

INTRODUCTION

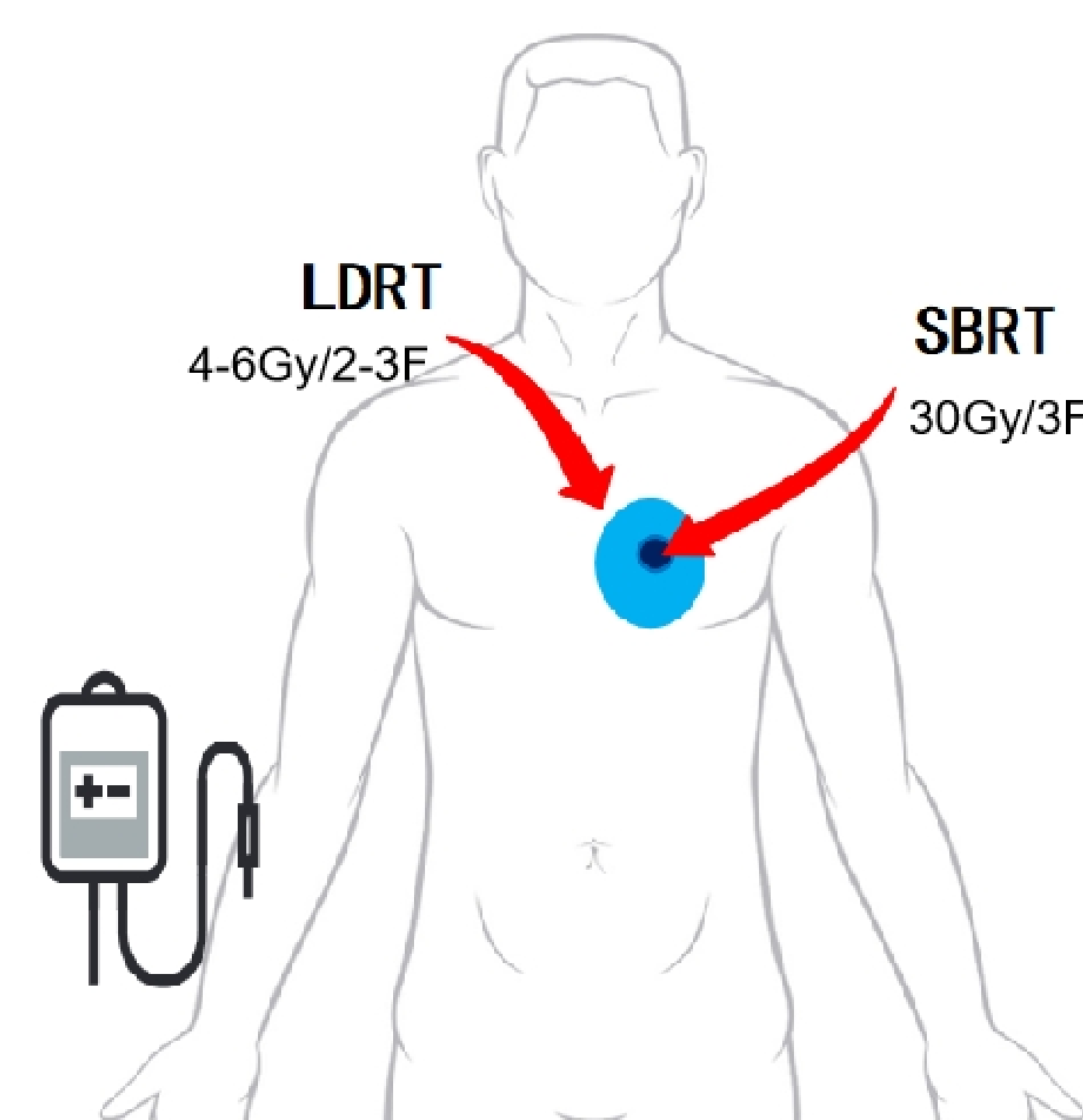
Low-dose radiotherapy (LDRT) may enhance the synergistic anti-tumor effect of combined immunotherapy and stereotactic body radiotherapy (SBRT). Our previous phase I study¹ first demonstrated that LDRT plus SBRT combined with PD-1 inhibitor was safe and promising as first-line treatment for metastatic non-small cell lung cancer (NSCLC), with an objective response rate of 60.7% and manageable safety profile. Neoadjuvant immunotherapy combined with chemotherapy (NeoICT) has become the standard of care for patients with resectable early-stage NSCLC. Nevertheless, pathological complete response (pCR) and major pathological response (MPR) rates remain suboptimal. Emerging evidence suggests that integrating radiotherapy with NeoICT may offer synergistic benefits. We hypothesized that adding LDRT and SBRT to neoadjuvant immuno-chemotherapy could further improve the pathological response in resectable NSCLC.

METHODS

This phase II, single-arm trial plans to enroll 30 patients aged 18-75 years with resectable stage IIA-IIIB NSCLC (NCT06877299). Eligible patients concurrently receive LDRT (4 Gy/2f or 6 Gy/3f) covering the entire tumor and SBRT (30 Gy/3f) delivered to a small subvolume within the same tumor, followed by three cycles of neoadjuvant tislelizumab (anti-PD-1) plus platinum-based chemotherapy every 3 weeks. Surgical resection is scheduled within 4-6 weeks after neoadjuvant therapy completion. Postoperatively, patients receive one cycle of tislelizumab plus platinum-based chemotherapy, followed by tislelizumab monotherapy for up to 13 cycles. The primary endpoint is pCR in the intention-to-treat population. Secondary endpoints include MPR, R0 resection rate, event-free survival (EFS), and safety. Exploratory analyses include minimal residual disease (MRD), tumor mutation burden (TMB), and whole-exome sequencing (WES) in tumor tissue and peripheral blood to identify predictive biomarkers. The trial is actively recruiting.

CONCLUSION

In patients with resectable early-stage NSCLC, neoadjuvant SBRT plus LDRT combined with NeoICT may enhance the pCR rate, with a manageable safety profile. Further enrollment and follow-up are ongoing.

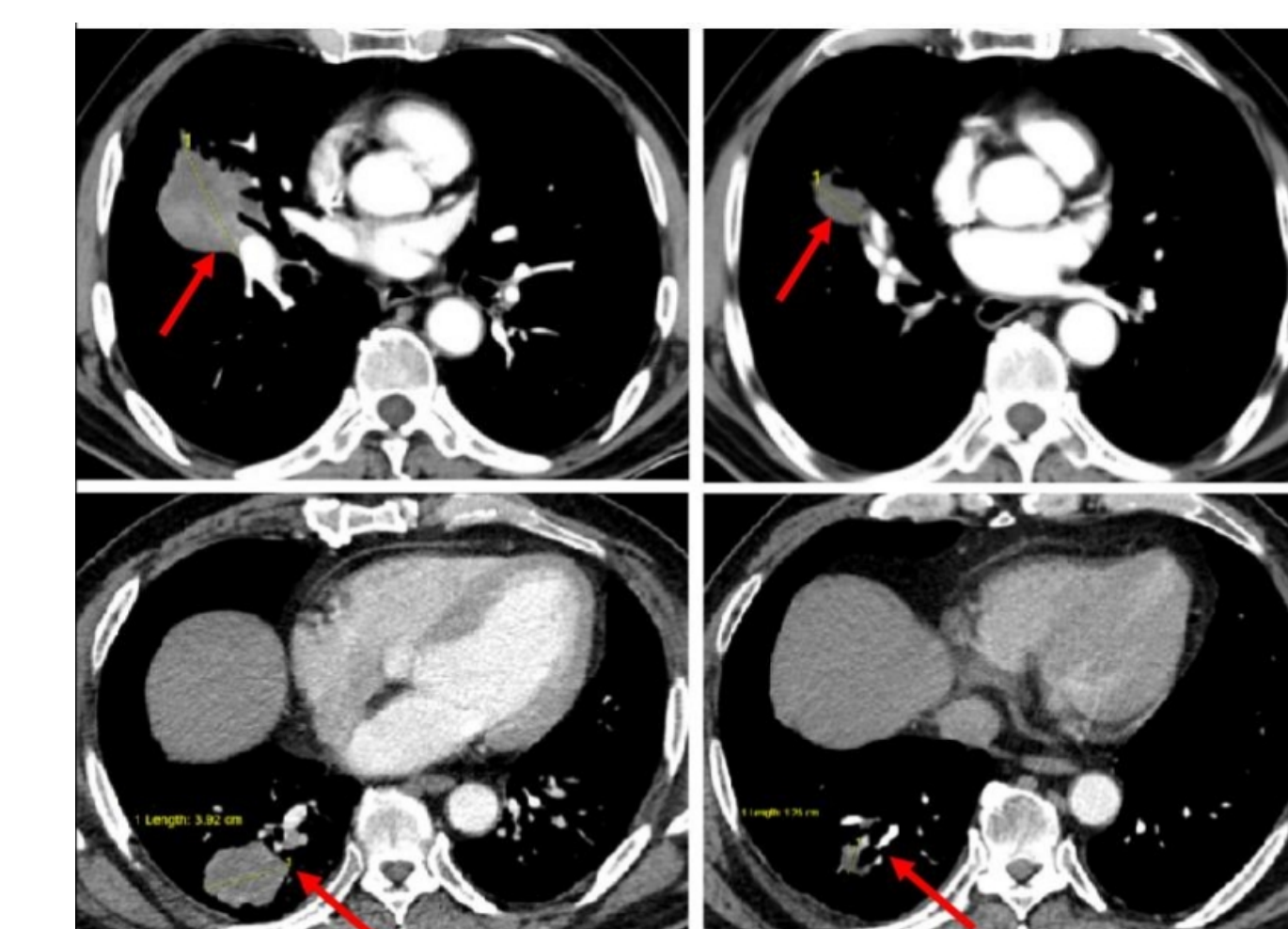
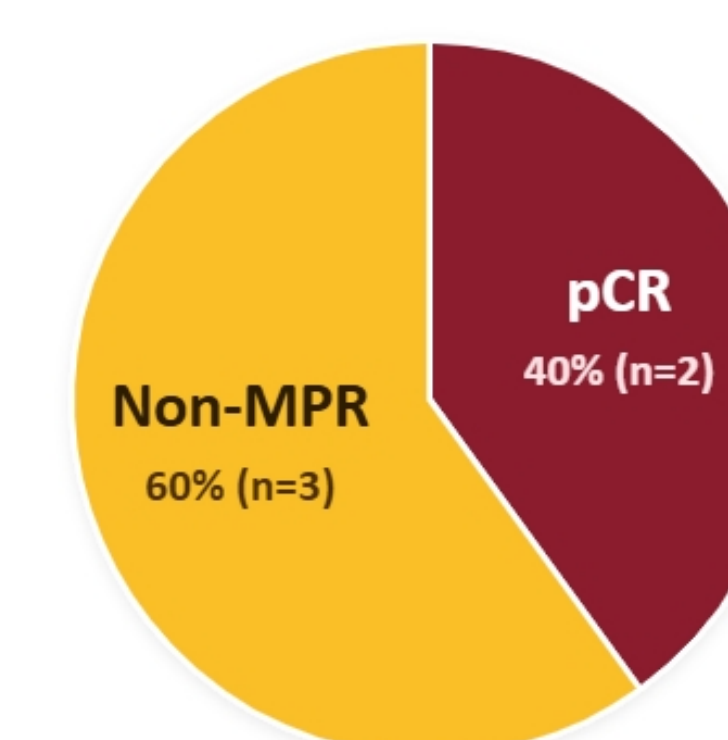


REFERENCES

¹Zhou X, Zhou L, Yao Z, et al. Safety and Tolerability of Low-Dose Radiation and Stereotactic Body Radiotherapy + Sintilimab for Treatment-Naïve Stage IV PD-L1+ Non-Small Cell Lung Cancer Patients. *Clin Cancer Res.* 2023 Oct 13;29(20):4098-4108.

RESULTS

Between June 2025 and January 2026, six patients were enrolled. Five patients completed neoadjuvant therapy and underwent surgery, with an R0 resection rate of 100% (5/5) and a pCR rate of 40% (2/5). The most common treatment-related adverse event was Grade 1-2 neutropenia, occurring in all six patients (100%). No Grade 4 or higher treatment-related adverse events were observed.



Characteristics	Surgical patients (n=5)	
Gender, n (%)	Male	5 (100.0)
Age, median (IQR)		55.00 [54.00, 63.00]
Histological type, n (%)	Squamous	3 (60.0)
	Adenocarcinoma	2 (40.0)
PD-L1 TPS, n (%)	<1%	4 (80.0)
	1-49%	1 (20.0)
Best efficacy, n (%)	PR	5 (100.0)
Pathological Response, n (%)	non-MPR	3 (60.0)
	pCR	2 (40.0)
Residual Viable Tumor percentage, n (%)	0	2 (40.0)
	15%	2 (40.0)
	45%	1 (20.0)
R0 resection, n (%)	Yes	5 (100.0)
Surgery time (min), median (IQR)		163.00 [162.00, 173.00]
Blood loss (mL), median (IQR)		20.00 [20.00, 50.00]