

# Outcome of non-responders to neoadjuvant immunotherapy compared to cisplatin-based chemotherapy before radical cystectomy in muscle-invasive bladder cancer



Abstract number:  
MP55-06



Bandini M. <sup>1</sup>, Zaffuto E. <sup>1</sup>, Marandino L. <sup>2</sup>, Scuderi S. <sup>1</sup>, Pederzoli F. <sup>3</sup>, Raggi D. <sup>2</sup>, Salonia A. <sup>1</sup>, Gandaglia G. <sup>1</sup>, Comana S. <sup>1</sup>, Barletta F. <sup>1</sup>, Pellegrino A. <sup>1</sup>, Burgio G. <sup>1</sup>, Moschini M. <sup>4</sup>, Fossati N. <sup>1</sup>, Briganti A. <sup>1</sup>, Montorsi F. <sup>1</sup>, Colombo R. <sup>1</sup>, Necchi A. <sup>2</sup>, Gallina A. <sup>1</sup>

<sup>1</sup> San Raffaele Hospital and Scientific Institute, Dept. of Urology, Milan, Italy, <sup>2</sup> Fondazione IRCCS Istituto Nazionale dei Tumori, Dept. of Oncology, Milan, Italy, <sup>3</sup> San Raffaele Hospital and Scientific Institute, Dept. of Pathology, Milan, Italy, <sup>4</sup> Klinik für Urologie, Luzerner Kantonsspital, Dept. of Urology, Lucerne, Switzerland

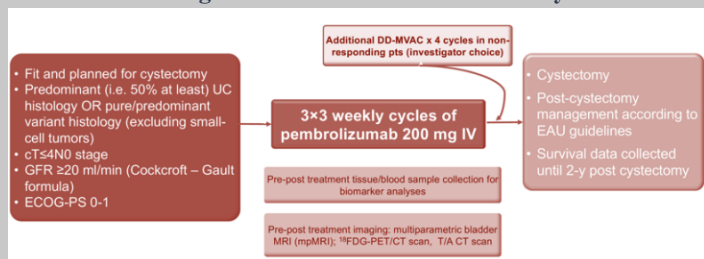
## Introduction

Patients (pts) with ypT2-4 or ypN+ response after neoadjuvant chemotherapy (CT) have a dismal prognosis regardless the use of adjuvant therapies. It is possible that similar pathologic responses after neoadjuvant immunotherapy (IO) portend different prognosis. Here, we compared the relapse-free survival (RFS) after RC in ypT2-4 or ypN+ pts after IO vs. CT.

## Materials & Methods

Between 2014 and 2019, we identified all patients with cT2-4N0 MIBC treated with neoadjuvant CT or IO (pembrolizumab), followed by RC, at our tertiary care institution. For this study purpose, only ypT2-4 or ypN+ pts were considered. Kaplan-Meier analyses examined the RFS according to neoadjuvant therapy group (CT VS. IO). Cox regression analysis examined the risk of relapse after adjusting for pT, pN, age at surgery, gender and use of adjuvant CT. Finally, actual rate of 1-year RFS after RC was plotted against pT, pN, and adjuvant CT-based risk of recurrence for pts treated with neoadjuvant CT or IO.

### Design of the amended PURE01 study



## Results

We retrospectively identified 47 and 42 ypT2-4 or ypN+ MIBC pts. Median follow-up was 12months (interquartile range [IQR] 6-17months). No baseline differences emerged between neoadjuvant treatment groups in terms of age, gender, ypT stage, ypN stage, and use of adjuvant CT (all  $p > 0.05$ ). At Kaplan-Meier and multivariable Cox-regression analyses, non-responder pts treated with IO (pembrolizumab) showed higher 1-year RFS (82% vs. 54%, adjusted HR: 0.38, 95% CI: 0.15-0.95,  $p=0.03$ ) compared with patients treated with neoadjuvant CT. The interaction between the use of neoadjuvant therapies (IO vs. CHT) and the risk of 1-year recurrence derived from ypT, ypN, and use of adjuvant CT-based model was statistically significant ( $p=0.0014$ ). Here, non-responder neoadjuvant IO-treated patients presented a clinically significant lower rate of 1-year recurrence for predicted probabilities of recurrence higher than 20%.

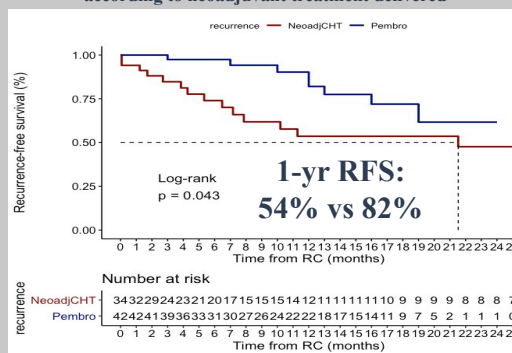
General characteristics of 88 patients with pT2-4 or pN+ treated with neoadjuvant CHT or IO

Variables	Overall (88)	Neoadjuvant CHT (46)	Neoadjuvant Pembrolizumab (42)	P
Median Age	68.8 (62.4-73.4)	71.1 (63.3-73.8)	66.5 (62-72)	0.4
No aCHT	67 (76.1)	34 (73.9)	33 (78.6)	
aCHT	11 (12.5)	2 (4.3)	9 (21.4)	0.1
Female	8 (9.1)	4 (8.7)	4 (9.5)	
Male	80 (90.9)	42 (91.3)	38 (90.5)	1.0
T<2	6 (6.8)	6 (13)	0 (0)	
T2-4	82 (93.2)	40 (87)	42 (100)	0.05
pN0-X	45 (51.1)	23 (50)	22 (52.4)	
pN1	15 (17)	5 (10.9)	10 (23.8)	
pN2	14 (15.9)	8 (17.4)	6 (14.3)	0.2
pN3	14 (15.9)	10 (21.7)	4 (9.5)	

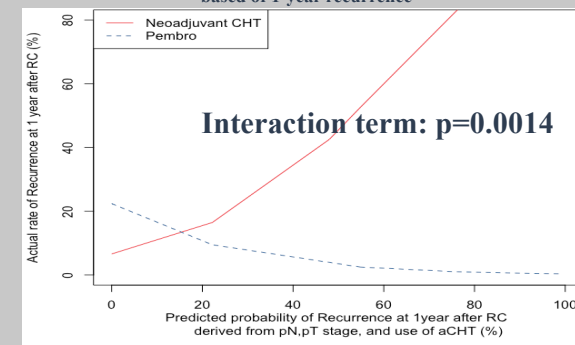
Cox regression analyses predicting the risk of recurrence after neoadjuvant therapy and RC

Cox regression	Univariate Table				Multivariate Table			
	HR	5%	95%	p	HR	5%	95%	p
Neoadjuvant pembrolizumab (Ref. CHT)	0.29	0.13	0.66	0.0029	0.38	0.15	0.95	0.03
age	1.06	1.01	1.11	0.02	1.11	1.04	1.18	0.002
Male	3.37	0.46	24.89	0.2	1.75	0.22	13.64	0.5
Adjuvant chemotherapy	2.50	0.85	7.35	0.09	3.45	1.08	11.08	0.037

Kaplan-Meier analysis examining recurrence-free survival according to neoadjuvant treatment delivered



Incremental utility analysis showing the increasing benefit associated with neoadjuvant IO according to T, N, and use of adjuvant CHT risk-based of 1-year recurrence



## Conclusions

The paradigm that non-responder ypT2-4 or ypN+ MIBC patients present adverse oncologic outcomes was confirmed after standard neoadjuvant chemotherapy, but not after neoadjuvant pembrolizumab. Neoadjuvant immunotherapy still shows an oncologic benefit even in patients with apparently unresponsive disease.