A phase II study of cisplatin and oral vinorelbine concomitantly with radiotherapy in locally advanced non-small-cell lung cancer treatment: Eficacy and safety results.

Authors: Sergio Vazquez[1], Oscar Juan[2], Jose Garcia[3], José Luis Fírvida[4], Francisco Aparisi[5], Jose Muñoz[6], Joaquin Casal[7],Vicente Giner[8], Regina Gironés[9], Martin Lazaro[7], Javier Garde[3], Alfredo Sánchez-Hernández[10]

[1]Hospital Universitario Lucus Augusti, Lugo/SPAIN, [2]Hospital Universitari i Politècnic la Fe, Valencia/SPAIN, [3]Hospital Arnau de Vilanova, Valencia/SPAIN, [4]Complexo Hospitalario Universitario de Ourense, Ourense/SPAIN, [5]Hospital Virgen de los Lirios, Alcoy/SPAIN, [6]Hospital Universitario Doctor Peset, Valencia/SPAIN, [7]Complexo Hospitalario Universitario de Vigo, Vigo/SPAIN, [8]Hospital de Sagunto, Sagunto/SPAIN, [9]Hospital Lluís Alcanyís, Xátiva/SPAIN, [10]Consorcio Hospitalario Provincial de Castellón, Castellón/SPAIN

Background:

It has been shown an improvement in survival with concurrent chemoradiation versus the sequential administration of both treatment modalities. In patients with unresectable stage III disease, chemotherapy may best be started soon after the diagnosis of unresectable NSCLC has been made. Cisplatin (CDDP) plus oral vinorelbine (OV) as induction and concomitant regimen with radiotherapy (RT) has shown good efficacy outcomes and safety profile (Vokes, Fournel, Krzakowski). The objective of this study was to evaluate the effectiveness and toxicities of the combination of CDDP and OV given at full doses concomitantly with RT in locally advanced (LA) non-small-cell lung cancer (NSCLC).

Methods:

Between February 2010 and December 2011, 48 chemo-naïve patients (p) with histologically confirmed unresectable stage IIIA/IIIB LA NSCLC were treated. Treatment consisted of 4 cycles (cy) of OV 60 mg/m2 on days 1 and 8 and CDDP 80 mg/m2 every 3 weeks plus RT 66 Gy starting on day 1, cy 2. The primary objective is the overall response rate (ORR) using RECIST 1.0. A standard Fleming two stage design was used. The sample size calculated with a type 1 error of 0.05 and type 2 error of 0.01, taking P0 20% and P1 40%. The study was approved by the local Ethical Committees of the participating institutions.

Results:

Patient's characteristics were: Median age 61 years (range 34-72); ≥ 65y 42%; males 89.6%; PS0 42% / PS1 58%; smokers 52%; adenocarcinoma 30% / squamous 64%; stage IIIA 46% / IIIB 54%. Median of days between initial diagnosis and study start was 28 days. 75% p completed the treatment as per protocol. Relative dose intensities of OV and CDDP were 97%/98%, respectively. 14.7% of cy were delayed, 11.8% due to toxicity. Dose of day 8 OV was canceled or delayed in 8.2% of cy. Hematological toxicities (% p): grade (g) 3/4 neutropenia 33.3%; g3 anemia 12.5%; g3/4 thrombocytopenia 16.6%; febrile neutropenia concomitant during CT-RT 14.6%. Non-hematological toxicities (% p): g3 esophagitis 12.5%; g3 dyspnea 4.2%, g3 vomiting 4.2%, g3-4 infection 4.2%. 2 treatment-related deaths were reported, both during cycle 1. 42 p (87.5%) received RT, 7.1% under 60 Gy, 23.8% with RT delays or interruptions due to adverse events. 44 p were evaluable for response. ORR 77.3% [CI 95%, 62.2-88.5], DCR 88.6% [CR 2 p (4.5%), PR 32 p (72.7%), SD 5 p (11.4%)]. Median follow-up was 19 months (m) (range 0.47-39.4). Median progression free survival (PFS), 12 m [CI 95%, 7.3-16.6]; 1-year PFS, 48.3% [CI 95%, 33.6-63], 2-year PFS, 30% [CI 95%, 15.8-44.2]. Median time to progression (TTP), 13.3 m [CI 95%, 9.7-16.9]; 1-year TTP, 51.7% [CI 95%, 36.9-66.6], 2-year TTP, 33.3% [18.5-48.1]. Median overall survival was not reached; 1-year and 2-year survival rates were, 72.3% [CI 95%, 59.6-85.1] and 49.4% [CI 95%, 33.8-64.9], respectively.

Conclusion:

This prospective phase II trial shows that the schedule of cisplatin plus oral vinorelbine concomitant with radiotherapy from 2nd cycle obtains a good efficacy with an acceptable safety profile. Clinical trial information: EudraCT Number: 2009-010436-17