Gemcitabine in the treatment of Non-Small Cell Lung Cancer (NSCLC): A meta-analysis of survival and progression free survival data

T. Le Chevalier[1], A. Brown[2], R. Natale[3], G. Scagliotti[4], J. Vansteenkiste[5], J.L. Van Meerbeeck[6], R. Rosell[7], R.M. Rudd[8], S. Danson[9], N. Thatcher[9], J. Schiller[10]; oral Session - Systematic Reviews of Evidence; Thursday,14 August 2003; Abstract: O-239; Citation: Lung Cancer 2003, Vol. 41, Supplement 2, Page 70

On behalf of the Gemzar NSCLC Meta-analysis Group. [1] Institute Gustave Roussy, France; [2] M-TAG, London, UK; [3] Cedars-Sinai Medical Center, Los Angeles, USA; [4] Università di Torino, Italy; [5] University Hospital Leuven, Belgium; [6] University Hospital Dijkzigt, Rotterdam, Netherlands; [7] Institut Catala dOncologia, Barcelona, Spain; [8] St. Bartholomews Hospital, London, UK; [9] Christie Hospital, Manchester, UK; [9] Christie Hospital, Manchester, UK; [10] University of Wisconsin, USA

Introduction: Significant advances in the treatment of advanced NSCLC prompted a formal evaluation of the efficacy of gemcitabine-platinum combinations, in comparison with standard and emergent (novel) treatments. A literature review defined the primary focus to any randomised trial of gemcitabine plus cisplatin or carboplatin versus a platinum based regimen[a]. Accordingly a meta-analysis of overall survival (OS) and time to progression (TTP) was performed.

Methods: A comprehensive search of published and unpublished sources was performed to identify all trials to December 2002. The hazard ratio (HR) was the summary statistic of choice, accounting for censoring and time-to-event. Where not reported or supplied by the investigator survival probabilities were estimated from Kaplan-Meier curves. The pooled HR was produced using a fixed effects meta-analysis. Statistical heterogeneity was addressed with a random effects model where appropriate. Estimation of absolute treatment benefit at one year was also performed.

Results: In total, 13 of the 15 potentially eligible trials were included (one trial was excluded due to flawed randomisation and one trial for data unavailability), resulting in a pool of 4556 patients. A total of 17 comparators were analysed: 12 against platinum-based doublets (11 novel agent-based doublets, VC (6), PC (2), PCb (2), DC (1) and one established agent doublet, EC), plus 5 against singlet/triplet agent regimens (MVC/ MIC (4) and C (1)). For OS a significant reduction in mortality in favour of the gemcitabine based arms was observed, HR 0.90 (0.84 to 0.96, $p < 0.001$), using the fixed effects model, with an absolute survival improvement of 3.9 % at 1 year. There was a significant reduction in the risk of TTP in favour of the gemcitabine regimens, HR 0.87 (0.82 to 0.93, $p < 0.001$), with the fixed effects model, with an absolute improvement of progression-free survival of 4.2 % at 1 year.

Conclusion: Overall the results demonstrate a slight but significant improvement in efficacy of gemcitabine plus a platinum agent when compared with platinum based comparators in survival and time to disease progression.

[a]C, cisplatin, Cb, carboplatin, D, docetaxel, E, etoposide, G, gemcitabine, I, ifosfamide, M, mitomycin, P, paclitaxel, V, vinorelbine.

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