GEMZAR RETROSPECTIVE ECONOMIC ANALYSIS OF CLINICAL TRIALS (GREAT2): A PATIENT-LEVEL COST COMPARISON OF THREE CHEMOTHERAPY REGIMENS IN THE TREATMENT OF NON-SMALL CELL LUNG CANCER IN FRANCE

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Introduction

Gemcitabine (Gemzar®) belongs to the new third-generation chemotherapeutic agents (vinorelbine-Navelbine®,docetaxel-Taxotere® and paclitaxel-Taxol®) that are now commonly used in combination with cisplatin or carboplatin in the 1st line treatment of advanced Non-Small Cell Lung Cancer (NSCLC).

In a phase III randomized clinical trial (Scagliotti et al, 2002)[1] for patients with advanced NSCLC, gemcitabine / cisplatin (Gem/Cis), paclitaxel / carboplatin (Pac/Carbo) and vinorelbine / cisplatin (Vin/Cis) showed no significant differences in efficacy with regards to overall survival and time to disease progression (TTP).

A cost -minimization analysis was performed based on resources used in this trial : only the French Ministry of Health's (MOH) perspective was considered.

Method

Aim

The aim of the analysis was to determine which of the three chemotherapy regimens described in the clinical trial was the most cost minimizing from the French Ministry of Health's perspective (MOH).

Study design

Trial data were associated to the following direct healthcare costs considered for each chemotherapy regimen described in the Scagliotti phase III randomized clinical trial :

- chemotherapy drugs acquisition costs (onerous drugs list - reimbursed over DRGs, GERS data),
- concomitant drugs acquisition costs (onerous drugs list - reimbursed over DRGs, GERS data),
- chemotherapy administration costs (national DRGs scale, published in August 2004),
- hospitalizations due to adverse events (national DRGs scale, published in August 2004).

Table 1: Regimens schedules

Novel agent	Treatment schedules	Session / cycle	Length	Average cycles per patient
Gemcitabine / Cisplatin	Gemcitabine1250 mg/m², D1,8 Cisplatin 75 mg/m² D2	3	21 days	4,02
Paclitaxel / Carboplatin	Paclitaxel 225 mg/m², D1 Carboplatin 400 mg/m², D1	1	21 days	4,23
Vinorelbine / Cisplatin	Vinorelbine 25 mg/m², D1,8,15,22 Cisplatin 100 mg/m² D1	4	28 days	3,25

Results

Chemotherapy drugs acquisition costs

Chemotherapy drugs acquisition costs were determined based on :

- a body square area of 1,8 m² / patient,
- an average chemotherapy cycles of 4,02 for Gem/Cis, 4,23 for Pac/Carbo and 3,25 for Vin/Cis,
- Cisplatin and Carboplatin costs were not reimbursed over but included in DRGs.

Table 2: Chemotherapy drugs acquisition

Regimen	Novel agent	Cost per mg	Drug cost per patient
Gem / Cis	Gemcitabine	0,202 €	**3 899,4 €**
Pac / Carbo	Paclitaxel	5,429 €	**9 875,4 €**
Vin / Cis	Vinorelbine	2,954 €	**1 920,6 €**

Concomitant medications costs

The only concomitant medication used in the Scagliotti trial and reimbursed over DRGs is Erythropoetine (EPO). The number of units used per patient is based on a 30-100 UI/Kg dosage (3 times / week). The EPO vials used in the clinical trial are presented in table 3.

Table 3: Concomitant medication costs

Regimen	EPO vials / patient	EPO Cost / unit	Cost / patient
Gem / Cis	3,31	123,10 €	407,5 €
Pac / Carbo	1,01		124,3 €
Vin / Cis	3,76		462,9 €

Chemotherapy drug administration costs

Whatever the chemotherapy regimen considered, the French Ministry of Health (MOH) reimburses the same DRG (DRG 8300) for each chemotherapy session over new agents used for the patient. Results are presented in table 4.

Table 4: Administration costs

Regimen	Sessions / cycle	Cycles / patient	DRG 8300	Total administration costs (€)
Gem / Cis	3	4,02	481,40 €	5 805,7 €
Pac / Carbo	1	4,23		2 036,3 €
Vin / Cis	4	3,25		6 258,2 €

Hospitalization for adverse events costs

- Only patients with grade 3/4 toxicities were considered for this evaluation and hospitalized. The frequency of these adverse events per patient are resumed in table 5.
- For anemia and thrombocytopenia, patients were transfused in a day care hospital.
- These toxicities were correlated with main French DRGs presented in table 6.
- DRGs indexed to toxicities frequencies enable us to determine adverse events hospitalization costs presented in table 7.

Table 5: frequency of adverse events

Toxicities grade 3 / 4 with hospitalization	Gem / Cis % patients	Pac / Carbo % patients	Vin / Cis % patients
Febrile neutropenia	0,5	1	3
Thrombocytopenia	8	2	8
Vomiting	6,6	0,5	12,6
Neuropathy	4	29,8	7
Anemia	17,7	6,1	19,2
Renal insufficiency	0,5	0	5

Table 6: Unit costs used in the analysis

Hospitalization	DRG (reference)	Costs (€)
Febrile neutropenia	6152	4 370,21 €
Vomiting	2104	3 118,80 €
Neuropathy	1667	3 896,08 €
Renal insufficiency	Jacobs C[3]	58 769,77 €
Transfusion for anemia	8306	722,71 €
Transfusion for thrombocytopenia	8306	722,71 €

Table 7: Hospitalization costs

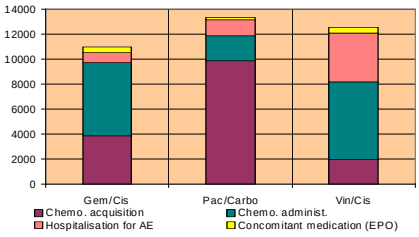
Toxicities with hospitalization	DRG cost (€)	Gemcitabine / Cisplatin		Paclitaxel / Carboplatin		Vinorelbine / Cisplatin	
		%	Cost	%	Cost	%	Cost
Febrile neutropenia	4370,21	0,5	21,85	1	43,70	3	131,11
Thrombocytopenia	722,71	8	57,8	2	14,45	8	57,8
Vomiting	3118,8	6,6	205,84	0,5	15,59	12,6	392,97
Neuropathy	3896,08	4	155,84	29,8	1161,03	7	272,72
Anemia	722,71	17,7	127,9	6,1	44,09	19,2	138,8
Renal insufficiency	58769,77	0,5	293,85	0	0	5	2938,49
Total cost due to hospitalization for adverse events (€)		**863,1 €**		**1 278,8 €**		**3 931,9 €**	

Total costs

Total costs per patient, including all direct costs developed previously, are presented in table 8.

Table 8: Total costs per patient

Regimen	Gemcitabine / Cisplatin	Paclitaxel / Carboplatin	Vinorelbine / Cisplatin
Chemotherapy drugs acquisition	3 899,4 €	9 875,36 €	1 920,6 €
Concomitant medications (EPO)	407,5 €	124,3 €	462,9 €
Chemotherapy administration	5 805,7 €	2 036,3 €	6 258,2 €
Hospitalization for adverse events	863,1 €	1 278,8 €	3 931,9 €
Total cost per patient	**10 975,7 €**	**13 314,8 €**	**12 573,6 €**



Discussion

Gem/Cis is the least expensive regimen for the French MOH when compared to Vin/Cis and Pac/Carbo in the 1st line NSCLC indication :

- a lower total cost for Gem/Cis regimen compared to Vin/Cis and Pac/Carbo (10 975,7 € vs 13 314,8 € and 12 573,6 € respectively),
- the total cost difference between Gem/Cis and Pac/Carbo (2 339,1 €) is explained by a higher chemotherapy acquisition cost which is not offset by lower costs elsewhere,
- the total cost difference between Gem/Cis and Vin/Cis (1 597,9 €) is explained by a higher rate of adverse events' hospitalizations.

CONCLUSIONS

- **Gemcitabine / Cisplatin administered at a 3-week cycle is cost minimizing when compared to Paclitaxel / Carboplatin at a 3-week cycle and Vinorelbine / Cisplatin at a 4-week cycle.**
- **Total direct chemotherapy costs must take into acount, besides drugs acquisition costs, drug administration and adverse events hospitalization costs.**
- **Notably, hospitalisation costs due to adverse events are a major cost driver for some chemotherapeutic regimens.**

References

[1]ScagliottiG. V. et al. Phase III randomized trial comparing three platinum based doublets in advanced non small cell lung cancer.
[2]Use as observed in Scagliotti et al.
[3]Jacobs C. The costs of dialysis treatments for patients with end-stage renal disease in France. Nephrology Dialysis Transplantation 1997; 12: (suppl 1): 29-32

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