Radiation Oncology trials using PET with FDG uptake among NSCLC patients

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Two radiation oncology trials presented at the IALSC World Conference on Lung Cancer Singapore highlight how some researchers are exploring use of higher radiation boost doses to only PET-positive regions in locally-advanced non-small cell lung cancer (NSCLC). A previous large RTOG phase III trial revealed that the unform delivery of a high dose to the entire tumor led to poorer survival.

In one study, Prof. Feng-Ming (Spring) Kong, Case Western Reserve University School of Medicine, in Cleveland, Ohio presented the results of a multicenter trial which aimed to determine whether adaptive isotoxic radiation dose escalation to mid-treatment FDG-PET provides superior local tumor control compared to a standard uniform dose of 60 Gy in patients with stage III NSCLC.

Prof. Kong and the research centers involved in the trials enrolled 138 patients with stage III NSCLC who were medically fit for concurrent chemoradiation. The patients were randomly assigned by a 1:2 ratio to standard (60 Gy) arm or to an adaptive-therapy arm, with dose individualized to 20 Gy mean lung dose (MLD), and adapted to residual tumor on the mid-treatment FDG-PET/CT. All patients had FDG-PET performed around 40 Gy mid-treatment, and radiation therapy was delivered in 30 daily fractions (Fx).

Of 138 patients enrolled between February 2012 and March 2017, 127 were eligible and analyzable, with 43 and 84 patients in the standard and adaptive arms, respectively, with a minimum follow-up of 3.7 and 3.4

years for surviving patients, also respectively.

The adaptive arm consisted of an initial plan of 2.2 Gy/Fx for 21 Fx followed by an adaptive radiation therapy boost to mid-treatment FDG-PET target using a variable prescription of 2.2-3.8 Gy/Fx for the final 9 Fx. The primary endpoint of this report was 2-year local-regional tumor progression free (LRPF), with inclusion of overall and in-field LRPF, assessed independently and blindly by radiologists.

There were no significant differences in lung, esophagus, and heart toxicities, though the adaptive arm had numerically higher mean doses of these organs at risk. The 2-year overall LRPF rates were 59.5% (95% CI: 37.9, 75.7) on the standard arm, and 54.6% (95% CI: 39.9, 67.0) on the adaptive arm. The median LRPF time was 27.5 months (95% CI: 14.3, not reached) on the standard arm and 28.4 months (95% CI: 19.1, not reached) on the adaptive arm. There were no significant differences in overall survival, progression-free survival, or lung cancer-specific survival between the two arms, according to the presentation by Dr. Kong.

"This is the first randomized trial that demonstrated the feasibility and safety of performing biologically adaptive radiation therapy escalation in a multicenter setting in patients with stage III NSCLC. This preliminary analysis did not show an improvement in overall local regional tumor control," Dr. Kong reported.

In the second study, Dr. Saskia Cooke, The Netherlands Cancer Institute in Amsterdam, Netherlands, reports on local and regional failure in the phase II PET-Boost trial (NCT01024829). In this study, patients with stage II-III non-small cell lung cancer (NSCLC) were treated with hypofractionated dose escalation to either the primary tumor as a whole (Arm A) or the high fluorodeoxyglucose (FDG)-uptake region inside the PT (> 50% SUVmax; Arm B).

The trial randomly assigned 107 patients—82% had stage III disease and most patients (72%) received concurrent chemoradiotherapy. In Arms A and B, median gross tumor volume (GTV) for the primary tumor was 100 and 115 cm^3, respectively; median GTV for the involved lymph nodes was 18 and 20 cm^3, respectively. Median fraction dose was 3.25 Gy to planning target volume (PTV) to the entire primary tumor and 3.50 Gy to PTV 50% SUVmax, resulting in total planned physical dose of 78.0 and 84.0 Gy, in 24 fractions. Median overall treatment time was 34 days in both arms, and median follow-up for CT scans in central review was 12.6 months.

In a previous report, the authors revealed that the primary tumor was non-measurable on follow-up in 27% of patients [Cooke S, 2020]. Of the 12 patients in Arm A who experienced locoregional failure, 2 had local failure (LF) without regional failure (RF) and 9 had RF without LF. Of the 15 patients in Arm B, 4 had LF without RF and 10 had RF without LF. In Arms A and B, respectively, the 2-year cumulative incidence of LF was 11% and 18%, and 28% and 25% for RF. The authors concluded that "dose escalation to the whole PT or 50% SUVmax in patients with NSCLC led to excellent local control rates in both treatment arms". However, few patients were evaluable for assessment of local failure at 2-years, grade 5 toxicity rates was previously reported to be 16% [van Diessen J, 2018], with 3-year OS rates of only 37% in armA and 33% in armB, respectively.

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