
ESCALATED DOSE FOR NON-SMALL-CELL LUNG CANCER WITH ACCELERATED HYPOFRACTIONATED THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY

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Purpose/Objective: Radiotherapy intensification by combining dose escalation and acceleration may improve local control in Non-Small-Cell Lung Cancer (NSCLC) but has a potential for significant toxicity. An institutional phase I/II trial (ICORG 99-09) was conducted to evaluate the safety and efficacy of an accelerated hypofractionated schedule using free-breathing 3-Dimensional Conformal Radiation Therapy (3-DCRT), omission of elective nodal irradiation and application of strict dose-volume-constraints (DVC).

Material/Methods: 46 patients (pts) with stage I-III medically inoperable / non-resectable NSCLC, weight loss less $\leq 10\%$ and KPS $\geq 70\%$ were treated with 3-DCRT delivering a radiation schedule of 72 Gy in 24 daily fractions, 5 fractions/week, over 32 days. The DVC were maximum dose to spinal cord $< 62\%$ and combined lung V25Gy $\leq 30\%$. Median age was 65 years (Range: 45-87) and 35 pts were male. Tumour stage was respectively I in 10 pts, II in 3 pts and III in 33 pts, and tumour was centrally located in 44 pts. 26 pts had induction chemotherapy. Primary endpoints were acute and late pulmonary (SWOG scale) and every other organs (RTOG/EORTC scale) toxicity. Secondary endpoints were response rate at 3 months (mths), time to tumour progression (TTP), time to tumour local progression (TTLP), time to distant progression (TTDP), progression free survival (PFS) and overall survival (OS).

Results: The main acute toxicities were pulmonary [26 pts: Grade (Gr)1 = 23 pts, Gr2 = 3 pts] and oesophageal [36 pts: Gr1 = 28pts, Gr2 = 5 pts, Gr3 = 3 pts] with one 4-day treatment interruption. With a median follow-up (f/u) of 24.2 mths [Range 6.9-75.5], 10 pts developed late pneumonitis [Gr1 = 9 pts, Gr3 = 1 pts]. Following two reported Gr 5 late oesophageal toxicity events (Thirion, ASCO 2004) an additional oesophageal DVC [98% isodose circumferential oesophagus ≤ 1 cm] was introduced. Since then 10 pts [median f/u =14.9 mths] were treated with no Gr5 toxicity and Gr1 = 1pt, Gr2 = 1pt, Gr3 = 1pt. Tumour response rate at 3 mths were: CR: 17.4%, PR: 32.6%, SD: 19.6% and PD: 23.9% [Non-evaluable: 6.5 %]. The other results for efficacy were: median TTP = 15.2 mths, median TTLP =12.6 mths, median TTDP = 10.9 mths and median OS=17.9 mths [1 yr OS=78%, 3 yr OS=26%].

Conclusions: The studied accelerated hypofractionated regime is feasible, with late oesophageal toxicity being the dose-limiting toxicity. The proposed oesophageal DVC is under prospective evaluation. The median survival and TTLP results are encouraging as 70% pts had Stage III disease.