studies, topical clonidine shown activity in reducing NF-κB activation and incidence of severe OM (SOM). In a randomized double blind, placebo-controlled study, a novel mucoadhesive buccal tablet (MBT) containing clonidine reduced the incidence of SOM in HNC patients being treated with CRT. We now report overall survival (OS), tolerability and systemic exposure of clonidine of study subjects.

Material and Methods: Clonidine MBT 50µg (n=56), 100µg (n=65) or matching placebo (n=62) were applied to the gum once daily 1-3 days prior to RT and then daily until the end of CRT (1.8-2.2 Gy/d, 5 times/week combined with a platinum based CT). AEs, vital signs and gingival tolerance by Silness-Loe index (global score from 0 to 9) were assessed twice a week; xerostomia and sedation (visual scale from 0 to 10) were evaluated once a week. Blood and saliva samples for clonidine levels were collected Q2 weeks. OS data will be collected until 2 years after last patient last visit. Patients received a median cumulative radiation dose of 66 Gy [min: 4; max: 78]. SOM was reported in 60% [95%CI: 47%; 72%] of placebo patients, 43% [95%CI: 29%; 57%] in clonidine 50µg MBT (p=0.063) and 48 % [95%CI: 35%; 61%] in clonidine 100µg MBT (p=0.169).

Results: All grade AE incidence was 91% in clonidine MBT groups and 98% in placebo group (p<0.10). No difference in heart rate and blood pressure was reported between groups. Reversible hypotension AEs were reported in 7% clonidine MBT 50µg patients, 6% clonidine MBT 100µg and 2% placebo-treated patients (p=ns). Sedation score slightly increased in all groups between week 1 and week 6 (overall from 1.5 ± 2.3 to 3.0 ±2.3) and was similar between groups (p=ns). Xerostomia grade ≥ 2 increased to 41% in clonidine MBT 50µg, 31% in clonidine MBT 100µg and 42% in placebo patients (p=ns). The mean plasma/saliva concentrations of clonidine were 0.087/154.2ng/mL in clonidine MBT 50µg and 0.134/301.1 ng/mL in clonidine MBT 100µg. With a median follow-up of 15 months, the median 1year-OS of 89.3% [95%CI: 73.9; 95.8] placebo and 89.7% [95%CI: 80.4; 94.8] clonidine MBT.

Conclusion: Clonidine MBT daily applied to the gum throughout CRT reduced the incidence of SOM and was well tolerated in HNC patients undergoing postoperative CRT. No significant systemic effects of clonidine were reported in the phase 2 study probably due to its low systemic levels.

PO-0637

RCT pilot study of Therabite vs wooden spatula in amelioration of trismus in H&N cancer patients

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Purpose or Objective: Specific objectives of the study were (i) to assess whether prophylactic exercise intervention prevented the worsening of jaw tightening that would be expected following radiotherapy (ii) to assess whether the Therabite® or wooden spatulas intervention improved patients' QOL as measured using validated questionnaires; (iii) to assess issues around power for sample size calculations, compliance and practical aspects of running a full RCT in this group of patients and (iv) whether the intervention reduced the level of post-treatment clinical management/health care utilisation required by mouth cancer patients

Material and Methods: All patients had some sense of subjective jaw tightening prior to study entry. Measurements of jaw opening and QOLs were taken pre and post radiotherapy 3 and 6 months. Patients were instructed to follow the 5-5-30 regimen daily, for 6 months. (5stretches, 5times, 30 second hold).

Results: 37 patients with stage 3/4 oral/oropharyngeal cancers were randomised to receive the therabite device and 34 the wooden spatulas for jaw exercises. The study has shown that mouth openings had increased on average in both groups following the exercise intervention. There was no statistically significant difference between the two interventions. There were problems with compliance. Lessons learnt from the semi structured telephone interviews, (15 patients) which would aid compliance included: (1) Allow patients to have more of a say in the exercise regimen ie reduce to 3 times a day. (2) Allow patients to take a variable break (up to 6 weeks) from the exercises when side effects of radiotherapy are at their worst. Mucositis, soreness and pain in mouth being reported during last few weeks and 4 weeks post radiotherapy. (3) More regular contact with the patients for encouragement and support. The study was designed to give an indication about the benefits of exercises and to inform feasibility to conduct a larger study

Conclusion: Prophylactic exercises during and after radiotherapy treatment can ameliorate trismus for stage 3 and 4 oral/oropharyngeal cancers. Keyword: Trismus, Radiotherapy This abstract presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Ref No: PB-PG-0610-22317). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Sponsor: The Christie NHS Foundation Trust

PO-0638

Adaptive dose painting by numbers for head and neck cancer: interim analysis of a randomised trial

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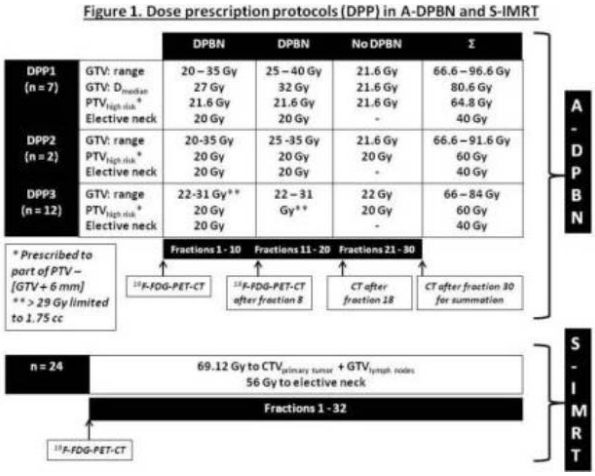
Purpose or Objective: A prospective randomized multi-centre phase II trial comparing standard IMRT (S-IMRT) to 3-phase adaptive dose painting by numbers (DPBN) for head and neck cancer (HNC) is currently recruiting patients. Unlike the fact that the initial dose prescription was derived from a phase I trial, we observed an unacceptable rate of late mucosal ulceration using this dose prescription in the DPBN group. This made us change the dose prescription in two steps. This interim analysis reports on acute and late toxicity and local (LC), regional (RC) and distant control (DC) in almost half of the patients to be included.

Material and Methods: From 2011, Q3 to 2015, Q3 53 patients received primary radio(chemo)therapy for HNC. We report on 45 patients who have ended therapy for 3 months. Patient, tumor and treatment characteristics can be found in Table 1

	3-phase adaptive DPBN (n = 21)	Standard IMRT (n = 24)	*p-value*
Median age (range; in years)	59 (40 – 74)	56 (48 – 68)	
Male / female	19 / 2	19 / 5	0.42
Site: - Oropharynx - Hypopharynx - Larynx	 14 5 2	 13 6 5	0.64
Stage grouping - I - II - III - IVA - IVB	 1 3 3 14 -	 - 2 6 12 4	0.25
T-staging - T1 - T2 - T3 - T4a - T4b	 4 7 5 4 1	 4 11 3 2 4	0.91
N-staging - N0 - N1 - N2a - N2b - N2c	 6 1 1 5 8	 2 7 2 4 9	0.13
Pre-IMRT neck dissection	6	1	0.04
Concomitant cisplatin	13	9	0.14

Fig. 1 demonstrates dose prescription protocols (DPP) of the DPBN- and S-IMRT group



Results: As previously reported (ESTRO 2015) we unexpectedly observed late grade (G)3 and 4 mucosal ulcers in 1/7 and 3/7 DPBN-patients in DPP1, respectively, that healed spontaneously (n = 1), after surgical intervention (n = 2) and is still persisting (n = 1) at 42 months. In order to avoid G4 mucosal late toxicity (LT) the DPBN-DPP has been adapted in 2 steps (Fig. 1): DPP1 used a median dose prescription that can result in increased doses in a GTV with > 50% voxels of low-uptake. This median dose prescription was abandoned in DPP2. In DPP3 the very-high dose region is limited to an absolute volume of 1.75 cc. In DPP2, 1/2 had G3 mucosal LT that healed spontaneously. In DPP3, 2/11 and 1/11 had G3 and G4 mucosal LT, respectively. In S-IMRT, there was no G3-4 mucosal LT (n = 20). Late G3 dysphagia was seen in 2/18 and 3/20 DPBN and S-IMRT patients at month 3, respectively. After 6 months, 6/15 and 2/13 patients had G≥2 dysphagia (p = 0.22) and PEG-tube was needed in 5/15 and 3/13 patients in DPBN and S-IMRT, respectively. G2 xerostomia was present in 6/13 and 7/13 patients in DPBN and S-IMRT, respectively.
Median follow-up is 12 (3-45) months. Nine patients deceased: 5 DPBN-patients (metastases in 3, complications after neck dissection for regional recurrence in 1 and unknown cause in 1) and 4 S-IMRT patients (2 metastases, 1 aspiration pneumonia and 1 cardial event). Local failure was seen in 1/21 (5%) and 4/24 (17%) in DPBN and S-IMRT, respectively. Regional failure was seen in 2/21 (10%) and 2/24 (8%) in DPBN and S-IMRT, respectively. Metastases were seen in 4/21 (19%) and 5/24 (21%) in DPBN and S-IMRT, respectively. At 1 year actuarial LC was 92% and 76% (p = 0.22), RC 86% and 87% (p = 0.9), DC 76% and 86% (p = 0.9) and OS 68% and 90% (p = 0.6) in DPBN and S-IMRT, respectively.

Conclusion: At short term, we did not observe significant differences yet in LC, RC, DC or OS in the first 45 patients. Due to mucosal LT, the DPBN-DPP has been adapted. Since then, G4 mucosal LT was observed in 1/12 patients. Strict follow-up of LT is being performed.

PO-0639

Graves ophthalmopathy: a network meta-analysis of treatments

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Purpose or Objective: Although several treatments have been evaluated in randomized clinical trials (RCTs) for Graves Ophthalmopathy (GO), many of these treatments have not been directly compared against each other and thus the relative efficacy among them is unclear. We conducted a network meta-analysis (NMA) to compare all regimens simultaneously.

Material and Methods: A systematic review was performed through MEDLINE, Cochrane Central Register of Controlled Trials and meeting abstracts to identify RCTs involving treatments for GO. Treatments included: Radiation 10 Gy in 10 fractions (RT10) or 20 Gy in 10 fraction (RT20), with oral glucocorticoid (RT20POGC), with intravenous glucocorticoid (RT20IVGC), with retrobulbar glucocorticoid injections (RT20RBGC); oral glucocorticoid (POGC); intravenous glucocorticoid (IVGC); surgical decompression (Decomp); somatostatin analogs i.e., Octreotide or Lanreotide (SSanlg); Cyclosporin alone (Cysprn), with oral glucocorticoid (CysprnPOGC); Ciamexone (Ciamex); rituximab (Ritux); peribulbar orbital glucocorticoid injection (BGCI) or no treatment/placebo/sham radiation (NoTx). Success of treatment was determined from overall clinical response, which was provided by most studies. If this was absent, then it was estimated from proportion of patient not needing further treatment, improvement in clinical activity score (CAS), ophthalmopathy index (OI) or proptosis was used in that order. Odds Ratio (OR) was calculated either directly or via standardized mean difference (SMD) in measures. A frequentist NMA was used to compare treatments. Fixed or random effect model was used based on any significant variation among ORs.

Results: 27 studies involving 1216 patients were identified, with 15 distinct treatments including NoTx. Fixed effect model was used, as there was no significant variation among ORs. RT20IVGC was significantly better that BGCI (OR 31.4 [5.1, 195.7]), Ciamex (OR 6.8 [1.4, 33.1]), Cysprn (OR 64.9 [10.6, 398.5]), Decomp (OR 25.8 [1.7, 392.8]), IVGC (OR 4.1 [1.5, 11.6]), NoTx (OR 18.9 [5.69, 62.6]), POGC (OR 11.8 [4.0, 34.6]), RT10 (OR 10.1 [1.9, 52.2]), RT20 (OR 8.4 [2.7, 25.9]), RT20POGC (OR 4.2 [1.3, 12.9]), RT20RBGC (OR 3.5 [1.2, 10.2]) and SSanlg (OR 11.1 [3.0, 40.4]), but did not reach significance compared to CysprnPOGC (OR 3.7 [0.8, 17.8]) or Ritux (OR 5.0 [0.9, 28.9]). IVGC was found to be significantly better than BGCI (OR 7.6), Cysprn (OR 15.7), NoTx (OR 4.6) and POGC (OR 2.9). Also, CysprnPOGC was significantly better than BGCI (OR 8.6), Cysprn (OR 17.7), NoTx (OR 5.1) and POGC (OR 3.2). RT20, RT20POGC and RT20RBGC were all significantly better than Cysprn (ORs 7.7, 15.6 & 18.6 respectively). RT20 and RT20RBGC were better