

# **Pembrolizumab post Trimodality Rx for MIBC**

**Shantanu Pendse. Nagpur.**

- **Increasing trend towards organ preservation.**
- **Unmet need for for improving on Recurrences ( Local > distant) in pts who undergo bladder preservation approach. 5 Yrs rec rate - 40%, DM rates - 30%.**
- **Even in pts who achieve CR.**
- **Cisplatin ineligibility is one more concern in some.**
- **Various trials to establish ICB as SOC in some phase , however more trials with RC > trimodality therapy.**

- **Stereotactic Ablative Body Radiotherapy (SABR) boost —> adds CR rate , well tolerated.**
- **Hypothesis —> Pembrolizumab as main therapy in pts who have received SABR and have achieved CR can add PFS.**

- **Investigator initiated.**
- **Phase 2.**
- **Single site.**
- **Primary End point - PFS.**
- **2ry end points - OS, Bladder- intact EFS( BI-EFS) and safety.**

# Eligibility

- **Primary bladder cancer**
- **Urothelial Carcinoma >50%.**
- **ECOG 0/1**
- **cT2-4, N0 .**
- **Maximal TURBT -> SABR boost with concurrent chemotherapy.**
- **Achieved T0/Ta/Tis.**
- **CR —. MRI and Cystoscopy Negative for residual invasive ca.**

- **N = 54 pts . Received Pembrolizumab 200 mg as maintenance therapy.**
- **1 year / 17 cycles.**
- **F/up - 30 days after last dose, 12 weekly survival visit.**

- **TURBT —> 18 Gy/ 3# SABR. Filling bladder. + Conventional Radiotherapy 45Gy/ 25# to Pelvic Lymph nodes with Empty bladder.**
- **Conc- Weekly Gemcitabine.**
- **Only those who achieved radiological + Cystoscopic CR received Main Pembrolizumab**
- **Others proceeded for Salvage RC.**

# General Treatment Schema

Maximal TURBT



SABR (18 Gy/ 3frs ) delivered to the tumor or tumor bed in the filling bladder

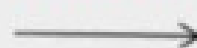


CFRT to the pelvic lymph nodes and empty bladder of 45 Gy/ 25 frs, and receive concomitant weekly Gemcitabine



Cystoscopy and MRI evaluation

No CR

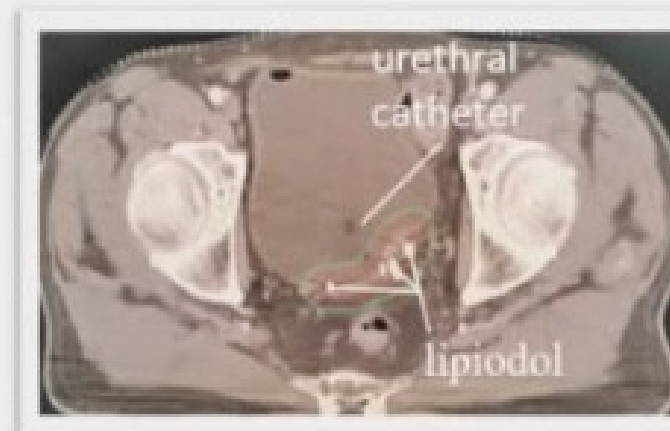
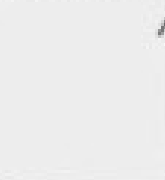


Salvage Radical Cystectomy

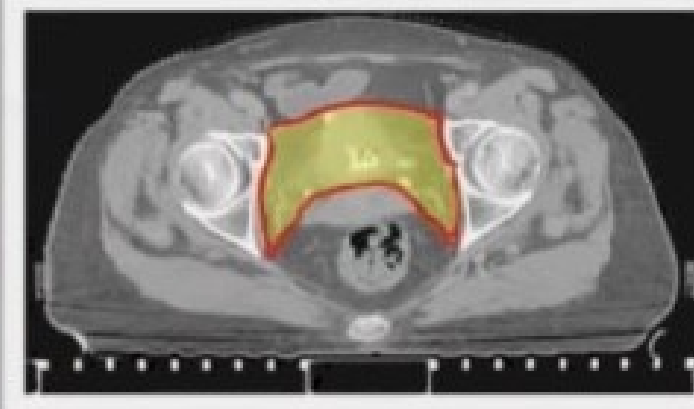
CR



Pembrolizumab maintenance → Invasive recurrence



18 Gy/ 3 frs to tumor bed



45 Gy/ 25 frs to the empty bladder and pelvic LNs



# Results – Baseline Characteristics

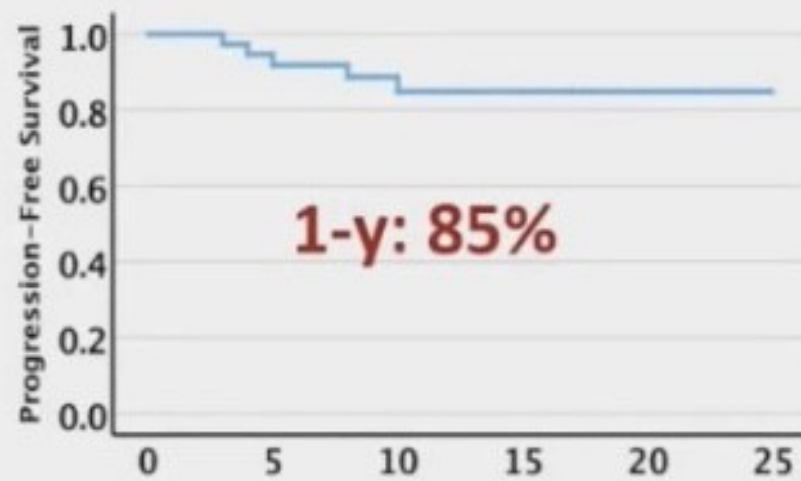
- At cutoff date of 7<sup>th</sup> Mar, 2024, 46 out of 54 patients with MIBC were enrolled.

Characteristic, n (%)	No. of patients (%)
Age, median (range)	69 years, (34, 86)
Gender	
Male	36 (78%)
Female	10 (22%)
Clinical T staging	
T2	39 (85%)
T3	7 (15%)
T4	0
TURBT	
Complete	18 (39%)
Incomplete	28 (61%)

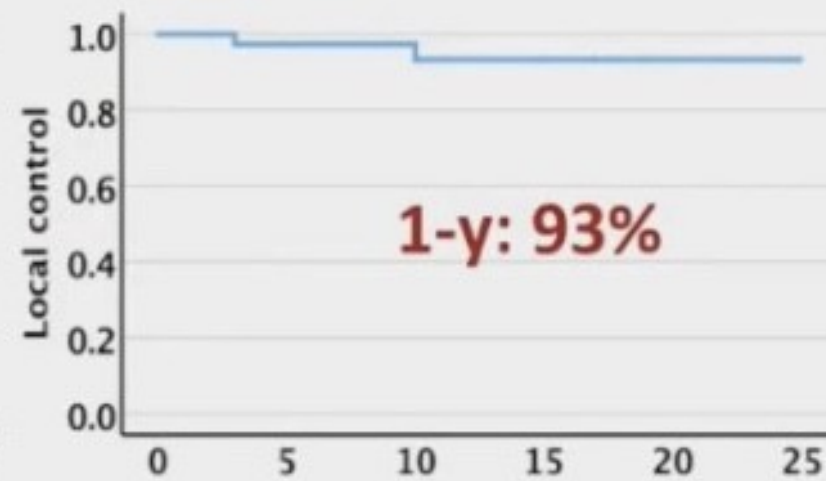
Characteristic, n (%)	No. of patients (%)
Concurrent chemotherapy	
Yes	44 (96%)
No	2 (4%)
Neo-adjuvant chemotherapy	
Yes	9 (20%)
No	37 (80%)
Hydronephrosis	
Yes	2 (4%)
No	44 (96%)

- **Median f/up - 10 months,**
- **10 participants completed 1 year of Pembrolizumab.**
- **1 year PFS - 85%**
- **Local Control - 93%**
- **OS - 97%.**

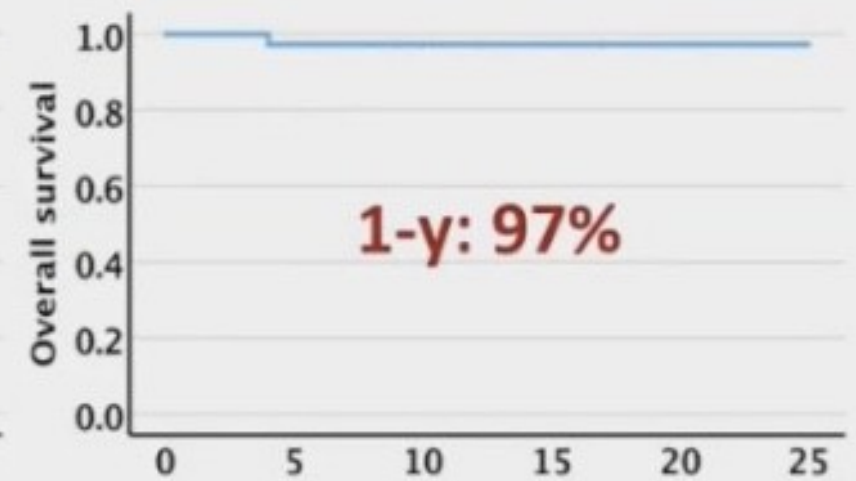
- The estimated 1-year Progression-free survival, local control and overall survival was 85%, 93% and 97%, respectively.



**PFS**

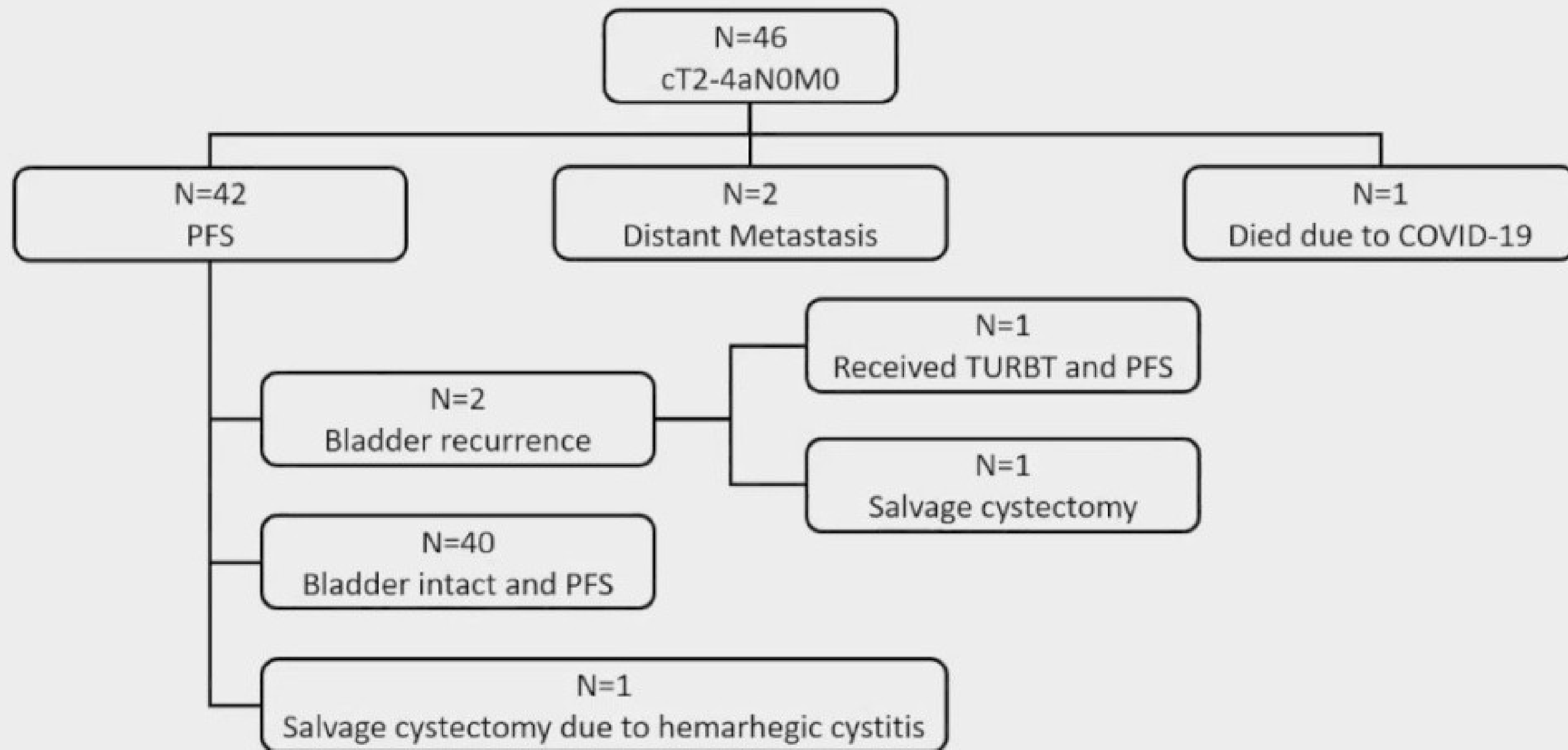


**LC**



**OS**

# Results - Efficacy



- **NONE GR 3 > HIGHER GU/ GI TOXICITIES — SURPRISING > SMALL SAMPLE SIZE . ?**
- **17 PTS DISCONTINUED PEMBRO.**
- **INTERESTING WITH INITIAL PAPERS ON PEMBRO - DOSE LIMITING TOXICITIES OF PEMBRO PARTICULARLY WITH HYPO-FRACTIONATED RT REGIMES.**

Safety Events	No. of patients (%)
<b>Immune-related AEs</b>	
Any grade treatment-related AEs	11 (24%)
Grade 3 treatment-related AEs	3 (7%)
Myocarditis	1 (2%)
Cystitis	1 (2%)
Pneumonitis	1 (2%)
<b>Immunotherapy discontinuation</b>	17
Death	1
Severe hematuria	1
Local recurrence	2
Distant metastasis (Bone and lung respectively)	2
High blood pressure	1
Atrial fibrillation	1
Coronary heart disease	1
Immune-related AEs	8

# **CONCLUDING REMARKS( AUTHOR)/ STRENGTH/ OPPORTUNITIES**

- **PROMISING EFFICACY IN EARLY ANALYSIS**
- **IRAEs c/w with previous studies**
- **Ongoing analysis of tissue specimen pending.**

# Concurrent durvalumab and radiation therapy (DUART) followed by adjuvant durvalumab in patients with localized urothelial cancer of bladder: results from phase II study, BTCRC-GU15-023

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Meeting Abstract: 2022 ASCO Genitourinary Cancers Symposium



**FREE ACCESS** | Urothelial Carcinoma | February 16, 2022

# **NEXT: A single-arm, phase 2, open-label study of adjuvant nivolumab after completion of chemo-radiation therapy in patients with localized muscle-invasive bladder cancer.**

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- **WHERE DOES THIS RX STAND IN CISPLATIN IN-ELEGIBLE PTS ?**
- **SMALL SAMPLE SIZE. SHORT F/UP.**
- **NO MOLECULAR PROFILING TILL DATE, NO PERIPHERAL MARKERS ASSESSED THAT CAN BE USED AS BIOMARKERS.**
- **DID NOT INCLUDE N+ PTS.**
- **DOES NOT ANSWER ROLE OF CONCURRENT ICB IF ANY.**
- **SINGLE CENTRE, NO COMPARATIVE ARM.**
- **Hence - NOT A PRACTICE CHANGING STUDY FOR ME .**