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LBA112

Neoadjuvant gemcitabine intravesical system (TAR-200) + cetrelimab (CET) or CET alone in patients (pts) with muscle-invasive bladder cancer (MIBC): SunRISe-4 (SR-4) primary analysis and biomarker results

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Background

SR-4 (NCT04919512) is an open-label, multicenter, parallel cohort (C) ph2 study assessing neoadjuvant TAR-200 + CET (C1) or CET alone (C2) in pts with MIBC scheduled for radical cystectomy (RC) and ineligible/refusing neoadjuvant platinum-based chemotherapy (NAC). Here we report efficacy and safety from the primary analysis of SR-4 and urinary and circulating tumor DNA (ut/ctDNA) minimal residual disease (MRD) as biomarkers of outcomes agnostic to treatment.

Methods

Eligible pts planned for RC had age ≥18 y, ECOG 0-1, cT2-T4a N0M0 MIBC and were ineligible/refusing NAC. Pts were randomized 5:3, stratified by TURBT completeness (residual tumor ≤3 cm permitted) and T stage, to receive TAR-200 + CET (C1) or CET alone (C2). Primary end point: pathologic complete response (pCR) rate at RC. Additional end points: pathologic overall response (pOR; defined as ≤ypT1) rate, recurrence-free survival (RFS), safety and ut/ctDNA. Side-by-side descriptive summary of efficacy was performed.

Results

Of 159 pts enrolled (median age 73 y, 83% male, 83% visibly complete TURBT, 24% variant histology, 81% cT2), 87% (88/101) in C1 and 79% (46/58) in C2 underwent RC. pCR, pOR and 1-y RFS rates were higher in C1 (38% [95% CI 27-49], 53% [43-64] and 77% [67-85]) than in C2 (28% [16-44], 44% [29-59] and 64% [47-77]). pCR was higher in C1 across stratification factors. ut/ctDNA MRD results are in the table. Across C1 and C2, utDNA MRD clearance (44%) and wk 12 MRD– were significantly correlated with pCR, but ctDNA clearance (55%) and wk 12 MRD– were not. Baseline and wk 12 ctDNA MRD– were associated with longer RFS vs ctDNA MRD+. No new safety signals were observed.Table: LBA112

Exploratory utDNA/ctDNA MRD analysis in SR-4 (C1 + C2)

	MRD+, % (n/N)	MRD–, % (n/N)	
utDNA	Baseline	82 (55/67)	18 (12/67)
Wk 12	52 (34/65)	48 (31/65)	
ctDNA	Baseline	51 (23/45)	49 (22/45)
Wk 12	27 (12/44)	73 (32/44)	
MRD association with pCR			
	pCR, % (n/N)	Non-pCR, % (n/N)	p value[a]

	MRD+, % (n/N)	MRD−, % (n/N)		
Wk 12 MRD−	utDNA	81 (22/27)	21 (7/33)	$<10^{-5}$
ctDNA	93 (13/14)	68 (19/28)	>0.1	
MRD clearance (Baseline MRD+ and Wk 12 MRD−)	utDNA	80 (12/15)	13 (2/15)	$<10^{-3}$
ctDNA	83 (5/6)	43 (6/14)	>0.1	
ctDNA MRD association with RFS				
	Median RFS, months (95% CI)	Hazard ratio (95% CI)	p value[b]	
Baseline ctDNA	MRD−	NR	4.4 (0.9-21.3)	0.04
MRD+	17.8 (14.5-NR)			
Wk 12 ctDNA	MRD−	NR	4.7 (1.2-17.4)	0.01
MRD+	14.5 (6.4-NR)			

NR, not reached. [a]Fisher's test. [b]Log-rank test.

Conclusions

At primary analysis, TAR-200 + CET showed high pCR, pOR and 1-y RFS, supporting a role for the combination in MIBC. Exploratory ut/ctDNA data support further investigation as predictive biomarkers for residual disease after neoadjuvant therapy in MIBC.

Clinical trial identification

NCT04919512.

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