



IASLC 2025 World
Conference on Lung Cancer
SEPTEMBER 6-9, 2025
BARCELONA, SPAIN

ID: #P1.11.07

Impact of Radiotherapy and Immune Checkpoint Inhibitor Combination in Advanced NSCLC: Real-World Data (RWD) Analysis

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BACKGROUND

Immune checkpoint inhibitors (ICIs) have become the standard treatment for advanced non-small cell lung cancer (NSCLC). Radiotherapy (RT) enhances local disease control and has immunomodulatory effects, making its combination with ICIs a potential therapeutic strategy. This study investigates how RT intent (palliative vs. radical) and sequencing with ICIs affect overall survival (OS) and progression-free survival (PFS) in patients from the Spanish Lung Cancer Group's Thoracic Tumor Registry (TTR).

METHODS

The TTR is a multicenter, observational cohort study of lung cancer in Spain. This retrospective analysis adhered to the Declaration of Helsinki and was approved by the Ethics Committees of all participating centers. The registry was authorized as a non-interventional study by the Spanish Medicines Agency. A total of 2,179 patients with stage IV NSCLC diagnosed at 66 Spanish centers between March 2009 and May 2023 and receiving ICIs—either as monotherapy or with chemotherapy (CT) in the first or second line—were included.

RESULTS

Among 2,179 patients, 475 (21.8%) received RT—88.0% for palliative intent and 12.0% for radical intent. The most common irradiation sites included bone (45.4%), the central nervous system (33.3%), and the lung (14.4%).

The median OS (mOS) was 19.4 months for the ICI group, 17.3 months for the ICI/RTpalliative group, and 27.3 months for the ICI/RTradical group ($p=0.002$). Compared to the ICI/RTpalliative group, patients treated with ICI (HR=0.80, 95% CI: 0.70-0.91) or ICI/RTradical (HR=0.67, 95% CI: 0.47-0.96) had better survival (Fig 1).

RESULTS

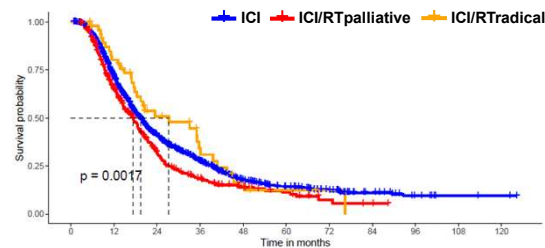


Fig 1. OS: ICI vs. ICI/RTpalliative vs. ICI/RTradical

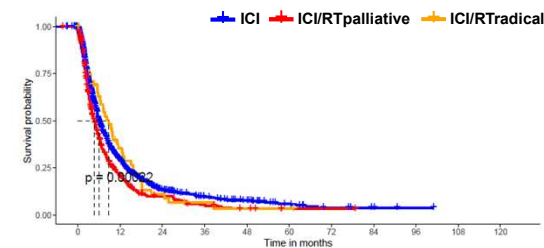


Fig 2. PFS: ICI vs. ICI/RTpalliative vs. ICI/RTradical

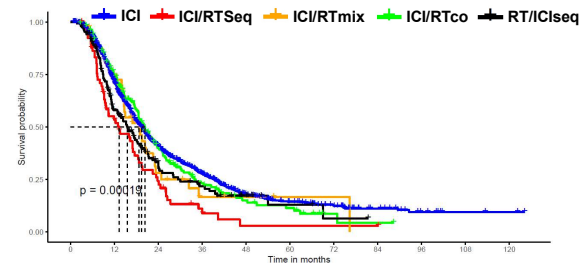


Fig 3. OS: ICI vs. ICI/RTseq vs. ICI/RTmix vs. ICI/RTco vs. RT/CIseq

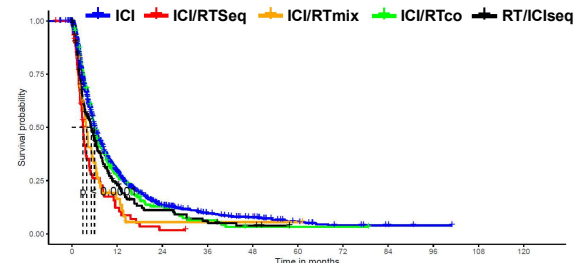


Fig 4. PFS: ICI vs. ICI/RTseq vs. ICI/RTmix vs. ICI/RTco vs. RT/CIseq

The median PFS (mPFS) was 6.0 months for the ICI group, 4.6 months for the ICI/RTpalliative group, and 8.7 months for the ICI/RTradical group ($p=0.00022$). Patients receiving ICI/RTpalliative had a significant worse prognosis than those in the ICI group (HR=1.29, 95% CI: 1.14-1.45) (Fig 2).

Regarding treatment sequencing, 14.9% patients received ICI before RT (ICI/RTseq), 39.6% concomitant ICI/RT (ICI/RTco), 35.8% RT before ICI (RT/CIseq), and 9.7% followed a mixed sequence (ICI/RTmix).

The mOS was 19.4 months for the ICI group, 13.3 months for the ICI/RTseq group, 20.3 months for the ICI/RTco group, 15.6 months for the RT/CIseq group, and 18.7 months for the ICI/RTmix ($p=0.00019$). Compared to the ICI group, patients receiving ICI/RTseq treatment (HR=1.76, 95% CI: 1.35-2.30) or RT/CIseq (HR=1.26, 95% CI: 1.03-1.54) were associated with worse survival (Fig 3).

The mPFS was 6.0 months for the ICI group, 2.9 months for the ICI/RTseq group, 5.9 months for the ICI/RTco group, and 3.9 months for the ICI/RTmix ($p<0.0001$). Patients receiving ICI/RTseq (HR=1.92, 95% CI: 1.48-2.48), RT/CIseq (HR=1.23, 95% CI: 1.03-1.47), or ICI/RTmix (HR=1.56, 95% CI: 1.14-2.13) had a worse prognosis than those in the ICI group (Fig 4).

CONCLUSIONS

This study highlights the impact of RT intent and sequencing on survival outcomes in advanced NSCLC patients receiving ICIs. Radical RT and concurrent ICI/RT were associated with improved outcomes, while palliative RT and sequential approaches correlated with worse prognosis. These findings support the need for optimized treatment strategies integrating RT and ICIs to enhance patient outcomes.