Abstract #: 849

Liquid Biopsy Guided Disitamab Vedotin combined with Toripalimab and radiotherapy for multimodal organ-sparing treatment of muscle invasive bladder cancer (DECIDING-I Study)

R. Zhang[1], L. Zhang[1], D. Jin[1], Y. Huang[1], L. Qian[1], H. Tang[2], F. Xie[2], C. Jia[2], Y. Zhang[2], X. Zhang[2], P. Du[2], S. Jia[2], G. Zhuang[1], H. Chen[1]
[1]Renji Hospital Affiliated to Shanghai Jiaotong University, Shanghai, China; [2]Huidu Shanghai Medical Sciences Ltd., Shanghai, China

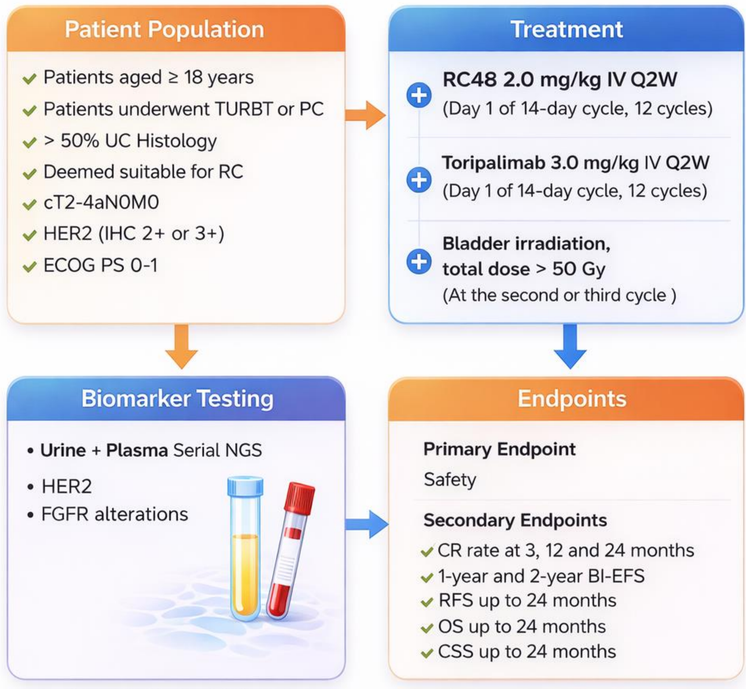
INTRODUCTION

Trimodal therapy remains the standard organ-sparing approach for muscle-invasive bladder cancer (MIBC), yet its clinical benefits are limited, and noninvasive biomarkers to guide dynamic treatment decisions are currently unavailable. There is an urgent need for innovative therapeutic strategies and reliable biomarkers to improve outcomes in localized HER2-positive MIBC.

METHODS

In this proof-of-concept study, we evaluated the safety and efficacy of disitamab vedotin (RC48, a HER2-targeted antibody-drug conjugate) combined with toripalimab (JS001, anti-PD-1) and radiotherapy in six patients with localized HER2-positive MIBC (DECIDING-1 study, ClinicalTrials.gov: NCT05979740). Longitudinal liquid biopsy analyses were performed using the PredicineCARE assay to profile circulating tumor DNA (ctDNA) and urinary tumor DNA (utDNA), assessing their utility in monitoring treatment response and detecting relapse.

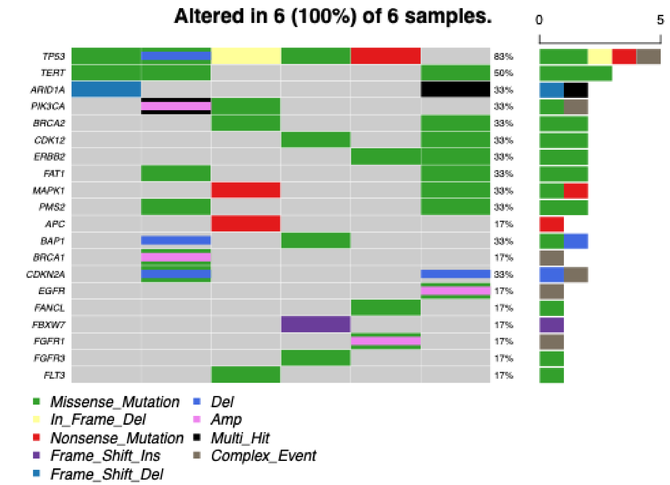
Fig. 1. Study design.



RESULTS

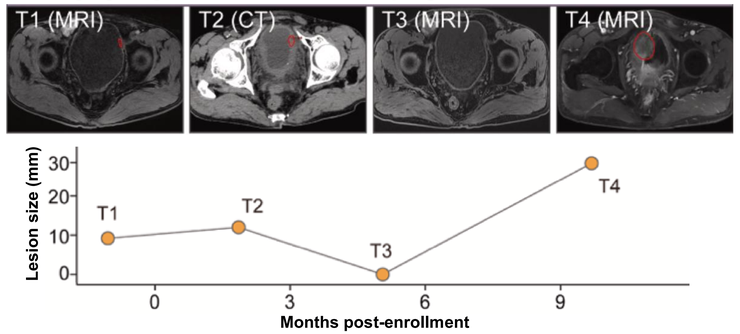
Six patients were enrolled in stage 1. Baseline utDNA signals were detected in all patients, with a median tumor fraction of 29.81% (range, 0.62%–54.19%). Overall, the assay identified 128 somatic mutations and 4 copy number variations. The most frequently altered genes at baseline were TP53 (5/6), TERT (3/6), and ARID1A, PIK3CA, BRCA2, CDK12, ERBB2, FAT1, MAPK1, and PMS2 (each 2/6). Plasma ctDNA results are not shown because few mutations were detectable in blood, limiting meaningful downstream analyses.

Fig. 2. The mutational landscape in baseline urine samples.



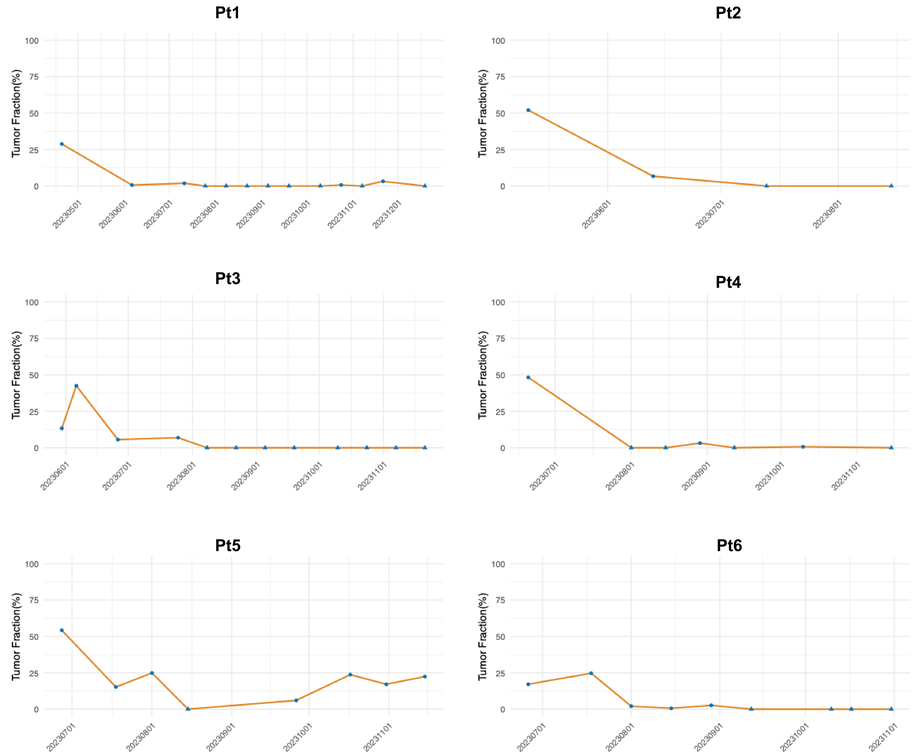
The combination regimen demonstrated a favorable safety profile, with no grade 4 treatment-related adverse events or treatment-related deaths. Five patients (83.3%) achieved a complete response and remained recurrence-free during follow-up, whereas one patient experienced disease progression approximately 9 months after enrollment.

Fig. 2. Imaging diagnosis revealed disease progression of Pt5



Longitudinal utDNA monitoring showed a marked decline in tumor fraction immediately after treatment initiation in all six patients. In most patients, tumor fraction fell below the limit of detection within 1–2 months, consistent with complete response and concordant with clinical assessments including imaging, diagnostic TUR, and urine cytology. Notably, one patient exhibited a rise in tumor fraction at 3 months post-treatment, which preceded clinically confirmed disease progression by approximately 6 months.

Fig. 4. Molecular response through utDNA tests



CONCLUSIONS

This study establishes the feasibility and efficacy of a novel bladder-preserving regimen combining HER2-targeted therapy, immunotherapy, and radiotherapy for HER2-positive MIBC. DECIDING-II is recruiting for validation in a larger cohort. Furthermore, utDNA emerges as a promising noninvasive biomarker for real-time monitoring and early relapse detection. These findings support further investigation of this approach as a potential paradigm shift in MIBC management.