

Adjuvant Intra-arterial Chemotherapy Following Surgery In Treating Patients With Locally Advanced Bladder Cancer: A China, prospective, Multicenter, randomized Phase III Trial

Lijuan Jiang¹, Kai Yao¹, Huancheng Tang¹, Yunlin Ye¹, Xiangdong Li¹, Bing Wang², Jing Li², Qun Xie³, Zike Qin¹, Fangjian Zhou¹, Zhuowei Liu^{1*}

1. Department of Urology, Cancer Center, Sun Yat-sen University, GuangZhou, China; 2. Department of Urology, Affiliated Cancer Hospital Of Guangzhou Medical University, China; 3. Department of Urology, Zhuhai People's Hospital, ZhuHai, China

BACKGROUND

- Patients with locally advanced urothelial carcinoma of the bladder (cT3-T4 or N+ M0) have poor survival after cystectomy.
- Neoadjuvant chemotherapy (NC) followed by radical cystectomy is recommended based on high-level data supporting for survival benefit.
- No high-level evidence definitive phase 3 data exists to support adjuvant chemotherapy for locally advanced bladder cancer.
- A trend for increasing use of NC, NC has been difficult to use in China over the past decade.

STUDY OBJECTIVE

To evaluate the benefit of adjuvant intraarterial chemotherapy (IAC) versus radical cystectomy alone in patients with locally advanced bladder cancer.

- ◆ Primary Objective: Disease free survival (DFS)
- ◆ Secondary Objectives: Overall survival (OS)

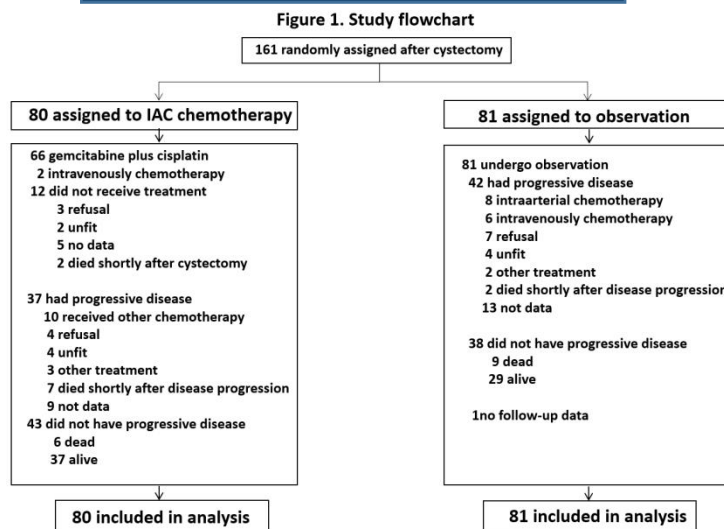
METHODS

- Patients with locally advanced urothelial carcinoma of the bladder after cystectomy were randomly assigned to 2 arms.
- Arm 1 (treatment): Surgery of percutaneous catheter system for arterial chemotherapy was done in the department of Invasive Technology.
- Arm 2 (control): No immediate post-surgery treatment. Patients undergo observation followed by intra-arterial cisplatin and gemcitabine at local relapse, or receive intravenously chemotherapy with cisplatin and gemcitabine at multiple metastases.
- All medications were administered using percutaneous catheter system via a modified Seldinger technique.
- Treatment would begin within 40 days is recommended.
- Patients were further to receive gemcitabine 800 mg/m² intra-arterial, cisplatin 25 mg/m² intra-arterial once a week for 3 weeks followed by 1-week rest period.
- Maximum of three cycles.

ACKNOWLEDGMENTS

We are very grateful to the patients, the investigators and their site staff members who worked for this study. This study was support by 5010 project of Sun Yat-sen University. This trial was registered with ClinicalTrials.gov, number NCT 01627197.

STUDY DESIGN



RESULTS

From July 2, 2012, to Dec 31, 2018, 161 patients (Table1) from 3 sites in China were randomly assigned after cystectomy: 80 were assigned to IAC and 81 to observation (figure 1). At a median follow-up of 33 months, two groups had significantly different disease-free survival (DFS) (P=0.021, 61.3% and 45.8%, respectively), the 5-year overall survival (OS) was 51.6%, with a statistical difference between the two groups (P=0.037, IAC group 62.5% and control group 43.9%, respectively)(figure 2). About 82.5% (66/80) of patients received the planned cycles, and hematologic toxicity was the most common (Table2).As of the data cutoff, 95 (59%) of 161 patients had progressed or died. 43(54%) patients in the IAC group, as did 51 (63%) in the control group (Table3).

Figure 2. Kaplan-Meier survival curves

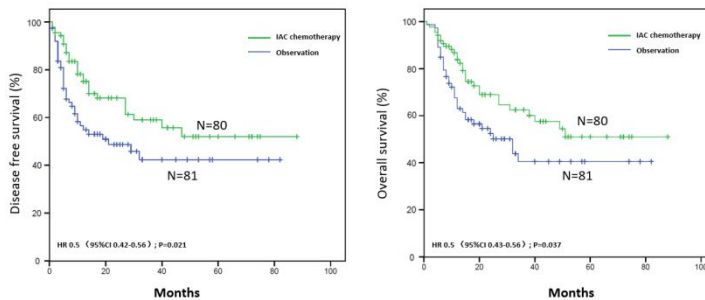


Table 1 : Baseline characteristics

	IAC (n=80)	Observation (n=81)
Age(years)		
≤60	28(35%)	26(32%)
>60	52(65%)	55(68%)
Sex		
Male	71(89%)	72(89%)
Female	9(11%)	9(11%)
WHO performance status		
0	40(50%)	39(48%)
1	39(49%)	41(51%)
2	1(1%)	1(1%)
pT category		
pT1	1(1%)	4(5%)
pT2	9(11%)	11(14%)
pT3	47(59%)	44(54%)
pT4a	22(28%)	22(27%)
pT4b	1(1%)	0
pN category		
pN0	34(43%)	34(42%)
pN1	14(17%)	19(23%)
pN2	18(23%)	22(27%)
pN3	14(17%)	6(8%)
pTN category		
pT1T2N+	10(13%)	15(18%)
pT3T4N-	34(42%)	34(42%)
pT3T4N+	36(45%)	32(40%)
pN by number of dissected nodes		
pN<15 nodes	11(14%)	15(19%)
pN≥15 nodes	24(30%)	19(24%)
pN+<15 nodes	10(12%)	10(12%)
pN+≥15 nodes	35(44%)	36(45%)

TABLES

Table 2: Haematological adverse events (AE)(n=66)

	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
Leucocytes	43(65%)	15(23%)	22(33%)	6(9%)	0
Neutrophils or granulocytes	17(26%)	17(26%)	16(24%)	12(18%)	4(6%)
Platelets	38(58%)	15(23%)	11(17%)	1(2%)	1(2%)
Haemoglobin	24(36%)	21(32%)	16(24%)	5(8%)	0

Data are number of patients with at least one event (% of patients).

Table 3 :Clinical outcomes during follow-up

	IAC (n=80)	Observation (n=81)
Survival status		
Alive	40(50%)	41(51%)
Dead	40(50%)	39(48%)
Cause of death		
Disease	32(40%)	28(35%)
Other	2(3%)	4(5%)
Unknown	6(7%)	7(9%)
Progression free survival		
Alive without progression	37(46%)	29(36%)
Progressed or died	43(54%)	51(63%)
First progression event		
Distant metastasis	18(22%)	17(21%)
Local or locoregional	19(24%)	25(31%)
Died without progression	6(8%)	9(11%)
Progression at any time during follow-up		
Any local or locoregional recurrence	20(25%)	28(35%)
Any distant progression	22(28%)	22(27%)

CONCLUSIONS

- ◆ Gemcitabine combined with cisplatin intraarterial adjuvant chemotherapy proved to be an effective adjuvant therapy for patients with locally advanced bladder cancer. The IAC showed improve DFS and OS in this study.