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PEMBROLIZUMAB WITH CHEMORADIOTHERAPY IN MUSCLE INVASIVE BLADDER CANCER
LONG-TERM FOLLOW UP OF EFFICACY OF THE PCR-MIB PHASE II CLINICAL TRIAL (ANZUP 1502)

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BACKGROUND

The addition of IO to chemoradiation prolongs OS in a range of non-bladder cancers[1,2]

We previously reported that pembrolizumab with chemoradiotherapy was feasible in MIBC at a median follow-up of 31 months[3]

Long-term follow-up is shown here of endpoints of efficacy with a median follow-up up 54 months

METHODS

Non randomised phase II trial
- 28 patients
- 6 Australian centres recruited from 2017- 2021

TURBT (Maximal) — Within 6 weeks

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Chemoradiotherapy* + Pembrolizumab — Weekly cisplatin 35mg/m^2 x 6 doses
- Dose reduction to 30mg/m^2 if CrCl 40-50ml/min
Week 1, 4 pembrolizumab IV 200mg
64Gy IMRT or 3DCRT to whole bladder in 32 fractions

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Pembrolizumab — Week 7, 10, 13, 16, 19 pembrolizumab IV 200mg

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Restaging Cystoscopy/CT CAP — Week 19
- 12 weeks post Chemoradiotherapy

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End of Treatment

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Post Treatment Review Restaging Cystoscopy/CT CAP — Week 31
- 24 weeks post Chemoradiotherapy

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Survival Follow Up
3 monthly for months 6-18
6 monthly for months 18-36
12 monthly for months 36-60
(minimum follow up 5 years) — CT CAP and Cystoscopy at each visit

KEY INCLUSION/EXCLUSION CRITERIA

Inclusion:
- T2-T4a, Nx or N0, M0 urothelial carcinoma of the bladder
- ECOG 0-1
- Creatinine Clearance >40 ml/min

Exclusion:
- Extensive CIS; bulky T3/T4a tumors
- moderate/severe hydronephrosis
- IO/cisplatin contraindications

STATISTICAL CONSIDERATIONS

Primary endpoint of the study was safety
- Considered definitely safe if 'unacceptable toxicity' events <30%, unsafe if >50%
- Unacceptable toxicity defined by criteria

Secondary endpoint was efficacy
- Best response at 3 and 6 months post-chemoradiation on cystoscopy
- Metastatic disease free survival, Locoregional disease free survival (pTxNxM0), Overall survival

BASELINE AND Rx CHARACTERISTICS

Baseline and treatment characteristics		Total n=28 (%)
Age, median in year (range)		72 (58-86)
Sex, n (%)	Male	26 (93)
	Female	2 (7)
ECOG performance state, n (%)	0	18 (64)
	1	10 (36)
Histology, n (%)	Urothelial	25 (89)
	Mixed urothelial/non-urothelial	3 (11)
	Associated CIS	9 (33)
Clinical T stage, n (%)	T2	26 (89)
	T3	2 (11)
Prior BCG, n (%)		2 (7)
Radiotherapy technique used	Inverse planned IMRT	16 (57)
	VMAT	7 (25)
	3D-RT	4(14)
	Other	1(4)

N = 28 (%)

SAFETY

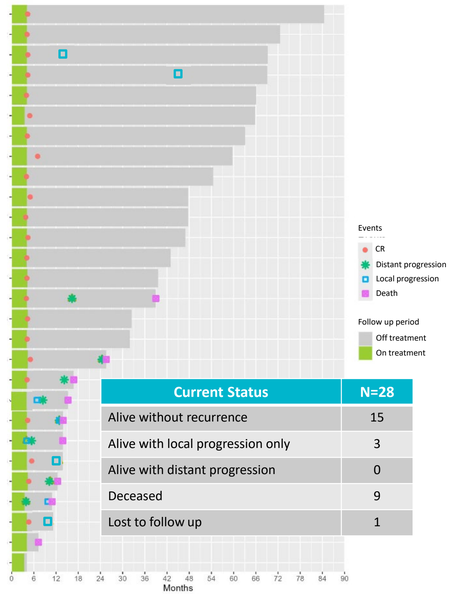
100% patients completed RTx

9/28 (32%, 16-52 95% CI) pts had a predefined toxicity event

3/28 patients had IO AEs requiring steroids. No new IO AEs reported here
- G3 colitis
- G3 polymyalgia
- G3 nephritis

1 pt died from COPD exacerbation

EFFICACY



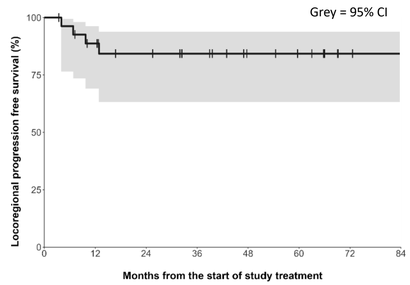
Current Status	N=28
Alive without recurrence	15
Alive with local progression only	3
Alive with distant progression	0
Deceased	9
Lost to follow up	1

EFFICACY

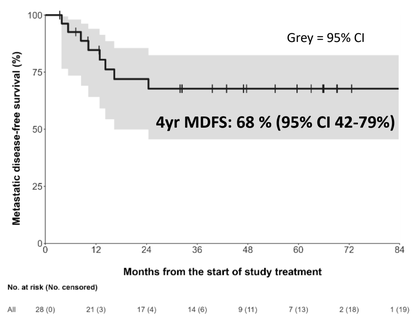
Best Response at Cystoscopy + Biopsy	Week 31 (6m)
Complete Response	23 (88% [70, 98])
Progression	3 (12% [2, 30])

2 non assessable patients
- One patient withdrew consent
- another ceased treatment due to severe COPD

Locoregional Progression-Free Survival (LPFS)

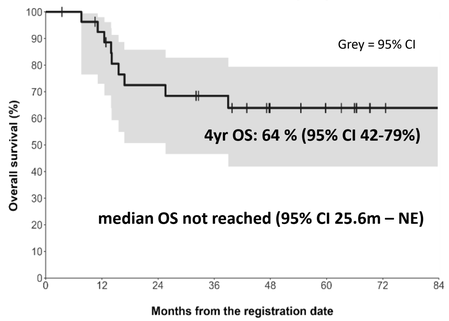


Metastatic Disease-Free Survival (MDFS)



EFFICACY

Overall Survival (OS)



CONCLUSION

No new safety issues identified
- **No new IO related side effects**

After 54 months follow-up

8/28 patients developed metastatic disease
- **all of whom are deceased**

3/28 patients developed non-muscle invasive local recurrences
- **all salvaged with local therapy/surgery**

No pt developed metastatic or non-met recurrences 2yrs post treatment

Keynote 992 accrued, results pending
- **Randomised trial CRT ± pembrolizumab**

#4577

1. Antonia et al, NEJM 2018
2. Lorusso et al, The Lancet 2024
3. Weickhardt et al, Eur Urology Oncology, 2023

Investigator Initiated Trial

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research trials outcomes

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