Long-term efficacy of Neoadjuvant Chemotherapy in Myoinvasive Urothelial Cancer - A retrospective study from The Canberra Hospital.

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Background

Most bladder cancers are myoinvasive at diagnosis, and half of them develop metastatic disease within two years and cause death [1-2]. Neoadjuvant therapy lowers recurrence risk by 19% with absolute disease-free survival of 7% and improves overall survival by 13% [3-4]. The purpose of this study is to look at the long-term efficacy of the neoadjuvant chemotherapy in patients with myoinvasive bladder cancer and to observe potential variables affecting the outcome. We assessed the response rate (RR), disease-free survival (DFS) and overall survival OS) in patients with myoinvasive bladder cancer who were treated with neoadjuvant chemotherapy over 11 years period at the Canberra hospital.

Methods

We conducted a retrospective analysis of the patients who received neoadjuvant chemotherapy for myoinvasive bladder cancer from 2009 to 2020 at the Canberra Hospital and affiliated satellite centers. The DFS and OS were calculated using Kaplan-Meier survival analysis. The treatment response was evaluated histologically as complete pathological response, partial response, or no response post chemotherapy.

Results

We screened 41 patients who received neoadjuvant chemotherapy. Of 41 patients, one patient died before surgery. Among the study cohort, the median age was 68. 56% of patients had Eastern Cooperative Oncology Group performance status 0. All received neoadjuvant chemotherapy with cisplatin and gemcitabine except 2 patients who had carboplatin instead of cisplatin. 75% of patients completed 4 cycles of neoadjuvant chemotherapy. Chemotherapy was discontinued in 5% of patients after 3 cycles due to non-hematological grade 3 toxicity. The response rate was 48%, of which 24% had a complete pathological response and 24% partially responded. Other 48% of patients had no response to the treatment. The median DFS and OS measured 17.5 months and 23.8 months, respectively. The 2, 5 and 7-year OS rates were 59%, 40% and 5% respectively. The recurrence rate and death rate were lower in patients who responded to neoadjuvant chemotherapy. The recurrence rate was 0%, 20%, and 62.5%, whereas the death rate was 10%, 20%, and 70% in the complete response, partial response, and no response groups. Neoadjuvant chemotherapy was generally well-tolerated, although grade 3 toxicity including neutropenia and anemia occurred in 34% patients. No chemotherapy-related death occurred.

Conclusion

Our retrospective study suggests that the neoadjuvant chemotherapy efficacy in patients treated at Canberra Hospital is similar to reported data from rest of the world. It improved DFS and OS in responders as compared to non-responders. It also indicates a relatively higher recurrence and death rate in non-responders, suggesting a need to develop further treatment options in this cohort.

References

1. Raghavan D, Shipley WU, Garnick MB, et al. Biology and management of bladder cancer. NEJM 1990; 322:1129
2. Stenzl A, Cowan NC, De Santis M, et al. The updated EAU guidelines on Muscle invasive and metastatic bladder cancer. Eur Urol 2009; 55:815.
3. C. Vale et al. Advanced Bladder Cancer Meta-Analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: a systemic review and meta-analysis. Lancet 2003; 361:1927
4. Meeks JJ, Bellmunt J, Bochner BH, et al. A systemic review of neoadjuvant and adjuvant chemotherapy for muscle-invasive bladder cancer. Eur Urol 2012; 62: 523

Patients' Characteristics		
Variable	Number of pts	%age
Age		
Median age – 68 years		
<70 years old	22	54%
>70 years old	19	46%
Gender		
Male	34	83%
Female	7	17%
ECOG Status		
PS 0	23	56%
PS 1	17	41%
PS 2	1	2%
Renal Function		
eGFR <60	4	10%
eGFR 60-90	21	51%
eGFR >90	14	34%
Pre-Chemo pathology		
pT1	1	2%
pT2	40	98%
Chemotherapy		
Cis/Gem	39	95%
Carbo/Gem	2	5%
Completed 4 cycles	31	89%
Changes in regimen	7	20%

Pathologic Response to chemotherapy		
Response	Number of pts	Percentage
Complete response	10	24%
Partial response	10	24 %
No response	20	48 %

Results	Months/Percentage
Median DFS	17.5 months
Median OS	23.8 months
2-year OS	59 %
5-year OS	40 %
7-year OS	22 %
10-year OS	10 %

Outcome based on Pathologic Response		
Response	Recurrence rate (%)	Death rate (%)
Complete response	0 %	10 %
Partial response	20 %	20 %
No response	62.5 %	70 %

Chemotherapy related toxicities				
Toxicity	Grade 1 and grade 2		Grade 2 and Grade 3	
	Number of patients	%age	Number of pts	%age
Hematologic				
Anaemia	8	23%	3	8%
Thrombocytopenia	7	20%	0	-
Neutropenia	5	14%	5	14%
Pancytopenia	5	14%	0	-
Non-Hematologic				
Nausea/Vomiting	17	48%	0	-
Fatigue	13	37%	0	-
Tinnitus	6	17%	1	3%
Thromboembolic event	2	5%	2	5%
Renal impairment	2	5%	1	3%
Neuropathy	2	5%	0	-
Anxiety	1	3%	1	3%
Fever	1	3%	0	-
Febrile neutropenia	0	-	0	-