

ORIGINAL ARTICLE

## PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer

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### ABSTRACT

#### BACKGROUND

The role of image-guided surveillance as compared with planned neck dissection in the treatment of patients with squamous-cell carcinoma of the head and neck who have advanced nodal disease (stage N2 or N3) and who have received chemoradiotherapy for primary treatment is a matter of debate.

#### METHODS

In this prospective, randomized, controlled trial, we assessed the noninferiority of positron-emission tomography-computed tomography (PET-CT)-guided surveillance (performed 12 weeks after the end of chemoradiotherapy, with neck dissection performed only if PET-CT showed an incomplete or equivocal response) to planned neck dissection in patients with stage N2 or N3 disease. The primary end point was overall survival.

#### RESULTS

From 2007 through 2012, we recruited 564 patients (282 patients in the planned-surgery group and 282 patients in the surveillance group) from 37 centers in the United Kingdom. Among these patients, 17% had nodal stage N2a disease and 61% had stage N2b disease. A total of 84% of the patients had oropharyngeal cancer, and 75% had tumor specimens that stained positive for the p16 protein, an indicator that human papillomavirus had a role in the causation of the cancer. The median follow-up was 36 months. PET-CT-guided surveillance resulted in fewer neck dissections than did planned dissection surgery (54 vs. 221); rates of surgical complications were similar in the two groups (42% and 38%, respectively). The 2-year overall survival rate was 84.9% (95% confidence interval [CI], 80.7 to 89.1) in the surveillance group and 81.5% (95% CI, 76.9 to 86.3) in the planned-surgery group. The hazard ratio for death slightly favored PET-CT-guided surveillance and indicated noninferiority (upper boundary of the 95% CI for the hazard ratio, <1.50;  $P=0.004$ ). There was no significant difference between the groups with respect to p16 expression. Quality of life was similar in the two groups. PET-CT-guided surveillance, as compared with neck dissection, resulted in savings of £1,492 (approximately \$2,190 in U.S. dollars) per person over the duration of the trial.

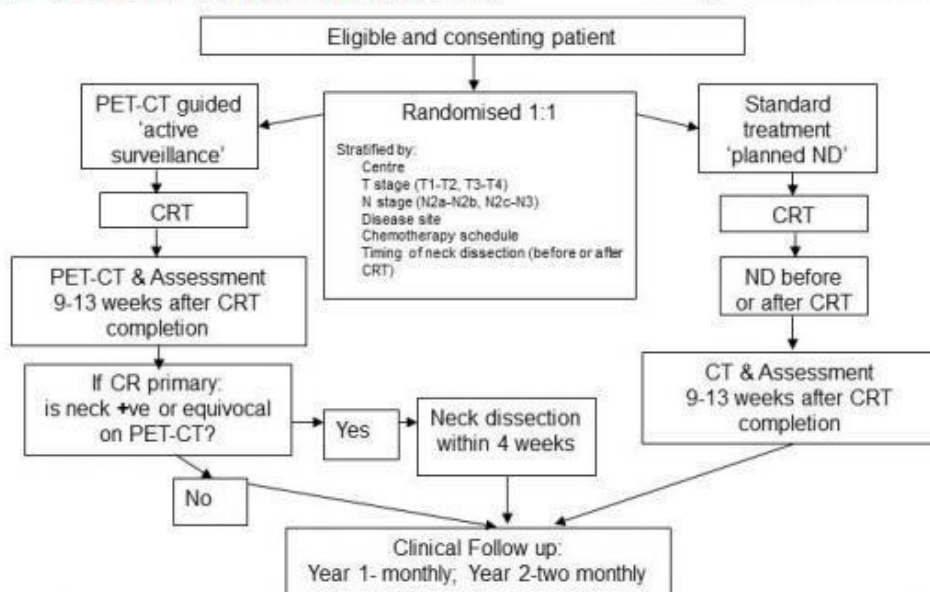
#### CONCLUSIONS

Survival was similar among patients who underwent PET-CT-guided surveillance and those who underwent planned neck dissection, but surveillance resulted in considerably fewer operations and it was more cost-effective. (Funded by the National Institute for Health Research Health Technology Assessment Programme and Cancer Research UK; PET-NECK Current Controlled Trials number, ISRCTN13735240.)

La gestione dei pazienti affetti da tumore del testa-collo localmente avanzati è tutt'oggi molto dibattuta. Varie meta-analisi di esperienze retrospettive monocentriche hanno mostrato come l'utilizzo della TC-PET nel follow-up abbia un'ottima specificità, risparmiando di fatto numerosi pazienti dalle comorbidità legate a una dissezione linfonodale laterocervicale. Gli autori di questo trial sono i primi a dimostrare in uno studio prospettico multicentrico la non-inferiorità della sorveglianza con PET-TC nei confronti di una dissezione linfonodale programmata.

## PET-Neck Trial schema

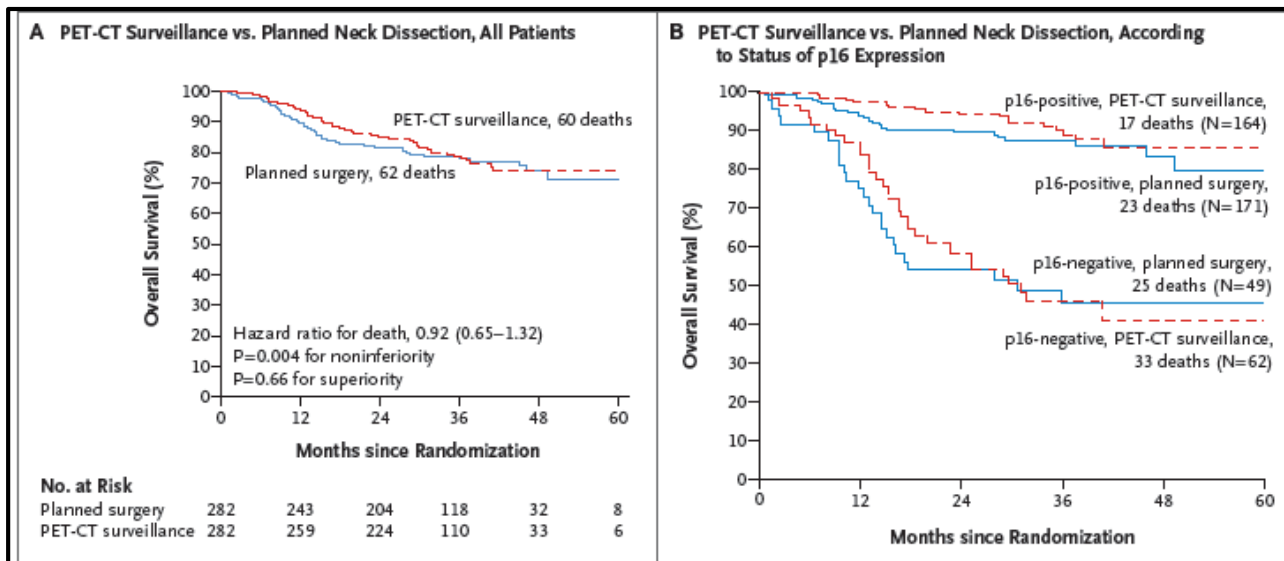
Pragmatic non-inferiority trial



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PRESENTED AT: ASCO Annual Meeting

564 pazienti prevalentemente affetti da tumori dell'orofaringe HPV-relati con stadio clinico N2 sono stati randomizzati nell'arco di 5 anni ad effettuare una dissezione linfonodale entro 4-8 settimane dal termine del trattamento radiochemioterapico vs sorveglianza mediante PET-TC effettuata a 3 mesi. Al termine dello studio i pazienti nel braccio di sorveglianza sottoposti a dissezione linfonodale per risposta incompleta e/o equivoca sono risultati essere in numero nettamente minore rispetto ai pazienti sottoposti ad intervento pianificato (54 vs 221). Le complicanze chirurgiche sono risultate analoghe fra i due bracci di trattamento così come la qualità della vita valutata mediante questionario EORTC e MD Anderson.



Come si evince dall'analisi di Kaplan-Meier sopraripportata la sopravvivenza a due anni non ha mostrato differenze significative fra i due bracci (84.5% vs 81.5%). Suddividendo inoltre i pazienti in p16+ e p16- si apprezza un'ulteriore conferma della miglior prognosi dei pazienti affetti da tumori HPV-relati, mentre non vi erano differenze circa l'utilizzo o meno della sorveglianza attiva mediante PET-TC.

### Conclusioni

La sorveglianza attiva mediante PET-TC può ad oggi ritenersi un'opzione da raccomandarsi in tutti i pazienti affetti da tumore del testa-collo con stadio clinico linfonodale N2; maggior cautela va adottata nei pazienti con malattia N3 data anche l'esiguo campione presente nello studio. Nei pazienti con tumori HPV-relati la rivalutazione con PET-TC a 3 mesi può sottostimare la risposta al trattamento, in quanto esperienze retrospettive hanno evidenziato una risposta più tardiva al trattamento radiochemioterapico ( si veda ad es.: Huang SH, O'Sullivan B, Xu W, et al. Temporal nodal regression and regional control after primary radiation therapy for N2-N3 head-and-neck cancer stratified by HPV status. *Int J Radiat Oncol Biol Phys* 2013; 87: 1078-85.)

Mehanna H, Wong WL, McConkey CC, Rahman JK, Robinson M, Hartley AG, Nutting C, Powell N, Al-Booz H, Robinson M, Junor E, Rizwanullah M, von Zeidler SV, Wiesmann H, Hulme C, Smith AF, Hall P, Dunn J; PET-NECK Trial Management Group. PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer. *N Engl J Med*. 2016 Apr 14;374(15):1444-54. doi: 10.1056/NEJMoa1514493.