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A prospective multicenter DAHANCA study of hyperfractionated accelerated RT for head and neck cancer

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Table 2 PET-positive lymph nodes in anal cancer patients with number of misses using different contouring guidelines¹

Location/ Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	Σ	
Para-aortic	6	6														1								13
RTOG	6	6														1								13
AGITG	6	6														1								13
BNG	6	6														1								13
Common iliac	13	1									1						1		1					17
RTOG	12	0								0							1	0						13
AGITG	12	0								0							1	0						13
BNG	12	0								0							1	0						13
External iliac	2	11		1		2					1		2	1	3	3								26
RTOG	0	0		0		0				0		0	0	0	0	0								0
AGITG	0	0		0		0				0		0	0	0	0	0								0
BNG	0	0		0		0				0		0	0	0	0	0								0
Internal iliac	1	5	1	1	1						1		1	1	4									16
RTOG	0	0	0	0	0					0		0	0	0	0									0
AGITG	0	0	0	0	0					0		0	0	0	0									0
BNG	0	0	0	0	0					0		0	0	0	0									0
Pre-sacral	3	1	1	1	2						1		2						2	1				14
RTOG	0	0	0	0	0					0		0	0						0	0				0
AGITG	0	0	0	0	0					0		0	0						0	0				0
BNG	0	0	0	0	0					0		0	0						0	0				0
Peri-sacral	1	2		1	2	1	1	1	2				2						2	1	2			19
RTOG	0	0		0	0	0	0	0	0			0							0	0	0			0
AGITG	0	0		0	0	0	0	0	0			0							0	0	0			0
BNG	0	0		0	0	0	0	0	0			0							0	0	0			0
Inguinal	2	5	1	14				1	1		1	6		2	16									49
RTOG	0	3	0	6				0	0		1	0		0	4									14
AGITG	0	1	0	3				0	0		1	0		0	2									7
BNG	0	0	0	3				0	0		1	0		0	1									5
Total LNs	3	32	1	38	1	2	2	3	4	5	3	3	1	10	3	13	19	1	2	4	3			154

Conclusion

In this study, we demonstrated patterns of LN involvement based on PET-imaging. In the pelvis, various recommendations are largely consistent and all LNs were covered by the recommended CTVs. LN "misses" appear generally cranially (common iliac or para-aortic) or caudally (inguinal) to the recommended CTVs. The established guidelines differ significantly, particular regarding the inguinal region. Based on our results, we finally presented our recommendation for contouring of the elective CTV of the inguinal region. Lymph node involvement of a larger number of patients should be investigated to enable final recommendations.

Proffered Papers: CL 8: Proffered papers : Head and Neck

OC-0387 radiotherapy with paclitaxel/cisplatin vs. fluorouracil/cisplatin for head and neck cancer

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Purpose or Objective

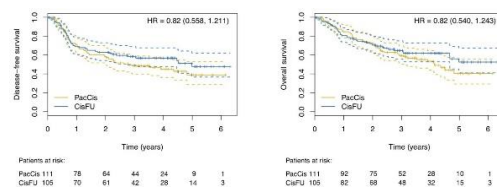
The utilization of taxanes has demonstrated promising results in squamous cell carcinoma of the head and neck (SCCHN) as induction chemotherapy prior to definitive chemoradiotherapy (CRT). The purpose of this multicenter, phase 3 trial was to investigate whether the incorporation of concurrent paclitaxel and cisplatin together with a slightly reduced total dose of radiotherapy (RT) is superior compared with standard fluorouracil-cisplatin based CRT.

Material and Methods

Previously untreated patients with non-metastatic SCCHN, stage III-IVB, were randomized to receive paclitaxel/cisplatin(PacCis)-CRT (arm A; paclitaxel 20 mg/m² on days 2, 5, 8, 11 and 25, 30, 33, 36; cisplatin 20 mg/m², days 1-4 and 29-32; RT to a total dose of 63.6 Gy) or fluorouracil/cisplatin(CisFU) -CRT (arm B; fluorouracil 600 mg/m²; cisplatin 20 mg/m², days 1-5 and 29-33; RT: 70.6 Gy). Primary endpoint was 3-year-disease free survival (3y-DFS). Secondary endpoints included overall survival (OS), locoregional failure rate (LFR), distant failure rate (DFR), and toxicity.

Results

A total of 221 patients have been enrolled in 14 sites between 2010 and 2015. With a median follow-up of 3.7 years, 3y-DFS in the CisFU arm and PacCis arm was 58.2% and 48.4%, respectively (HR 0.82, 95% CI 0.56-1.21, p=0.52). The 3y-OS amounted to 64.6% in the CisFU arm, and to 59.2% in the PacCis arm (HR 0.82, 95% CI 0.54-1.24, p=0.43). There were no significant differences for LFR and DFR. In the subgroup of p16-positive oropharyngeal carcinomas, 3y-DFS and 3y-OS was 84.6% vs 83.9% (p=0.653), and 92.3% vs. 83.5% (p=0.76) in arm A and B, respectively. Hematological toxicities grade 3-4 were significantly reduced in arm A (anemia, p=0.01; leukocytopenia, p=0.003).



Conclusion

Paclitaxel/cisplatin-CRT with a slightly reduced total RT-dose is not superior to standard fluorouracil/cisplatin-CRT. Subgroup analyses indicate that a reduced radiation dose seems to be sufficient for p16+ oropharyngeal cancer and/ or in non-smokers.

OC-0388 A prospective multicenter DAHANCA study of hyperfractionated accelerated RT for head and neck cancer

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Purpose or Objective

The DAHANCA9 hyperfractionation study and the MARCH meta-analysis (Bourhis et al, Lancet 2006) on altered fractionation showed that Hyperfractionated Accelerated Radiotherapy (HART) is superior in terms of loco-regional control (LRC) and overall survival (OS) compared to conventional or moderately accelerated radiotherapy for Head and Neck Squamous Cell Carcinomas (HNSCC). Since 2007, HART has been included as a treatment option in the Danish DAHANCA radiotherapy guidelines. The aim of the present study was to evaluate this treatment strategy using LRC, OS and late morbidity as endpoints.

Material and Methods

Prospectively registered patients (pts) with HNSCC treated with HART according to national guidelines prescribed as 76Gy/56fx, 10 fx/week, as primary treatment were identified in the DAHANCA database and updated. The study was evaluated as intention to treat and elective neck-dissection was not an option.

Results

From July 2007 to December 2017, 271 pts with HNSCC treated with HART were identified in four national cancer centers that on a regular basis offers HART according to treatment guidelines. The median age was 64 years (32-81 years) and 74% were males. The majority of pts were WHO PS 0-1 (94%) and only 6% were WHO PS \geq 2. Most (84%) were current or previous smokers with a smoking history of median 42 pack-years (1-140 pack-years). The primary site was larynx in 65 cases (24%); 176 cases were in the pharynx (65%) and 30 pts had oral cavity cancer (11%). In total, 62% of the cases were stage III-IV (UICC7). In the pharynx, 138 cases (78%) were of oropharyngeal origin and of those, 48% were HPV/p16+. The proportion of pts receiving HART as planned was 96%. No patients received adjuvant or concomitant chemotherapy. As per September 1st 2018, 50 loco-regional failures (19% of the pts) were detected with a median follow-up time of 29 months: 47 occurred in T-site and 15 in N-site. Among those, 12 pts had both T- and N-site failure. Three-year actuarial LRC was 81% and OS was 68%. LRC at three years was significantly different for stage I-II and stage III-IV HNSCC (90% vs. 74%, HR 0.44 (range 0.23-0.81)) but not significantly better for HPV/p16+ oropharyngeal carcinomas compared to the HPV/p16- oropharynx pts (94% vs 89%). The proportion of pts reporting severe late dysphagia was 16%, and 9% reported late, severe dryness of the mouth; 8% were observed with late tardive edema of the larynx, 10% with severe mucosal atrophy and 5% with severe fibrosis of the subcutaneous tissue in the neck region.

Conclusion

Hyperfractionated accelerated radiotherapy is an attractive treatment approach in patients with HNSCC. Three-year loco-regional control as observed in this study is more than 80% and that is reflected in an acceptable overall survival. In this study, HART produced equally good results for HPV/p16+ and HPV/p16- oropharyngeal cancer patients. Severe late morbidity is reasonably low and comparable to treatment with chemo-radiotherapy.

OC-0389 Individualized prophylactic irradiation based on sentinel lymph node(s) identification in cN0 HNSCC

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Purpose or Objective

Due to a risk of occult nodal metastases in clinically node-negative (cN0) head and neck squamous cell carcinoma

(HNSCC) patients, prophylactic and often bilateral neck irradiation is mandatory. However, it leads to a large irradiation of healthy tissues and could miss unexpected nodal basins drained by the tumor. This prospective, non-randomized, interventional phase II study investigated how sentinel lymph node (SLN) mapping by SPECT/CT may help to individualize prophylactic neck irradiation and its potential impact on radiation-related toxicities and tumor control. The final results are presented.

Material and Methods

Forty-four patients with newly diagnosed cN0 squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx were included and treated with upfront (chemo)radiotherapy with a curative intent. After simulation, all patients were imaged in treatment position with SPECT/CT after ^{99m}Tc nanocolloid injection around the tumor. The neck levels containing up to four hottest SLN were selected for prophylactic irradiation (CTVn-LS). A comparative virtual planning was performed by including the levels selected on the basis of the current international guidelines (CTVn-IG). Dosimetric data to the different organs-at-risk (OAR) were compared between both plans. Normal tissue complication probability (NTCP) models for xerostomia and dysphagia as well as quality of life assessments (EORTC C30 and H&N35 scales) are being investigated to predict the clinical benefit of this technique.

Results

Lymphatic migration was observed in all of the 44 patients. Four patients (9%) presented an unpredicted lymphatic drainage and 21 patients (48%) had only an unilateral drainage. The volumes of CTVn-LS and PTVn-LS (median volumes of 91.8 cc and 219.1 cc, respectively) were systematically smaller than CTVn-IG and PTVn-IG (median volumes of 188.3 cc and 405.3 cc, respectively). This led to a significant dose decrease in identified OAR, particularly to the contralateral parotid gland, contralateral submandibular gland, inferior constrictor muscle for oral/oropharynx tumors and superior constrictor muscle for larynx/hypopharynx tumors (Table 1). NTCP values and QoL data processing is still work in progress and will be presented during the congress. At a median follow-up of 42 months, 3 patients experienced a regional relapse: 2 in an irradiated area (4.5%) and 1 in a non-irradiated area (2.3%). Currently, 4 patients had a local recurrence and 6 patients died (2 patients from geriatric degradation and 4 patients experienced fatal local relapse).

Comparative dosimetry of clinically significant organs-at-risk

OARs	IG plan Median Dmean (Gy)	LS plan Median Dmean (Gy)	p-Value*	Median ΔDmean (Gy)
Unilateral lymph drainage on SPECT/CT (n = 21)				
Oral cavity and oropharynx carcinoma				
Parotid gland (ipsilateral)	28.5	29.7	0.69	-0.1
Parotid gland (contralateral)	25.3	18.6	0.03	10.4
Submandibular gland (ipsilateral)	45.0	47.1	0.87	0.4
Submandibular gland (contralateral)	49.8	20.9	<0.01	28.0
Superior PCM	57.3	55.2	0.09	1.0
Middle PCM	38.2	32.2	0.14	7.1
Inferior PCM	33.8	13.4	0.01	22.5
Hypopharynx and larynx carcinoma				
Parotid gland (ipsilateral)	18.9	18.0	0.03	1.9
Parotid gland (contralateral)	19.5	4.0	<0.01	15.2
Submandibular gland (ipsilateral)	39.2	36.3	0.08	3.1
Submandibular gland (contralateral)	41.6	11.0	<0.01	29.1
Superior PCM	56.0	20.9	<0.01	34.4
Middle PCM	49.1	42.2	0.22	6.2
Inferior PCM	58.6	57.3	0.66	2.2
Bilateral lymph drainage on SPECT/CT (n = 22)				
Oral cavity and oropharynx carcinoma				
Parotid gland (ipsilateral)	27.15	25.75	0.43	1.5
Parotid gland (contralateral)	25.05	23.67	0.45	1.7
Submandibular gland (ipsilateral)	50.15	46.3	0.55	0.4
Submandibular gland (contralateral)	42.1	38.4	0.31	1.5
Superior PCM	54.25	45.2	0.06	6.0
Middle PCM	47.6	44.2	0.70	0.8
Inferior PCM	46.7	19.05	<0.01	24.9
Hypopharynx and larynx carcinoma				
Parotid gland (ipsilateral)	20.7	18.9	0.02	0.3
Parotid gland (contralateral)	20.2	18.7	0.02	0.6
Submandibular gland (ipsilateral)	39.5	26.95	0.06	1.8
Submandibular gland (contralateral)	37.25	33.55	0.04	2.8
Superior PCM	36.95	30.55	0.05	6.0
Middle PCM	56.3	56.15	0.44	0.4
Inferior PCM	60.05	58.3	0.74	0.3

Abbreviations: IG: International guidelines; LS: Lymphoscintigraphy; PCM: pharyngeal constrictor muscle

* Mann-Whitney-U test, two-sided test.

Conclusion

SLN mapping using SPECT/CT allowed to significantly reduce the prophylactically irradiated neck volumes in cN0 HNSCC patients. This resulted in a significant dose decrease in OAR, especially in patients presenting an unilateral lymphatic drainage, while uncompromising the