ORAL VINORELBINE IN THE TREATMENT OF NON SMALL CELL LUNG CANCER

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OBJECTIVES : Since May 2001, vinorelbine has been available to be administered in oral form at home in the treatment of non small cell lung cancer. Its efficacy is similar to that of IV vinorelbine, gastro-intestinal toxicity are more frequent. the periodicity of the treatment follow up in a hospital environment is poorly defined. The aim of this study is to position oral vinorelbine among the other treatment options for which no direct comparison is available and to establish the regimen which minimises costs whilst ensuring patient safety.

METHODS :

5 Cytotoxics agents compared:

- Vinorelbine PO (NVB O) (60 mg/m2 the first 3 weeks, then 80 mg/m2/week)
- Vinorelbine IV (NVB IV) (30 mg/m2/week)
- Gemcitabine (GEM IV) (1g/m2, 3 weeks followed by a week of rest)
- Docetaxel (TXT IV) (100 mg/m2, every 3 weeks)
- Paclitaxel (TXL IV) (200 mg/m2, every 3 weeks)

4 Scenarii of management care under oral vinorelbine :

scenario 1 : : an initial Day Hospitalisation

D1	D8	D15	D21	D29	D36	D43	D50	D57	D64
DH	GPV	GPV	OV	GPV	GPV	OV	GPV	GPV	OV

scenario 2 : a Day Hospitalisation every 9 weeks

D1	D8	D15	D21	D29	D36	D43	D50	D57	D64
DH	GPV	GPV	OV	GPV	GPV	OV	GPV	GPV	DH

scenario 3 : a Day Hospitalisation every 6 weeks

D1	D8	D15	D21	D29	D36	D43	D50	D57	D64
DH	GPV	GPV	OV	GPV	GPV	DH	GPV	GPV	OV

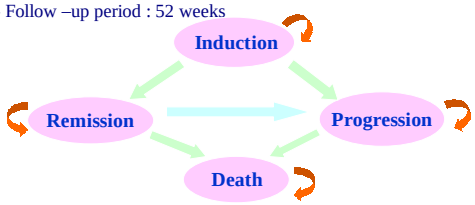
scenario 4 : a Day Hospitalisation every 3 weeks

D1	D8	D15	D21	D29	D36	D43	D50	D57	D64
DH	GPV	GPV	DH	GPV	GPV	DH	GPV	GPV	DH

DH : Day Hospitalisation, **OV**: Outpatient Visit, **GPV** : General Practioner Visit

A Simplified Markov Model :

- 6 Clinical States : Induction, Death (DC), drop-out (DO), remission (OR+SD) with or without reduction dose (REM_R et REM), progression (PD).
- Cycle duration : one week - Follow –up period : 52 weeks
- No adjustement for timing



Assumptions:

- At each cycle : Remission (CR+PR+SD), Progression, Death occurs
- Probability of relapse obtained from the TTP - probability of death
- Probability of global survival obtained from GS and live expectancy of a healthy patient
- Cost of severe toxicities applied to the entire cohort (ITT)

Efficacy and safety :

- Efficacy equivalence of oral and intravenous regimen has been demonstrated in a randomised clinical trial of 115 patients[1]. The same trial has shown more frequent severe gastro-intestinal toxicities.
- 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

	NVB [2]	GEM[3]	TXT[4]	TXL [5]
GS (weeks)	31	29 (21-31)	26 (19-25,5)	29 (24,6-44)
TTP (weeks)	10 [6]	13 (9,5-17)	12,6 (9,9-16,6)	13 (8,6-16,6) [8]
ORR (%)	14	18 (9,6-29,2)	19,6 (12-29)	16 (8-26)
SR (%)	43	42	42,4	43 [8]

GS : Global Survival, TTP : Time To Progression, ORR : Overal Response Rate, SR : Stable Rate

Table 2 : Safety

	NVB IV [2]		NVB O [2]		GEM [3]		TXT[4]		TXL [5]	
	n	%	n	%	n	%	n	%	n	%
Febrile neutropaenia/sepsis	7/199	3,5	3/77[1]	4	1/161 [10]	1	15/137	11	8/79	10
Blood transfusion	26/143[9]	18	26/143[9]	18	10/72	14	0	0	0/51[8]	0
Neurotoxicity	18/199	9	18/199	9	0/161[10]	0	13/137	9,5	4/79	5
Nausea - Vomiting	6/115 [6]	5	14/77[1]	18	8/72	11	7/137	5	4/79	5

Unit Costs:

The costs of IV hospital treatments were estimated from the perspective of the Health Care System using the French DRG national costs scale 1999,

- from the DRG 681 "Day Hospitalisation for chemotherapy", the "medicinal" products component has been excluded
- And replaced by the actual costs directly linked to the use of a specific cytotoxic agent (the acquisition cost and its associated expenses)

In the case of oral Navelbine, allocated values are based on :

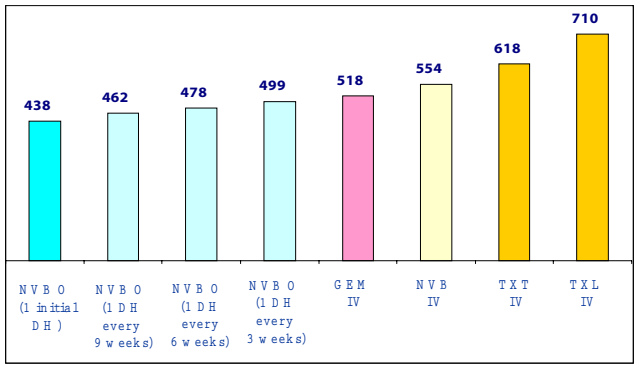
- the type of management used for the chemotherapy administration,
- and on the price of the oral form and associated expenses

The costs of toxicity reactions were calculated using the french DRG national costs scale 1999

RESULTS :

In terms of mean weekly treatment cost, the oral form was the least expensive strategy and produced savings of 80 to 270 € compared to intravenous treatments.

Graph 1 : Mean weekly treatment costs (€)



The estimated treatment toxicity costs are of :

- 305 € for gemcitabine IV
- 396 € for vinorelbine IV
- 560 € for vinorelbine PO
- 583 € for docetaxel IV
- 629 € for paclitaxel IV

With the assumption of equivalent efficacy, over a period of 52 weeks, the least expensive regimen was the one involving a permanent management of the patient at home after an initial day hospitalisation : 5 940 euros. It produced savings per patient and per year equal to 930 € compared to gemcitabine, and 2 320 to 3 670 € compared to the taxanes,
Oral vinorelbine based on day hospitalisations every 3 weeks has almost the same cost than gemcitabine and allows savings of 1430 to 2550 € per patient and per year compared to taxanes.

Table3: Oral Vinorelbine Savings per patient and per year (€)

Strategy	Annual Cost ( )	Incremental cost ( )	
Oral Vinorelbine (1 Initial DH)	5 939	-	
Oral Vinorelbine (DH every 9 weeks)	6 186		
Oral Vinorelbine (DH every 6 weeks)	6 360		
Gemcitabine	6 873	+930	
OralVinorelbine (DH every 3 weeks)	6 890		-
Navelbine IV	7 406	+1 467	+ 1 463
Docetaxel	8 255	+2320	+ 2 355
Paclitaxel	9 399	+ 3 670	+ 2 458

Sensitivity analysis :

In order to obtain equivalent cost between the least expensive form of management of navelbine and intravenous gemcitabine,

- The cost of the capsules of 20 mg and 30 mg of the oral form should be multiplied by 1.2,
- Or the cost of toxicities due to navelbine by 4.

CONCLUSION : With the assumption of equivalent efficacy, over a period of 52 weeks, oral vinorelbine releases savings of 950 € per patient followed compared to management with gemcitabine, and of 1 400 to 3 500 € per patient, compared the taxanes.

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