A COST MINIMIZATION ANALYSIS OF FIRST-LINE POLYCHEMOTHERAPY REGIMENS IN THE TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER

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OBJECTIVES : Five polychemotherapy regimens: gemcitabine-cisplatine (GC), vinorelbine-cisplatine (VC), docetaxel-cisplatine (DC), paclitaxel-cisplatine (PC) and paclitaxel-carboplatine (PCa), are commonly used in first-line treatment of advanced non-small cell lung cancer. Whereas taxanes have to be administrated within a conventional day-hospitalization setting [1,2], gemcitabine and vinorelbine could be administrated without platinium in home-hospitalization. The purpose of the study is to find out which case management minimizes costs for the French National Health Insurance while ensuring patient safety.

METHODS

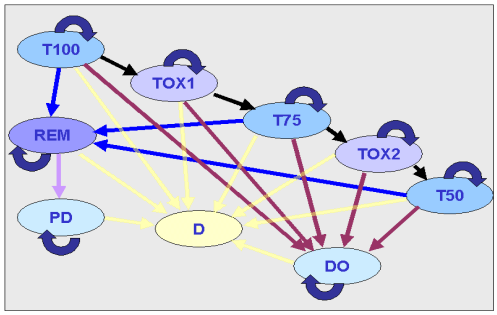
5 Therapeutic Options compared :

	D1	D8	D15	D22	D29	
Gemcitabine-Cisplatin (GC)[1]	1250mg/m²	1250mg/m²		1250mg/m²	1250mg/m²	
	75mg/m²			75mg/m²		
Vinorelbine-Cisplatin (VC)[1]	25mg/m²	25mg/m²	25mg/m²	25mg/m²	25mg/m²	25mg/m²
	100mg/m²				100mg/m²	
Docetaxel-Cisplatin (DC)[1-2]	75mg/m²			75mg/m²		
	75mg/m²			75mg/m²		
Paclitaxel-Cisplatin (PC)[3]	175mg/m²			175mg/m²		
	80mg/m²			80mg/m²		
Paclitaxel-Carboplatin(PCa)[1-2]	225mg/m²			225mg/m²		
	AUC=6			AUC=6		

DH : Conventional Day Hospitalisation; **HH :** Home Hospitalisation [1,2]

A Simplified Markov Model :

- 13 Clinical States : Treatment without reduction dose (T100), Severe Toxicities (TOX1 : Febrile Neutropenia FN1, Blood transfusion BT1, Nausea /Vomiting NV1 : not showed in the graph), and possible reappearances (TOX2 : FN2, BT2, NV2), Early treatment stop because of progression or severe toxicities (DO), Treatment with 75% or 50% reduction dose (T75, T50), Remission (REM : OR+SD), Progression (PD), and Death (D).
- Cycle duration : one week Follow –up period : 52 weeks



Assumptions:

- At each cycle : Remission (CR+PR+SD), Progression, Death occurs
- Probability of relapse obtained from the Time To Progression (TTP) - probability of death [3]
- Probability of overall survival obtained from the Median Survival (MS) and live expectancy of a healthy patient
- At each state of health, is associated a chemotherapy cost with or without reduction dose, and a cost of severe toxicity.

Efficacy and safety :

The small differences in effectiveness between treatments lead us to assume that all the products have the same effectiveness. Therefore we choose to carry a cost minimization study.

Table1 :Efficacy

	GC [4]	VC [4]	PCa [4]	DC [5]	PC [6]
MS (weeks)	42 [37-48]	41 [36-48]	43 [39-54]	49 [44-54]	35[27-43]
TTP (weeks)	23 [19-27]	20 [17-24]	24 [20-28]	22 [21-25]	15 [12-17] [7]
ORR (%)	30 [24-37]	30 [24-36]	32 [25-38]	31,6 [27-36]	31,8 [24-39]
Non assessable (%)	13*	23*	14	15,7	4,6
TTF (weeks)	15	16	12 [5]	15	15
Second lign (%)	37	33,5	37	35,3	57,5

MS : Median Survival, TTP : Time to Progression; ORR : Overall Response Rate, TTF : Time to Treatment Failure; * significantly different (p<0,02)

Table 2 : Safety

Toxicities Grade3/4 WHO	GC [4]	VC [4]	PCa [4]	DC [5]	PC [6]
Febrile Neutropenia (FN)	1/205-0,5%	6/203-3%	2/203-1%	20/406-409%	2/159-1,3%
Blood Transfusion (BT)	16/205-8%	16/203-8%	4/204-2%	42/406-10,3%	16/205-8%
Nausea-vomiting (NV)	13/205-6,6%	13/205-13,6%	1/204-0,5%	40/406-9,9%	14/159-8,8%

Unit Costs:

- The costs of IV hospital treatments were calculated, in the perspective of the Health Care System, by adding DRG costs (T2A, GHS 2004) [9], onerous drug reimbursed over DRGs, and transportation expenses.
- Platinium components included in DRG costs were not added.
- The costs of chemotherapy courses administrated at home were based on the IRDES charges model [10].
- Costs of febrile neutropenia, blood transfusion, nausea and vomiting, diagnosis and palliative care were estimated by DRG costs and transportation expenses.
- A univariate sensitivity analysis was performed, in order to identify the main cost drivers.

RESULTS

With the assumption of no difference of therapeutic efficacy, over a period of 52 weeks,

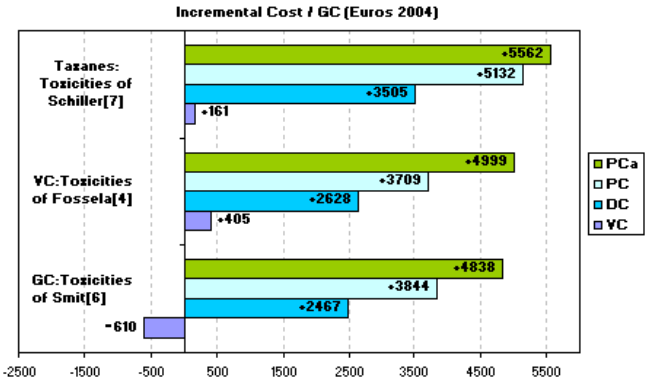
- The annual hospital and ambulatory follow--up costs of GC and VC are of 7,281 and 7,442 €. Administrated within a conventional day-hospitalisation, their annual follow up costs are of 8,408 and 9,831 €.
- Taxanes hospital administration have annual follow-up costs of 10,066 €, 10,999€, and 12,280 € respectively.

Table 3: Annual Follow-up Costs (€)

	Annual hospital and ambulatory follow--up **Cost (€ 2004)**	Incremental Cost
GC	7281	
VC	7442	+161
DC	9909	+2628
PC	10066	+2785
PCa	12280	+4999

Sensitivity analysis :

- By integrating the toxicity data of Smit [6] directly comparing GC with PC with high rates of blood transfusions, the incremental costs with taxanes remains located between 2467 and 4838 €.
- If one integrates data of Fossela [5] comparing DC, PC, and Pca, or Schiller [7] comparing VC and DC, GC remains the less expensive strategy, with an incremental cost from 161 to 5562 €



- In order to obtain equivalent cost between GC and DC, the cost of docetaxel should be divided by 1,6 or gemcitabine cost multiplied by 2.

CONCLUSION : When the patient's safety and his will to receive chemotherapy at home are met in an environment where equivalent efficacy exists between chemotherapy regimens, an economic analysis can quantify the financial consequences on the French Health Insurance, of the drug choice made by prescribers.

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