~have~~ include~~d~~ing a mixed population (i.e. low- and high-risk), we will not include studies if less than 75% of the included patients are considered to be high-risk soft tissue sarcoma patients.		
	14		"ICD 10 codes: C 48 and C49.0-C49.9. Since ICD-codes follow organ of origin, other organ specific ICD 10 codes may be applicable (for instance in case of a sarcoma of the pancreas, the correct code will be C25)	1	Changed accordingly.
	19		Add to references: *Issels RD, Lindner LH, Verweij J, Wessalowski R, Reichardt P, Wust P, Ghadjar P, Hohenberger P, Angele M, Salat C, Vujaskovic Z, Daugaard S, Mella O, Mansmann U, Dürr HR, Knösel T, Abdel-Rahman S, Schmidt M, Hiddemann W, Jauch KW, Belka C, Gronchi A; European Organization for the Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group and the European Society for Hyperthermic Oncology.* **Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia on Long-term Outcomes Among Patients With Localized High-Risk Soft Tissue Sarcoma: The EORTC 62961-ESHO 95 Randomized Clinical Trial.** JAMA Oncol. 2018 Apr 1;4(4):483-492. doi: 10.1001/jamaoncol.2017.4996. PMID: 29450452	1	Changed accordingly.
	19		May be considered as reference: *Issels R, Lindner LH.* **Regional hyperthermia for high-risk soft tissue sarcoma treatment: present status and next questions.** Curr Opin Oncol. 2016 Sep;28(5):447-52. doi:	2	We will evaluate the suggested references during the screening process where we select studies for inclusion in the assessment.

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			10.1097/CCO.0000000000000316. Review. PMID: 27455134		
	19		May be considered as reference: *Issels R, Kampmann E, Kanaar R, Lindner LH.* **Hallmarks of hyperthermia in driving the future of clinical hyperthermia as targeted therapy: translation into clinical application.** Int J Hyperthermia. 2016;32(1):89-95. doi: 10.3109/02656736.2015.1119317. Epub 2016 Jan 24. Review. PMID: 26803991	2	See reply above.
	19		May be considered as reference: *Ott OJ, Schmidt M, Semrau S, Strnad V, Matzel KE, Schneider I, Raptis D, Uter W, Grützmann R, Fietkau R.* **Chemoradiotherapy with and without deep regional hyperthermia for squamous cell carcinoma of the anus.** Strahlenther Onkol. 2018 Nov 2. doi: 10.1007/s00066-018-1396-x. [Epub ahead of print], PMID:30390114	2	See reply above.
	19		May be considered as reference: *Elming PB, Sørensen BS, Oei AL, Franken NAP, Crezee J, Overgaard J, Horsman MR.* **Hyperthermia: The Optimal Treatment to Overcome Radiation Resistant Hypoxia.** Cancers (Basel). 2019 Jan 9;11(1). pii: E60. doi: 10.3390/cancers11010060. Review. PMID: 30634444	2	See reply above.
	19		May be considered as reference: **Datta NR, Stutz E, Gomez S, Bodis S.**	2	See reply above.

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			Efficacy and Safety Evaluation of the Various Therapeutic Options in Locally Advanced Cervix Cancer: A Systematic Review and Network Meta-Analysis of Randomized Clinical Trials. Int J Radiat Oncol Biol Phys. 2019 Feb 1;103(2):411-437. doi: 10.1016/j.ijrobp.2018.09.037. Epub 2018 Nov 1. Review. PMID:30391522		

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