A Cost-Utility Analysis of First-line Chemotherapy regimens in the treatment of Metastatic Breast Cancer after Anthracycline Failure
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OBJECTIVES : Four chemotherapy regimens: gemcitabine-paclitaxel (Gem/Pac), paclitaxel in monotherapy (Pac), docetaxel in monotherapy (Doc) and docetaxel-capcitabine in association (Doc/Cap), are commonly used in the first-line treatment of metastatic breast cancer after anthracyclines failure. The purpose of the study is to rank these strategies according to their incremental cost-utility ratios.

METHODS


4 Treatments and administration regimens :
- CapDoc: Cap: 1250 mg/m² x2, from D1 to D14, Doc: 75 mg/m² on D[1]
- Doc: 100 mg/m² on D [1,2]
- Pac: 175 mg/m² on D[2,3]
- Gem/Pac: Gem: 1250 mg/m² on D1 and D8, Pac: 175 mg/m² on D1 [3]

A Simplified Markov Model :
- Cycle duration : one week. Follow – up period : 5 years
- 6 Clinical States : induction of treatment (Induction), skipped Dose (SD) and Reduction dose of 25 or 50% (RD50, RD100) after severe toxicities, after the Tumor Extension Assessment, the remission in absence or in presence of neurotoxicities (REM and REM-NP), absence of treatment (PD), drop-out from the study (DO) and death (D)

Assumptions :
- At each cycle : Remission (CRs+PRs+SD), Progression, death occurs
- Probability of relapse obtained from the Time To Progression (TTP) – probability of death [4] Probability of overall survival obtained from the Median Survival (MS) and live expectancy of a healthy patient
- The health-related-quality-of-life score was used as a quality adjustment of life expectancy
- Each state of health is associated with a acquisition and administration chemotherapy cost with or without reduction dose, and a cost of severe toxicity.

RESULTS

The Gem/Pac strategy appears to be the most effective compared to Doc, Pac and Doc/Cap.
- In terms of survival, Gem/Pac has an additional efficacy of 16.9 weeks and an incremental cost of 5,586 € compared to Doc/Pac, with an incremental cost-effectiveness ratio (ICER) of 16,789 € per year of life gained.

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<tr>
<th>Table 2 - Global survival (%)</th>
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<td>Endpoints</td>
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<tr>
<td>CapDoc</td>
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<td>Gem/Pac</td>
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- In terms of survival adjusted to quality of life, the efficacy gain is 12.8 weeks and the ICER is 21.060 € per year of life gained.
- When the DM is administered at home, the Gem/Pac ICER is 14.0 € per year of life gained.

The representation of 5,000 points (figure 1) on the cost-effectiveness plane makes it possible to better take into account of the outliers.

If one observes the values of Gem/Pac compared to Cap-Doc (figure 2),
- there is a small proportion of cases where ΔE < 0 (12.2 %, points to the left of the light dotted line).
- 5.9% (297 points) correspond to ΔE > 0 and ΔC/R < 959 €/week (points between the light and dark dotted lines)
- and 92.8% (4642 points) are below the threshold of 50,000 €/year or 959 €/week (points to the right of the dark dotted line).

The probability that the gemcitabine-paclitaxel association is acceptable compared to the other association with the 95% threshold of life gained is then 93 %.

CONCLUSION : The incremental cost-effectiveness ratios of Gem/Pac regimen are between 10,000 and 22,000 € per year of life gained, still below the limits recognized as reasonable at the international level. Another advantage of the Gem/Pac combination therapy is to allow home care on day 8 of the cycle. The higher cost stems essentially from the additional weeks spent in remission and therefore in treatment.

Quality of Life:
- Health-related Quality of Life coefficients extracted from the Launois’ cost–utility study [5] which demonstrated the impact of the response, and the interaction between response and toxicity in the patient’s judgement. A no-claim bonus of 5% was allotted to patients who took advantages of home care.

Unit Costs:
- The costs were calculated by adding DRG costs, onshore drug costs reimbursed over DRGs, and transportation expenses [6]
- Costs of severe toxicities (baloed gastro-intestinal disorders, neurotoxicities), diagnosis and palliative care, were taken into account.
- Direct medical and indirect costs were excluded.

Discounting:
- From NICE’s recommendations, costs were discounted at 3.5% annually, and efficacy, safety and utility parameters at 1.5% per annum.

Probabilistic Analysis:
- Twelve variables of the model have a which can be subject to uncertainty, each one of these variables was characterized by a distribution.
- Concerning monotherapies for which each parameter is available in two clinical trials, a mix of the two densities was performed, taking into account of the number of patients observed in the two studies for the same arm.
- A Monte Carlo simulation was undertaken by randomly sampling from each of the parameter distributions and calculating the expected costs and efficacy and their confidence limits of each strategy. A total of 5,000 replications were performed.

References

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Figure 1 - Cost-effectiveness frontier

Figure 2 - A and D Distributions (ICER= 959 €/week). Doc vs Cap Doc

Figure 3 - A and D Distributions (ICER= 959 €/week). Cap vs Doc Doc

Table 1 - Efficacy and safety : table 1, 2