Adjuvant chemotherapy in patients with muscle invasive bladder cancer after radical cystectomy: now or never?

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Disclosure slide

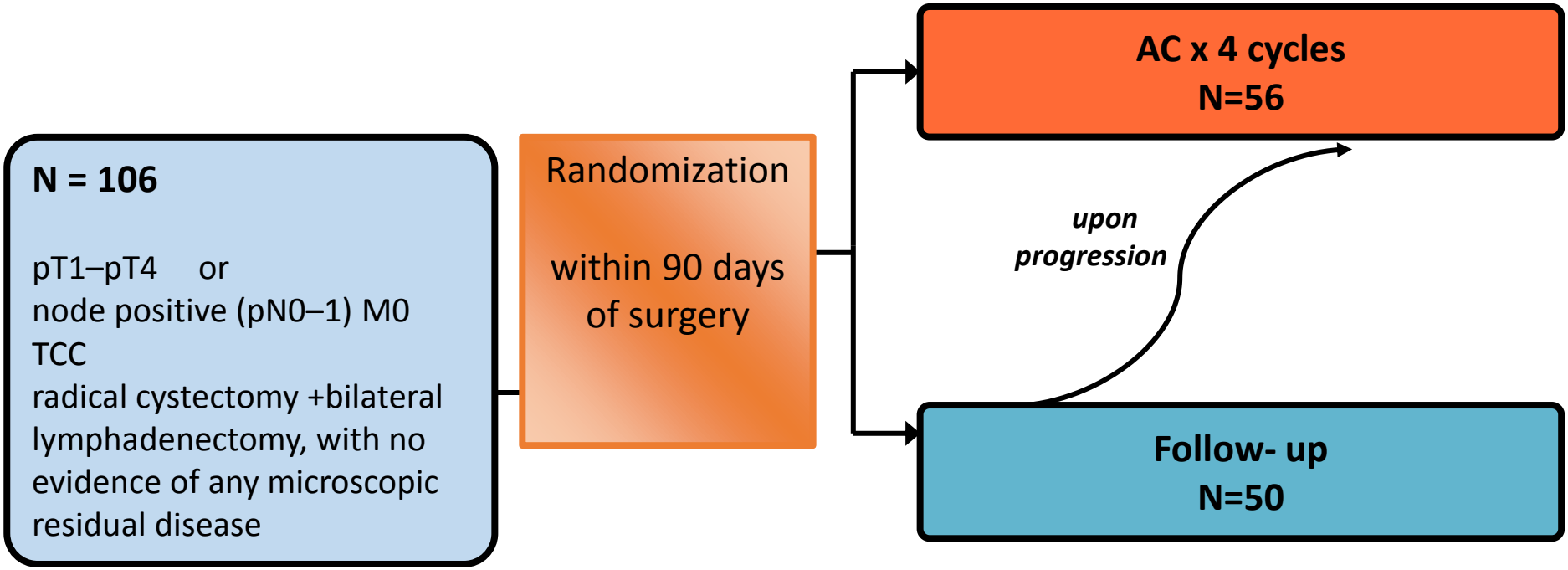
- Nothing to declare

Aim/Background

- Addressing the need for immediate adjuvant chemotherapy, in the form of gemcitabine – cisplatin, after cystectomy and if this translates to a survival benefit was the main aim of this study.
- DFS and toxicity were secondary aims.

Methods

Study Design



AC= gemcitabine 1000 mg/m^2 days 1, 8 ,15
+
cisplatin 70 mg/m^2 day 1 / 28 days.

Results

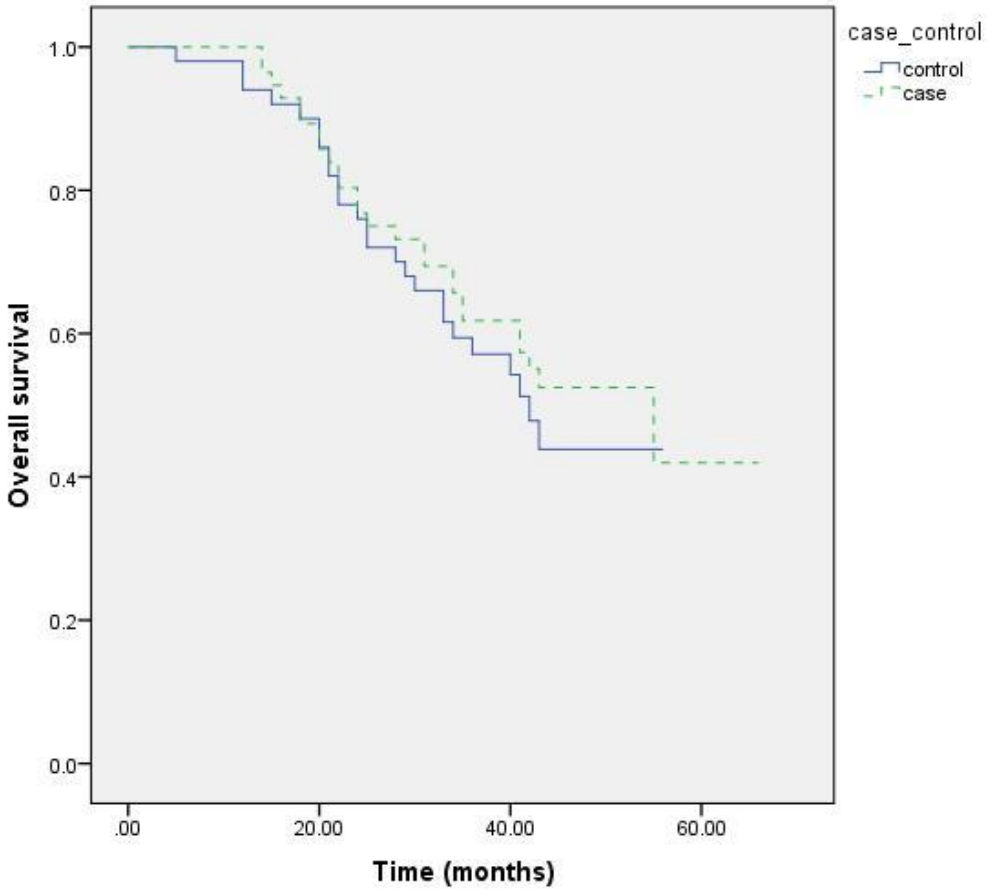
Patients' baseline characteristics

	Control (arm A; n= 50) (%)	Adjuvant chemotherapy (arm B; n= 56) (%)	P value
Age (mean;sd years)	58±10.7	57sd±10.8	7.2
Gender (Male/Female)	44(88)/ 6(12)	49 (87.5)/ 7(12.5)	0.94
Smoking	38 (76)	40(71.4)	0.59
History of bilharziasis	29 (58)	32 (57.1)	0.93
Performance status (ECOG)			0.79
0	22 (44)	25 (44.6)	
1	26 (52)	30 (53.6)	
2	2 (4)	1 (1.8)	
Tumour stage			0.34
T1	5 (10)	1 (1.8)	
T2	9 (18)	8 (14.3)	
T3	30 (60)	39 (69.6)	
T4	6 (12)	8 (14.3)	
Lymph node status			0.57
N0	26 (52)	26 (46.4)	
N1	24 (48)	30 (53.6)	
Tumor grade			0.61
1	4 (8)	2 (3.6)	
2	20 (40)	24 (42.9)	
3	26 (52)	30 (53.6)	
Squamous differentiation	24 (48)	25 (44.6)	0.73
Lymphovascular invasion	14 (28)	17 (30.4)	0.79

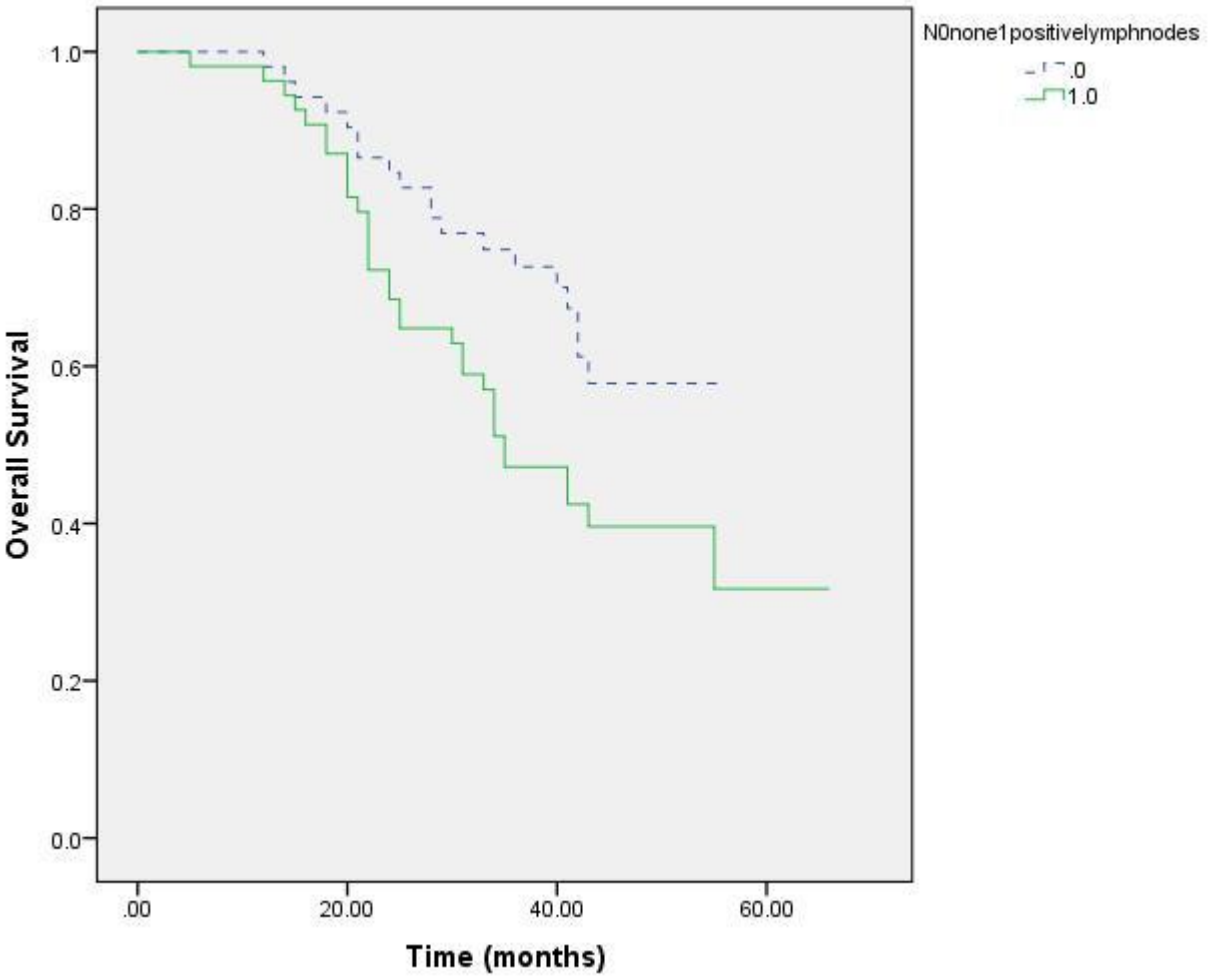
Results

- At a median follow-up of 38 months (interquartile range 25-44.25), 51 patients had died (arm A, N = 25; arm B, N = 26).
- The 5-year OS of the whole series was 47 % (standard error 9%), with no significant difference between the two arms (p = 0.565).
- The median overall survival was 44 months, 42 in the control group and was 55 months in the AC arm (hazard ratio 1.2; 95% CI 0.69-2.1, p=0.51).

Kaplan- Meier Survival curves for the Adjuvant Chemotherapy (B) and Control group (A) for overall survival.
(hazard ratio 1.2; 95% CI 0.69-2.1) p=0.51

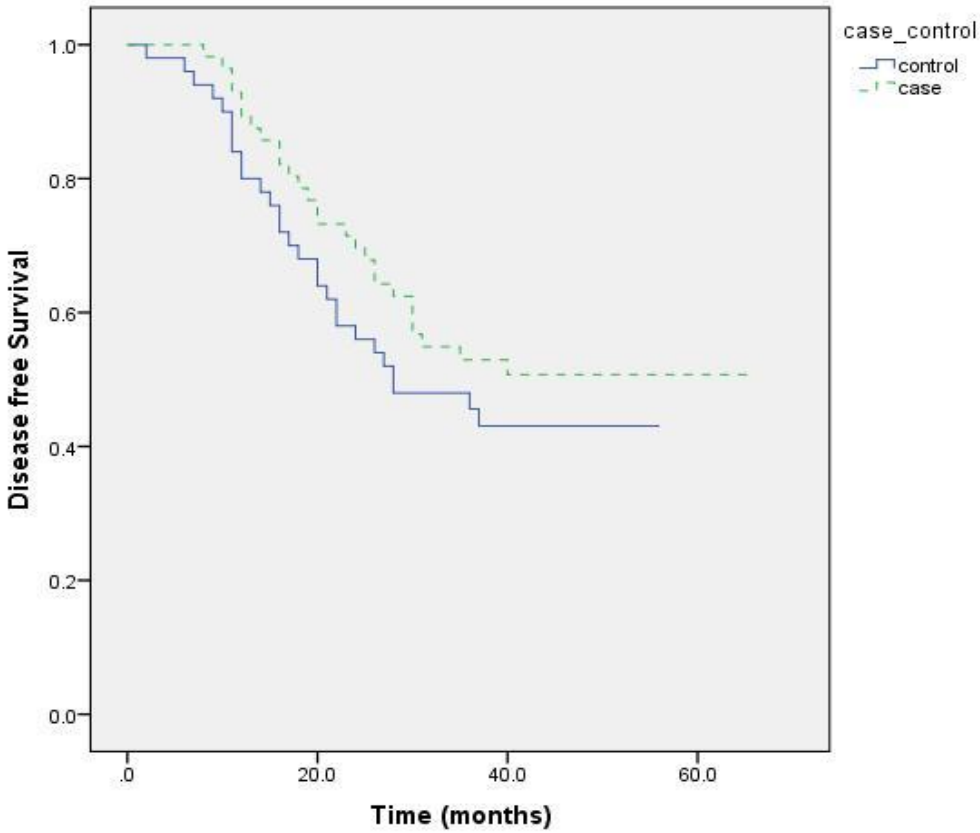


- The only significant predictor of overall survival. independently via cox regress tumour stage, LVI (pN1 versu 0.002). The 5 y (standard erro pN1 it was 30% months.



The 5 year DFS for the entire study group was 46% (SE 5%) with no significant difference between the two arms (p = 0.255): 43%±7 in the control group and 50% ±7 in the AC arm with a hazard ratio of 1.35; CI 0.79-2.3, p=0.262.

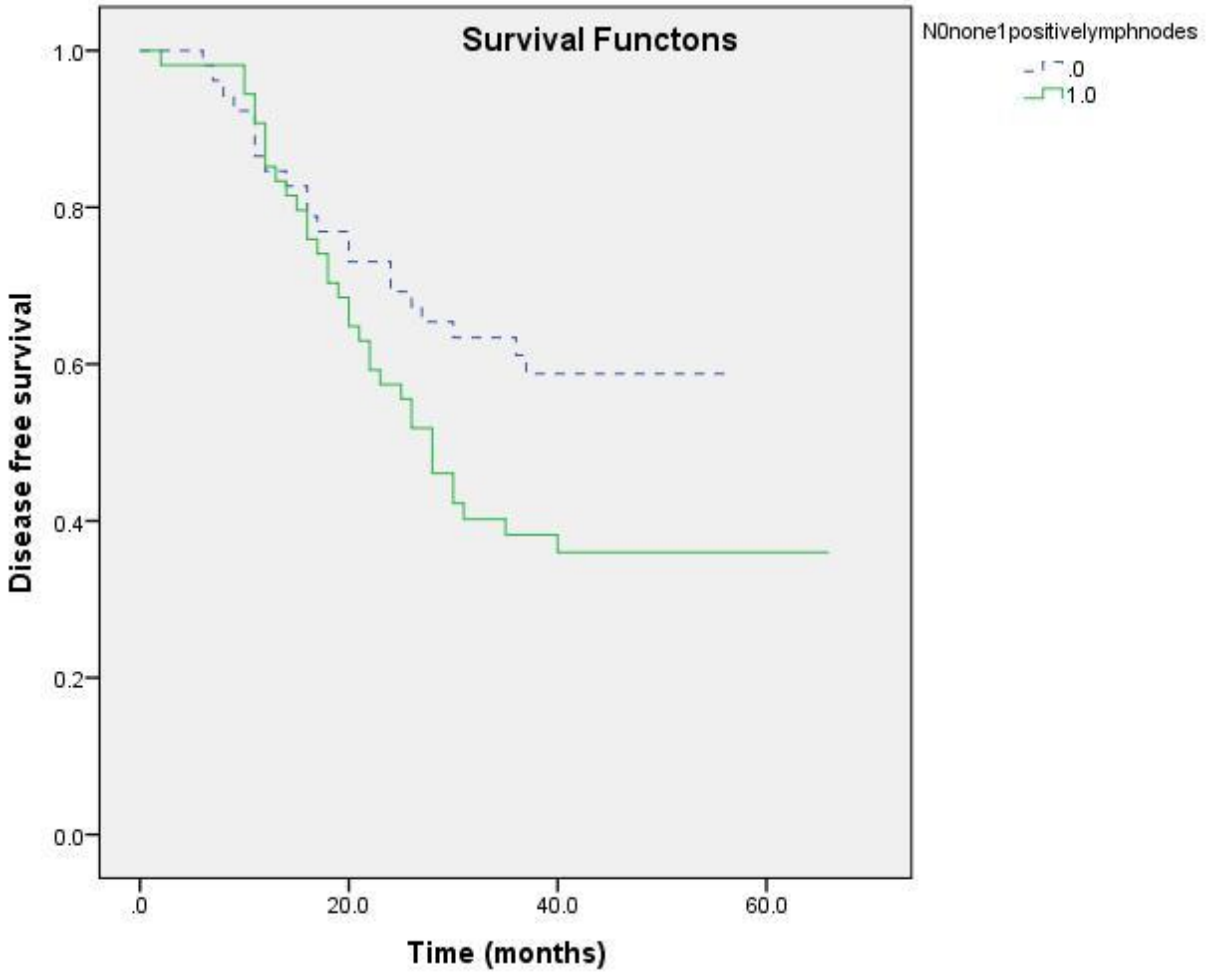
Median DFS was 37.1 and control groups resp



Kaplan- Meier Survival curves for the Adjuvant Chemotherapy (B) and Control group (A) for disease-free survival.

Hazard ratio of 1.35; CI 0.79-2.3, p=0.262

- The only significant predictor of disease free survival, independently of treatment arm, was nodal status via cox regression a
tumour stag
differentiati
HR 2.7; 95%



- All patients received the planned four cycles; although there were delays in some cases (27 patients; 48.2%) that required prompt management to resume treatment.
- No drug toxicity-related death was observed.
- Relapsed patients in either group received appropriate treatments.

Toxicity

	AC arm (n=56)	
Adverse event	Any grade	Grade 3/4
Vomiting	24 (42.8%)	0
Fever	27(48.2%)	3(5.4%)
Hypertransaminasemia	2(3.6%)	0
Serum creatinine	32(57.1%)	3(5.4%)
Hearing	1(1.8%)	0
Anemia	29(51.8%)	0
Neutropenia	40 (71.4%)	10(17.9%)
Leukopenia	35(62.5%)	3(5.4%)
Thrombocytopenia	37(66.1%)	0

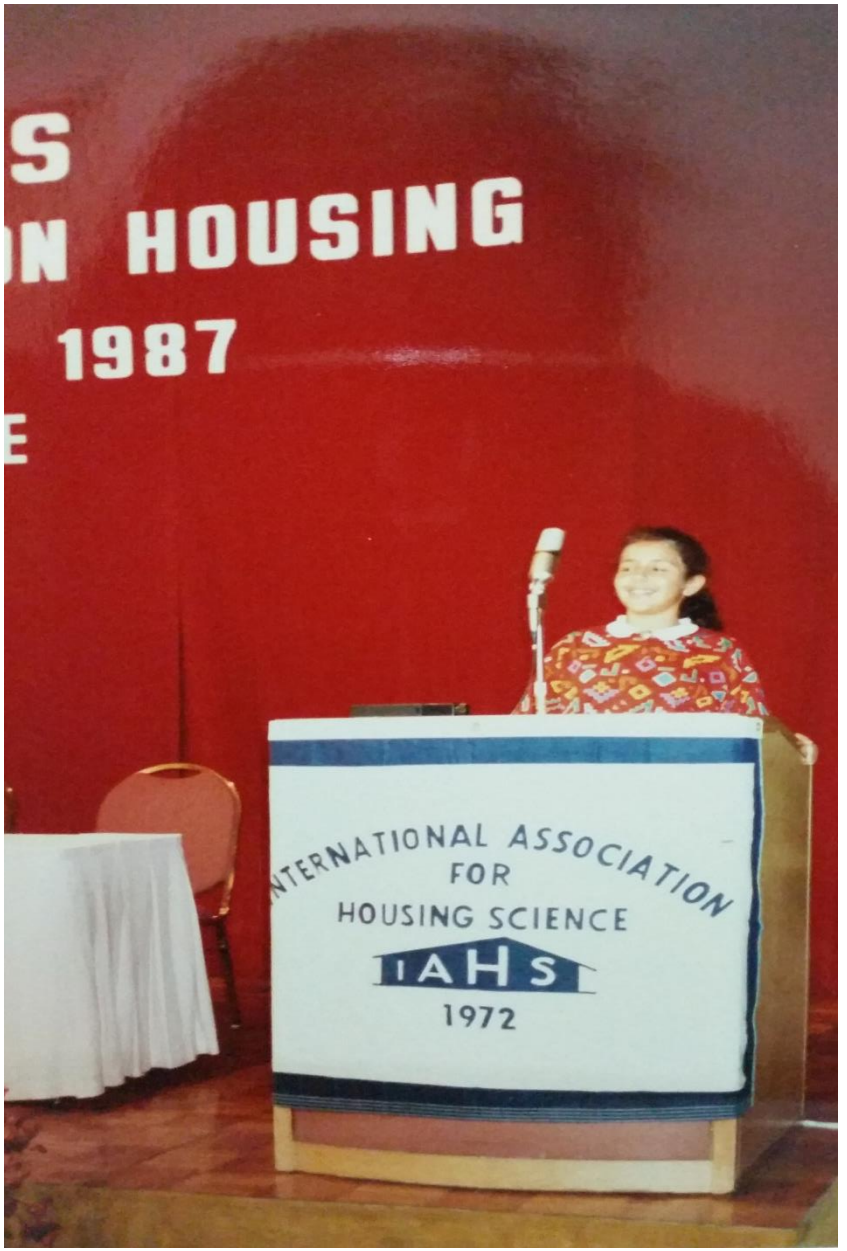
Adverse events were scored by Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

Conclusions

- Finally, this trial of adjuvant chemotherapy after radical cystectomy for advanced bladder carcinoma, is limited in sample size. Data assessing quality of life and response/ toxicity to second line or salvage chemotherapy was not collected; this could have clarified the lack of benefit observed in terms of OS and DFS.

- Lymph node positivity was found to be the most important determinant of survival benefit and DFS from immediate post-cystectomy chemotherapy, but incomplete data on the adequacy of lymphadenectomy in the pathology reports require further validation necessary to emphasize this point.

- Both OS and DFS failed to show a significant improvement with immediate versus deferred chemotherapy after radical cystectomy and bilateral lymphadenectomy for patients with muscle-invasive bladder cancer.



Thank you