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Title: Ifosfamide (IFO) is a valuable alternative to cisplatin (CDDP) for first-line chemotherapy (CT) in advanced non-small cell lung cancer (NSCLC): A meta-analysis

Dr. Thierry 13936 Berghmans thierry.berghmans@bordet.be MD ¹, Ms. Marianne 13937 Paesmans marianne.paesmans@bordet.be ², Dr. Anne-Pascale 13938 Meert ap.meert@bordet.be MD ¹, Dr. Marcello 13939 Tiseo mtiseo@ao.pr.it MD ³ and Prof. Jean-Paul 13940 Sculier sculier@bordet.be MD ¹. ¹ Department of Oncological Intensive Care and Emergencies & Clinic of Thoracic Oncology, Institut Jules Bordet, Brussels, Belgium, 1000 ; ² Data Centre, Institut Jules Bordet, Brussels, Belgium, 1000 and ³ Medical Oncology, University Hospital of Parma, Parma, Italy .

Body: Background: CDDP is the cornerstone of CT in advanced NSCLC while presenting with substantial acute and chronic toxicity. IFO-based regimens were tested in 3 phase III trials with conflicting results. We aimed to compare IFO to CDDP regimens by meta-analysing those studies. Methods: From each trial, we extracted an estimate of the hazard ratio (HR) for group comparisons and aggregated them into a combined HR. Individual patients' data were used when available; otherwise HR and 95% CI were provided by the authors. Results: Three trials are available for the meta-analysis. Sculier et al (2002) compared CDDP (plus carboplatin) with either gemcitabine (GEM)(CCG) or IFO (CCI) to IFO-GEM (IG). Berghmans et al (yet unpublished) randomised patients to CDDP-IFO-GEM (GIP), IG or CDDP-Docetaxel (DP). In the FAST trial (Boni et al, 2012), cisplatin-based regimens (GIP, CDDG-GEM) were compared to GEM-vinorelbine (VNR) and IFO-GEM-VNR.

Meta-analysis results

	N patients	Q HET	HR	95% CI
GIP vs IG (Berghmans et al)	460		0.96	0.79-1.16
GIP vs IFO-GEM-VNR (Boni et al)	221		1.40	1.06-1.85
CCI vs IG (Sculier et al)	188		0.75	0.55-1.02
CDDP-IFO vs IFO without CDDP	869	p=0.01	1.01	0.73-1.38
DP vs IG (Berghmans et al)	462		0.93	0.77-1.14
CDDP-GEM vs IFO-GEM-VNR (Boni et al)	217		1.26	0.96-1.65
CCG vs IG (Sculier et al)	186		0.92	0.68-1.24
CDDP without IFO vs IFO without CDDP	865	p=0.17	1.01	0.88-1.16

Q HET: heterogeneity test; CI = confidence interval Conclusion: Regimens with cisplatin and with ifosfamide are associated with similar survival (at least no detectable difference), suggesting that ifosfamide-based doublets are an alternative to cisplatin-based ones.