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Pathologic Outcomes After Neoadjuvant Chemotherapy in Primary versus Secondary Muscle Invasive Bladder Cancer – A Single Institution Experience

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INTRODUCTION

- Neoadjuvant chemotherapy (NAC) followed by radical cystectomy (RC) is the standard of care for muscle invasive bladder cancer (MIBC)
- Retrospective studies have demonstrated that patients with non-muscle invasive bladder cancer (NMIBC) progressing to MIBC (secondary MIBC) have worse clinical outcomes than similarly treated patients with primary MIBC
  - Thought to be related to the changes in tumor genomics due to prior treatment in NMIBC patients
  - It is important to improve patient selection for NAC to prevent toxicity of therapy as well as delays to RC
- It is unknown whether pathologic response rates differ between primary and secondary MIBC patients undergoing NAC and RC
- **Objective**: To investigate the pathologic response rates of patients with primary versus secondary MIBC treated with NAC

METHODS

- Retrospective review of RC patients at University of Florida from 2011 to 2021
- Inclusion criteria:
  - Patients treated with NAC and RC
  - Patients presenting with MIBC at time of cancer diagnosis were defined as primary MIBC
  - Patients with a history of intravesical therapy who progressed to MIBC were defined as secondary MIBC
- 169 primary MIBC and 34 secondary MIBC patients identified
- Rates of complete response (pT0) and downstaging (<pT2) were investigated

RESULTS

Variables	Primary MIBC NAC + RC (N=169)	Secondary MIBC NAC + RC (N=34)	p value
Median age at RC	68	72	0.18
Male gender, n (%)	133 (79)	30 (88)	0.24
Clinical stage, n (%)			0.42
cT2	147 (87)	27 (79)	
cT3	22 (13)	7 (21)	
Pathologic stage, n (%)			0.52
pT0	29 (17)	7 (21)	
pTa	3 (2)	0 (0)	
pTis	25 (15)	3 (9)	
pT1	6 (4)	1 (3)	
pT2	36 (21)	3 (9)	
pT3	43 (25)	9 (26)	
pT4	27 (16)	11 (32)	
ypN stage, n (%)			0.25
pN0	136 (80)	24 (71)	
pN1	10 (6)	2 (6)	
pN2	10 (6)	6 (18)	
pN3	6 (4)	1 (3)	
pNx	7 (4)	1 (3)	
Variant histology on RC specimen			
Present	49 (29)	8 (24)	0.52
Surgical margins, n (%)			
Positive	33 (20)	9 (26)	0.36
Excluding ureter and prostate	22 (13)	8 (24)	0.19

Table 1. Baseline demographics and clinical characteristics of patients with primary and secondary MIBC who were treated with NAC prior to RC (n=203)

Authors	Type of study	N	Primary MIBC w/ pT0	Secondary MIBC w/ pT0	p value	Primary MIBC w/ downstaging*	Secondary MIBC w/ downstaging*	p value
Pietzak et al (2018)	Retrospective	245 P-MIBC 43 S-MIBC	15%	0%	NR	45%	26%	**0.02**
D'Andrea et al (2022)	Retrospective, multi-institutional	350 P-MIBC 64 S-MIBC	33%	17%	**0.01**	51%	34%	**0.02**
Benidir et al (2022)	Retrospective	285 P-MIBC 48 S-MIBC	28%	33%	0.41	51%	54%	0.67
Miyagi et al (2023)	Retrospective	169 P-MIBC 34 S-MIBC	17%	21%	0.33	37%	32%	0.70

Table 2. Summary of other studies investigating response to NAC in primary and secondary MIBC.
*Downstaging defined as <pT2 or <pT1.

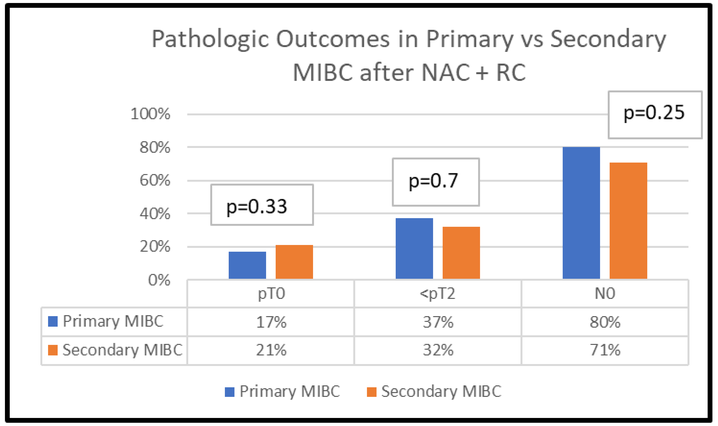

Figure 1. Pathologic outcomes in primary vs secondary MIBC after NAC and RC

CONCLUSIONS

- Controversial data exist regarding benefit of NAC in secondary MIBC (Table 2)
- We found no significant association between tumor status and pathologic outcomes (Figure 1)
  - pT0 rate of 17% vs 21% for primary vs secondary MIBC
  - <pT2 rate of 37% vs 32% for primary vs secondary MIBC
- Our findings are in accordance with results reported for a retrospective study of 333 patients
- Our findings support the rationale to continue to counsel patients with MIBC to undergo NAC prior to RC
- Investigation of CSS and OS outcomes is needed to further evaluate the clinical benefit of NAC in secondary MIBC patients
- Investigation into tumor genomics of MIBC patients will improve our ability to predict tumor response to NAC