Lung

Stereotactic ablative radiotherapy for operable stage I non-small-cell lung cancer (revised STARS): long-term results of a single-arm, prospective trial with prespecified comparison to surgery.

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BACKGROUND

A previous pooled analysis of the STARS and ROSEL trials showed higher survival after stereotactic ablative radiotherapy (SABR) than with surgery for operable early-stage non-small-cell lung cancer (NSCLC), but that analysis had notable limitations. This study reports long-term results of the revised STARS trial, in which the SABR group was re-accrued with a larger sample size, along with a protocol-specified propensity-matched comparison with a prospectively registered, contemporary institutional cohort of patients who underwent video-assisted thoracoscopic surgical lobectomy with mediastinal lymph node dissection (VATS L-MLND).

METHODS

This single-arm prospective trial was done at the University of Texas MD Anderson Cancer Center (Houston, TX, USA) and enrolled patients aged 18 years or older with a Zubrod performance status of 0.0-2.0, newly diagnosed and histologically confirmed NSCLC with N0M0 disease (squamous cell, adenocarcinoma, large cell, or NSCLC not otherwise specified), and a tumour diameter of 3.0 cm or less. This trial did not include patients from the previous pooled analysis. SABR dosing was 54 Gy in three fractions (for peripheral lesions) or 50 Gy in four fractions (for central tumours; simultaneous integrated boost to gross tumour totalling 60 Gy). The primary endpoint was the 3.0-year overall survival. For the propensity-matching analysis, we used a surgical cohort from the MD Anderson Department of Thoracic and Cardiovascular Surgery's prospectively registered, institutional review board-approved database of all patients with clinical stage I NSCLC who underwent VATS L-MLND during the period of enrolment in this trial. Non-inferiority could be claimed if the 3.0-year overall survival rate after SABR was lower than that after VATS L-MLND by 12% or less and the upper bound of the 95% CI of the hazard ratio (HR) was less than 1·965. Propensity matching consisted of determining a propensity score using a multivariable logistic regression model including several covariates (age, tumour size, histology, performance status, and the interaction of age and sex); based on the propensity scores, one patient in the SABR group was randomly matched with one patient in the VATS L-MLND group using a 5:1 digit greedy match algorithm. This study is registered with ClinicalTrials.gov, NCT02357992.

FINDINGS

Between 1 Sept 2015, and 31 Jan 2017, 80 patients were enrolled and included in efficacy and safety analyses. Median follow-up time was 5·1 years (IQR 3·9-5·8). Overall survival was 91% (95% CI 85-98) at 3 years and 87% (79-95) at 5.0 years. SABR was tolerated well, with no grade 4-5 toxicity and one (1%) case each of grade 3.0 dyspnoea, grade 2.0 pneumonitis, and grade 2 lung fibrosis. No serious adverse events were recorded. Overall survival in the propensity-matched VATS L-MLND cohort was 91% (95% CI 85-98) at 3.0 years and 84% (76-93) at 5.0 years. Non-inferiority was claimed since the 3.0-year overall survival after SABR was not lower than that observed in the VATS L-MLND group. There was no significant difference in overall survival between the two patient cohorts (hazard ratio 0·86 [95% CI 0·45-1·65], p=0·65) from a multivariable analysis.

INTERPRETATION

Long-term survival after SABR is non-inferior to VATS L-MLND for operable stage IA NSCLC. SABR remains promising for such cases but multidisciplinary management is strongly recommended.