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 regime which minimises costs whilst ensuring patient safety.

METHODS:
5 Cytotoxic agents compared:
- Vinorelbine PO (NVB O) (60 mg/m2 the 1st 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 Scenario of management care under oral vinorelbine :

**scenario 1 : an initial Day Hospitalisation**

**scenario 2 : a Day Hospitalisation every 9 weeks**

**scenario 3 : a Day Hospitalisation every 6 weeks**

**scenario 4 : a Day Hospitalisation every 3 weeks**

DH : Day Hospitalisation, OV : Outpatient Visit, GPV : General Practitioner 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 REMR), progression (PD).
- Cycle duration : one week - Follow –up period : 52 weeks
- No adjustment 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)

**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 costs are of:
- 305 € for gemcitabine IV
- 396 € for paclitaxel 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.

**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 leads us to assume that all the products have the same effectiveness. Therefore we choose to carry a cost minimization study.

Table 1: Efficacy

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<tbody>
<tr>
<td>31</td>
<td>29 (21-31)</td>
<td>26 (19-25.5)</td>
<td>29 (24.6-44)</td>
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<tr>
<td>TTP (weeks)</td>
<td>10 [6]</td>
<td>13 (9.5-16)</td>
<td>12.6 (9.6-16.6)</td>
<td>13 (8.6-16.6) [8]</td>
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<tr>
<td>ORR (%)</td>
<td>14</td>
<td>18 (9.6-29.2)</td>
<td>19.6 (12-29)</td>
<td>16 (8-26)</td>
</tr>
<tr>
<td>SR (%)</td>
<td>43</td>
<td>42</td>
<td>42.4</td>
<td>43 [8]</td>
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GS: Global Survival, TTP: Time To Progression, ORR : Overall Response Rate, SR : Stable Rate

**Table 2 : Safety**

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<tr>
<td>7/199</td>
<td>3.5</td>
<td>3/7/11</td>
<td>4</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>26/144 [9]</td>
<td>18</td>
<td>26/144 [9]</td>
</tr>
<tr>
<td>Neurotoxicity</td>
<td>18/199</td>
<td>9</td>
<td>18/199</td>
</tr>
<tr>
<td>Nausea - Vomiting</td>
<td>6/115 [8]</td>
<td>5</td>
<td>14/77/1</td>
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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

**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 by management with gemcitabine, and of 1 400 to 3 500 € per patient compared the taxanes.

**References:**