



Integration of Consolidation Chemotherapy After Concurrent Chemoradiation in the Treatment of Locally Advanced Uterine Cervical Cancer

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Received: 16 August 2022 / Revised: 16 August 2022 / Accepted: 18 October 2022

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Abstract

Background Despite the current standard of concurrent chemoradiation (CCRT), around 30–40% are still dying from locally advanced cervical cancer. Increasing the radiation dose further was not a feasible option, but addition of chemotherapy further was tried due to the different toxicity profiles of it. So, the use of consolidation chemotherapy beyond CCRT has been studied.

Aim To evaluate the efficacy, toxicity, tumour response and loco-regional control following consolidation chemotherapy after concurrent chemoradiation in locally advanced carcinoma cervix (LACC).

Methods The patients were randomized into two arms: the conventional arm (control arm, $n = 30$) patients received conventional treatment with weekly injection cisplatin (35 mg/m^2) concurrently with pelvic external beam radiation ($50 \text{ Gy}/25 \text{ fraction}$, $2 \text{ Gy}/\text{fraction}$, $5 \text{ fraction weekly}$) followed by intracavitary radiotherapy of 21 Gy in 3 fractions of 7 Gy each by HDR brachytherapy. In the interventional arm (study arm, $n = 30$), patients received the standard treatment followed by 3 cycles of consolidation chemotherapy (paclitaxel + carboplatin) every three weekly.

Results Haematological toxicity (grade 3 anaemia and grade 1 leucopenia, grade 1 and 2 thrombocytopenia) was higher in the study group. Renal, hepatic and gastrointestinal toxicity was more in the study arm. Peripheral neuropathy was mostly seen in the study arm. Median follow-up was 9 months. Treatment response was better, and the rate of recurrence was less in the study arm.

Conclusion Addition of few cycles of consolidation chemotherapy after standard treatment is beneficial in patients with LACC with manageable toxicity and good compliance.

Keywords Cervical cancer · LACC · Concurrent chemoradiation · Consolidation chemotherapy

Introduction

Cervical cancer is a global health problem in women [1]. Globally cervical cancer continues to be the most common cancer among females, being the 4th most common after breast, colorectal and lung cancer [2]. Worldwide cancer incidence and mortality are growing at an alarming rate [3, 4]. As per GLOBOCON 2018 data, cervical cancer is

the second most common cancer in low- and middle-income countries (LMICs) [3]. In India, its incidence varies from 13 to 24/100,000 women per year [5]. Although the incidence of carcinoma cervix has declined in the urban population, in the rural areas, it continues to be highly prevalent [6]. It is one of the leading causes of cancer mortality, accounting for 17% of all cancer deaths among women aged between 30 and 69 years [7]. It is estimated that cervical cancer will occur in approximately 1 in 53 Indian women during their lifetime compared with 1 in 100 women in more developed regions in the world [8–10]. Incorporation of concomitant chemotherapy into radiotherapy schedules is in fact the most recent major breakthrough in treatment of locally advanced cervical cancer

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(LACC) at the end of 1990's when results of 5 randomized studies comparing concomitant chemoradiotherapy with radiotherapy alone in this setting were published. Despite an overall survival gain accomplished with concomitant chemoradiotherapy, unfortunately, a significant proportion of patients 30–40% are still dying from LACC [11–15]. Lymph node metastasis is one of the most significant prognostic factors of cervical cancer. According to the literature, the incidence of lymph node involvement increases with the FIGO stage, and it occurs in 12–22% of stage IB, 10–27% of stage IIA and 34–43% of stage IIB [16]. Locoregional recurrences are the main cause of failure. Whilst, local control is becoming a reality in therapy of patients with LACC, distant control of the disease has become a major issue [17]. The incidence of distant relapse ranges between 7 and 11% in lower stages of disease (IA2-IIA) and between 16 and 22% in higher stages of the disease (IIB- IVA) [12, 14, 15, 18]. It is generally suspected that the ability of radiotherapy to cure locally advanced cervical disease is limited by the size of the tumour [19]. In the last 7 years, the use of systemic chemotherapy beyond concomitant phase of CT and RT has been studied as treatment intensification strategy [20], by addition of consolidation chemotherapy after definitive CCRT [21]. A 2008 meta-analysis of RCT's strongly suggested that addition of consolidation chemotherapy to CCRT is beneficial [22]. According to these studies, it then seems to be justified to hypothesize such an approach, i.e. application of consolidation chemotherapy is better [1]. Chemotherapy consisting of paclitaxel plus carboplatin (TC) has been shown to be effective in patients with advanced or recurrent cervical cancer [21].

In developing countries including India, studies incorporating the use of adjuvant chemotherapy (ACT) in LACC after CCRT is done as an attempt to improve survival [23]. In our study, the idea behind giving consolidation chemotherapy was to consolidate local control of the disease achieved by concomitant chemoradiotherapy and to eradicate potential distant micro-metastasis.

So, with an aim to achieve better local and distant control and to improve the prognosis of locally advanced cervical cancer patients, we have designed this study to see the efficacy, toxicity, tumour response and locoregional control of consolidation chemotherapy following concurrent chemoradiation by subjecting our patients to 3 cycles of consolidation chemotherapy after 3–5 weeks of completion of CCRT, with paclitaxel (175 mg/m²) and carboplatin (AUC: 5.0, Calvert's formula) every 21 days.

Materials and Methods

Study Design

This is a comparative, prospective, randomized, interventional study. It was carried out at the oncology centre in a tertiary care hospital in a developing country over a duration of one and half years. Institutional ethics committee approval was obtained at the beginning of the study.

Sample Size

The sample size was calculated using statistical software Epi info 2000 (CDC Atlanta, USA). Data are presented as Mean \pm SD, median and ranges or numbers and percentages of patients. Patients were randomly selected and divided into two groups of minimum of 30 patients in each group.

Inclusion Criteria

The inclusion criteria were age more than 18 years and less than 70 years, histopathologically proven malignancy of cervix, locally advanced disease (FIGO stage IIB-IVA), Karnofsky performance status at least 40, Eastern cooperative oncology group (ECOG) performance status 0-1-2, normal cardiovascular function, normal blood counts, normal serum levels of blood urea, serum creatinine and bilirubin and who gave consent for the study.

Treatment Protocol

There were two arms in the study, study arm (arm 1) and control arm (arm 2) having 30 patients in each. The patients were randomized by simple random sampling technique. In arm 1, patients received concurrent chemoradiotherapy with weekly cisplatin 35 mg/m² followed by 3 cycles of consolidation chemotherapy after 3–5 weeks of completion of CCRT, with paclitaxel and carboplatin (Paclitaxel in a dosage of 175 mg/m² and Carboplatin (AUC: 5.0, Calvert's formula) every 21 days. In arm 2, patients were planned for only concurrent chemoradiotherapy. In both the arms, the external beam radiotherapy (EBRT) treatment schedule was 5000 cGy in 25 fractions, 200 cGy/fraction, 5 fraction/week which was delivered using Co60 teletherapy machine followed by ICRT of 2100 cGy in 3 fractions at point A, 700 cGy/fraction at point A, 1fraction/week by high dose rate (HDR) brachytherapy. The gap between EBRT and ICRT was kept as 1 week. The patients were monitored for therapy-induced acute toxicities weekly during treatment

and up to 3 months posttreatment. Thereafter, they were reviewed every 12 weekly for delayed toxicities.

Results

Patient-Related Characteristics

Patients enrolled were more than 18 years and less than 70 years. Mean age of the patients was 47.3 years (range 35–61 years) and 50.7 years (range 35–69 years) in the study and control arm, respectively. Majority of patients in this study belonged to 41–50 year group in both arms. *P* value was 0.255, which was non-significant. More patients belong to the rural background in both the groups, 93% (study arm) and 97% (control group). *P* value was 0.554, which was non-significant. Among the study group, 29 patients (96.7%) had ECOG score 1, and only 1 patient (3.3%) had ECOG score 2. In the control group, 28 patients (93.3%) had ECOG score 1 and 2 patients (6.7%) had ECOG score 2. Majority had ECOG- 1 (95%) score. The *P* value was 0.554 which was non-significant. This study had 17 (57%) patients in study group and 26 (87%) of patients in the control group belonging to upper lower (class IV) socioeconomic status and 13 (43%) patients in study group and 4 (13%) of control group belonging to lower middle (class III) socio-economic status. In total, most of the patients (72%) were from upper lower (class IV) socioeconomic status. The *P* value was 0.01 which was significant. Tobacco addiction was seen in 72% of the patients enrolled and absent in 28%. The *P* value was found to be 0.39 which was statistically non-significant (Table 1).

Disease-Related Characteristics

Only histopathologically proven cases were included in the study. Most of patients 55 out of 60 patients (92%) had squamous cell carcinoma (SCC) as histopathology. In the study group, 27 (90%) patients had squamous cell carcinoma, and in the control group, SCC was seen in 28 (93%) patients. Adenocarcinoma was seen in 3(10%) patients in the study group and in 2 (6.7%) patients in the control group. *P* value was 0.64, which was non-significant.

Among the study group, only 1 patient (3.3%) had well differentiated, 27 (90%) had moderately differentiated and 2 (6.7%) had poorly differentiated tumour. In the control group, 3 patients (10%) had well differentiated, 27 (90%) had moderately differentiated, and none of the patients had poorly differentiated tumour. The *P* value was 0.223 which was non-significant. In the study group, 23 (76.7%) patients had pelvic nodes alone and 7 (23.3%) had pelvic + para-aortic nodes at the time of enrolment in the

study. In the control group, 22 (73.3%) had pelvic nodes alone and 8 (26.7%) had para-aortic nodes. The *P* value was 0.766, which was non-significant. In the study group, 3 (10%) patients belong to stage IIB, 7 (23.7%) patients belong to stage IIIB, 13 (43%) patients belonged to stage IIIC1, and 7 (23%) patients belonged to stage IIIC2. In control group, 1 (3.3%) patient belong to stage IIB, 11 (37%) patients belonged to stage IIIB, 10 (33%) patients belonged to stage IIIC1, and 8 (27%) patients belong to stage IIIC2. The *P* value was 0.504 which was non-significant. Majority of the patients belonged to stage IIIC1 (38%).

In both the arms, majority had tumour size < 6 cm, 18 (60%) patients in study arm and 21(70%) in the control arm. The *P* value was 0.417 which was non-significant (Table 1).

Treatment-Related Characteristics

Majority of the patients in both arms received 5 cycles of concurrent chemotherapy along with radiation, 57% in study arm and 63% in control arm 0.17% of study arm and 27% of control arm received 4 cycles of concurrent chemotherapy. *P* value was non-significant. In the study group, 28 patients (93.3%) received 3 cycles and 2 patients (6.7%) received 2 cycles of consolidation chemotherapy. The *P* value was statistically significant (*P* value: < 0.001).

Majority of the patients completed treatment within 18–20 weeks, 17 (56.7%) patients in the study arm and 12(40%) patients in the control arm. Only 1 patient (3.3%) in each group completed treatment between 27 and 29 weeks. *P* value was 0.029 which was statistically significant.

The tumour response was assessed after each cycle of chemotherapy and at 3rd, 6th, 9th,12th and 18th month. Median follow-up was of 9 months. The treatment response was assessed according to the Response Evaluation Criteria in Solid Tumours (RECIST 1.1 criteria) (Table 2). At 3 months follow-up, complete response was seen in 70% of study group and 46.6% of control group. 16.6% of the study group and 30% of the control group showed partial response. 3.3% of study population and 10% of control population showed progressive disease. Stable disease was not found in any group. *P* value was 0.03 which was statistically significant. There was one death in the study arm due to disease progression.

At 6 months follow-up, 73.3% of study population and in 63.3% of control population showed complete response (CR). Stable disease was not found in any. Progressive disease was seen in 10% of study and 13.3% of control population. It was statistically insignificant with *P* value being 0.20.

Table 1 Patient-related and disease-related characteristics

Patient characteristics	Study		Control		Total		X^2	Df	P
	N	%	N	%	N	%			
<i>Age (in years)</i>									
< 40	7	23.3	6	20	13	21.7	4.059	3	0.255
41–50	15	50	12	40	27	45			
51–60	7	23.3	6	20	13	21.7			
> 60	1	3.3	6	20	7	11.7			
<i>Place of residence</i>									
Rural	28	93	29	97	57	95	0.351	1	0.554
Urban	2	6.7	1	3.3	3	5			
<i>ECOG</i>									
0	0	0	0	0	0	0	0.351	1	.554
1	29	96.7	28	93.3	57	95			
2	1	3.3	2	6.7	3	5			
<i>Socio-economic status</i>									
Lower middle	13	43	4	13	17	28	6.648	1	0.01
Upper lower	17	57	26	87	43	72			
<i>Tobacco addiction</i>									
Absent	7	23	10	33	17	28	0.739	1	0.39
Present	23	77	20	67	43	72			
<i>HPR</i>									
AD	3	10	2	6.7	5	8.3	0.218	1	0.64
SCC	27	90	28	93	55	92			
<i>Grade</i>									
1	1	3.3	3	10	4	6.7	3	2	0.223
2	27	90	27	90	54	90			
3	2	6.7	0	0	2	3.3			
<i>Lymph node</i>									
Pelvic	23	76.7	22	73.3	45	75.0	0.089	2	0.766
Pelvic + Paln	7	23.3	8	26.7	15	25.0			
<i>Stage</i>									
2B	3	10	1	3.3	4	6.7	2.347	3	0.504
3B	7	23.7	11	37	18	30.3			
3C1	13	43	10	33	23	38			
3C2	7	23	8	27	15	25			
2B	3	10	1	3.3	4	6.7			
2B	3	10	1	3.3	4	6.7			
<i>Tumour size</i>									
< 6 CM	18	60	21	70	39	65	.659	1	0.417
≥ 6 CM	12	40	9	30	21	35			

At 9 months follow-up, 50% in the study group and 53.3% in the control group had complete response. Progressive disease was seen in 13.3% of the study group and 16.6% of the control group.

At 12 months follow-up, complete response was seen in 33.3% of the study population and 23.3% of the control population. Progressive disease was seen in 16.6% of the study population and 20% of the control population. 13 patients in the study arm and 17 patients in the control arm

were lost to follow-up which is speculated to be due to COVID-19 pandemic in the country.

At 18 months follow-up, of the 6 patients who reported 5 patients in the study arm had shown complete response and of the 7 patients who reported in the control arm, 3 patients had shown complete response. Majority of the patients were loss to follow-up which is speculated to be due to the pandemic situation and lockdown measures in the country.

Table 2 Treatment response during follow-up

Treatment Response at 3rd month follow-up	Study		Control		P value
	N	%	N	%	
CR	21	70	14	46.6	0.03
PD	1	3.3	3	10	
PR	5	16.6	9	30	
Default	1	3.3	0	0	
LFU	1	3.3	4	13.3	
Death	1	3.3	0	0	
<hr/>					
Treatment response at 6th-month follow-up	Study		Control		P value
	N	%	N	%	
CR	22	73.3	19	63.3	0.20
PD	3	10	4	13.3	
PR	0	0	3	10	
default	1	3.3	0	0	
LFU	3	10	4	13.3	
death	1	3.3	0	0	
<hr/>					
Treatment response at 9th-month follow-up	Study		Control		
	N	%	N	%	
CR	15	50	16	53.3	
PD	4	13.3	5	16.6	
PR	0	0	3	10	
Default	1	3.3	0	0	
LFU	9	30	6	20	
Death	1	3.3	0	0	
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Treatment response at 12th-month follow-up	Study		Control		
	N	%	N	%	
CR	10	33.3	7	23.3	
PD	5	16.6	6	20	
PR	0	0	0	0	
Default	1	3.3	0	0	
LFU	13	43.3	17	56.6	
Death	1	3.3	0	0	
<hr/>					
Treatment Response At 18th-month follow-up	Study		Control		
	N	%	N	%	
CR	5	16.6	3	10	
PD	1	3.3	4	13.3	
PR	0	0	0	0	
Default	1	3.3	0	0	
LFU	22	73.3	23	76.6	
Death	1	3.3	0	0	

Toxicity-Related Characteristics

Toxicities were divided into acute and late. Acute toxicities were graded using Common Terminology Criteria for Adverse Events (CTCAE v5.0), and late toxicities were graded using the RTOG late radiation morbidity scoring scheme.

Grading was done between 0 and 5, grade 0 was taken as nil toxicity, and grade 5 was taken as death.

Acute Toxicity

Renal Toxicity

In the study group, grade 1 creatinine levels were seen in 15 patients (53.5%) and grade 2 creatinine levels were seen in 4 patients (14.2%) after 3rd cycle of consolidation chemotherapy (Fig. 1). During consolidation chemotherapy phase after 3rd cycle, 15 patients (53.5%) had abnormal blood urea levels.

Hepatotoxicity

Hepatotoxicity was assessed by measuring total serum bilirubin levels. During the consolidation phase, grade 1 hyperbilirubinemia was seen in 5 patients after 3rd cycle of

consolidation chemotherapy and in none in the control arm (Fig. 2).

Radiation Dermatitis

At the end of EBRT, all patients had grade 2 dermatitis in both arms. At the end of ICRT, all the patients in both arms had grade 1 dermatitis.

Gastrointestinal Toxicity

In patients who received consolidation chemotherapy grade 3 nausea was seen in majority. By the end of 3rd cycle, 16 patients (57.1%) had grade 3 nausea.

In the consolidation phase, most of the patients had grade 2 vomiting after each cycle of chemotherapy. Grade 3 vomiting was seen in 7 patients after 3rd cycle chemotherapy.

In the consolidation phase, majority of the patients had grade 1 diarrhoea after each cycle, while grade 2 diarrhoea was seen in 13(46.6%) patients after 3rd cycle chemotherapy. Grade 3 diarrhoea was seen in only 1 patient after 3rd consolidation chemotherapy. Grade 1 diarrhoea was seen in 16 patients(53.3%) and grade 2 diarrhoea in 14 patients (46.6%) in control arm after EBRT (Fig. 3).

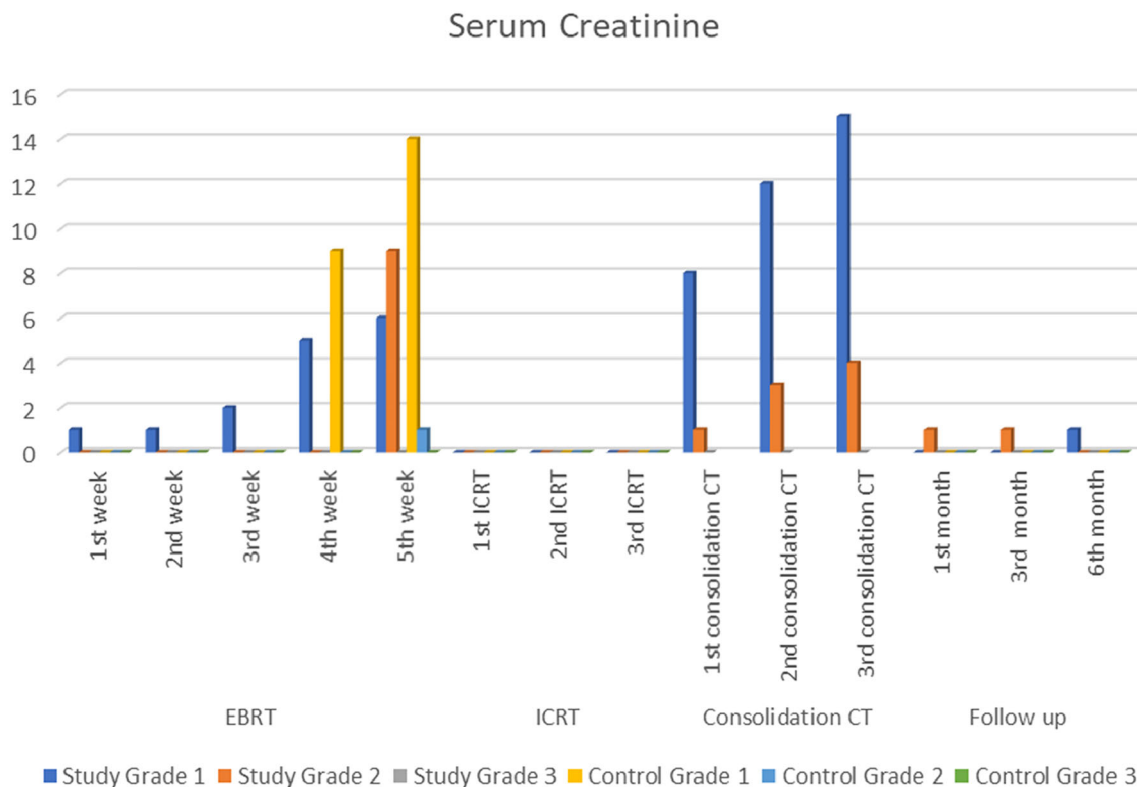


Fig. 1 Shows comparison of serum creatinine in the study group and control group

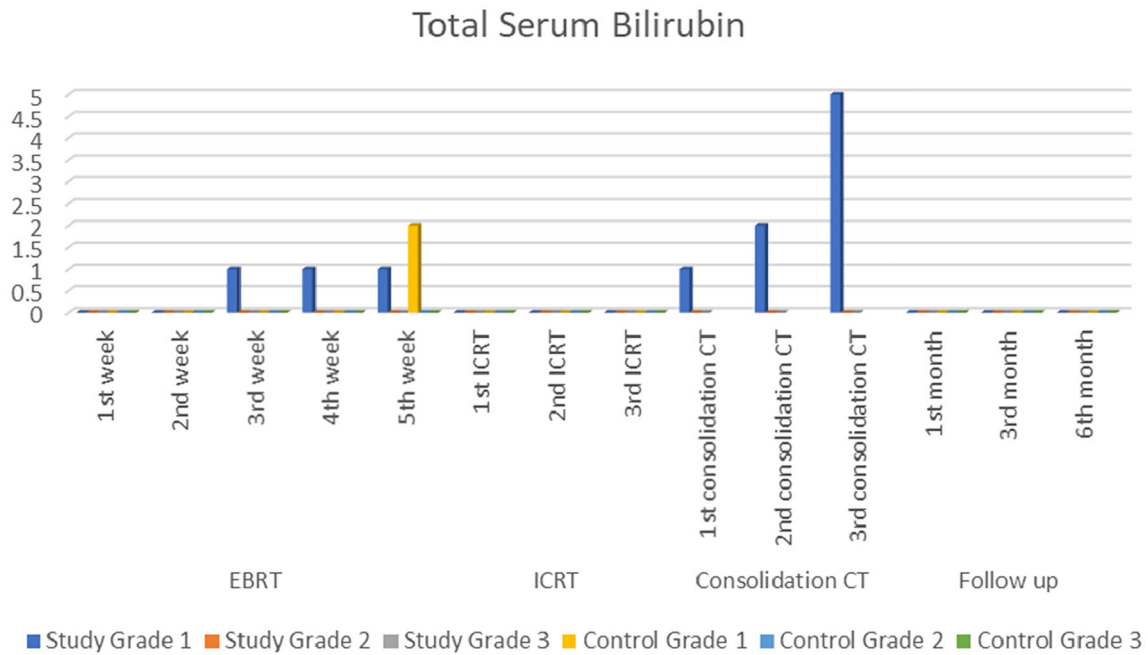


Fig. 2 Shows comparison of total serum bilirubin between study group and control group

Genitourinary Toxicity

Acute Cystitis

At the end of EBRT, grade 2 cystitis was seen in all patients in both arms. During ICRT phase, grade 1 cystitis was seen in a mean percentage of 54.4% in study arm and in 51.1% in control arm. Grade 2 cystitis was seen in a mean percentage of 45.5% of study patients and 48.8% of control patients. During consolidation chemotherapy, cystitis was not seen in any (Fig. 4).

Rectal and Vaginal Mucositis

At the end of EBRT, grade 2 and grade 3 mucositis was mostly seen. Grade 2 mucositis was seen in 93.3% of the study population and 86.6% of the control population. Grade 3 mucositis was seen in 2 patients (6.6%) in the study arm and in 4 patients (13.3%) in the control arm.

During ICRT, grade 1 and grade 2 mucositis was most common. At the end of ICRT, Grade 1 mucositis was seen in 15 patients (50%) in the study arm and 24 patients (80%) in the control arm. Grade 2 mucositis was seen in 15 patients (50%) in the study arm and 6 patients (20%) in the control arm.

Haematological Toxicity

Anaemia

At the end of EBRT, grade 3 anaemia was seen in 13 patients (43.3%) in study arm and 19 patients (63.3%) in the control arm.

In the consolidation phase, grade 2 anaemia was seen in majority of patients after each cycle chemotherapy. Grade 3 anaemia was seen in 11 patients (39.2%) after 3rd cycle chemotherapy (Fig. 5).

Leucopenia

At the end of EBRT, grade 1 leucopenia was seen in 13 patients (43.3%) in the study group and 8 patients (26.6%) in the control group. Grade 2 leucopenia was seen in 3 patients (10%) each in both arms. *P* value was 0.378, which was statistically non-significant.

At the end of ICRT, grade 2 leucopenia was seen in 1 patient (3.3%) only in the study arm. Grade 1 leucopenia was seen in 2 patients (6.6%) only in the study arm.

In the consolidation phase, grade 1 leucopenia was seen in 19(67.8%) patients after last cycle of chemotherapy. Grade 2 leucopenia was seen in 7 patients, and Grade 3 leucopenia was seen in 2 patients (6.6%) after last cycle chemotherapy (Fig. 6).

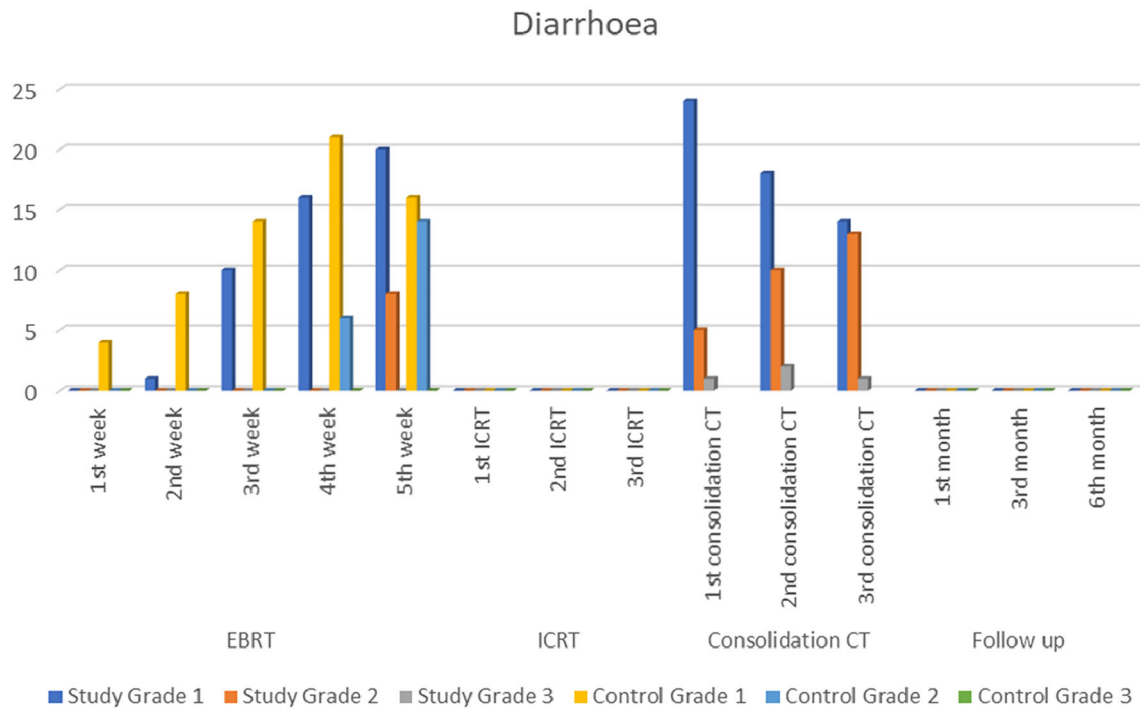


Fig. 3 Shows comparison of diarrhoea between study group and control group

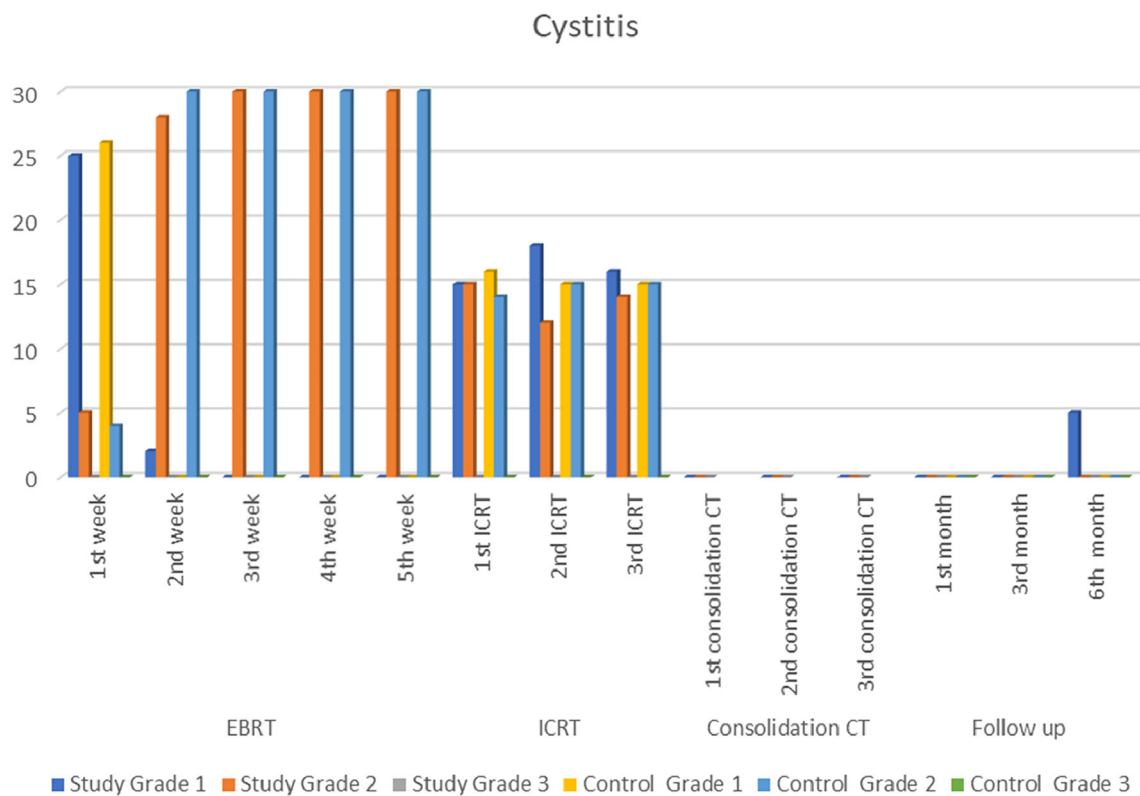


Fig. 4 Shows comparison of cystitis of between study group and control group

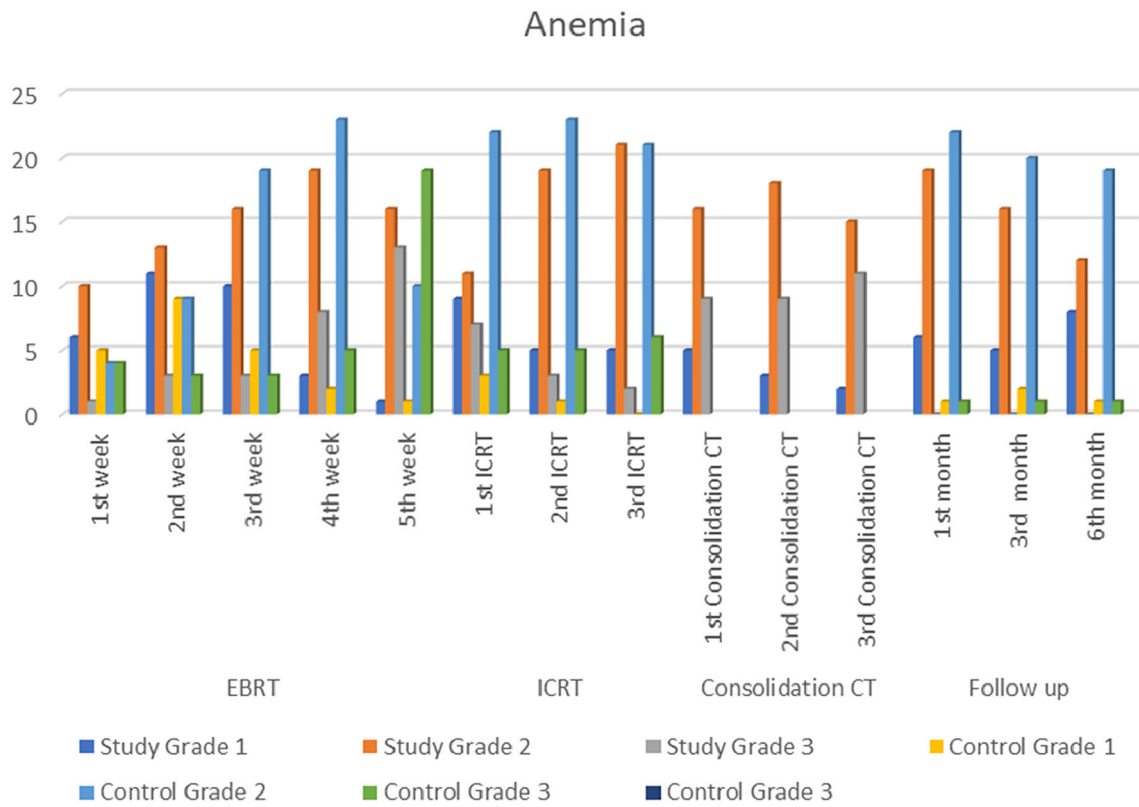


Fig. 5 Shows comparison of anaemia between study and control group

Thrombocytopenia

At the end of EBRT, 5 patients (16.6%) in the study arm and 6 patients (20%) in the control arm had grade 1 thrombocytopenia. Grade 2 thrombocytopenia was seen in 3 patients (10%) only in the control arm. *P* value was 0.179, which was statistically non-significant.

During the consolidation phase, grade 1 thrombocytopenia was seen in 5 patients (17.8%) after 3rd cycle. Grade 2 thrombocytopenia was seen in 3 patients (10.7%) after 3rd cycle (Fig. 7).

Peripheral Neuropathy

At the end of EBRT treatment, Grade 2 peripheral neuropathy was seen in 23.3% of patients in the study and control arm and was seen in 70–100% of the patients receiving consolidation chemotherapy.

Grade 3 neuropathy was seen only during consolidation chemotherapy, in 8 patients (28.5%) in the study arm after 3rd cycle chemotherapy (Fig. 8).

Late Toxicity

Anaemia

Grade 2 anaemia was seen in 12 patients (44.4%) of the study group and in 19 patients (73.1%) in the control group. Grade 3 anaemia was seen only in 1 patient (3.8%) in the control arm and none in the study arm. *P* value was 0.227 which was statistically non-significant.

In the follow-up period, none of the patients had leucopenia and thrombocytopenia.

Peripheral Neuropathy

It was not seen as a late toxicity in any patient in either arm.

Miscellaneous

Grade 1 proctitis was seen in 8 patients (29.6%) in the study arm and in 2 patients (7.6%) in the control arm. *P* value was 0.041 which was statistically significant.

Grade 1 cystitis was seen in 5 /27(18.5%) of study population when compared to the control group. *P* value was 0.020, which was statistically significant.

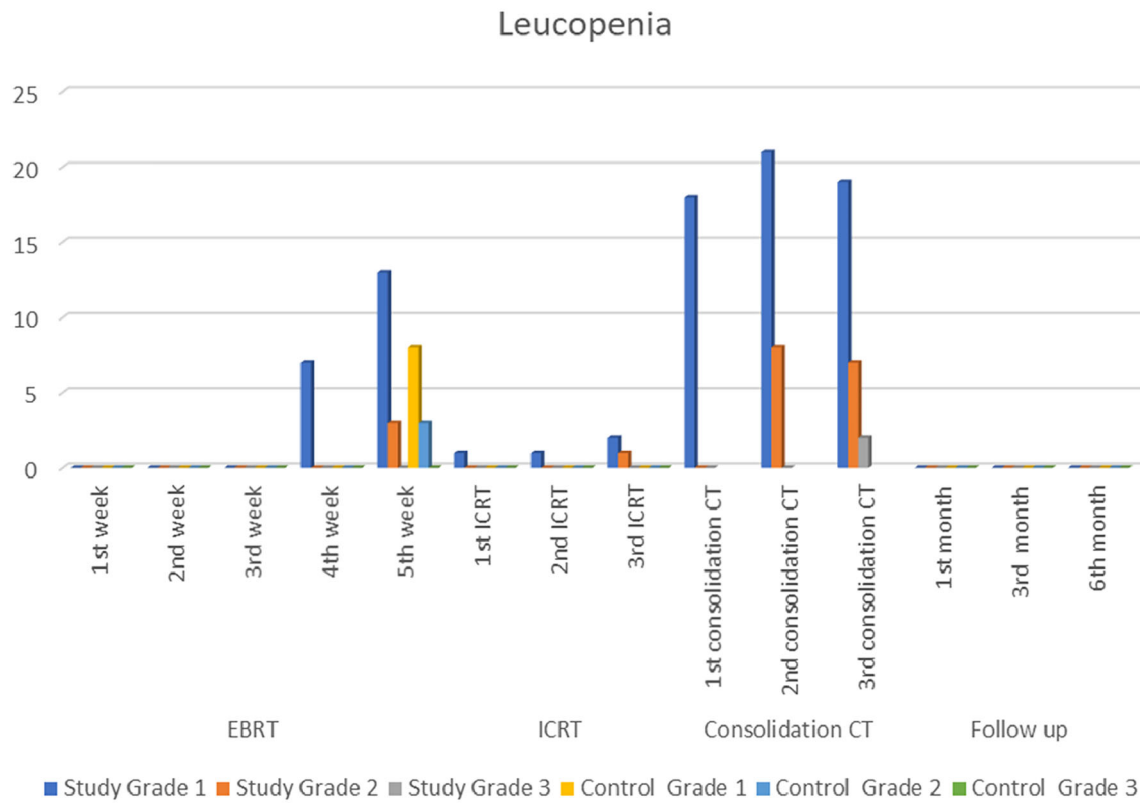


Fig. 6 Shows comparison of leucopenia between study group and control group

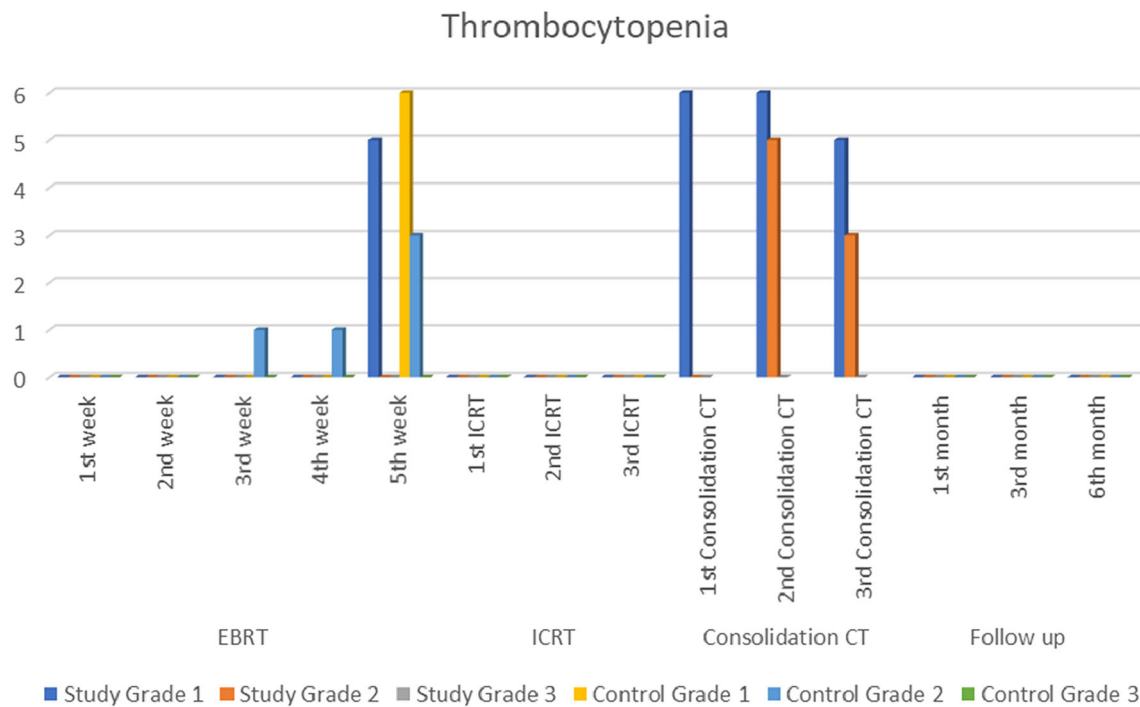


Fig. 7 Shows comparison of thrombocytopenia between study group and control group

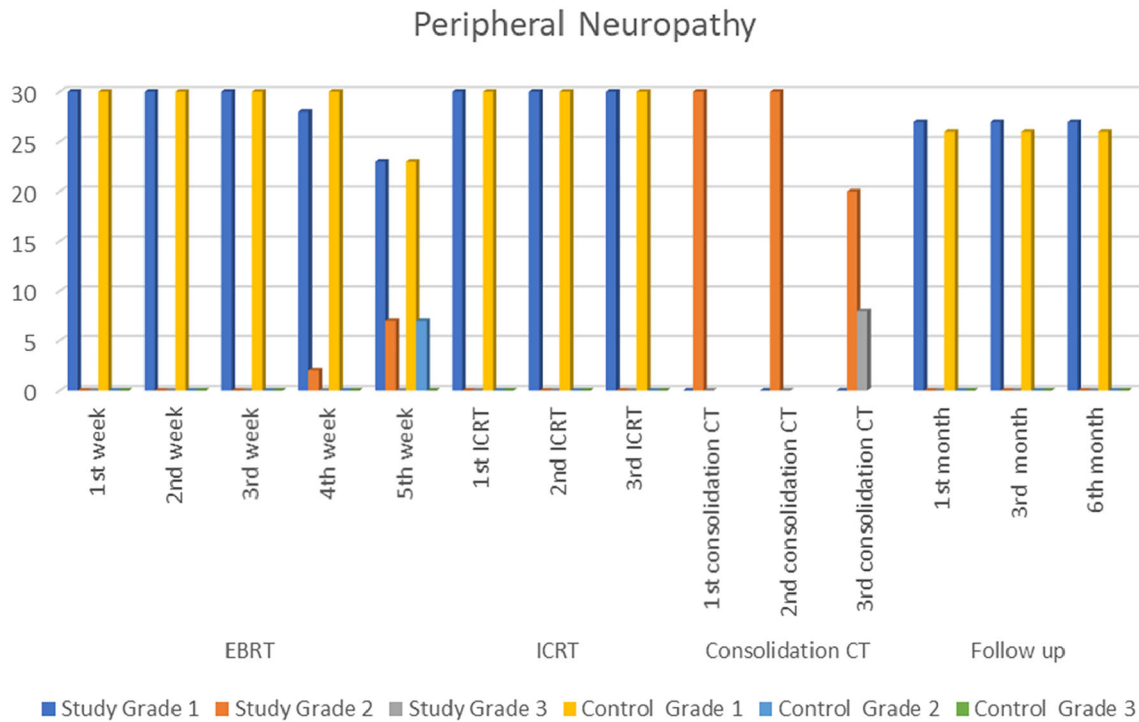


Fig. 8 Shows comparison of peripheral neuropathy between study group and control group

Discussion

Cervical cancer is an ominous disease when it presents in locally advanced stages. To date, the standard of care for locally advanced disease is pelvic radiotherapy with concurrent cisplatin-based chemotherapy followed by brachytherapy [24].

Despite an increase in survival, we have reached a plateau in the last two decades where the 5-year survival remains static at 50–60%. Several attempts have been made to modify existing CCRT protocols in an attempt to improve survival or decrease toxicity [25]. In general consolidation chemotherapy was seen to be well tolerated. The rate of haematological toxicity was found to be higher in the study group. Grade 3 anaemia was more common in the study group, seen in 13 patients (43.3%) at the end of EBRT and in 11 patients (39.2%) at the end of consolidation chemotherapy. Grade 1 and 2 leucopenia and thrombocytopenia were seen in the study and control group at the end of EBRT and during ICRT, but maximum number of patients presenting with grade 1 leucopenia was seen during consolidation chemotherapy, in 67.8% at the end of 3rd cycle of consolidation chemotherapy. Grade 3 leucopenia was only seen in patients receiving consolidation chemotherapy. (7.1%). These findings were similar to those seen in studies done by Jelavic et al., Mabuchi et al., Kim et al., Choi et al. and Abe et al. [1, 21, 26–28]. Grade 1 and 2 thrombocytopenia was seen in patients during EBRT,

but majority of the patients showed it during consolidation chemotherapy. These findings were similar to the studies of Jelavic et al. [1].

The incidence of nausea and vomiting was more frequent in the study arm during consolidation chemotherapy, with mean percentage of 47.5% having grade 2 and 43.4% having grade 3 nausea and a mean percentage of 65.6% having grade 2 and 17.2% having grade 3 vomiting. Grade 4 nausea and vomiting were not found in both the groups. These findings were similar to the studies conducted by Jelavic et al., Vrdoljak et al., Choi et al. and Zhang et al. [1, 29–31].

Diarrhoea was a major toxicity seen in the study group during consolidation chemotherapy. Grade 1 diarrhoea was seen in a mean percentage of 63.3%. It was managed by probiotics and proper oral hydration. Grade 2 diarrhoea was seen in a mean percentage of 32.1% of the study population. Grade 3 was seen in a mean percentage of 4.46%. This was similar to those seen in study by Peters et al. and Kim et al. [15, 28].

Rectal and vaginal mucositis/inflammation were seen in both study and control population, grade 2 and 3 being most common in the 4th and 5th week of EBRT.

Grade 1 proctitis was seen in 29.6% of study and 7.6% of control population. Grade 2 proctitis was not seen in either groups. This was similar to the results seen in Vrdoljak et al. and Zhang et al. [30, 31].

Acute cystitis was more commonly seen in both the groups during EBRT and ICRT. Grade 2 cystitis was seen in all patients in both the groups from 3rd week of EBRT and seen in a mean percentage of 45.5% of the study population during ICRT and 48.8% of the control population during ICRT. The results were similar to the study done by Zhao et al. [32] Only 18.5% of the study population had grade 1 chronic cystitis at the end of 6th-month follow-up.

Radiation dermatitis, grade 2, was seen in majority of patients after 3rd week of EBRT and was seen in a mean percentage of 10% of the study population and 13.3% of the control population during ICRT. This was similar to the result seen in the study done by Zhao et al. [32].

Peripheral neuropathy was more common in the study population as it was most common side effect of paclitaxel. Grade 2 and grade 3 peripheral neuropathy was mostly seen during consolidation chemotherapy. Grade 2 was seen in a mean percentage of 90.4% of study population, whereas grade 3 neuropathy was seen in a mean percentage of 9.5%. This finding was similar to that seen in study by Pandya et al. [23].

Median treatment duration was 18–20 weeks with minimal duration of 18 weeks and maximum duration of 29 weeks. Treatment duration was significantly associated with treatment outcome, *P* value being 0.029.

At 6 months follow-up, CR was higher in the study arm. This finding was similar to the study done by Singh et al. [33].

At 12 months follow-up, higher CR was seen in the study group. This was similar to the findings seen in studies by Wong et al. and Vrdoljak et al. [30, 34].

The response to treatment did not depend on a specific age group. Patients with ECOG 1 and those belonging to urban population had good response due to better living conditions, awareness and good compliance to treatment seen in them.

Patients receiving 4–5 cycles of concurrent chemotherapy had better response than patients receiving less than 4 cycles and patients with treatment duration of 18–20 weeks had better response than those with treatment duration more than 22 weeks.

Patients with well to moderately differentiated tumours had a better response to treatment than poorly differentiated had significance though grade did not have any significance in the chemoradiation era as shown in many studies.

A 9-month median follow-up was quite encouraging, but a longer follow up is warranted for further establishing the role of this treatment protocol in overall, disease-free and recurrence-free survival of the patient and it needs further evaluation.

Conclusion

Advanced cervical cancer is a very threatening disease. Although the survival with the standard treatment has been found to good, failure rates are found to be high in patients with high-risk factors after CCRT.

Therefore, additional researches focussed on the role of consolidation chemotherapy after standard concurrent chemoradiation and ICRT was necessary. With this aim, in this prospective study, we have evaluated in our tertiary care setup, the impact on the efficacy, toxicity, tumour response and locoregional control by the addition of 3 cycles of consolidation chemotherapy with paclitaxel and carboplatin in patients with locally advanced carcinoma cervix, and the results were quite encouraging.

Limitation of the Study

A longer follow-up data are required to comment on disease-free survival and overall survival.

Acknowledgements Nil

Declarations

Conflicts of interest Nil.

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