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Research Article

The Addition of Docetaxel to Platinum Based Concurrent Chemoradiation Improves the Response and Survival in Patients with Locally Advanced Squamous Cell Carcinoma of Head and Neck; Phase II Study

Amal Rayan,[1] Samir Shehata,[1] Mohamed Modather Aboshanif,[2] Doaa Abdel Aleem,[1] Maha Salah El-Naggar[1]

[1]Department of Clinical Oncology, Faculty of Medicine, Assiut University, Assiut, Egypt
[2]Department of ENT, Otorhinolaryngology, Assiut University Hospital, Assiut University, Assiut, Egypt

Abstract

Objectives: We aimed from the current study to explore the added benefits of docetaxel to platinum based CCRT in locally advanced HNSCC regarding response rates, locoregional control (LRC), progression free survival (PFS).

Methods: Cisplatin 80 mg/m^2 was given on days 1, 22, 45 of radiotherapy. Weekly docetaxel 20 mg/m^2 without cisplatin and 15 mg/m^2 with cisplatin. 3DCRT was given using linear accelerator (Varian Clinac DMX) with multiple X-ray energies 6, 10, 12, & 15 MV.

Results: 41 patients were recruited in this study, complete response at primary and regional sites were developed in 75.5% and 85.4% respectively, pathologic complete response was found in 65.9%, the median progression free survival for all patients was 12 months, however for surviving patients up to end of study was not reached and the mean was 22.6 months, locoregional control (LRC) was 97.6%, one-year LRC was 63.4%, regional response was the independent prognostic factor for progression free survival ($p<0.001$, HR=11.84 (3.2-44.39)).

Conclusion: Intensification of treatment for inoperable squamous cell carcinoma of head and neck is a target for different clinical trials, the current protocol is associated with high response rate, improved survival than standard treatment approaches with controllable side effects.

Keywords: Cisplatin, concurrent chemoradiation, docetaxel, progression free survival, squamous cell carcinoma of head and neck

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Globally, squamous cell carcinoma of head and neck (HNSCC) is the seventh most common cancer, accounting for more than 660,000 new cases and 325,000 deaths annually.[1] Lifestyle with consumption of alcohol and smoking, and HPV infection represent the main etiology for HNSCC. Despite decline of smoking in developed countries, still the incidence is rising and is proposed to rise due to changes in the involved site with prevalence of oropharyngeal carcinoma in developed countries and tobacco smoking in developing countries.[2] In Egypt, the incidence is lacking, with only the results of Ibrahim et al.[3] published in 2014 to report the projected incidence of HNSCC in 2020

Address for correspondence: Amal Rayan, MD. Department of Clinical Oncology, Faculty of Medicine, Assiut University, Assiut, Egypt
Phone: 00201022454482 **E-mail:** amalrayan@aun.edu.eg

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reaching about 1.49% of the total cancer burden derived from large hospital registries in the three geographical strata of Egypt.

Based on several randomized trials, cisplatin at a dose of 100 mg/m^2 given concurrently with radical radiotherapy (CCRT) is established as the standard non-surgical treatment for locally advanced HNSCC,[4] however, the ConCERT trial proved that weekly cisplatin at a dose of 40mg/m^2 is non inferior to 3-weekly cisplatin with better toxicity profile and fewer supportive care needs and hospitalization.[5] In the later trial, complete response rate was significantly higher compared to standard 3-weekly regimen which was translated to improved 2-year locoregional control (LRC) but without comparable improvement in median overall survival, median progression free survival, and median time to locoregional progression between both 3-weekly and weekly cisplatin.[5]

Being an aggressive disease with poor locoregional control and survival, so the need to add other agents to the standard protocol to empower the results of CCRT, docetaxel is believed to have two fold antineoplastic activity; inhibition of microtubular depolarization and induction of bcl-2 phosphorylation,[6] although no synergistic interplay between Docetaxel and platinum compounds, several phase I studies proved the feasibility of this combination and the activity against a variety of malignancies.[7, 8]

To our knowledge, there is no study up till now evaluating the effectiveness and toxicity patterns of both platinum and docetaxel based CCRT, so we aimed from the current study to explore the added benefits of docetaxel to platinum based CCRT in locally advanced HNSCC regarding response rates, one-year locoregional control (LRC), one-year and median PFS, and toxicity profiles.

Patients

This study was a single arm phase II prospective study, conducted in the clinical oncology department in collaboration of ENT department, Assiut university, patients were recruited from ENT department during the period from 1st of January 2021 to 30th of June 2022. The inclusion criteria were as follows: (1) biopsy proven squamous cell carcinoma, (2) age ≥18 years up to 80 years, (3) ECOG-PS 0-2, (4) T3-T4, N0, Nx, or N+, M0 of any head and neck site except nasopharynx and salivary glands (5) adequate hemogram (HB>11 gm/dL, neutrophil ≥ 1500 cell/mm^3, platelets ≥100 cell/mm^3), adequate blood chemistry (creatinine ≤1.5, bilirubin <1mg/dL, albumin >3.5, serum potassium 3.5-5.2 mEq/L), accepted audiogram (6) patients received neoadjuvant chemotherapy and those with recurrent lesion at least 5 years later after total laryngectomy were included. We excluded patients with prior chemotherapy and radiotherapy to head and neck, excruciating infection, history of multiple malignancies.

Methods

Before the Protocol

All patients underwent thorough clinical examination, multislice CT head, neck, and chest with contrast (MRI head and neck with contrast or PET/CT in some cases were done), bone scan, abdominal U/S, CBC, blood chemistries and electrolytes, and audiography.

During Treatment

Repeated clinical examination to determine their toxicity grades, required treatments for toxicities, repeated CBC, blood chemistries and electrolytes every 3 weeks and according to symptoms developed during treatment.

Post Treatment Assessment

Clinical examination, multislice CT imaging was done at least 4 weeks after end of protocol, endoscopy, and biopsy 8-10 weeks later, audiogram 4-8 weeks later then every 6 months accordingly.

Treatment Protocol

Chemotherapy Regimen

Cisplatin 80 mg/m^2 (substituted by carboplatin AUC=5 in cases of mild sensorineural hearing loss, or raised renal chemistry) on days 1, 22, 43 of radiotherapy, the 3rd cycle was omitted in those finished their radiotherapy before reaching the third cycle because of renal impairment or development of severe mucositis. Weekly docetaxel 20 mg/m^2 without cisplatin and 15 mg/m^2 with cisplatin.

Before chemotherapy, patients were prepared 30 minutes before with IV dexamethasone 10 mg and IV cimetidine 200 mg, IM diphenhydramine 40 mg, and adequate hydration.

Adverse Effects

Treatment related adverse events were graded according to CTCAE v.4, 4 treatment interruptions were required in some patients because of grade 4 mucositis, skin ulceration, inflammatory thyroid cartilage fistula (in one patient), and raised creatinine then they resumed their treatment protocol with dose reduction 25-50%, replacement of cisplatin with carboplatin, or omission of platinum.

Supportive Measures During Treatment

Weekly clinical examination, mouth wash, antifungal oral gel, anti-inflammatory, IV arginine (dipeptiven infusion), fluids, nutritional support.

Radiotherapy

3DCRT was given using linear accelerator (Varian Clinac DMX) with multiple X-ray energies 6, 10, 12, & 15 MV, target volumes were determined according to tumor site and draining LNs with gross tumor volume (GTV) included primary site and LNs >1cm, radiotherapy dose was 70 Gy over 35 fractions over 7 weeks, clinical tumor volume included GTV+ a margin for microscopic spread to a dose of 60 Gy/30 fractions/ 6 weeks, and high risk nodal CTV for a dose of 54/27 fractions/5.5 weeks.

Response Evaluation

RECIST ver.1.1 was used to determine the response 4-6 weeks following the end of protocol on imaging (target lesions were the primary lesion with a length >1 cm and 4 LNs with shortest axial diameter ≥1.5 cm, other lesions were considered non-target, summation of all longest diameters (SLD) of target lesions were carried out within 4-weeks before CCRT and non-target lesions were evaluated as disappear, stable, or progress) by also summating the longest diameters or SLD of target lesion and evaluation of non-target lesions; complete response (CR) defined as complete disappearance of all target and non-target lesions, partial response (PR); defined as ≥30% decrease SLD, no new lesions, and no progression of non-target lesions, stable disease (SD); defined as no PR and no PD, progressive disease (PD); ≥20% increase SLD, new lesions, or progression of non-target lesions, after imaging, narrow band endoscopy with biopsy was done 6-8 weeks after the end of protocol to determine their pathologic response.

Follow Up

Was calculated from time of diagnosis to last follow, end of study, or death, it ranged from 7-29 months with a median of 18 months, the patients were followed up every 3 months for 2 years then every 6 months thereafter, follow up was mainly done by clinical examination, laboratory evaluation, multislice CT head and neck with contrast, and endoscopy if indicated.

Ethical Considerations

- The study was conducted in full concordance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of Egypt.

Nature of the study was clarified to all participants and made assurances that participants' confidentiality was protected. Participation was entirely voluntary, and they were able to withdraw at any time without providing reason and their data were destroyed if they wish.

- The research was conducted only by scientifically qualified and trained personnel. No risks (physical, psychological, social, legal, or economic) expected from participation in the research.
- The researchers also fully explained the nature of the research at the start of work and informed consents were obtained from all relatives of cases. The study also was approved by ethics committee of faculty of medicine, Assiut university (IRB no 17200581) and registered in ClinicalTrials.gov. (ID: NCT04780750).

Statistical Analysis

All data were analysed using IBM-SPSS 26, descriptive statistics including percentages, mean, standard deviation, and median, inferential statistics including independent sample t-test, one way Anova with homogeneity test for equality of variances (robust test was used instead of Anova in case of inequal variances), and bivariate Pearson correlation were used for univariate analysis of the effect of different variables on progression free survival (PFS), while cox regression analysis with enter methods and stepwise forward methods were run for multivariate analysis. Kaplan-Meier test for calculation and graphing of PFS.

Progression free survival was analysed and graphed by Kaplan-Meier test using log rank test for comparison, it was calculated from time of diagnosis to time of death or progression. All results were considered significant at p-value<5%.

Results

Forty-one patients with squamous cell carcinoma of head and neck were recruited after ethical approval and continued for one year. The follow up period will be intended to continue for 5 years to fully determine the actual progression free survival, and to better describe the late effects of the protocol. Despite being preliminary results but they were interesting. The median age was 60 years, most patients were male (70.7%), patients were selected to have acceptable PS (PS≤2) with PS 0-1 represented in about 75.6%, Table 1.

Table 1. Demographic characteristics of patients

Characteristics	Descriptive
-Age (mean± SD), Range, median	55.2±16 years, 21-80 years, 60 years
-Sex (male/female)	29/12 (2.4:1)
-Performance status	
PS-0	13 (31.7%)
PS-1	18 (43.9%)
PS-2	10 (24.4%)
-Tracheostomy	12 (29.3%)
-Smoking	
Smokers	17 (41.5%)
Ex-smokers	11 (26.8%)
Never-smokers	13 (31.7%)

Data were expressed as number, mean, median, percentage, and range.

Table 2. Clinicopathologic characteristics of patients

Characteristics	Descriptive
Tumor site	
Larynx	14 (34.1%)
Hypopharynx	10 (24.4%)
Tongue	7 (17.1%)
Check	5 (12.2%)
PNS	4 (9.8%)
Oropharynx	1 (2.4%)
T-stage	
T1	3 (7.3%)
T2	10 (24.4%)
T3	20 (48.8%)
T4	8 (19.5%)
N-stage	
N0	11 (26.8%)
N1	7 (17.1%)
N2	18 (43.9%)
N3	5 (12.2%)
Pathologic grade	
G1	2 (4.9%)
G2	23 (56.1%)
G3	13 (31.7%)
G4	3 (7.3%)
Pre CCRT chemotherapy	
No	25 (61%)
Cetuximab, carboplatin, paclitaxel regimen	10 (24.4%)
TPF regimen	6 (14.6%)
Platinum received.	
Cisplatin	19 (46.3%)
Carboplatin	22 (53.7%)
Dose reduction	3 (7.3%)
Pre CCRT audiogram	
Normal	22 (53.7%)
Mild SNHL	13 (31.7%)
Moderate SNHL	6 (14.7%)
Number of platinum cycles	
2	5 (12.2%)
3	36 (87.8%)
Time interval before CCRT	
Mean±SD	4± 2.9 months
Median	2 months
Time before CCRT for those received neoadjuvant chemotherapy	
Mean± SD, median	7.3±1.9, 7 months
Events	
Died	5 (12.2%)
Progressed	5 (12.2%)
Alive (free)	31 (75.6%)

Data were expressed as number, percentage, mean±SD, and median.

Larynx and hypopharynx were the most common sites detected among study patients, >60% of patients had T3-4, also >50% had N2-3 diseases, grade 2 was the predominant one while dedifferentiation was reported in nearly 40% of them, moreover, 39% of patients received neoadjuvant chemotherapy either due to large tumor volume that could not be adequately covered by radiation fields (i.e. hypopharyngeal lesion extending to esophagus), or technical delay in radiotherapy delivery with median time delay before CCRT was 7 months. >50% of patients received carboplatin instead of cisplatin due to mild to moderate SNHL or intolerable side effects, 5 patients died mainly due to other causes and side effects, and 5 patients progressed, Table 2.

Response Patterns Among 41 Patients with Locally Advanced HNSCC

Complete radiologic response on the primary and regional sites were the predominant pattern of response that was accordingly translated into pCR in most cases, locoregional control was 97.6%, one-year LRC was 63.4% that was explained by ending of study with early analysis as most of patients were still under follow up, Table 3.

Survival Analysis

The median PFS for all events was 12 months, and the mean was 13.5± 1.1 with 95% CI= 11.4-15.6 months, one-year PFS was 63.4%, and two-year PFS was 12.2%, Figure 1.

The mean PFS of alive patients at the time of analysis was 22.6±1.5 months 95% CI (19.6-25.5) (excluding dead and progressed patients), the median PFS was not reached, Figure 2.

Table 3. Response rates among study population.

Response type	Descriptive
Radiologic response of primary	
CR	31 (75.6%)
PR	7 (17.1%)
SD	2 (4.9%)
PD	1 (2.4%)
Radiologic response of regional LNs	
CR	35 (85.4%)
PR	3 (7.3%)
SD	1 (2.4%)
PD	0 (0%)
Pathologic response of primary lesions	
pCR	27 (65.9%)
non-pCR	14 (34.1%)

Data were expressed as number and percentage.

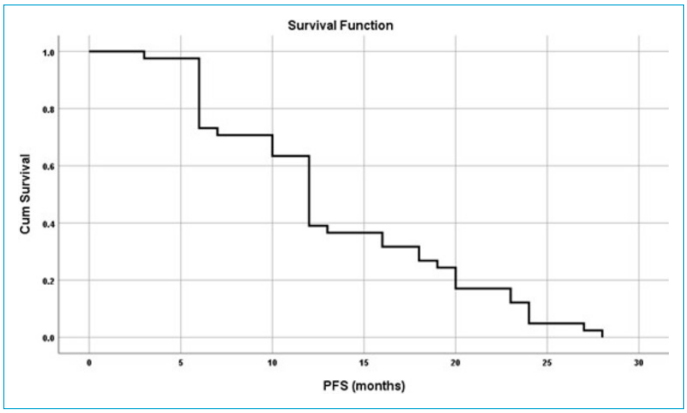

Figure 1. PFS for all patients.

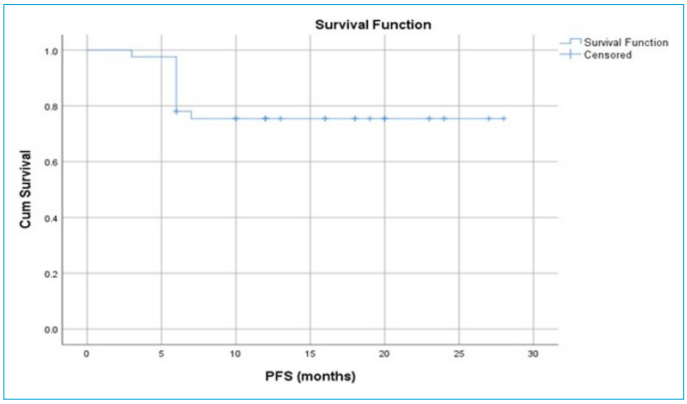

Figure 2. PFS for living patients up to the time of analysis.

Several variables impacted PFS in univariate analysis, where male patients, <N3, non-pharyngeal primary site, no neoadjuvant treatment, cisplatin use, short interval before CCRT, and CR radiologically or pathologically evidenced had higher PFS compared to counterparts. However, in multivariate analysis using enter method, the primary site had no overall significant impact, however laryngeal site had 1.6% lower risk of death or progression, likewise those receiving no neoadjuvant treatment had 1.5% lower risk. Moreover, for each increase in CR rate in the primary site, regional site, and pCR by one, the hazard of death and progression decreased by 13.9%, 11.84%, and 18.5% with significant impact, Table 4.

However, using multivariate analysis with stepwise forward method (Omnibus test showed Chi^2=19.71, p<0.001), all variables were not significant and those with significant effect in enter method (radiologic primary response, radiologic regional response, and pCR) had a high multicollinearity with each other (VIF>4, condition index>30), so they were removed from the model, and only regional radiologic response persisted and considered an independent prognostic factor for PFS. Those with complete radiologic response of LNs was associated with more than 11% lower risk of death or progression compared to those without CR.

The mean PFS for all regional radiologic responses; CR, PR, SD were 24.8±1.3, 5.3±0.3, 6.0 months, log rank= 23.5, p<0.001, Figure 3.

Furthermore, the mean PFS for all radiologic primary responses; CR, PR, SD, & PD were 26.5±1.04, 7.9±1.0, 6±0.0, & 6±0.0 respectively, log rank=22.6, p<0.001, Figure 4.

The mean PFS for pCR compared to those with non-pCR were 27.1±0.91, 12.14±2.2 months respectively, log rank=17.1, p<0.001, Figure 5.

Ototoxicity Among Study Population

Although, 41.5% of patients with normal pre-audiogram continued to have normal post audiogram, but 12.5% (5 patients) developed mild SNHL in post audiogram, while those with moderate SNHL continued to be the same with significant impact, p<0.001, Table 5A.

Other Toxicities

Grade III-IV hematologic, cutaneous, and mucositis were developed in 14.6%, 19.5%, & 70.7%, severe laryngopharyngeal oedema as evaluated by follow up fiberoptic endoscopy was detected in 19.5%, and acute renal impairment was discovered in 9.8%, in addition to fatigue, dysphagia, sinusitis, gastroenteritis, pneumonia, and fungal pneumonitis were reported in few cases, although all these toxicities were resolved and improved by supportive treatment but over a prolonged duration, Figure 6, Table 5B.

Discussion

Despite the great progress in diagnostic procedures and therapeutic management of HNSCC, still the 3-year survival is <50% in hypopharyngeal and oropharyngeal cancers and slightly >50% in laryngeal and oral cancers,[9] although not mentioned in our results but most patients came from rural areas where lack of awareness of cancer manifestations, shortage of medical resources as a result of disorganized health system, and lack of access to specialized health care center are main factors for delayed diagnosis of cancer. Moreover, delayed diagnosis of squamous cell carcinoma is a considerable cause for incurability of this tumor.

The standard treatment for locoregionally advanced HNSCC is concurrent chemoradiation which results in improvement of local control and survival compared with radiotherapy alone,[10-12] the optimum chemotherapy regimen is not yet fully determined, in spite cisplatin-based combinations were considered standard particularly cis-

Table 4. Univariate and multivariate analyses of PFS

Variable	Univariate analysis		Multivariate analysis	
	Mean±SD	p	p	HR (95% CI)
Age	55.2±15.95 r=0.09	0.6	0.8	1.004 (0.96-1.045)
Sex				
Male	15.14±7.2	0.002	0.9	2.4 (0.7-8.4)
Female	9.5±3.7			
PS				
PS=0	14.9±7.04	0.7	0.9	0.75 (0.15-3.74)
PS=1	13±7.05			0.78 (0.2-3.4)
PS=2	12.5±6.7			Reference
Smoking				
Smokers	24.5±1.6	0.07	0.5	Reference
Ex-smokers	24.1±2.5		0.7	1.5 (0.21-10.8)
Never-smokers	12.2±1.7		0.07	4.3 (0.87-21.5)
Tracheostomy				
Yes	13.9±7.4	0.8	0.9	0.96 (0.27-3.36)
No	13.3±6.8			Reference
T-staging				
T1	10±0.0	0.5	0.99	HR=0
T2	15.7±7.0		0.4	0.5 (0.08-2.8)
T3	13.8±7.6		0.5	0.6 (0.14-2.5)
T4	11.3±5.7		0.7	Reference
N-staging				
N0	10±4.5	0.01	0.96	0.96 (0.2-4.95)
N1	17.6±7.5		0.3	0.3 (0.03-3.1)
N2	15.6±6.9		0.11	0.2 (0.03-1.6)
N3	7.8±3.2		0.3	Reference
Grade				
G1	12±8.5	0.4	0.8	1.54 (0.096-24.6)
G2	15.04±7.4		0.6	0.51 (0.06-4.6)
G3	11.2±5.8		0.97	0.98 (0.1-8.8)
G4	12.7±5.8		0.7	Reference
Site of primary				
Oral cavity	13.4±4.6	0.023	0.95	0.0 (0.0-2.93)
PNS	12.5±4.7		0.3	0.35 (0.04-2.8)
Larynx	17.7±8.2		0.05	0.2 (0.04-0.96)
Pharynx	8.6±4.4		0.2	Reference
Neoadjuvant treatment				
No	15.7±7.6	0.005	0.04	0.23 (0.06-0.93)
Cetuximab-based regimen	11.2±3.3		0.1	0.27 (0.05-1.5)
TPF regimen	8±3.1		0.09	Reference
Dose reduction				
Yes	10.3±7.5	0.4	0.1	0.3 (0.06-1.4)
No	13.7±6.9			Reference
Platinum				
Cisplatin	17.1±6.7	0.001	0.09	3.82 (0.81-10.04)
Carboplatin	10.4±5.4			Reference
Number of platinum cycles				
2 cycles	17±9.9	0.2	0.8	1.3 (0.2-10.2)
3 cycles	13±6.4			Reference
Interval before CCRT	r=-0.437	0.004	0.2	1.12 (0.93-1.35)
Radiologic response of primary				B=-2.9
CR	15.5±6.6	<0.001	0.001	13.9 (2.88-66.63)
Non-CR	7.3±2.5			Reference
Radiologic response of LNs		<0.001	B=2.4	B=-2.5
CR	14.6±6.6		<0.001	11.84 (3.2-44.39)
Non-CR	5.4±1.3			Reference
Pathologic response				B=-2.9
pCR	15.4±6.5	0.011	0.006	18.5 (2.3-147.5)
non-pCR	9.8±6.1			Reference

Data analyzed using Cox regression for multivariate analysis, and independent sample t-test, one-way Anova, and bivariate Pearson correlation for univariate analysis.

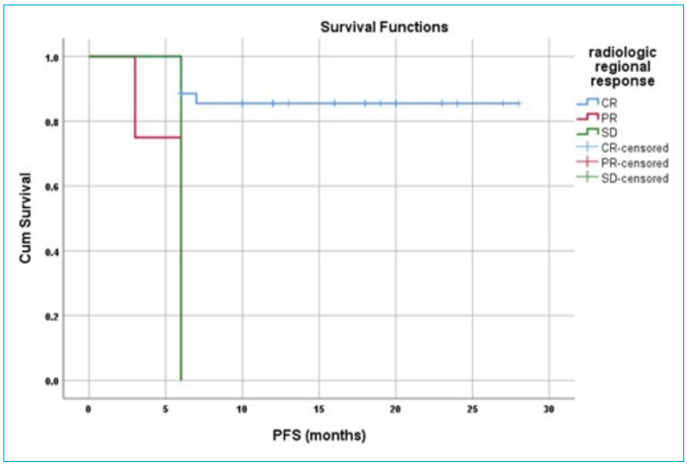

Figure 3. Differences in PFS according to regional LN response.

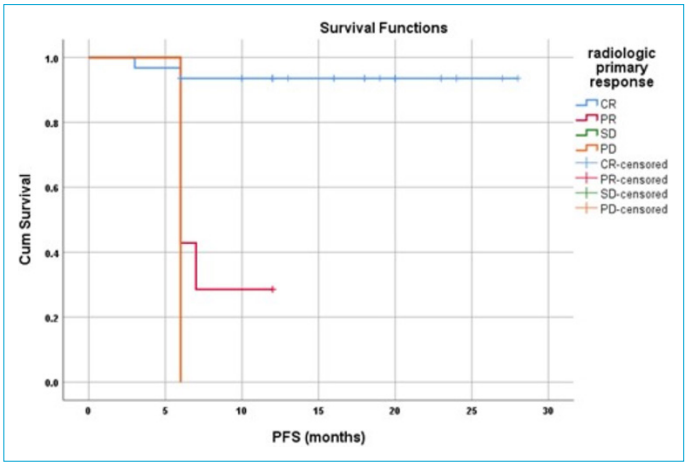

Figure 4. Differences in PFS according to primary response.

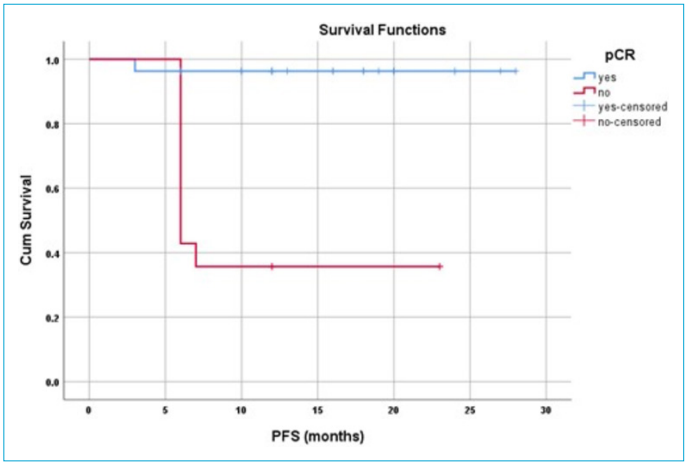

Figure 5. Differences in PFS according to pathologic response.

platin and fluorouracil, also weekly cisplatin was equally effective to 3-weekly cisplatin.[13] Docetaxel showed an overall response rate of 21% and 42% in patients with recurrent and metastatic HNSCC,[14] several phase I-II studies of docetaxel-RT showed promising results with lo-

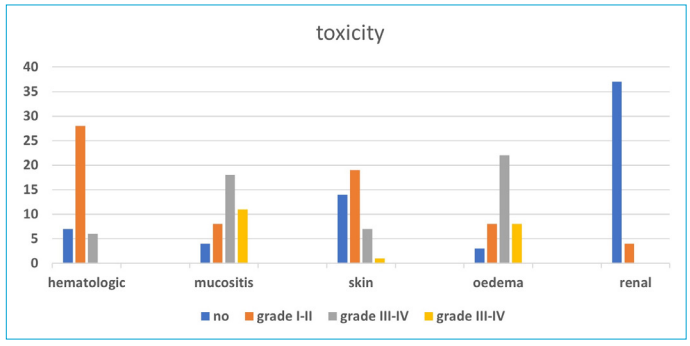

Figure 6. Toxicity patterns.

coregional control of 64% and 3-year OS of 47%,[15-17] but with grade III skin toxicities of 23%, grade III dysphagia of 38% and 41% of patients required nasogastric tubing and gastrostomy feeding, furthermore, grade III toxicities increased to 49% with combined cisplatin and 5FU regimen with RT, these toxicities were considered higher when compared to ours, where grade III hematologic, grade III-IV mucositis, grade III-IV skin reactions, and severe laryngopharyngeal oedema were detected in 14.6%, 70.7%, 19.5%, and 19.5%.

The role of docetaxel alone as a radiosensitizer was further evaluated in phase III randomized study in comparison with radiotherapy in patients non-eligible to cisplatin, the 2-year disease free survival, median survival, and 2-year overall survival were significantly prolonged with docetaxel-RT, but with higher incidence of grade ≥3 mucositis, odynophagia, and dysphagia,[18] in addition the value of chemotherapy added to RT is considered controversial in elderly patients more than 80 years, the higher incidence of frailty, comorbidities, and higher vulnerability to chemotherapy related-side effects in older patients result in decreased efficacy of chemoradiation in this group of patients as evidenced by the MACH-NC study,[4, 19] so we excluded those older than 80 years from participating in the current study.

The addition of chemotherapy to definitive RT in locally advanced HNSCC improved 5-year survival by 6.5% compared with RT,[20] also concurrent chemoradiation increased the median survival by one year compared to sequential chemoradiation in another meta-analysis,[21] the standard treatment regimen consisted of 3-weekly cisplatin with a dose of 100 mg/m^2 on days 1, 22, 43 of 7-weeks course of radiotherapy,[22, 23] because of adverse events concerns of this regimen, dose modifications were required in up to 40% of patients.[24] Suboptimal doses of cisplatin impaired significantly patients' outcomes, a finding led to development of alternative treatment schedules of cisplatin including weekly low dose cisplatin of 30-40 mg/m^2 [25, 26] have been frequently used.

Table 5A. Ototoxicity among study population.

Pre-audiogram	Post-audiogram			p
	Normal	Mild SNHL	Moderate SNHL	
Normal (n=22)	17 (41.5%)	5 (12.2%)	0 (0%)	<0.001
Mild SNHL (n=14)	5 (12.5%)	6 (14.6%)	3 (7.3%)	
Moderate SNHL (n=5)	0 (0%)	0 (0%)	5 (12.5%)	

Data analyzed by Chi² test; percentages were calculated from total number of patients.

Table 5B. toxicities among study population

Hematologic		Mucositis		Skin		Oedema		Renal	
no	7	G I	4	G I	14	no	3	No	37
G I-II	28	G II	8	G II	19	mild	8	Yes	4
G III-IV	6	G III	18	G III	7	moderate	22		
		G IV	11	G IV	1	severe	8		

Data expressed as numbers.

Recently, a randomized phase III non-inferiority study suggested that 3-weekly cisplatin regimen was associated with superior 2-year locoregional control of 73.1% compared with 58.5% for once-weekly cisplatin with an absolute difference of 14.6% (95% CI, 5.7% to 23.5%); p=.014; hazard ratio (HR=1.76, 95% CI= 1.11 to 2.79), with comparable median PFS and median OS,[25] in a similar multicenter retrospective study, improvement in the median PFS and OS of 3-weekly cisplatin over once weekly cisplatin could not be confirmed in the whole cohort,[27] however, in the previous study, 35.1% of patients received cisplatin in the adjuvant setting, of them 32.7% received once-weekly cisplatin, moreover, 36% of the total cohort received 2 cycles instead of 3 cycles that might explained the results on PFS, and OS.

Cisplatin dose of >200mg/m^2 was considered mandatory for survival benefit in CCRT of HNSCC,[28] to recoup for reduced dose of cisplatin (80mg/m^2), with cumulative dose of 240 mg/m^2 delivered to 34.1%, and 160mg/m^2 to 12.2% of patients, docetaxel was added in the current regimen, for cisplatin-ineligible patients, carboplatin was received in combination with docetaxel, a previous study compared cisplatin-based to carboplatin-based chemoradiation and the treatment results revealed comparability regarding locoregional control, metastasis free survival, overall survival, and toxicities, even in subgroup analysis,[29] moreover several previous studies indicated conflicting results in comparing cisplatin to carboplatin in CCRT, four studies detected superiority of cisplatin, one study suggested superiority of carboplatin while six indicated similar efficacy between both.[30-41]

Regarding to chemotherapy compliance, neoadjuvant platinum-based chemotherapy combinations were received to 39% of our patients that contributed partly to SNHL which detected in 46.3% in pre-CCRT, so that 12.2% of patients received 2 cycles of cisplatin instead of 3 cycles, and >50% of patients received carboplatin, acute renal impairment was developed in 9.8%, grade III-IV mucositis and severe laryngeal oedema which developed in >70% and 19.5% respectively could be explained by neoadjuvant chemotherapy received. The current protocol was considered tolerable with manageable toxicities, although it could be considered an aggressive regimen for those patients who were considered debilitated and frail by the nature of this tumor.

Conclusion

Intensification of treatment for inoperable squamous cell carcinoma of head and neck is a target for different clinical trials, the current protocol is associated with high response rate, improved survival than standard treatment approaches with controllable side effects.

Disclosures

Ethics Committee Approval: This study was approved by Assiut University, Faculty of Medicine Ethics Committee (IRB No: 17200581, Date: 31/5/2021).

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Conflict of Interest: None declared.

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