Radiotherapy (RT) and efficacy of immune checkpoint inhibitors (ICI), chemotherapy (CTX) and chemoinmunotherapy (CIT) in patients with non-small cell lung cancer (NSCLC)

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Abstract

Background: Preclinical and retrospective clinical studies have suggested that low RT doses enhance the activity of ICIs induced by the so-called abscopal effect—a systemic immune response to intra-abdominal tumor growth. Here we investigated whether low-dose RT could benefit tumor control and abscopal effects in patients with NSCLC.

Methods: In this study, we included a total of 1079 NSCLC patients with stage IIIA, IIIB, or IV disease. Atezolizumab and carboplatin-paclitaxel were given as first-line chemotherapy in combination with different doses of radiotherapy to all patients. The objective response rate (ORR) was calculated for all subgroups.

Results: In a Cox proportional hazards analysis (CPHA), we identified that the hazard ratio (HR) for OS in the 2 Gy group was 0.80 (95% CI 0.69–0.93, p = 0.004). The CPHA was calculated using the Cox-Proportional Hazards method.

Conclusion: We found that a lower RT dose of 2 Gy was associated with improved outcomes compared to the standard 5 Gy RT dose in patients with NSCLC.

Source of funding: Kantonsspital Graubünden

Clinical trial identification: OAK: NCT01368827
IMpower130: NCT02261783
IMpower150: NCT02661423

Figure 1: Kaplan-Meier estimates for the probability of OS in IMpower130, IMpower150 and OAK stratified for prior and prior chemotherapy. Hazard ratios are shown in the Kaplan-Meier curves and multivariate hazard ratios stratified for sex, ever-smoking status (only IMpower150 and PD-L1 status can be found in the online abstract). Neither prior nor on-study radiotherapy was associated with improved outcomes in contrast to previous results [Shavershidian et al., Cancer Res 2017].

Figure 2: Kaplan-Meier estimates for the probability of OS stratified by RT doses 2 Gy (Arm A) vs 5 Gy (Arm B) in IMpower150. A ≤ 2 Gy: Arm A vs Arm B (p = 0.0187); Arm B ≥ 5 Gy: HR = 1.187 (95% CI 1.008–1.404). IMpower150 (n = 2391).

Summary

- Neither prior nor on-study radiotherapy was associated with improved outcomes irrespective of the intention to treat.
- In this comprehensive analysis of 3,000 NSCLC patients we found no evidence for the so-called abscopal effect, which postulated that local radiotherapy could stimulate a systemic immune response.
- Higher single dose fraction > 5 Gy might be associated with prolonged overall survival suggesting that radiotherapy schedules can be further optimized in the context of immunotherapy NSCLC and novel systemic treatments.

Conflict of interest: All the authors were involved in the analysis of the data and the interpretation of the results. The authors have no other conflicts of interest to declare.